

Table 14-1.01
Summary of Populations

| | Placebo (N=86) | Xanomeline Low Dose (N=84) | Xanomeline High Dose (N=84) | Total (N=254) |
|-----------------------|-------------------|----------------------------------|-----------------------------------|------------------|
| Intent-To-Treat (ITT) | 86 (100%) | 84 (100%) | 84 (100%) | 254 (100%) |
| Safety | 86 (100%) | 84 (100%) | 84 (100%) | 254 (100%) |
| Efficacy | 79 (92%) | 81 (96%) | 74 (88%) | 234 (92%) |
| Complete Week 24 | 60 (70%) | 28 (33%) | 30 (36%) | 118 (46%) |
| Complete Study | 58 (67%) | 25 (30%) | 27 (32%) | 110 (43%) |

NOTE: N in column headers represents number of subjects entered in study (i.e., signed informed consent). The ITT population includes all subjects randomized. The Safety population includes all randomized subjects known to have taken at least one dose of randomized study drug. The Efficacy population includes all subjects in the safety population who also have at least one post-baseline ADAS-Cog and CIBIC+ assessment.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\adsl1.sas

21:02 Monday, June 26, 2006

Table 14-1.02
Summary of End of Study Data

| | Placebo (N=86) | Xanomeline Low Dose (N=84) | Xanomeline High Dose (N=84) | Total (N=254) | p-value[1] |
|--|-------------------|----------------------------------|-----------------------------------|------------------|------------|
| Completion Status: | | | | | |
| Completed Week 24 | 60 (70%) | 28 (33%) | 30 (36%) | 118 (46%) | <.0001 |
| Early Termination (prior to Week 24) | 26 (30%) | 56 (67%) | 54 (64%) | 136 (54%) | |
| Missing | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | |
| Reason for Early Termination (prior to Week 24): | | | | | |
| Adverse Event | 8 (9%) | 44 (52%) | 39 (46%) | 91 (36%) | <.0001 |
| Death | 1 (1%) | 1 (1%) | 0 (0%) | 2 (1%) | |
| Lack of Efficacy[2] | 3 (3%) | 0 (0%) | 1 (1%) | 4 (2%) | 0.3281 |
| Lost to Follow-up | 1 (1%) | 0 (0%) | 0 (0%) | 1 (0%) | |
| Subject decided to withdraw | 9 (10%) | 8 (10%) | 8 (10%) | 25 (10%) | |
| Physician decided to withdraw subject | 1 (1%) | 0 (0%) | 2 (2%) | 3 (1%) | |
| Protocol criteria not met | 1 (1%) | 0 (0%) | 2 (2%) | 3 (1%) | |
| Protocol violation | 1 (1%) | 1 (1%) | 1 (1%) | 3 (1%) | |
| Sponsor decision | 1 (1%) | 2 (2%) | 1 (1%) | 4 (2%) | |
| Missing | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | |

[1] Fisher's exact test.

[2] Based on either patient/caregiver perception or physician perception.

Table 14-1.03
Summary of Number of Subjects By Site

| Pooled Id | Site Id | Placebo (N=86) | | | Xanomeline Low Dose (N=84) | | | Xanomeline High Dose (N=84) | | | Total (N=254) | | |
|--------------|------------|-------------------|-----|-----|----------------------------------|-----|-----|-----------------------------------|-----|-----|------------------|-----|-----|
| | | ITT | Eff | Com | ITT | Eff | Com | ITT | Eff | Com | ITT | Eff | Com |
| 701 | 701 | 14 | 14 | 11 | 13 | 13 | 5 | 14 | 14 | 7 | 41 | 41 | 23 |
| 703 | 703 | 6 | 5 | 4 | 6 | 5 | 1 | 6 | 5 | 2 | 18 | 15 | 7 |
| 704 | 704 | 9 | 9 | 5 | 8 | 7 | 3 | 8 | 8 | 0 | 25 | 24 | 8 |
| 705 | 705 | 5 | 3 | 2 | 5 | 5 | 3 | 6 | 4 | 1 | 16 | 12 | 6 |
| 708 | 708 | 9 | 9 | 7 | 8 | 8 | 2 | 8 | 5 | 2 | 25 | 22 | 11 |
| 709 | 709 | 7 | 7 | 5 | 7 | 6 | 2 | 7 | 7 | 3 | 21 | 20 | 10 |
| 710 | 710 | 11 | 8 | 6 | 10 | 10 | 2 | 10 | 8 | 5 | 31 | 26 | 13 |
| 713 | 713 | 3 | 3 | 3 | 3 | 3 | 2 | 3 | 2 | 2 | 9 | 8 | 7 |
| 716 | 716 | 8 | 8 | 7 | 8 | 8 | 3 | 8 | 8 | 3 | 24 | 24 | 13 |
| 718 | 718 | 4 | 4 | 3 | 5 | 5 | 1 | 4 | 4 | 1 | 13 | 13 | 5 |
| 900 | 702 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 0 |
| 900 | 706 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 0 | 3 | 3 | 1 |
| 900 | 707 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 2 | 2 | 1 |
| 900 | 711 | 1 | 1 | 1 | 1 | 1 | 0 | 2 | 1 | 0 | 4 | 3 | 1 |
| 900 | 714 | 2 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 1 | 6 | 6 | 4 |
| 900 | 715 | 3 | 2 | 2 | 3 | 3 | 1 | 2 | 2 | 0 | 8 | 7 | 3 |
| 900 | 717 | 2 | 2 | 0 | 2 | 2 | 2 | 3 | 3 | 3 | 7 | 7 | 5 |
| TOTAL | | 86 | 79 | 60 | 84 | 81 | 28 | 84 | 74 | 30 | 254 | 234 | 118 |

Note: ITT: Number of subjects in the ITT population, Eff: Number of subjects in the Efficacy population;
Com: Number of subjects completing Week 24.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\adsl4.sas

21:02 Monday, June 26, 2006

Table 14-2.01
Summary of Demographic and Baseline Characteristics

| | | Placebo (N=86) | Xanomeline Low Dose (N=84) | Xanomeline High Dose (N=84) | Total (N=254) | p-value [1] |
|---------------|-----------------|-------------------|----------------------------------|-----------------------------------|------------------|----------------|
| Age (y) | n | 86 | 84 | 84 | 254 | 0.5934 |
| | Mean | 75.2 | 75.7 | 74.4 | 75.1 | |
| | SD | 8.59 | 8.29 | 7.89 | 8.25 | |
| | Median | 76.0 | 77.5 | 76.0 | 77.0 | |
| | Min | 52.0 | 51.0 | 56.0 | 51.0 | |
| | Max | 89.0 | 88.0 | 88.0 | 89.0 | |
| | <65 yrs | 14 (16%) | 8 (10%) | 11 (13%) | 33 (13%) | 0.1439 |
| | 65-80 yrs | 42 (49%) | 47 (56%) | 55 (65%) | 144 (57%) | |
| | >80 yrs | 30 (35%) | 29 (35%) | 18 (21%) | 77 (30%) | |
| Sex | n | 86 | 84 | 84 | 254 | 0.1409 |
| | Male | 33 (38%) | 34 (40%) | 44 (52%) | 111 (44%) | |
| | Female | 53 (62%) | 50 (60%) | 40 (48%) | 143 (56%) | |
| Race (Origin) | n | 86 | 84 | 84 | 254 | 0.6477 |
| | Caucasian | 75 (87%) | 72 (86%) | 71 (85%) | 218 (86%) | |
| | African Descent | 8 (9%) | 6 (7%) | 9 (11%) | 23 (9%) | |
| | Hispanic | 3 (3%) | 6 (7%) | 3 (4%) | 12 (5%) | |
| | Other | 0 | 0 | 1 (1%) | 1 (<1%) | |
| MMSE | n | 86 | 84 | 84 | 254 | 0.5947 |
| | Mean | 18.0 | 17.9 | 18.5 | 18.1 | |
| | SD | 4.27 | 4.22 | 4.16 | 4.21 | |
| | Median | 19.5 | 18.0 | 20.0 | 19.0 | |

[1] P-values are results of ANOVA treatment group comparison for continuous variable and Pearson's chi-square test for categorical variables.

NOTE: Duration of disease is computed as months between date of enrollment and date of onset of the first definite symptoms of Alzheimer's disease.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\adsl3.sas

21:02 Monday, June 26, 2006

Table 14-2.01
Summary of Demographic and Baseline Characteristics

| | | Placebo (N=86) | Xanomeline Low Dose (N=84) | Xanomeline High Dose (N=84) | Total (N=254) | p-value [1] |
|----------------------|-------------|-------------------|----------------------------------|-----------------------------------|------------------|----------------|
| | Min | 10.0 | 10.0 | 10.0 | 10.0 | |
| | Max | 23.0 | 24.0 | 24.0 | 24.0 | |
| Duration of disease | n | 86 | 84 | 84 | 254 | 0.1530 |
| | Mean | 42.7 | 48.7 | 40.5 | 43.9 | |
| | SD | 30.24 | 29.58 | 24.69 | 28.40 | |
| | Median | 35.3 | 40.3 | 36.0 | 36.3 | |
| | Min | 7.2 | 7.8 | 2.2 | 2.2 | |
| | Max | 183.1 | 130.8 | 135.0 | 183.1 | |
| | | | | | | |
| | <12 months | 5 (6%) | 3 (4%) | 4 (5%) | 12 (5%) | 0.7885 |
| | >=12 months | 81 (94%) | 81 (96%) | 80 (95%) | 242 (95%) | |
| Years of education | n | 86 | 84 | 84 | 254 | 0.3875 |
| | Mean | 12.6 | 13.2 | 12.5 | 12.8 | |
| | SD | 2.95 | 4.15 | 2.92 | 3.38 | |
| | Median | 12.0 | 12.0 | 12.0 | 12.0 | |
| | Min | 6.0 | 3.0 | 6.0 | 3.0 | |
| | Max | 21.0 | 24.0 | 20.0 | 24.0 | |
| | | | | | | |
| Baseline weight (kg) | n | 86 | 83 | 84 | 253 | 0.0030 |
| | Mean | 62.8 | 67.3 | 70.0 | 66.6 | |
| | SD | 12.77 | 14.12 | 14.65 | 14.13 | |
| | Median | 60.6 | 64.9 | 69.2 | 66.7 | |
| | Min | 34.0 | 45.4 | 41.7 | 34.0 | |
| | Max | 86.2 | 106.1 | 108.0 | 108.0 | |
| | | | | | | |

[1] P-values are results of ANOVA treatment group comparison for continuous variable and Pearson's chi-square test for categorical variables.

NOTE: Duration of disease is computed as months between date of enrollment and date of onset of the first definite symptoms of Alzheimer's disease.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\adsl3.sas

21:02 Monday, June 26, 2006

Table 14-2.01
Summary of Demographic and Baseline Characteristics

| | | Placebo (N=86) | Xanomeline Low Dose (N=84) | Xanomeline High Dose (N=84) | Total (N=254) | p-value [1] |
|----------------------|--------|-------------------|----------------------------------|-----------------------------------|------------------|----------------|
| Baseline height (cm) | n | 86 | 84 | 84 | 254 | 0.1262 |
| | Mean | 162.6 | 163.4 | 165.8 | 163.9 | |
| | SD | 11.52 | 10.42 | 10.13 | 10.76 | |
| | Median | 162.6 | 162.6 | 165.1 | 162.9 | |
| | Min | 137.2 | 135.9 | 146.1 | 135.9 | |
| | Max | 185.4 | 195.6 | 190.5 | 195.6 | |
| Baseline BMI | n | 86 | 83 | 84 | 253 | 0.0133 |
| | Mean | 23.6 | 25.1 | 25.3 | 24.7 | |
| | SD | 3.67 | 4.27 | 4.16 | 4.09 | |
| | Median | 23.4 | 24.3 | 24.8 | 24.2 | |
| | Min | 15.1 | 17.7 | 13.7 | 13.7 | |
| | Max | 33.3 | 40.1 | 34.5 | 40.1 | |
| | <25 | 59 (69%) | 47 (56%) | 44 (52%) | 150 (59%) | 0.2326 |
| | 25-<30 | 21 (24%) | 27 (32%) | 28 (33%) | 76 (30%) | |
| | >=30 | 6 (7%) | 10 (12%) | 12 (14%) | 28 (11%) | |

[1] P-values are results of ANOVA treatment group comparison for continuous variable and Pearson's chi-square test for categorical variables.

NOTE: Duration of disease is computed as months between date of enrollment and date of onset of the first definite symptoms of Alzheimer's disease.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\adsl3.sas

21:02 Monday, June 26, 2006

Table 14-3.01

Primary Endpoint Analysis: ADAS Cog (11) - Change from Baseline to Week 24 - LOCF

| | Placebo (N=79) | Xanomeline Low Dose (N=81) | Xanomeline High Dose (N=74) |
|-------------------------------------|-------------------|----------------------------------|-----------------------------------|
| Baseline | | | |
| n | 79 | 81 | 74 |
| Mean (SD) | 24.1 (12.19) | 24.4 (12.92) | 21.3 (11.74) |
| Median (Range) | 21.0 (5;61) | 21.0 (5;57) | 18.0 (3;57) |
| Week 24 | | | |
| n | 79 | 81 | 74 |
| Mean (SD) | 26.7 (13.79) | 26.4 (13.18) | 22.8 (12.48) |
| Median (Range) | 24.0 (5;62) | 25.0 (6;62) | 20.0 (3;62) |
| Change from Baseline | | | |
| n | 79 | 81 | 74 |
| Mean (SD) | 2.5 (5.80) | 2.0 (5.55) | 1.5 (4.26) |
| Median (Range) | 2.0 (-11;16) | 2.0 (-11;17) | 1.0 (-7;13) |
| p-value(Dose Response) [1] [2] | | | 0.245 |
| p-value(Xan - Placebo) [1] [3] | | 0.569 | 0.233 |
| Diff of LS Means (SE) | | -0.5 (0.82) | -1.0 (0.84) |
| 95% CI | | (-2.1;1.1) | (-2.7;0.7) |
| p-value(Xan High - Xan Low) [1] [3] | | | 0.520 |
| Diff of LS Means (SE) | | | -0.5 (0.84) |
| 95% CI | | | (-2.2;1.1) |

[1] Based on Analysis of covariance (ANCOVA) model with treatment and site group as factors and baseline value as a covariate.

[2] Test for a non-zero coefficient for treatment (dose) as a continuous variable.

[3] Pairwise comparison with treatment as a categorical variable: p-values without adjustment for multiple comparisons.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rtf_eff1.sas

21:05 Monday, June 26, 2006

Table 14-3.02
Primary Endpoint Analysis: CIBIC+ - Summary at Week 24 - LOCF

| | Placebo (N=79) | Xanomeline Low Dose (N=81) | Xanomeline High Dose (N=74) |
|-------------------------------------|-------------------|----------------------------------|-----------------------------------|
| Week 24 | | | |
| n | 79 | 81 | 74 |
| Mean (SD) | 4.3 (0.77) | 4.2 (0.79) | 4.3 (0.81) |
| Median (Range) | 4.0 (2;6) | 4.0 (2;6) | 4.0 (3;6) |
| p-value(Dose Response) [1] [2] | | | 0.960 |
| p-value(Xan - Placebo) [1] [3] | | 0.489 | 0.799 |
| Diff of LS Means (SE) | | -0.1 (0.13) | 0.0 (0.13) |
| 95% CI | | (-0.3;0.2) | (-0.2;0.3) |
| p-value(Xan High - Xan Low) [1] [3] | | | 0.349 |
| Diff of LS Means (SE) | | | 0.1 (0.13) |
| 95% CI | | | (-0.1;0.4) |

[1] Based on Analysis of covariance (ANCOVA) model with treatment and site group as factors.

[2] Test for a non-zero coefficient for treatment (dose) as a continuous variable.

[3] Pairwise comparison with treatment as a categorical variable: p-values without adjustment for multiple comparisons.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rtf_eff1.sas

21:05 Monday, June 26, 2006

Table 14-3.03
ADAS Cog (11) - Change from Baseline to Week 8 - LOCF

| | Placebo (N=79) | Xanomeline Low Dose (N=81) | Xanomeline High Dose (N=74) |
|------------------------------------|-------------------|----------------------------------|-----------------------------------|
| Baseline | | | |
| n | 79 | 81 | 74 |
| Mean (SD) | 24.1 (12.19) | 24.4 (12.92) | 21.3 (11.74) |
| Median (Range) | 21.0 (5;61) | 21.0 (5;57) | 18.0 (3;57) |
| Week 8 | | | |
| n | 79 | 81 | 74 |
| Mean (SD) | 25.0 (13.10) | 26.2 (12.98) | 22.3 (12.41) |
| Median (Range) | 22.0 (5;62) | 25.0 (5;62) | 19.0 (2;62) |
| Change from Baseline | | | |
| n | 79 | 81 | 74 |
| Mean (SD) | 0.8 (4.81) | 1.8 (4.14) | 1.0 (3.62) |
| Median (Range) | 1.0 (-12;16) | 2.0 (-12;14) | 1.0 (-8;13) |
| p-value(Dose Response) [1][2] | | | 0.497 |
| p-value(Xan - Placebo) [1][3] | | 0.099 | 0.751 |
| Diff of LS Means (SE) | | 1.1 (0.65) | 0.2 (0.67) |
| 95% CI | | (-0.2;2.4) | (-1.1;1.5) |
| p-value(Xan High - Xan Low) [1][3] | | | 0.195 |
| Diff of LS Means (SE) | | | -0.9 (0.66) |
| 95% CI | | | (-2.2;0.4) |

[1] Based on Analysis of covariance (ANCOVA) model with treatment and site group as factors and baseline value as a covariate.

[2] Test for a non-zero coefficient for treatment (dose) as a continuous variable.

[3] Pairwise comparison with treatment as a categorical variable: p-values without adjustment for multiple comparisons.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rtf_eff1.sas

21:05 Monday, June 26, 2006

Table 14-3.04
CIBIC+ - Summary at Week 8 - LOCF

| | Placebo (N=79) | Xanomeline Low Dose (N=81) | Xanomeline High Dose (N=74) |
|------------------------------------|-------------------|----------------------------------|-----------------------------------|
| Week 8 | | | |
| n | 77 | 81 | 73 |
| Mean (SD) | 3.9 (0.73) | 4.0 (0.72) | 4.1 (0.75) |
| Median (Range) | 4.0 (2;6) | 4.0 (2;6) | 4.0 (2;6) |
| p-value(Dose Response) [1][2] | | | 0.167 |
| p-value(Xan - Placebo) [1][3] | | 0.754 | 0.128 |
| Diff of LS Means (SE) | | 0.0 (0.12) | 0.2 (0.12) |
| 95% CI | | (-0.2;0.3) | (-0.1;0.4) |
| p-value(Xan High - Xan Low) [1][3] | | | 0.218 |
| Diff of LS Means (SE) | | | 0.1 (0.12) |
| 95% CI | | | (-0.1;0.4) |

[1] Based on Analysis of covariance (ANCOVA) model with treatment and site group as factors.

[2] Test for a non-zero coefficient for treatment (dose) as a continuous variable.

[3] Pairwise comparison with treatment as a categorical variable: p-values without adjustment for multiple comparisons.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rtf_eff1.sas

21:05 Monday, June 26, 2006

Table 14-3.05
ADAS Cog (11) - Change from Baseline to Week 16 - LOCF

| | Placebo (N=79) | Xanomeline Low Dose (N=81) | Xanomeline High Dose (N=74) |
|------------------------------------|-------------------|----------------------------------|-----------------------------------|
| Baseline | | | |
| n | 79 | 81 | 74 |
| Mean (SD) | 24.1 (12.19) | 24.4 (12.92) | 21.3 (11.74) |
| Median (Range) | 21.0 (5;61) | 21.0 (5;57) | 18.0 (3;57) |
| Week 16 | | | |
| n | 79 | 81 | 74 |
| Mean (SD) | 26.1 (14.16) | 26.0 (13.05) | 22.5 (12.33) |
| Median (Range) | 23.0 (5;63) | 25.0 (5;62) | 20.0 (4;62) |
| Change from Baseline | | | |
| n | 79 | 81 | 74 |
| Mean (SD) | 2.0 (5.89) | 1.6 (4.10) | 1.2 (4.33) |
| Median (Range) | 2.0 (-17;23) | 2.0 (-9;14) | 1.0 (-11;13) |
| p-value(Dose Response) [1][2] | | | 0.412 |
| p-value(Xan - Placebo) [1][3] | | 0.724 | 0.392 |
| Diff of LS Means (SE) | | -0.3 (0.77) | -0.7 (0.79) |
| 95% CI | | (-1.8;1.2) | (-2.2;0.9) |
| p-value(Xan High - Xan Low) [1][3] | | | 0.606 |
| Diff of LS Means (SE) | | | -0.4 (0.78) |
| 95% CI | | | (-1.9;1.1) |

[1] Based on Analysis of covariance (ANCOVA) model with treatment and site group as factors and baseline value as a covariate.

[2] Test for a non-zero coefficient for treatment (dose) as a continuous variable.

[3] Pairwise comparison with treatment as a categorical variable: p-values without adjustment for multiple comparisons.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rtf_eff1.sas

21:05 Monday, June 26, 2006

Table 14-3.06
CIBIC+ - Summary at Week 16 - LOCF

| | Placebo (N=79) | Xanomeline Low Dose (N=81) | Xanomeline High Dose (N=74) |
|------------------------------------|-------------------|----------------------------------|-----------------------------------|
| Week 16 | | | |
| n | 79 | 81 | 74 |
| Mean (SD) | 4.2 (0.70) | 4.0 (0.77) | 4.0 (0.75) |
| Median (Range) | 4.0 (3;6) | 4.0 (2;6) | 4.0 (2;5) |
| p-value(Dose Response) [1][2] | | | 0.214 |
| p-value(Xan - Placebo) [1][3] | | 0.219 | 0.272 |
| Diff of LS Means (SE) | | -0.1 (0.12) | -0.1 (0.12) |
| 95% CI | | (-0.4;0.1) | (-0.4;0.1) |
| p-value(Xan High - Xan Low) [1][3] | | | 0.916 |
| Diff of LS Means (SE) | | | 0.0 (0.12) |
| 95% CI | | | (-0.2;0.2) |

[1] Based on Analysis of covariance (ANCOVA) model with treatment and site group as factors.

[2] Test for a non-zero coefficient for treatment (dose) as a continuous variable.

[3] Pairwise comparison with treatment as a categorical variable: p-values without adjustment for multiple comparisons.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rtf_eff1.sas

21:05 Monday, June 26, 2006

Table 14-3.07

ADAS Cog (11) - Change from Baseline to Week 24 - Completers at Wk 24-Observed Cases-Windowed

| | Placebo (N=60) | Xanomeline Low Dose (N=28) | Xanomeline High Dose (N=30) |
|------------------------------------|-------------------|----------------------------------|-----------------------------------|
| Baseline | | | |
| n | 59 | 27 | 30 |
| Mean (SD) | 23.2 (11.74) | 24.0 (13.89) | 20.5 (11.50) |
| Median (Range) | 21.0 (5;51) | 20.0 (5;57) | 18.0 (3;49) |
| Week 24 | | | |
| n | 59 | 27 | 30 |
| Mean (SD) | 25.3 (13.32) | 24.1 (11.87) | 21.8 (12.60) |
| Median (Range) | 23.0 (5;58) | 22.0 (8;51) | 18.5 (3;44) |
| Change from Baseline | | | |
| n | 59 | 27 | 30 |
| Mean (SD) | 2.1 (5.89) | 0.1 (5.86) | 1.3 (4.51) |
| Median (Range) | 2.0 (-11;16) | 1.0 (-11;12) | 1.0 (-7;13) |
| p-value(Dose Response) [1][2] | | | 0.234 |
| p-value(Xan - Placebo) [1][3] | | 0.105 | 0.461 |
| Diff of LS Means (SE) | | -2.1 (1.26) | -0.9 (1.22) |
| 95% CI | | (-4.6;0.4) | (-3.3;1.5) |
| p-value(Xan High - Xan Low) [1][3] | | | 0.430 |
| Diff of LS Means (SE) | | | 1.2 (1.47) |
| 95% CI | | | (-1.8;4.1) |

[1] Based on Analysis of covariance (ANCOVA) model with treatment and site group as factors and baseline value as a covariate.

[2] Test for a non-zero coefficient for treatment (dose) as a continuous variable.

[3] Pairwise comparison with treatment as a categorical variable: p-values without adjustment for multiple comparisons.

Note that only assessments falling within the assessment window are included in the summary for a visit.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rtf_eff1.sas

21:05 Monday, June 26, 2006

Table 14-3.08
ADAS Cog (11) - Change from Baseline to Week 24 in Male Subjects - LOCF

| | Placebo (N=33) | Xanomeline Low Dose (N=34) | Xanomeline High Dose (N=39) |
|------------------------------------|-------------------|----------------------------------|-----------------------------------|
| Baseline | | | |
| n | 33 | 34 | 39 |
| Mean (SD) | 22.8 (13.45) | 23.3 (14.03) | 20.8 (11.11) |
| Median (Range) | 19.0 (5;61) | 21.5 (7;57) | 17.0 (3;51) |
| Week 24 | | | |
| n | 33 | 34 | 39 |
| Mean (SD) | 24.7 (13.89) | 25.7 (14.72) | 22.7 (12.32) |
| Median (Range) | 20.0 (5;62) | 24.0 (6;57) | 21.0 (3;51) |
| Change from Baseline | | | |
| n | 33 | 34 | 39 |
| Mean (SD) | 1.9 (6.14) | 2.5 (5.61) | 1.8 (3.77) |
| Median (Range) | 1.0 (-11;16) | 1.0 (-6;14) | 1.0 (-7;13) |
| p-value(Dose Response) [1][2] | | | 0.873 |
| p-value(Xan - Placebo) [1][3] | | 0.712 | 0.915 |
| Diff of LS Means (SE) | | 0.5 (1.30) | 0.1 (1.25) |
| 95% CI | | (-2.1;3.1) | (-2.4;2.6) |
| p-value(Xan High - Xan Low) [1][3] | | | 0.783 |
| Diff of LS Means (SE) | | | -0.3 (1.26) |
| 95% CI | | | (-2.9;2.2) |

[1] Based on Analysis of covariance (ANCOVA) model with treatment and site group as factors and baseline value as a covariate.

[2] Test for a non-zero coefficient for treatment (dose) as a continuous variable.

[3] Pairwise comparison with treatment as a categorical variable: p-values without adjustment for multiple comparisons.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rtf_eff1.sas

21:05 Monday, June 26, 2006

Table 14-3.09
ADAS Cog (11) - Change from Baseline to Week 24 in Female Subjects - LOCF

| | Placebo (N=46) | Xanomeline Low Dose (N=47) | Xanomeline High Dose (N=35) |
|------------------------------------|-------------------|----------------------------------|-----------------------------------|
| Baseline | | | |
| n | 46 | 47 | 35 |
| Mean (SD) | 25.1 (11.25) | 25.2 (12.15) | 21.8 (12.54) |
| Median (Range) | 23.5 (5;51) | 21.0 (5;55) | 18.0 (5;57) |
| Week 24 | | | |
| n | 46 | 47 | 35 |
| Mean (SD) | 28.1 (13.70) | 26.9 (12.09) | 22.9 (12.84) |
| Median (Range) | 24.0 (8;59) | 25.0 (8;62) | 19.0 (4;62) |
| Change from Baseline | | | |
| n | 46 | 47 | 35 |
| Mean (SD) | 3.0 (5.57) | 1.7 (5.54) | 1.1 (4.77) |
| Median (Range) | 3.0 (-8;16) | 2.0 (-11;17) | 0.0 (-7;13) |
| p-value(Dose Response) [1][2] | | | 0.094 |
| p-value(Xan - Placebo) [1][3] | | 0.160 | 0.135 |
| Diff of LS Means (SE) | | -1.6 (1.10) | -1.8 (1.20) |
| 95% CI | | (-3.7;0.6) | (-4.2;0.6) |
| p-value(Xan High - Xan Low) [1][3] | | | 0.843 |
| Diff of LS Means (SE) | | | -0.2 (1.21) |
| 95% CI | | | (-2.6;2.2) |

[1] Based on Analysis of covariance (ANCOVA) model with treatment and site group as factors and baseline value as a covariate.

[2] Test for a non-zero coefficient for treatment (dose) as a continuous variable.

[3] Pairwise comparison with treatment as a categorical variable: p-values without adjustment for multiple comparisons.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rtf_eff1.sas

21:05 Monday, June 26, 2006

Table 14-3.10
ADAS Cog (11) - Mean and Mean Change from Baseline over Time

| | | | | | | | | ---Change from baseline--- | | | | | | | |
|----------|--------------------|----|------|-------|------|------|------|----------------------------|-------------|------|------|------|------|------|--|
| | | nc | Mean | Std | Med. | Min. | Max. | Bsln Mean | Bsln Std | Mean | Std | Med. | Min. | Max. | |
| Placebo | Baseline | 79 | 24.1 | 12.19 | 21.0 | 5 | 61 | | | | | | | | |
| | Week 8 (Windowed) | 79 | 25.0 | 13.10 | 22.0 | 5 | 62 | 24.1 | 12.19 | 0.8 | 4.81 | 1.0 | -12 | 16 | |
| | Week 16 (Windowed) | 68 | 25.1 | 13.42 | 21.0 | 5 | 63 | 23.4 | 11.32 | 1.7 | 5.92 | 2.0 | -17 | 23 | |
| | Week 24 (Windowed) | 65 | 25.7 | 13.90 | 23.0 | 5 | 59 | 23.6 | 12.13 | 2.1 | 5.99 | 2.0 | -11 | 16 | |
| | Week 8 LOCF | 79 | 25.0 | 13.10 | 22.0 | 5 | 62 | 24.1 | 12.19 | 0.8 | 4.81 | 1.0 | -12 | 16 | |
| | Week 16 LOCF | 79 | 26.1 | 14.16 | 23.0 | 5 | 63 | 24.1 | 12.19 | 2.0 | 5.89 | 2.0 | -17 | 23 | |
| | Week 24 LOCF | 79 | 26.7 | 13.79 | 24.0 | 5 | 62 | 24.1 | 12.19 | 2.5 | 5.80 | 2.0 | -11 | 16 | |
| Xan.Low | Baseline | 81 | 24.4 | 12.92 | 21.0 | 5 | 57 | | | | | | | | |
| | Week 8 (Windowed) | 81 | 26.2 | 12.98 | 25.0 | 5 | 62 | 24.4 | 12.92 | 1.8 | 4.14 | 2.0 | -12 | 14 | |
| | Week 16 (Windowed) | 42 | 26.2 | 12.23 | 25.0 | 8 | 53 | 25.0 | 12.52 | 1.2 | 4.33 | 1.0 | -8 | 13 | |
| | Week 24 (Windowed) | 49 | 25.6 | 13.81 | 24.0 | 7 | 57 | 24.4 | 13.76 | 1.3 | 6.05 | 1.0 | -11 | 17 | |
| | Week 8 LOCF | 81 | 26.2 | 12.98 | 25.0 | 5 | 62 | 24.4 | 12.92 | 1.8 | 4.14 | 2.0 | -12 | 14 | |
| | Week 16 LOCF | 81 | 26.0 | 13.05 | 25.0 | 5 | 62 | 24.4 | 12.92 | 1.6 | 4.10 | 2.0 | -9 | 14 | |
| | Week 24 LOCF | 81 | 26.4 | 13.18 | 25.0 | 6 | 62 | 24.4 | 12.92 | 2.0 | 5.55 | 2.0 | -11 | 17 | |
| Xan.High | Baseline | 74 | 21.3 | 11.74 | 18.0 | 3 | 57 | | | | | | | | |
| | Week 8 (Windowed) | 74 | 22.3 | 12.41 | 19.0 | 2 | 62 | 21.3 | 11.74 | 1.0 | 3.62 | 1.0 | -8 | 13 | |
| | Week 16 (Windowed) | 40 | 21.9 | 12.39 | 19.5 | 4 | 49 | 21.1 | 11.79 | 0.8 | 4.92 | 1.0 | -11 | 10 | |
| | Week 24 (Windowed) | 41 | 21.8 | 12.38 | 19.0 | 3 | 45 | 20.1 | 11.13 | 1.7 | 4.74 | 1.0 | -7 | 13 | |
| | Week 8 LOCF | 74 | 22.3 | 12.41 | 19.0 | 2 | 62 | 21.3 | 11.74 | 1.0 | 3.62 | 1.0 | -8 | 13 | |
| | Week 16 LOCF | 74 | 22.5 | 12.33 | 20.0 | 4 | 62 | 21.3 | 11.74 | 1.2 | 4.33 | 1.0 | -11 | 13 | |
| | Week 24 LOCF | 74 | 22.8 | 12.48 | 20.0 | 3 | 62 | 21.3 | 11.74 | 1.5 | 4.26 | 1.0 | -7 | 13 | |

Table 14-3.11

ADAS Cog (11) - Repeated Measures Analysis of Change from Baseline to Week 24

| | Placebo (N=79) | Xanomeline Low Dose (N=81) | Xanomeline High Dose (N=74) |
|-----------------------------|-------------------|----------------------------------|-----------------------------------|
| LS Means (SE) | 1.6 (0.49) | 1.5 (0.52) | 1.1 (0.56) |
| p-value(Xan - Placebo) | | 0.955 | 0.556 |
| Diff of LS Means (SE) | | -0.0 (0.70) | -0.4 (0.72) |
| 95% CI | | (-1.4;1.3) | (-1.9;1.0) |
| p-value(Xan High - Xan Low) | | | 0.606 |
| Diff of LS Means (SE) | | | -0.4 (0.75) |
| 95% CI | | | (-1.9;1.1) |

Note: The change from baseline is calculated as the post-baseline score minus the baseline score. The covariates included in the MMRM model are treatment, site group, time and treatment by time interaction, baseline ADAS-Cog (11) score, and baseline ADAS-Cog (11) score by time interaction.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rtf_eff_mmrms.sas

21:06 Monday, June 26, 2006

Table 14-3.12
Mean NPI-X Total Score from Week 4 through Week 24 - Windowed

| | Placebo (N=79) | Xanomeline Low Dose (N=81) | Xanomeline High Dose (N=74) |
|------------------------------------|-------------------|----------------------------------|-----------------------------------|
| Baseline | | | |
| n | 79 | 81 | 74 |
| Mean (SD) | 9.5 (12.10) | 8.7 (9.82) | 11.9 (13.70) |
| Median (Range) | 5.0 (0;66) | 4.0 (0;32) | 8.0 (0;61) |
| Mean of Weeks 4-24 | | | |
| n | 78 | 75 | 69 |
| Mean (SD) | 9.3 (11.18) | 9.1 (12.10) | 9.6 (11.60) |
| Median (Range) | 5.5 (0;65) | 3.8 (0;51) | 4.4 (0;46) |
| p-value(Dose Response) [1][2] | | | 0.637 |
| p-value(Xan - Placebo) [1][3] | | 0.760 | 0.517 |
| Diff of LS Means (SE) | | 0.3 (1.13) | -0.7 (1.15) |
| 95% CI | | (-1.9;2.6) | (-3.0;1.5) |
| p-value(Xan High - Xan Low) [1][3] | | | 0.350 |
| Diff of LS Means (SE) | | | -1.1 (1.17) |
| 95% CI | | | (-3.4;1.2) |

[1] Based on Analysis of covariance (ANCOVA) model with treatment and site group as factors and baseline value as a covariate.

[2] Test for a non-zero coefficient for treatment (dose) as a continuous variable.

[3] Pairwise comparison with treatment as a categorical variable: p-values without adjustment for multiple comparisons.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rtf_eff1.sas

21:05 Monday, June 26, 2006

Table 14-3.13
CIBIC+ - Categorical Analysis - LOCF

| | Assessment | Placebo (N=79) | Xanomeline Low Dose (N=81) | Xanomeline High Dose (N=74) | p-value [1] |
|---------|----------------------|-------------------|----------------------------------|-----------------------------------|----------------|
| Week 8 | n | 77 | 81 | 73 | 0.2727 |
| | Marked improvement | 0 | 0 | 0 | |
| | Moderate improvement | 1 (1%) | 2 (2%) | 1 (1%) | |
| | Minimal improvement | 19 (25%) | 16 (20%) | 13 (18%) | |
| | No Change | 45 (58%) | 48 (59%) | 38 (52%) | |
| | Minimal worsening | 10 (13%) | 14 (17%) | 20 (27%) | |
| | Moderate worsening | 2 (3%) | 1 (1%) | 1 (1%) | |
| | Marked worsening | 0 | 0 | 0 | |
| Week 16 | n | 79 | 81 | 74 | 0.4003 |
| | Marked improvement | 0 | 0 | 0 | |
| | Moderate improvement | 0 | 3 (4%) | 2 (3%) | |
| | Minimal improvement | 12 (15%) | 12 (15%) | 13 (18%) | |
| | No Change | 41 (52%) | 46 (57%) | 39 (53%) | |
| | Minimal worsening | 25 (32%) | 19 (23%) | 20 (27%) | |
| | Moderate worsening | 1 (1%) | 1 (1%) | 0 | |
| | Marked worsening | 0 | 0 | 0 | |
| Week 24 | n | 79 | 81 | 74 | 0.6180 |
| | Marked improvement | 0 | 0 | 0 | |
| | Moderate improvement | 1 (1%) | 1 (1%) | 0 | |
| | Minimal improvement | 9 (11%) | 14 (17%) | 11 (15%) | |
| | No Change | 38 (48%) | 37 (46%) | 33 (45%) | |
| | Minimal worsening | 28 (35%) | 27 (33%) | 25 (34%) | |
| | Moderate worsening | 3 (4%) | 2 (2%) | 5 (7%) | |
| | Marked worsening | 0 | 0 | 0 | |

[1] Overall comparison of treatments using CMH test (Pearson Chi-Square), controlling for site group.
Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rtf_eff_cat.sas 21:06 Monday, June 26, 2006

Table 14-4.01
Summary of Planned Exposure to Study Drug, as of End of Study

| | | Completers at Week 24 | | | Safety Population [1] | | |
|-------------------------------------|--------|-----------------------|----------------------------------|-----------------------------------|-----------------------|----------------------------------|-----------------------------------|
| | | Placebo (N=60) | Xanomeline Low Dose (N=28) | Xanomeline High Dose (N=30) | Placebo (N=86) | Xanomeline Low Dose (N=84) | Xanomeline High Dose (N=84) |
| Average daily dose (mg) | n | 60 | 28 | 30 | 86 | 84 | 84 |
| | mean | 0.0 | 54.0 | 77.0 | 0.0 | 54.0 | 71.6 |
| | std | 0.00 | 0.00 | 0.58 | 0.00 | 0.00 | 8.11 |
| | median | 0.0 | 54.0 | 76.9 | 0.0 | 54.0 | 75.1 |
| | min | 0.0 | 54.0 | 76.1 | 0.0 | 54.0 | 54.0 |
| | max | 0.0 | 54.0 | 78.6 | 0.0 | 54.0 | 78.6 |
| Cumulative dose at end of study [2] | n | 60 | 28 | 30 | 86 | 84 | 84 |
| | mean | 0.0 | 9918.6 | 14089.5 | 0.0 | 5347.3 | 7551.0 |
| | std | 0.00 | 603.84 | 481.01 | 0.00 | 3680.35 | 5531.04 |
| | median | 0.0 | 9936.0 | 14080.5 | 0.0 | 4455.0 | 5778.0 |
| | min | 0.0 | 7884.0 | 12960.0 | 0.0 | 108.0 | 54.0 |
| | max | 0.0 | 11448.0 | 15417.0 | 0.0 | 11448.0 | 15417.0 |

[1] Includes completers and early terminators.

[2] End of Study refers to week 26/Early Termination.

Source: C:\cdisc_pilot\PROGRAMS\DRIFT\TFLs\adsl12.sas

21:02 Monday, June 26, 2006

Table 14-5.01
Incidence of Treatment Emergent Adverse Events by Treatment Group

| System Organ Class/ Preferred Term | Placebo (N=86) | | Xanomeline Low (N=84) | | Xanomeline High (N=84) | | Fisher's Exact p-values Placebo vs. Placebo vs. Low Dose High Dose | |
|---------------------------------------|-------------------|-------|--------------------------|-------|---------------------------|-------|--|--------|
| | n(%) | [AEs] | n(%) | [AEs] | n(%) | [AEs] | | |
| ANY BODY SYSTEM | 65 (75.6%) | [281] | 77 (91.7%) | [412] | 76 (90.5%) | [433] | 0.007* | 0.014* |
| CARDIAC DISORDERS | 12 (14.0%) | [26] | 13 (15.5%) | [30] | 15 (17.9%) | [30] | 0.831 | 0.534 |
| SINUS BRADYCARDIA | 2 (2.3%) | [2] | 7 (8.3%) | [10] | 8 (9.5%) | [12] | 0.097* | 0.056* |
| MYOCARDIAL INFARCTION | 4 (4.7%) | [4] | 2 (2.4%) | [4] | 4 (4.8%) | [8] | 0.682 | >0.99 |
| ATRIAL FIBRILLATION | 1 (1.2%) | [1] | 1 (1.2%) | [1] | 3 (3.6%) | [5] | >0.99 | 0.365 |
| ATRIAL FLUTTER | 0 | | 1 (1.2%) | [1] | 1 (1.2%) | [2] | 0.494 | 0.494 |
| CARDIAC DISORDER | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| SUPRAVENTRICULAR | 1 (1.2%) | [2] | 1 (1.2%) | [2] | 1 (1.2%) | [1] | >0.99 | >0.99 |
| EXTRASYSTOLES | | | | | | | | |
| VENTRICULAR EXTRASYSTOLES | 0 | | 2 (2.4%) | [4] | 1 (1.2%) | [1] | 0.243 | 0.494 |
| ATRIAL HYPERTROPHY | 1 (1.2%) | [2] | 0 | | 0 | | >0.99 | >0.99 |
| ATRIOVENTRICULAR BLOCK | 1 (1.2%) | [1] | 1 (1.2%) | [1] | 0 | | >0.99 | >0.99 |
| FIRST DEGREE | | | | | | | | |
| ATRIOVENTRICULAR BLOCK | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| SECOND DEGREE | | | | | | | | |
| BRADYCARDIA | 1 (1.2%) | [4] | 0 | | 0 | | >0.99 | >0.99 |
| BUNDLE BRANCH BLOCK LEFT | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| BUNDLE BRANCH BLOCK RIGHT | 1 (1.2%) | [2] | 1 (1.2%) | [1] | 0 | | >0.99 | >0.99 |

Note: Treatment emergent events are defined as events which start on or after the start of treatment.

Note: Adverse events are coded using MedDRA.

Note: Percentages are based on the number of subjects in the safety population within each treatment group.

Note: P-values are based on Fisher's Exact test for the comparison of placebo versus each active treatment group. An asterisk is appended to p-values that are less than 0.15.

Note: The column [AE] represents the total number of times an event was recorded.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\aetable.sas

21:41 Monday, June 26, 2006

Table 14-5.01
Incidence of Treatment Emergent Adverse Events by Treatment Group

| System Organ Class/ Preferred Term | Placebo (N=86) | | Xanomeline Low (N=84) | | Xanomeline High (N=84) | | Fisher's Exact p-values Placebo vs. Placebo vs. Low Dose High Dose | |
|---------------------------------------|-------------------|-------|--------------------------|-------|---------------------------|-------|--|-------|
| | n(%) | [AEs] | n(%) | [AEs] | n(%) | [AEs] | | |
| CARDIAC FAILURE | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| CONGESTIVE | | | | | | | | |
| PALPITATIONS | 0 | | 2 (2.4%) | [2] | 0 | | 0.243 | |
| SINUS ARRHYTHMIA | 1 (1.2%) | [2] | 0 | | 0 | | >0.99 | >0.99 |
| SUPRAVENTRICULAR | 0 | | 1 (1.2%) | [2] | 0 | | 0.494 | |
| TACHYCARDIA | | | | | | | | |
| TACHYCARDIA | 1 (1.2%) | [2] | 0 | | 0 | | >0.99 | >0.99 |
| VENTRICULAR HYPERTROPHY | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| WOLFF-PARKINSON-WHITE | 0 | | 1 (1.2%) | [2] | 0 | | 0.494 | |
| SYNDROME | | | | | | | | |
| CONGENITAL, FAMILIAL AND | 0 | | 1 (1.2%) | [1] | 2 (2.4%) | [2] | 0.494 | 0.243 |
| GENETIC DISORDE | | | | | | | | |
| VENTRICULAR SEPTAL DEFECT | 0 | | 1 (1.2%) | [1] | 2 (2.4%) | [2] | 0.494 | 0.243 |
| EAR AND LABYRINTH DISORDERS | 1 (1.2%) | [2] | 2 (2.4%) | [2] | 1 (1.2%) | [1] | 0.618 | >0.99 |
| VERTIGO | 0 | | 1 (1.2%) | [1] | 1 (1.2%) | [1] | 0.494 | 0.494 |
| CERUMEN IMPACTION | 0 | | 1 (1.2%) | [1] | 0 | | 0.494 | |
| EAR PAIN | 1 (1.2%) | [2] | 0 | | 0 | | >0.99 | >0.99 |
| EYE DISORDERS | 2 (2.3%) | [5] | 2 (2.4%) | [2] | 1 (1.2%) | [2] | >0.99 | >0.99 |

Note: Treatment emergent events are defined as events which start on or after the start of treatment.

Note: Adverse events are coded using MedDRA.

Note: Percentages are based on the number of subjects in the safety population within each treatment group.

Note: P-values are based on Fisher's Exact test for the comparison of placebo versus each active treatment group. An asterisk is appended to p-values that are less than 0.15.

Note: The column [AE] represents the total number of times an event was recorded.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\aetable.sas

21:41 Monday, June 26, 2006

Table 14-5.01
Incidence of Treatment Emergent Adverse Events by Treatment Group

| System Organ Class/ Preferred Term | Placebo (N=86) | | Xanomeline Low (N=84) | | Xanomeline High (N=84) | | Fisher's Exact p-values Placebo vs. Placebo vs. Low Dose High Dose | |
|---------------------------------------|-------------------|-------|--------------------------|-------|---------------------------|-------|--|--------|
| | n(%) | [AEs] | n(%) | [AEs] | n(%) | [AEs] | | |
| VISION BLURRED | 0 | | 1 (1.2%) | [1] | 1 (1.2%) | [2] | 0.494 | 0.494 |
| CONJUNCTIVAL HAEMORRHAGE | 0 | | 1 (1.2%) | [1] | 0 | | 0.494 | |
| CONJUNCTIVITIS | 1 (1.2%) | [2] | 0 | | 0 | | >0.99 | >0.99 |
| EYE ALLERGY | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| EYE PRURITUS | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| EYE SWELLING | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| GASTROINTESTINAL DISORDERS | 17 (19.8%) | [26] | 14 (16.7%) | [22] | 20 (23.8%) | [36] | 0.692 | 0.58 |
| VOMITING | 3 (3.5%) | [3] | 3 (3.6%) | [4] | 7 (8.3%) | [9] | >0.99 | 0.209 |
| NAUSEA | 3 (3.5%) | [3] | 3 (3.6%) | [5] | 6 (7.1%) | [13] | >0.99 | 0.326 |
| DIARRHOEA | 9 (10.5%) | [10] | 4 (4.8%) | [5] | 4 (4.8%) | [4] | 0.248 | 0.248 |
| SALIVARY HYPERSECRETION | 0 | | 0 | | 4 (4.8%) | [5] | | 0.058* |
| ABDOMINAL DISCOMFORT | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| ABDOMINAL PAIN | 1 (1.2%) | [1] | 3 (3.6%) | [3] | 1 (1.2%) | [2] | 0.365 | >0.99 |
| GASTROINTESTINAL HAEMORRHAGE | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| STOMACH DISCOMFORT | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| CONSTIPATION | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| DYSPEPSIA | 1 (1.2%) | [2] | 1 (1.2%) | [2] | 0 | | >0.99 | >0.99 |
| DYSPHAGIA | 0 | | 1 (1.2%) | [1] | 0 | | 0.494 | |
| FLATULENCE | 1 (1.2%) | [2] | 0 | | 0 | | >0.99 | >0.99 |

Note: Treatment emergent events are defined as events which start on or after the start of treatment.

Note: Adverse events are coded using MedDRA.

Note: Percentages are based on the number of subjects in the safety population within each treatment group.

Note: P-values are based on Fisher's Exact test for the comparison of placebo versus each active treatment group. An asterisk is appended to p-values that are less than 0.15.

Note: The column [AE] represents the total number of times an event was recorded.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\aetable.sas

21:41 Monday, June 26, 2006

Table 14-5.01
Incidence of Treatment Emergent Adverse Events by Treatment Group

| System Organ Class/ Preferred Term | Placebo (N=86) | | Xanomeline Low (N=84) | | Xanomeline High (N=84) | | Fisher's Exact p-values Placebo vs. Placebo vs. Low Dose High Dose | |
|---|-------------------|-------|--------------------------|-------|---------------------------|-------|--|--------|
| | n(%) | [AEs] | n(%) | [AEs] | n(%) | [AEs] | | |
| GASTROESOPHAGEAL REFLUX DISEASE | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| GLOSSITIS | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| HIATUS HERNIA | 1 (1.2%) | [2] | 0 | | 0 | | >0.99 | >0.99 |
| RECTAL HAEMORRHAGE | 0 | | 1 (1.2%) | [2] | 0 | | 0.494 | |
| GENERAL DISORDERS AND ADMINISTRATION SIT | 21 (24.4%) | [46] | 47 (56.0%) | [118] | 40 (47.6%) | [124] | 0.000* | 0.002* |
| APPLICATION SITE PRURITUS | 6 (7.0%) | [10] | 22 (26.2%) | [32] | 22 (26.2%) | [35] | 0.001* | 0.001* |
| APPLICATION SITE ERYTHEMA | 3 (3.5%) | [3] | 12 (14.3%) | [20] | 15 (17.9%) | [23] | 0.015* | 0.003* |
| APPLICATION SITE IRRITATION | 3 (3.5%) | [7] | 9 (10.7%) | [18] | 9 (10.7%) | [16] | 0.078* | 0.078* |
| APPLICATION SITE DERMATITIS | 5 (5.8%) | [9] | 9 (10.7%) | [15] | 7 (8.3%) | [12] | 0.277 | 0.563 |
| APPLICATION SITE VESICLES | 1 (1.2%) | [2] | 4 (4.8%) | [5] | 6 (7.1%) | [6] | 0.208 | 0.062* |
| FATIGUE | 1 (1.2%) | [2] | 5 (6.0%) | [5] | 5 (6.0%) | [5] | 0.115* | 0.115* |
| APPLICATION SITE PAIN | 0 | | 0 | | 2 (2.4%) | [2] | | 0.243 |
| APPLICATION SITE PERSPIRATION | 0 | | 0 | | 2 (2.4%) | [3] | | 0.243 |
| APPLICATION SITE SWELLING | 0 | | 1 (1.2%) | [1] | 2 (2.4%) | [3] | 0.494 | 0.243 |
| CHEST DISCOMFORT | 0 | | 0 | | 2 (2.4%) | [2] | | 0.243 |

Note: Treatment emergent events are defined as events which start on or after the start of treatment.

Note: Adverse events are coded using MedDRA.

Note: Percentages are based on the number of subjects in the safety population within each treatment group.

Note: P-values are based on Fisher's Exact test for the comparison of placebo versus each active treatment group. An asterisk is appended to p-values that are less than 0.15.

Note: The column [AE] represents the total number of times an event was recorded.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\aetable.sas

21:41 Monday, June 26, 2006

Table 14-5.01
Incidence of Treatment Emergent Adverse Events by Treatment Group

| System Organ Class/ Preferred Term | Placebo (N=86) | | Xanomeline Low (N=84) | | Xanomeline High (N=84) | | Fisher's Exact p-values Placebo vs. Placebo vs. Low Dose High Dose | |
|---------------------------------------|-------------------|-------|--------------------------|-------|---------------------------|-------|--|-------|
| | n(%) | [AEs] | n(%) | [AEs] | n(%) | [AEs] | | |
| CHEST PAIN | 0 | | 0 | | 2 (2.4%) | [2] | | 0.243 |
| MALAISE | 0 | | 1 (1.2%) | [2] | 2 (2.4%) | [3] | 0.494 | 0.243 |
| OEDEMA PERIPHERAL | 2 (2.3%) | [3] | 1 (1.2%) | [1] | 2 (2.4%) | [3] | >0.99 | >0.99 |
| APPLICATION SITE | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| DISCHARGE | | | | | | | | |
| APPLICATION SITE REACTION | 1 (1.2%) | [2] | 0 | | 1 (1.2%) | [1] | >0.99 | >0.99 |
| APPLICATION SITE | 0 | | 2 (2.4%) | [2] | 1 (1.2%) | [1] | 0.243 | 0.494 |
| URTICARIA | | | | | | | | |
| ASTHENIA | 1 (1.2%) | [2] | 0 | | 1 (1.2%) | [1] | >0.99 | >0.99 |
| CHILLS | 1 (1.2%) | [3] | 1 (1.2%) | [2] | 1 (1.2%) | [1] | >0.99 | >0.99 |
| FEELING ABNORMAL | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| FEELING COLD | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| PAIN | 0 | | 1 (1.2%) | [2] | 1 (1.2%) | [1] | 0.494 | 0.494 |
| PYREXIA | 2 (2.3%) | [2] | 0 | | 1 (1.2%) | [1] | 0.497 | >0.99 |
| APPLICATION SITE BLEEDING | 0 | | 1 (1.2%) | [1] | 0 | | 0.494 | |
| APPLICATION SITE | 0 | | 1 (1.2%) | [1] | 0 | | 0.494 | |
| DESQUAMATION | | | | | | | | |
| APPLICATION SITE | 0 | | 1 (1.2%) | [1] | 0 | | 0.494 | |
| DISCOLOURATION | | | | | | | | |
| APPLICATION SITE | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| INDURATION | | | | | | | | |

Note: Treatment emergent events are defined as events which start on or after the start of treatment.

Note: Adverse events are coded using MedDRA.

Note: Percentages are based on the number of subjects in the safety population within each treatment group.

Note: P-values are based on Fisher's Exact test for the comparison of placebo versus each active treatment group. An asterisk is appended to p-values that are less than 0.15.

Note: The column [AE] represents the total number of times an event was recorded.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\aetable.sas

21:41 Monday, June 26, 2006

Table 14-5.01
Incidence of Treatment Emergent Adverse Events by Treatment Group

| System Organ Class/ Preferred Term | Placebo (N=86) | | Xanomeline Low (N=84) | | Xanomeline High (N=84) | | Fisher's Exact p-values Placebo vs. Placebo vs. Low Dose High Dose | |
|---------------------------------------|-------------------|-------|--------------------------|-------|---------------------------|-------|--|-------|
| | n(%) | [AEs] | n(%) | [AEs] | n(%) | [AEs] | | |
| APPLICATION SITE WARMTH | 0 | | 1 (1.2%) | [2] | 0 | | 0.494 | |
| INFLAMMATION | 0 | | 1 (1.2%) | [1] | 0 | | 0.494 | |
| OEDEMA | 0 | | 2 (2.4%) | [2] | 0 | | 0.243 | |
| SECRETION DISCHARGE | 0 | | 1 (1.2%) | [2] | 0 | | 0.494 | |
| SUDDEN DEATH | 0 | | 1 (1.2%) | [1] | 0 | | 0.494 | |
| SWELLING | 0 | | 1 (1.2%) | [1] | 0 | | 0.494 | |
| ULCER | 0 | | 1 (1.2%) | [1] | 0 | | 0.494 | |
| HEPATOBIILIARY DISORDERS | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| HYPERBILIRUBINAEMIA | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| IMMUNE SYSTEM DISORDERS | 0 | | 1 (1.2%) | [2] | 0 | | 0.494 | |
| HYPERSENSITIVITY | 0 | | 1 (1.2%) | [2] | 0 | | 0.494 | |
| INFECTIONS AND INFESTATIONS | 16 (18.6%) | [35] | 9 (10.7%) | [16] | 13 (15.5%) | [20] | 0.194 | 0.685 |
| NASOPHARYNGITIS | 2 (2.3%) | [4] | 4 (4.8%) | [9] | 6 (7.1%) | [8] | 0.441 | 0.166 |
| UPPER RESPIRATORY TRACT INFECTION | 6 (7.0%) | [12] | 1 (1.2%) | [2] | 3 (3.6%) | [5] | 0.117* | 0.496 |
| CYSTITIS | 1 (1.2%) | [1] | 0 | | 1 (1.2%) | [1] | >0.99 | >0.99 |
| HORDEOLUM | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| INFLUENZA | 1 (1.2%) | [2] | 1 (1.2%) | [1] | 1 (1.2%) | [1] | >0.99 | >0.99 |

Note: Treatment emergent events are defined as events which start on or after the start of treatment.

Note: Adverse events are coded using MedDRA.

Note: Percentages are based on the number of subjects in the safety population within each treatment group.

Note: P-values are based on Fisher's Exact test for the comparison of placebo versus each active treatment group. An asterisk is appended to p-values that are less than 0.15.

Note: The column [AE] represents the total number of times an event was recorded.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\aetable.sas

21:41 Monday, June 26, 2006

Table 14-5.01
Incidence of Treatment Emergent Adverse Events by Treatment Group

| System Organ Class/ Preferred Term | Placebo (N=86) | | Xanomeline Low (N=84) | | Xanomeline High (N=84) | | Fisher's Exact p-values Placebo vs. Low Dose vs. Placebo vs. High Dose | |
|---|-------------------|-------|--------------------------|-------|---------------------------|-------|---|-------|
| | n(%) | [AEs] | n(%) | [AEs] | n(%) | [AEs] | | |
| LOWER RESPIRATORY TRACT INFECTION | 0 | | 0 | | 1 (1.2%) | [2] | | 0.494 |
| RHINITIS | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| URINARY TRACT INFECTION | 2 (2.3%) | [4] | 0 | | 1 (1.2%) | [1] | 0.497 | >0.99 |
| BRONCHITIS | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| CELLULITIS | 0 | | 1 (1.2%) | [1] | 0 | | 0.494 | |
| CERVICITIS | 1 (1.2%) | [2] | 0 | | 0 | | >0.99 | >0.99 |
| EAR INFECTION | 2 (2.3%) | [4] | 0 | | 0 | | 0.497 | 0.497 |
| GASTROENTERITIS VIRAL | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| LOCALISED INFECTION | 1 (1.2%) | [2] | 0 | | 0 | | >0.99 | >0.99 |
| PNEUMONIA | 0 | | 1 (1.2%) | [2] | 0 | | 0.494 | |
| VAGINAL MYCOSIS | 1 (1.2%) | [2] | 0 | | 0 | | >0.99 | >0.99 |
| VIRAL INFECTION | 0 | | 1 (1.2%) | [1] | 0 | | 0.494 | |
| INJURY, POISONING AND PROCEDURAL COMPLIC | 4 (4.7%) | [9] | 5 (6.0%) | [12] | 5 (6.0%) | [8] | 0.745 | 0.745 |
| CONTUSION | 1 (1.2%) | [1] | 1 (1.2%) | [3] | 2 (2.4%) | [3] | >0.99 | 0.618 |
| HIP FRACTURE | 1 (1.2%) | [2] | 0 | | 2 (2.4%) | [2] | >0.99 | 0.618 |
| EXCORIATION | 2 (2.3%) | [3] | 1 (1.2%) | [2] | 1 (1.2%) | [1] | >0.99 | >0.99 |
| FACIAL BONES FRACTURE | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| FALL | 1 (1.2%) | [2] | 2 (2.4%) | [2] | 1 (1.2%) | [1] | 0.618 | >0.99 |

Note: Treatment emergent events are defined as events which start on or after the start of treatment.

Note: Adverse events are coded using MedDRA.

Note: Percentages are based on the number of subjects in the safety population within each treatment group.

Note: P-values are based on Fisher's Exact test for the comparison of placebo versus each active treatment group. An asterisk is appended to p-values that are less than 0.15.

Note: The column [AE] represents the total number of times an event was recorded.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\atable.sas

21:41 Monday, June 26, 2006

Table 14-5.01
Incidence of Treatment Emergent Adverse Events by Treatment Group

| System Organ Class/ Preferred Term | Placebo (N=86) | | Xanomeline Low (N=84) | | Xanomeline High (N=84) | | Fisher's Exact p-values Placebo vs. Placebo vs. Low Dose High Dose | |
|---------------------------------------|-------------------|-------|--------------------------|-------|---------------------------|-------|--|-------|
| | n(%) | [AEs] | n(%) | [AEs] | n(%) | [AEs] | | |
| JOINT DISLOCATION | 0 | | 1 (1.2%) | [1] | 0 | | 0.494 | |
| SKIN LACERATION | 1 (1.2%) | [1] | 2 (2.4%) | [2] | 0 | | 0.618 | >0.99 |
| WOUND | 0 | | 1 (1.2%) | [2] | 0 | | 0.494 | |
| INVESTIGATIONS | 10 (11.6%) | [19] | 6 (7.1%) | [7] | 6 (7.1%) | [8] | 0.432 | 0.432 |
| BIOPSY | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| BIOPSY PROSTATE | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| BLOOD CHOLESTEROL | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| INCREASED | | | | | | | | |
| BLOOD GLUCOSE INCREASED | 0 | | 1 (1.2%) | [1] | 1 (1.2%) | [2] | 0.494 | 0.494 |
| ELECTROCARDIOGRAM T WAVE | 2 (2.3%) | [3] | 1 (1.2%) | [1] | 1 (1.2%) | [1] | >0.99 | >0.99 |
| INVERSION | | | | | | | | |
| WEIGHT DECREASED | 0 | | 0 | | 1 (1.2%) | [2] | | 0.494 |
| BLOOD ALKALINE | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| PHOSPHATASE INCREASED | | | | | | | | |
| BLOOD CREATINE | 1 (1.2%) | [2] | 0 | | 0 | | >0.99 | >0.99 |
| PHOSPHOKINASE INCREASED | | | | | | | | |
| BLOOD URINE PRESENT | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| BODY TEMPERATURE | 0 | | 1 (1.2%) | [1] | 0 | | 0.494 | |
| INCREASED | | | | | | | | |
| CYSTOSCOPY | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |

Note: Treatment emergent events are defined as events which start on or after the start of treatment.

Note: Adverse events are coded using MedDRA.

Note: Percentages are based on the number of subjects in the safety population within each treatment group.

Note: P-values are based on Fisher's Exact test for the comparison of placebo versus each active treatment group. An asterisk is appended to p-values that are less than 0.15.

Note: The column [AE] represents the total number of times an event was recorded.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\aetable.sas

21:41 Monday, June 26, 2006

Table 14-5.01
Incidence of Treatment Emergent Adverse Events by Treatment Group

| System Organ Class/ Preferred Term | Placebo (N=86) | | Xanomeline Low (N=84) | | Xanomeline High (N=84) | | Fisher's Exact p-values Placebo vs. Placebo vs. Low Dose High Dose | |
|---|-------------------|-------|--------------------------|-------|---------------------------|-------|--|-----------|
| | n(%) | [AEs] | n(%) | [AEs] | n(%) | [AEs] | Low Dose | High Dose |
| ELECTROCARDIOGRAM ST SEGMENT DEPRESSIO | 4 (4.7%) | [4] | 1 (1.2%) | [2] | 0 | | 0.368 | 0.121* |
| ELECTROCARDIOGRAM T WAVE AMPLITUDE DEC | 1 (1.2%) | [1] | 1 (1.2%) | [1] | 0 | | >0.99 | >0.99 |
| HEART RATE INCREASED | 1 (1.2%) | [2] | 0 | | 0 | | >0.99 | >0.99 |
| HEART RATE IRREGULAR | 1 (1.2%) | [4] | 0 | | 0 | | >0.99 | >0.99 |
| NASAL MUCOSA BIOPSY | 0 | | 1 (1.2%) | [1] | 0 | | 0.494 | |
| METABOLISM AND NUTRITION DISORDERS | 6 (7.0%) | [8] | 1 (1.2%) | [1] | 2 (2.4%) | [4] | 0.117* | 0.278 |
| DECREASED APPETITE | 1 (1.2%) | [2] | 0 | | 1 (1.2%) | [2] | >0.99 | >0.99 |
| INCREASED APPETITE | 1 (1.2%) | [2] | 0 | | 1 (1.2%) | [2] | >0.99 | >0.99 |
| DEHYDRATION | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| DIABETES MELLITUS | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| FOOD CRAVING | 1 (1.2%) | [1] | 1 (1.2%) | [1] | 0 | | >0.99 | >0.99 |
| HYPONATRAEMIA | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| MUSCULOSKELETAL AND CONNECTIVE TISSUE DI | 4 (4.7%) | [6] | 7 (8.3%) | [10] | 7 (8.3%) | [10] | 0.367 | 0.367 |
| BACK PAIN | 1 (1.2%) | [2] | 1 (1.2%) | [1] | 3 (3.6%) | [4] | >0.99 | 0.365 |
| ARTHRALGIA | 1 (1.2%) | [1] | 2 (2.4%) | [4] | 1 (1.2%) | [1] | 0.618 | >0.99 |

Note: Treatment emergent events are defined as events which start on or after the start of treatment.

Note: Adverse events are coded using MedDRA.

Note: Percentages are based on the number of subjects in the safety population within each treatment group.

Note: P-values are based on Fisher's Exact test for the comparison of placebo versus each active treatment group. An asterisk is appended to p-values that are less than 0.15.

Note: The column [AE] represents the total number of times an event was recorded.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\aetable.sas

21:41 Monday, June 26, 2006

Table 14-5.01
Incidence of Treatment Emergent Adverse Events by Treatment Group

| System Organ Class/ Preferred Term | Placebo (N=86) | | Xanomeline Low (N=84) | | Xanomeline High (N=84) | | Fisher's Exact p-values Placebo vs. Placebo vs. Low Dose vs. High Dose | |
|---|-------------------|-------|--------------------------|-------|---------------------------|-------|---|--------|
| | n(%) | [AEs] | n(%) | [AEs] | n(%) | [AEs] | | |
| ARTHRITIS | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| FLANK PAIN | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| MUSCLE SPASMS | 0 | | 1 (1.2%) | [1] | 1 (1.2%) | [2] | 0.494 | 0.494 |
| MYALGIA | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| MUSCULAR WEAKNESS | 0 | | 1 (1.2%) | [2] | 0 | | 0.494 | |
| PAIN IN EXTREMITY | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| SHOULDER PAIN | 1 (1.2%) | [2] | 2 (2.4%) | [2] | 0 | | 0.618 | >0.99 |
| NEOPLASMS BENIGN, MALIGNANT AND UNSPECIF | 0 | | 2 (2.4%) | [3] | 1 (1.2%) | [1] | 0.243 | 0.494 |
| PROSTATE CANCER | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| COLON CANCER | 0 | | 1 (1.2%) | [1] | 0 | | 0.494 | |
| MALIGNANT FIBROUS HISTIOCYTOMA | 0 | | 1 (1.2%) | [2] | 0 | | 0.494 | |
| NERVOUS SYSTEM DISORDERS | 8 (9.3%) | [11] | 20 (23.8%) | [40] | 25 (29.8%) | [41] | 0.013* | 0.001* |
| DIZZINESS | 2 (2.3%) | [3] | 8 (9.5%) | [13] | 11 (13.1%) | [15] | 0.056* | 0.009* |
| HEADACHE | 3 (3.5%) | [3] | 3 (3.6%) | [4] | 5 (6.0%) | [8] | >0.99 | 0.493 |
| SYNCOPE | 0 | | 4 (4.8%) | [6] | 3 (3.6%) | [4] | 0.058* | 0.118* |
| BURNING SENSATION | 0 | | 0 | | 2 (2.4%) | [2] | | 0.243 |
| AMNESIA | 0 | | 0 | | 1 (1.2%) | [2] | | 0.494 |

Note: Treatment emergent events are defined as events which start on or after the start of treatment.

Note: Adverse events are coded using MedDRA.

Note: Percentages are based on the number of subjects in the safety population within each treatment group.

Note: P-values are based on Fisher's Exact test for the comparison of placebo versus each active treatment group. An asterisk is appended to p-values that are less than 0.15.

Note: The column [AE] represents the total number of times an event was recorded.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\aetable.sas

21:41 Monday, June 26, 2006

Table 14-5.01
Incidence of Treatment Emergent Adverse Events by Treatment Group

| System Organ Class/ Preferred Term | Placebo (N=86) | | Xanomeline Low (N=84) | | Xanomeline High (N=84) | | Fisher's Exact p-values Placebo vs. Low Dose vs. Placebo vs. High Dose | |
|---|-------------------|-------|--------------------------|-------|---------------------------|-------|---|-------|
| | n(%) | [AEs] | n(%) | [AEs] | n(%) | [AEs] | | |
| COGNITIVE DISORDER | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| HYPERSOMNIA | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| LETHARGY | 0 | | 1 (1.2%) | [1] | 1 (1.2%) | [1] | 0.494 | 0.494 |
| PARAESTHESIA | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| PAROSMIA | 0 | | 0 | | 1 (1.2%) | [2] | | 0.494 |
| PARTIAL SEIZURES WITH SECONDARY GENERA | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| SOMNOLENCE | 2 (2.3%) | [3] | 3 (3.6%) | [5] | 1 (1.2%) | [1] | 0.68 | >0.99 |
| SYNCOPE VASOVAGAL | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| TRANSIENT ISCHAEMIC ATTACK | 0 | | 2 (2.4%) | [3] | 1 (1.2%) | [1] | 0.243 | 0.494 |
| BALANCE DISORDER | 0 | | 1 (1.2%) | [3] | 0 | | 0.494 | |
| COMPLEX PARTIAL SEIZURES | 0 | | 1 (1.2%) | [1] | 0 | | 0.494 | |
| COORDINATION ABNORMAL | 0 | | 1 (1.2%) | [1] | 0 | | 0.494 | |
| HEMIANOPIA HOMONYMOUS | 0 | | 1 (1.2%) | [1] | 0 | | 0.494 | |
| PARAESTHESIA ORAL | 0 | | 1 (1.2%) | [1] | 0 | | 0.494 | |
| PARKINSON'S DISEASE | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| PSYCHOMOTOR HYPERACTIVITY | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| STUPOR | 0 | | 1 (1.2%) | [1] | 0 | | 0.494 | |
| PSYCHIATRIC DISORDERS | 10 (11.6%) | [12] | 10 (11.9%) | [14] | 8 (9.5%) | [11] | >0.99 | 0.804 |

Note: Treatment emergent events are defined as events which start on or after the start of treatment.

Note: Adverse events are coded using MedDRA.

Note: Percentages are based on the number of subjects in the safety population within each treatment group.

Note: P-values are based on Fisher's Exact test for the comparison of placebo versus each active treatment group. An asterisk is appended to p-values that are less than 0.15.

Note: The column [AE] represents the total number of times an event was recorded.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\atable.sas

21:41 Monday, June 26, 2006

Table 14-5.01
Incidence of Treatment Emergent Adverse Events by Treatment Group

| System Organ Class/ Preferred Term | Placebo (N=86) | | Xanomeline Low (N=84) | | Xanomeline High (N=84) | | Fisher's Exact p-values Placebo vs. Placebo vs. Low Dose High Dose | |
|---------------------------------------|-------------------|-------|--------------------------|-------|---------------------------|-------|--|-------|
| | n(%) | [AEs] | n(%) | [AEs] | n(%) | [AEs] | | |
| INSOMNIA | 2 (2.3%) | [3] | 0 | | 2 (2.4%) | [2] | 0.497 | >0.99 |
| AGITATION | 2 (2.3%) | [2] | 2 (2.4%) | [2] | 1 (1.2%) | [1] | >0.99 | >0.99 |
| CONFUSIONAL STATE | 2 (2.3%) | [2] | 3 (3.6%) | [3] | 1 (1.2%) | [1] | 0.68 | >0.99 |
| DELIRIUM | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| DELUSION | 1 (1.2%) | [1] | 0 | | 1 (1.2%) | [1] | >0.99 | >0.99 |
| HALLUCINATION | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| HALLUCINATION, VISUAL | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| LIBIDO DECREASED | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| LISTLESS | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| NIGHTMARE | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| ANXIETY | 0 | | 3 (3.6%) | [4] | 0 | | 0.118* | |
| COMPLETED SUICIDE | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| DEPRESSED MOOD | 0 | | 1 (1.2%) | [2] | 0 | | 0.494 | |
| DISORIENTATION | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| IRRITABILITY | 1 (1.2%) | [2] | 1 (1.2%) | [1] | 0 | | >0.99 | >0.99 |
| RESTLESSNESS | 0 | | 1 (1.2%) | [2] | 0 | | 0.494 | |
| RENAL AND URINARY DISORDERS | 4 (4.7%) | [5] | 3 (3.6%) | [3] | 3 (3.6%) | [4] | >0.99 | >0.99 |
| CALCULUS URETHRAL | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| MICTURITION URGENCY | 1 (1.2%) | [1] | 1 (1.2%) | [1] | 1 (1.2%) | [2] | >0.99 | >0.99 |
| NEPHROLITHIASIS | 1 (1.2%) | [1] | 0 | | 1 (1.2%) | [1] | >0.99 | >0.99 |

Note: Treatment emergent events are defined as events which start on or after the start of treatment.

Note: Adverse events are coded using MedDRA.

Note: Percentages are based on the number of subjects in the safety population within each treatment group.

Note: P-values are based on Fisher's Exact test for the comparison of placebo versus each active treatment group. An asterisk is appended to p-values that are less than 0.15.

Note: The column [AE] represents the total number of times an event was recorded.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\aetable.sas

21:41 Monday, June 26, 2006

Table 14-5.01
Incidence of Treatment Emergent Adverse Events by Treatment Group

| System Organ Class/ Preferred Term | Placebo (N=86) | | Xanomeline Low (N=84) | | Xanomeline High (N=84) | | Fisher's Exact p-values Placebo vs. Low Dose vs. Placebo vs. High Dose | |
|---|-------------------|-------|--------------------------|-------|---------------------------|-------|---|--------|
| | n(%) | [AEs] | n(%) | [AEs] | n(%) | [AEs] | | |
| DYSURIA | 1 (1.2%) | [1] | 1 (1.2%) | [1] | 0 | | >0.99 | >0.99 |
| INCONTINENCE | 0 | | 1 (1.2%) | [1] | 0 | | 0.494 | |
| POLLAKEIURIA | 1 (1.2%) | [2] | 0 | | 0 | | >0.99 | >0.99 |
| REPRODUCTIVE SYSTEM AND BREAST DISORDERS | 2 (2.3%) | [4] | 0 | | 1 (1.2%) | [1] | 0.497 | >0.99 |
| BENIGN PROSTATIC HYPERPLASIA | 1 (1.2%) | [2] | 0 | | 1 (1.2%) | [1] | >0.99 | >0.99 |
| PELVIC PAIN | 1 (1.2%) | [2] | 0 | | 0 | | >0.99 | >0.99 |
| RESPIRATORY, THORACIC AND MEDIASTINAL DI | 8 (9.3%) | [12] | 9 (10.7%) | [14] | 10 (11.9%) | [22] | 0.803 | 0.626 |
| COUGH | 1 (1.2%) | [1] | 5 (6.0%) | [7] | 5 (6.0%) | [7] | 0.115* | 0.115* |
| NASAL CONGESTION | 3 (3.5%) | [3] | 1 (1.2%) | [1] | 3 (3.6%) | [4] | 0.621 | >0.99 |
| EPISTAXIS | 0 | | 1 (1.2%) | [1] | 2 (2.4%) | [2] | 0.494 | 0.243 |
| ALLERGIC GRANULOMATOUS ANGIITIS | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| DYSPNOEA | 1 (1.2%) | [1] | 1 (1.2%) | [1] | 1 (1.2%) | [1] | >0.99 | >0.99 |
| PHARYNGEAL ERYTHEMA | 0 | | 0 | | 1 (1.2%) | [2] | | 0.494 |
| PHARYNGOLARYNGEAL PAIN | 0 | | 1 (1.2%) | [1] | 1 (1.2%) | [1] | 0.494 | 0.494 |
| PRODUCTIVE COUGH | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |

Note: Treatment emergent events are defined as events which start on or after the start of treatment.

Note: Adverse events are coded using MedDRA.

Note: Percentages are based on the number of subjects in the safety population within each treatment group.

Note: P-values are based on Fisher's Exact test for the comparison of placebo versus each active treatment group. An asterisk is appended to p-values that are less than 0.15.

Note: The column [AE] represents the total number of times an event was recorded.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\atable.sas

21:41 Monday, June 26, 2006

Table 14-5.01
Incidence of Treatment Emergent Adverse Events by Treatment Group

| System Organ Class/ Preferred Term | Placebo (N=86) | | Xanomeline Low (N=84) | | Xanomeline High (N=84) | | Fisher's Exact p-values Placebo vs. Low Dose vs. Placebo vs. High Dose | |
|---|-------------------|-------|--------------------------|-------|---------------------------|-------|---|--------|
| | n(%) | [AEs] | n(%) | [AEs] | n(%) | [AEs] | | |
| RESPIRATORY TRACT CONGESTION | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| RHINORRHOEA | 0 | | 1 (1.2%) | [2] | 1 (1.2%) | [2] | 0.494 | 0.494 |
| DYSPHONIA | 0 | | 1 (1.2%) | [1] | 0 | | 0.494 | |
| EMPHYSEMA | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| HAEMOPTYSIS | 1 (1.2%) | [2] | 0 | | 0 | | >0.99 | >0.99 |
| POSTNASAL DRIP | 1 (1.2%) | [2] | 0 | | 0 | | >0.99 | >0.99 |
| RALES | 1 (1.2%) | [2] | 0 | | 0 | | >0.99 | >0.99 |
| SKIN AND SUBCUTANEOUS TISSUE DISORDERS | 20 (23.3%) | [45] | 39 (46.4%) | [111] | 40 (47.6%) | [104] | 0.002* | 0.001* |
| PRURITUS | 8 (9.3%) | [11] | 21 (25.0%) | [31] | 26 (31.0%) | [38] | 0.008* | 0.000* |
| ERYTHEMA | 8 (9.3%) | [12] | 14 (16.7%) | [22] | 14 (16.7%) | [22] | 0.175 | 0.175 |
| RASH | 5 (5.8%) | [9] | 13 (15.5%) | [18] | 9 (10.7%) | [15] | 0.048* | 0.277 |
| HYPERHIDROSIS | 2 (2.3%) | [2] | 4 (4.8%) | [5] | 8 (9.5%) | [10] | 0.441 | 0.056* |
| SKIN IRRITATION | 3 (3.5%) | [4] | 6 (7.1%) | [13] | 5 (6.0%) | [8] | 0.326 | 0.493 |
| RASH PRURITIC | 0 | | 1 (1.2%) | [2] | 2 (2.4%) | [3] | 0.494 | 0.243 |
| ACTINIC KERATOSIS | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| BLISTER | 0 | | 5 (6.0%) | [8] | 1 (1.2%) | [2] | 0.028* | 0.494 |
| PRURITUS GENERALISED | 0 | | 1 (1.2%) | [4] | 1 (1.2%) | [1] | 0.494 | 0.494 |
| RASH MACULO-PAPULAR | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |

Note: Treatment emergent events are defined as events which start on or after the start of treatment.

Note: Adverse events are coded using MedDRA.

Note: Percentages are based on the number of subjects in the safety population within each treatment group.

Note: P-values are based on Fisher's Exact test for the comparison of placebo versus each active treatment group. An asterisk is appended to p-values that are less than 0.15.

Note: The column [AE] represents the total number of times an event was recorded.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\aetable.sas

21:41 Monday, June 26, 2006

Table 14-5.01
Incidence of Treatment Emergent Adverse Events by Treatment Group

| System Organ Class/ Preferred Term | Placebo (N=86) | | Xanomeline Low (N=84) | | Xanomeline High (N=84) | | Fisher's Exact p-values Placebo vs. Placebo vs. Low Dose High Dose | |
|---------------------------------------|-------------------|-------|--------------------------|-------|---------------------------|-------|--|-------|
| | n(%) | [AEs] | n(%) | [AEs] | n(%) | [AEs] | | |
| SKIN ODOUR ABNORMAL | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| URTICARIA | 0 | | 1 (1.2%) | [3] | 1 (1.2%) | [2] | 0.494 | 0.494 |
| ALOPECIA | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| COLD SWEAT | 1 (1.2%) | [3] | 0 | | 0 | | >0.99 | >0.99 |
| DERMATITIS CONTACT | 0 | | 1 (1.2%) | [2] | 0 | | 0.494 | |
| DRUG ERUPTION | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| RASH ERYTHEMATOUS | 0 | | 1 (1.2%) | [1] | 0 | | 0.494 | |
| SKIN EXFOLIATION | 0 | | 1 (1.2%) | [2] | 0 | | 0.494 | |
| SKIN ULCER | 1 (1.2%) | [2] | 0 | | 0 | | >0.99 | >0.99 |
| SOCIAL CIRCUMSTANCES | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| ALCOHOL USE | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| SURGICAL AND MEDICAL PROCEDURES | 2 (2.3%) | [2] | 1 (1.2%) | [1] | 2 (2.4%) | [2] | >0.99 | >0.99 |
| ACROCHORDON EXCISION | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| SKIN LESION EXCISION | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| CATARACT OPERATION | 1 (1.2%) | [1] | 1 (1.2%) | [1] | 0 | | >0.99 | >0.99 |
| EYE LASER SURGERY | 1 (1.2%) | [1] | 0 | | 0 | | >0.99 | >0.99 |
| VASCULAR DISORDERS | 3 (3.5%) | [7] | 3 (3.6%) | [3] | 1 (1.2%) | [1] | >0.99 | 0.621 |

Note: Treatment emergent events are defined as events which start on or after the start of treatment.

Note: Adverse events are coded using MedDRA.

Note: Percentages are based on the number of subjects in the safety population within each treatment group.

Note: P-values are based on Fisher's Exact test for the comparison of placebo versus each active treatment group. An asterisk is appended to p-values that are less than 0.15.

Note: The column [AE] represents the total number of times an event was recorded.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\aetable.sas

21:41 Monday, June 26, 2006

Table 14-5.01
Incidence of Treatment Emergent Adverse Events by Treatment Group

| System Organ Class/ Preferred Term | Placebo (N=86) | | Xanomeline Low (N=84) | | Xanomeline High (N=84) | | Fisher's Exact p-values Placebo vs. Placebo vs. Low Dose High Dose | |
|---------------------------------------|-------------------|-------|--------------------------|-------|---------------------------|-------|--|-----------|
| | n(%) | [AEs] | n(%) | [AEs] | n(%) | [AEs] | Low Dose | High Dose |
| WOUND HAEMORRHAGE | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |
| HOT FLUSH | 0 | | 1 (1.2%) | [1] | 0 | | 0.494 | |
| HYPERTENSION | 1 (1.2%) | [2] | 1 (1.2%) | [1] | 0 | | >0.99 | >0.99 |
| HYPOTENSION | 2 (2.3%) | [3] | 1 (1.2%) | [1] | 0 | | >0.99 | 0.497 |
| ORTHOSTATIC HYPOTENSION | 1 (1.2%) | [2] | 0 | | 0 | | >0.99 | >0.99 |

Note: Treatment emergent events are defined as events which start on or after the start of treatment.

Note: Adverse events are coded using MedDRA.

Note: Percentages are based on the number of subjects in the safety population within each treatment group.

Note: P-values are based on Fisher's Exact test for the comparison of placebo versus each active treatment group. An asterisk is appended to p-values that are less than 0.15.

Note: The column [AE] represents the total number of times an event was recorded.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\aetable.sas

21:41 Monday, June 26, 2006

Table 14-5.02

Incidence of Treatment Emergent Serious Adverse Events by Treatment Group

| System Organ Class/ Preferred Term | Placebo (N=86) | | Xanomeline Low (N=84) | | Xanomeline High (N=84) | | Fisher's Exact p-values Placebo vs. Placebo vs. Low Dose High Dose | |
|---|-------------------|-------|--------------------------|-------|---------------------------|-------|--|-------|
| | n(%) | [AEs] | n(%) | [AEs] | n(%) | [AEs] | | |
| ANY BODY SYSTEM | 0 | | 1 (1.2%) | [1] | 2 (2.4%) | [2] | 0.494 | 0.243 |
| NERVOUS SYSTEM DISORDERS | 0 | | 1 (1.2%) | [1] | 2 (2.4%) | [2] | 0.494 | 0.243 |
| SYNCOPE | 0 | | 1 (1.2%) | [1] | 1 (1.2%) | [1] | 0.494 | 0.494 |
| PARTIAL SEIZURES WITH SECONDARY GENERALIZATION | 0 | | 0 | | 1 (1.2%) | [1] | | 0.494 |

Note: Treatment emergent events are defined as events which start on or after the start of treatment.

Note: Adverse events are coded using MedDRA.

Note: Percentages are based on the number of subjects in the safety population within each treatment group.

Note: P-values are based on Fisher's Exact test for the comparison of placebo versus each active treatment group. An asterisk is appended to p-values that are less than 0.15.

Note: The column [AE] represents the total number of times an event was recorded.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\saetable.sas

21:44 Monday, June 26, 2006

Table 14-6.01
Summary Statistics for Continuous Laboratory Values

| Placebo | | | | Xanomeline Low | | | | Xanomeline High | | | |
|--------------------------|----|---------------|------------------------|----------------|---------------|------------------------|----|-----------------|------------------------|--|--|
| Visit | N | Mean (SD) | Change | N | Mean (SD) | Change | N | Mean (SD) | Change | | |
| | | | from Bsln Mean (SD) | | | from Bsln Mean (SD) | | | from Bsln Mean (SD) | | |
| CHEMISTRY | | | | | | | | | | | |
| ALANINE AMINOTRANSFERASE | | | | | | | | | | | |
| Bsln | 86 | 17.6 (9.22) | | 82 | 18.0 (8.72) | | 84 | 19.2 (10.05) | | | |
| Wk 2 | 83 | 18.0 (12.53) | 0.2 (7.90) | 80 | 20.9 (10.55) | 2.8 (8.18) | 78 | 21.0 (8.87) | 1.6 (6.83) | | |
| Wk 4 | 79 | 18.7 (12.91) | 0.7 (8.66) | 72 | 17.5 (7.66) | -0.7 (5.08) | 72 | 21.3 (9.51) | 2.1 (7.08) | | |
| Wk 6 | 73 | 17.0 (9.92) | -0.3 (7.78) | 62 | 17.0 (7.98) | -0.8 (4.87) | 66 | 21.2 (9.49) | 1.6 (6.11) | | |
| Wk 8 | 72 | 16.7 (9.34) | -1.1 (5.05) | 60 | 17.6 (7.86) | 0.2 (5.45) | 56 | 22.8 (17.49) | 3.2 (17.24) | | |
| Wk 12 | 67 | 18.0 (9.16) | 0.0 (8.07) | 51 | 18.5 (12.68) | 0.1 (9.27) | 50 | 21.0 (10.18) | 0.7 (8.74) | | |
| Wk 16 | 68 | 17.1 (7.39) | -0.8 (7.94) | 42 | 17.3 (7.51) | 0.7 (5.80) | 37 | 19.6 (7.61) | -0.3 (7.58) | | |
| Wk 20 | 65 | 16.1 (6.56) | -1.9 (7.49) | 30 | 16.7 (6.33) | 0.9 (4.77) | 31 | 19.6 (6.82) | -0.3 (8.63) | | |
| Wk 24 | 57 | 17.9 (15.61) | -0.3 (16.62) | 26 | 18.2 (9.17) | 1.6 (5.66) | 30 | 21.0 (8.70) | 0.2 (8.25) | | |
| Wk 26 | 57 | 16.0 (5.98) | -2.1 (7.70) | 25 | 17.8 (9.51) | 1.5 (6.26) | 27 | 18.9 (7.02) | -2.0 (7.01) | | |
| End[1] | 84 | 18.1 (16.74) | 0.4 (15.40) | 82 | 18.3 (8.26) | 0.3 (7.25) | 80 | 19.5 (7.44) | 0.1 (8.08) | | |
| ALBUMIN | | | | | | | | | | | |
| Bsln | 86 | 39.8 (2.81) | | 82 | 39.8 (2.56) | | 84 | 40.3 (2.84) | | | |
| Wk 2 | 83 | 38.9 (3.11) | -1.0 (2.49) | 80 | 38.7 (3.17) | -1.1 (2.71) | 78 | 38.9 (2.76) | -1.4 (2.59) | | |
| Wk 4 | 79 | 38.8 (3.29) | -1.0 (2.69) | 72 | 38.6 (2.80) | -1.2 (2.66) | 72 | 39.1 (3.05) | -1.3 (2.70) | | |
| Wk 6 | 73 | 39.1 (2.56) | -1.0 (2.25) | 62 | 38.4 (2.60) | -1.2 (2.49) | 66 | 39.5 (2.76) | -1.0 (2.60) | | |
| Wk 8 | 72 | 39.8 (3.51) | -0.4 (2.70) | 60 | 39.1 (2.93) | -0.5 (2.73) | 56 | 39.8 (2.33) | -0.9 (2.21) | | |
| Wk 12 | 67 | 39.5 (3.49) | -0.5 (2.31) | 51 | 38.9 (2.18) | -0.9 (2.19) | 50 | 39.8 (2.45) | -0.6 (2.77) | | |
| Wk 16 | 68 | 40.4 (3.02) | 0.4 (2.45) | 42 | 39.1 (2.98) | -0.4 (2.78) | 37 | 39.9 (1.92) | -0.7 (2.76) | | |
| Wk 20 | 65 | 39.6 (3.47) | -0.5 (2.86) | 30 | 38.6 (2.66) | -1.2 (2.55) | 31 | 39.6 (1.85) | -1.4 (2.86) | | |
| Wk 24 | 57 | 39.7 (3.34) | -0.2 (2.88) | 26 | 40.4 (2.52) | 0.4 (2.40) | 30 | 40.5 (2.10) | -0.5 (2.65) | | |

[1] Last observed value while on treatment (prior to or at Week 24)

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_lb_cont.sas

21:05 Monday, June 26, 2006

Table 14-6.01
Summary Statistics for Continuous Laboratory Values

| Placebo | | | | Xanomeline Low | | | | Xanomeline High | | | |
|----------------------------|----|---------------|------------------|----------------|---------------|------------------|----|-----------------|------------------|--|--|
| | | | Change from Bsln | | | Change from Bsln | | | Change from Bsln | | |
| Visit | N | Mean (SD) | Mean (SD) | N | Mean (SD) | Mean (SD) | N | Mean (SD) | Mean (SD) | | |
| Wk 26 | 57 | 39.8 (3.02) | 0.0 (2.26) | 25 | 39.2 (2.39) | -1.0 (2.85) | 27 | 40.0 (2.26) | -1.2 (2.78) | | |
| End[1] | 84 | 39.6 (3.32) | -0.2 (2.69) | 82 | 39.2 (2.97) | -0.5 (2.64) | 80 | 39.8 (2.48) | -0.6 (2.64) | | |
| ALKALINE PHOSPHATASE | | | | | | | | | | | |
| Bsln | 86 | 77.7 (58.11) | | 81 | 73.3 (20.72) | | 83 | 71.0 (38.85) | | | |
| Wk 2 | 84 | 77.7 (69.50) | 0.1 (15.51) | 80 | 73.0 (21.87) | 0.3 (10.25) | 78 | 72.2 (40.22) | -0.1 (8.09) | | |
| Wk 4 | 82 | 78.0 (69.43) | 0.4 (14.16) | 72 | 73.2 (23.17) | -0.3 (11.12) | 72 | 71.3 (40.65) | -0.7 (6.88) | | |
| Wk 6 | 75 | 68.4 (21.53) | -0.4 (10.40) | 64 | 72.7 (23.15) | -1.0 (10.83) | 67 | 71.5 (43.40) | -0.2 (12.65) | | |
| Wk 8 | 73 | 70.0 (27.15) | -0.0 (10.67) | 60 | 72.9 (23.84) | 0.5 (14.09) | 56 | 74.0 (45.60) | 0.8 (13.54) | | |
| Wk 12 | 67 | 72.1 (32.73) | 1.8 (17.18) | 52 | 69.5 (20.55) | -1.5 (9.41) | 50 | 71.9 (46.65) | -1.7 (8.53) | | |
| Wk 16 | 68 | 70.6 (29.49) | 0.3 (16.98) | 42 | 69.5 (19.43) | -1.7 (8.61) | 37 | 74.7 (54.78) | -1.4 (8.29) | | |
| Wk 20 | 65 | 72.6 (37.41) | 1.9 (25.77) | 31 | 70.6 (22.20) | -2.2 (9.90) | 31 | 73.5 (55.23) | -2.7 (8.35) | | |
| Wk 24 | 56 | 80.6 (68.06) | 10.1 (58.71) | 27 | 72.0 (21.80) | -0.4 (8.93) | 30 | 64.4 (17.63) | -2.4 (7.44) | | |
| Wk 26 | 57 | 81.0 (79.33) | 10.1 (72.41) | 25 | 68.6 (21.08) | -4.1 (10.74) | 27 | 61.9 (16.60) | -3.9 (7.65) | | |
| End[1] | 84 | 84.6 (84.86) | 7.1 (49.37) | 82 | 71.6 (23.80) | -1.1 (13.09) | 80 | 70.3 (37.91) | -1.6 (12.00) | | |
| ASPARTATE AMINOTRANSFERASE | | | | | | | | | | | |
| Bsln | 86 | 23.2 (7.50) | | 82 | 23.4 (8.24) | | 84 | 23.1 (6.61) | | | |
| Wk 2 | 83 | 23.6 (12.35) | 0.2 (8.96) | 80 | 24.7 (8.06) | 1.6 (6.53) | 78 | 23.4 (5.20) | 0.4 (5.63) | | |
| Wk 4 | 79 | 23.9 (14.93) | 0.5 (11.33) | 72 | 22.3 (6.75) | -1.4 (6.40) | 72 | 23.8 (5.85) | 0.6 (5.75) | | |
| Wk 6 | 73 | 22.0 (6.40) | -0.9 (6.38) | 62 | 22.1 (6.11) | -0.4 (4.19) | 66 | 24.1 (7.84) | 0.4 (6.10) | | |
| Wk 8 | 72 | 22.3 (7.05) | -1.1 (4.84) | 60 | 22.7 (5.95) | 0.3 (4.02) | 56 | 25.7 (13.33) | 1.6 (13.98) | | |
| Wk 12 | 67 | 22.8 (7.64) | -0.6 (7.06) | 51 | 24.2 (15.87) | 1.5 (12.39) | 50 | 23.3 (6.11) | -1.2 (6.26) | | |
| Wk 16 | 68 | 22.8 (6.42) | -0.6 (6.43) | 42 | 22.4 (10.34) | 0.6 (7.62) | 37 | 23.1 (5.78) | -0.7 (4.17) | | |
| Wk 20 | 65 | 21.9 (5.90) | -1.6 (6.07) | 30 | 20.7 (5.74) | 0.4 (4.60) | 31 | 24.0 (6.90) | -0.3 (6.18) | | |
| Wk 24 | 57 | 25.2 (21.02) | 1.2 (20.43) | 26 | 22.4 (10.78) | 2.1 (6.58) | 30 | 24.4 (7.29) | -0.2 (5.48) | | |
| Wk 26 | 57 | 21.5 (6.99) | -2.5 (7.29) | 25 | 22.1 (11.85) | 1.4 (7.69) | 27 | 21.6 (5.71) | -3.1 (4.17) | | |

[1] Last observed value while on treatment (prior to or at Week 24)

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_lb_cont.sas

21:05 Monday, June 26, 2006

Table 14-6.01
Summary Statistics for Continuous Laboratory Values

| Placebo | | | | Xanomeline Low | | | | Xanomeline High | | | | |
|-----------|----|---------------|--------------|---------------------|--------------|--------------|----|---------------------|--------------|---|-----------|---------------------|
| | | | | Change from Bsln | | | | Change from Bsln | | | | Change from Bsln |
| Visit | N | Mean (SD) | Mean (SD) | N | Mean (SD) | Mean (SD) | N | Mean (SD) | Mean (SD) | N | Mean (SD) | Mean (SD) |
| End[1] | 84 | 25.1 (21.33) | 1.8 (19.03) | 82 | 23.2 (8.21) | -0.3 (8.06) | 80 | 22.7 (6.13) | -0.4 (6.36) | | | |
| BILIRUBIN | | | | | | | | | | | | |
| Bsln | 86 | 9.7 (3.96) | | 82 | 9.4 (4.01) | | 84 | 11.0 (5.35) | | | | |
| Wk 2 | 83 | 10.8 (12.26) | 1.1 (10.29) | 79 | 9.4 (4.16) | -0.0 (3.08) | 78 | 10.4 (3.94) | -0.6 (3.62) | | | |
| Wk 4 | 79 | 11.1 (13.57) | 1.4 (11.65) | 71 | 9.2 (3.84) | -0.3 (2.70) | 72 | 10.9 (5.62) | -0.3 (3.07) | | | |
| Wk 6 | 73 | 9.6 (3.78) | 0.1 (2.88) | 62 | 9.5 (4.03) | -0.0 (2.99) | 66 | 10.9 (4.89) | -0.6 (3.18) | | | |
| Wk 8 | 72 | 9.4 (3.89) | -0.4 (3.43) | 60 | 9.6 (4.72) | 0.5 (3.11) | 56 | 10.8 (5.21) | -0.7 (3.21) | | | |
| Wk 12 | 67 | 9.5 (3.56) | -0.1 (2.83) | 51 | 8.8 (4.15) | 0.1 (2.64) | 50 | 11.5 (6.16) | -0.3 (4.78) | | | |
| Wk 16 | 68 | 10.0 (3.63) | 0.2 (2.68) | 42 | 8.8 (3.91) | 0.4 (2.14) | 37 | 11.6 (4.89) | -0.7 (4.28) | | | |
| Wk 20 | 65 | 10.1 (5.19) | 0.3 (3.58) | 30 | 8.8 (4.51) | 0.3 (2.82) | 31 | 11.8 (8.69) | -0.2 (6.41) | | | |
| Wk 24 | 55 | 9.4 (3.39) | 0.1 (2.75) | 25 | 10.1 (4.44) | 1.1 (2.84) | 30 | 12.3 (6.52) | -0.6 (2.89) | | | |
| Wk 26 | 57 | 10.0 (4.73) | 0.4 (3.57) | 25 | 10.2 (6.21) | 1.4 (3.44) | 27 | 12.2 (6.82) | -0.6 (5.31) | | | |
| End[1] | 82 | 11.2 (13.42) | 1.4 (11.28) | 80 | 9.8 (4.29) | 0.5 (3.08) | 80 | 11.1 (5.36) | -0.0 (3.16) | | | |
| CALCIUM | | | | | | | | | | | | |
| Bsln | 86 | 2.3 (0.09) | | 82 | 2.3 (0.11) | | 84 | 2.3 (0.10) | | | | |
| Wk 2 | 84 | 2.3 (0.09) | -0.0 (0.10) | 80 | 2.3 (0.12) | -0.0 (0.10) | 78 | 2.3 (0.11) | -0.0 (0.11) | | | |
| Wk 4 | 82 | 2.3 (0.09) | -0.0 (0.09) | 72 | 2.3 (0.10) | -0.0 (0.08) | 72 | 2.3 (0.10) | -0.0 (0.10) | | | |
| Wk 6 | 75 | 2.3 (0.09) | -0.0 (0.10) | 64 | 2.3 (0.10) | -0.0 (0.08) | 67 | 2.3 (0.09) | -0.0 (0.10) | | | |
| Wk 8 | 73 | 2.3 (0.09) | -0.0 (0.09) | 60 | 2.3 (0.12) | -0.0 (0.09) | 56 | 2.3 (0.12) | -0.0 (0.11) | | | |
| Wk 12 | 67 | 2.3 (0.09) | -0.0 (0.08) | 52 | 2.3 (0.10) | -0.0 (0.07) | 50 | 2.3 (0.09) | -0.0 (0.09) | | | |
| Wk 16 | 68 | 2.3 (0.10) | -0.0 (0.11) | 42 | 2.3 (0.11) | -0.0 (0.08) | 37 | 2.3 (0.11) | -0.0 (0.12) | | | |
| Wk 20 | 66 | 2.3 (0.09) | -0.0 (0.09) | 31 | 2.3 (0.10) | -0.0 (0.09) | 31 | 2.3 (0.08) | -0.0 (0.09) | | | |
| Wk 24 | 57 | 2.3 (0.09) | -0.1 (0.10) | 27 | 2.3 (0.11) | -0.0 (0.12) | 30 | 2.3 (0.10) | -0.1 (0.12) | | | |
| Wk 26 | 57 | 2.3 (0.10) | -0.0 (0.10) | 25 | 2.3 (0.10) | -0.0 (0.08) | 27 | 2.3 (0.09) | -0.0 (0.10) | | | |
| End[1] | 84 | 2.3 (0.09) | -0.0 (0.10) | 82 | 2.3 (0.10) | -0.0 (0.10) | 80 | 2.3 (0.10) | -0.0 (0.11) | | | |

[1] Last observed value while on treatment (prior to or at Week 24)

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_lb_cont.sas

21:05 Monday, June 26, 2006

Table 14-6.01
Summary Statistics for Continuous Laboratory Values

| Visit | Placebo | | | Xanomeline Low | | | Xanomeline High | | |
|-------------|---------|---------------|-------------------------------|----------------|---------------|-------------------------------|-----------------|---------------|-------------------------------|
| | N | Mean (SD) | Change from Bsln Mean (SD) | N | Mean (SD) | Change from Bsln Mean (SD) | N | Mean (SD) | Change from Bsln Mean (SD) |
| CHLORIDE | | | | | | | | | |
| Bsln | 86 | 105.7 (3.19) | | 82 | 105.8 (3.25) | | 83 | 105.4 (3.33) | |
| Wk 2 | 84 | 106.0 (3.12) | 0.3 (3.40) | 80 | 105.6 (3.12) | -0.0 (3.44) | 77 | 104.4 (3.49) | -0.8 (3.88) |
| Wk 4 | 82 | 105.6 (3.53) | -0.1 (4.24) | 72 | 105.5 (2.88) | -0.3 (3.72) | 72 | 105.0 (3.46) | -0.4 (3.94) |
| Wk 6 | 75 | 105.5 (3.14) | -0.1 (3.61) | 64 | 106.3 (3.07) | 0.6 (3.78) | 67 | 105.3 (3.09) | -0.3 (3.47) |
| Wk 8 | 73 | 106.0 (3.34) | 0.3 (3.52) | 60 | 105.6 (3.01) | -0.2 (3.47) | 56 | 105.2 (3.57) | -0.1 (3.71) |
| Wk 12 | 67 | 105.3 (2.93) | -0.3 (3.75) | 52 | 105.7 (3.21) | -0.4 (3.63) | 49 | 105.2 (2.40) | -0.1 (2.64) |
| Wk 16 | 68 | 105.5 (3.16) | -0.0 (3.57) | 42 | 106.2 (2.93) | 0.2 (3.17) | 37 | 105.9 (2.66) | 0.6 (2.54) |
| Wk 20 | 65 | 106.0 (3.68) | 0.6 (4.13) | 31 | 106.3 (2.75) | -0.1 (2.41) | 31 | 105.4 (3.03) | -0.2 (3.69) |
| Wk 24 | 57 | 105.5 (3.14) | -0.1 (3.82) | 27 | 105.3 (2.52) | -1.2 (2.95) | 30 | 105.3 (3.21) | -0.1 (3.06) |
| Wk 26 | 57 | 106.2 (2.58) | 0.8 (3.33) | 25 | 105.7 (2.35) | -0.5 (2.72) | 27 | 105.7 (3.44) | 0.4 (2.92) |
| End[1] | 84 | 105.6 (3.42) | -0.1 (3.86) | 82 | 105.5 (3.37) | -0.1 (3.31) | 80 | 105.0 (3.20) | -0.5 (3.17) |
| CHOLESTEROL | | | | | | | | | |
| Bsln | 86 | 5.8 (1.07) | | 82 | 5.7 (1.00) | | 84 | 5.8 (1.02) | |
| Wk 2 | 84 | 5.6 (1.02) | -0.1 (0.54) | 80 | 5.6 (0.92) | -0.1 (0.50) | 78 | 5.6 (0.93) | -0.2 (0.53) |
| Wk 4 | 82 | 5.5 (0.94) | -0.2 (0.57) | 72 | 5.5 (0.97) | -0.2 (0.49) | 72 | 5.5 (1.00) | -0.3 (0.51) |
| Wk 6 | 75 | 5.6 (0.95) | -0.1 (0.67) | 64 | 5.4 (0.95) | -0.2 (0.55) | 67 | 5.5 (0.91) | -0.3 (0.64) |
| Wk 8 | 73 | 5.5 (1.02) | -0.2 (0.71) | 60 | 5.5 (0.96) | -0.2 (0.49) | 56 | 5.5 (0.94) | -0.3 (0.54) |
| Wk 12 | 67 | 5.5 (0.92) | -0.2 (0.57) | 52 | 5.3 (0.90) | -0.3 (0.47) | 50 | 5.4 (0.91) | -0.3 (0.63) |
| Wk 16 | 68 | 5.6 (0.98) | -0.1 (0.58) | 42 | 5.3 (1.00) | -0.3 (0.48) | 37 | 5.4 (0.94) | -0.2 (0.55) |
| Wk 20 | 66 | 5.5 (0.94) | -0.2 (0.68) | 31 | 5.2 (0.86) | -0.4 (0.46) | 31 | 5.3 (0.85) | -0.3 (0.49) |
| Wk 24 | 57 | 5.5 (1.01) | -0.3 (0.68) | 27 | 5.4 (0.94) | -0.2 (0.65) | 30 | 5.3 (0.89) | -0.3 (0.50) |
| Wk 26 | 57 | 5.5 (0.94) | -0.3 (0.62) | 25 | 5.2 (0.76) | -0.4 (0.64) | 27 | 5.4 (0.90) | -0.2 (0.81) |
| End[1] | 84 | 5.5 (1.02) | -0.3 (0.76) | 82 | 5.4 (0.96) | -0.3 (0.56) | 80 | 5.4 (0.89) | -0.4 (0.60) |

[1] Last observed value while on treatment (prior to or at Week 24)

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_lb_cont.sas

21:05 Monday, June 26, 2006

Table 14-6.01
Summary Statistics for Continuous Laboratory Values

| Visit | Placebo | | | Xanomeline Low | | | Xanomeline High | | |
|-----------------|---------|----------------|-------------------------------|----------------|----------------|-------------------------------|-----------------|----------------|-------------------------------|
| | N | Mean (SD) | Change from Bsln Mean (SD) | N | Mean (SD) | Change from Bsln Mean (SD) | N | Mean (SD) | Change from Bsln Mean (SD) |
| CREATINE KINASE | | | | | | | | | |
| Bsln | 86 | 86.9 (43.71) | | 82 | 100.6 (68.87) | | 84 | 104.0 (71.75) | |
| Wk 2 | 83 | 90.3 (66.11) | 2.4 (57.72) | 80 | 106.1 (83.92) | 6.0 (84.97) | 78 | 93.8 (53.19) | -12.0 (52.92) |
| Wk 4 | 79 | 96.9 (124.45) | 8.3 (116.54) | 72 | 93.2 (51.67) | -7.8 (55.54) | 72 | 100.6 (58.39) | -4.8 (53.80) |
| Wk 6 | 73 | 88.0 (42.36) | -0.3 (40.55) | 62 | 89.0 (44.29) | -13.7 (59.25) | 66 | 123.5 (227.36) | 17.8 (187.17) |
| Wk 8 | 72 | 93.8 (45.84) | 1.2 (46.26) | 60 | 90.0 (39.16) | -8.3 (61.09) | 56 | 91.8 (52.25) | -9.3 (59.25) |
| Wk 12 | 67 | 101.8 (78.66) | 8.9 (67.77) | 51 | 94.7 (53.59) | -7.2 (65.59) | 50 | 96.6 (60.55) | -2.8 (66.47) |
| Wk 16 | 68 | 104.9 (66.37) | 12.7 (52.13) | 42 | 97.5 (56.39) | -6.9 (72.02) | 37 | 86.1 (47.70) | -1.6 (24.32) |
| Wk 20 | 65 | 93.8 (46.56) | 1.0 (42.07) | 30 | 111.6 (137.04) | 21.5 (136.75) | 31 | 97.5 (68.57) | 6.0 (28.57) |
| Wk 24 | 57 | 127.4 (207.98) | 32.6 (200.00) | 26 | 83.6 (38.60) | 0.8 (21.99) | 30 | 90.9 (53.97) | -1.1 (23.40) |
| Wk 26 | 57 | 94.1 (51.03) | 2.0 (46.93) | 25 | 69.9 (23.70) | -15.0 (17.45) | 27 | 93.0 (59.94) | 1.4 (43.90) |
| End[1] | 84 | 112.6 (173.34) | 24.6 (165.91) | 82 | 98.2 (61.12) | -1.9 (67.09) | 80 | 95.1 (56.32) | -9.9 (60.94) |
| CREATININE | | | | | | | | | |
| Bsln | 86 | 97.7 (17.78) | | 82 | 103.5 (20.01) | | 84 | 103.7 (19.37) | |
| Wk 2 | 84 | 99.0 (17.51) | 1.4 (8.06) | 80 | 106.2 (21.26) | 2.3 (10.51) | 78 | 106.3 (21.18) | 2.8 (9.50) |
| Wk 4 | 82 | 98.6 (18.56) | 1.1 (11.40) | 72 | 105.1 (19.83) | 2.0 (8.13) | 72 | 105.8 (20.66) | 2.6 (10.43) |
| Wk 6 | 75 | 101.7 (18.46) | 3.3 (12.14) | 64 | 104.4 (19.85) | 1.7 (9.31) | 67 | 105.8 (20.87) | 3.2 (9.94) |
| Wk 8 | 73 | 99.1 (16.07) | -0.0 (9.88) | 60 | 104.3 (21.27) | 1.8 (7.54) | 56 | 106.1 (22.24) | 3.2 (9.14) |
| Wk 12 | 67 | 101.5 (16.53) | 2.4 (9.68) | 52 | 101.8 (17.72) | 1.8 (7.99) | 50 | 108.2 (20.48) | 5.8 (10.95) |
| Wk 16 | 68 | 100.4 (16.43) | 1.2 (10.57) | 42 | 98.5 (16.63) | -1.3 (9.29) | 37 | 102.5 (17.86) | 2.2 (9.18) |
| Wk 20 | 66 | 100.3 (17.92) | 1.3 (11.31) | 31 | 97.2 (17.23) | -1.8 (8.17) | 31 | 103.5 (19.66) | 3.1 (11.76) |
| Wk 24 | 57 | 99.3 (15.85) | 0.8 (11.37) | 27 | 99.2 (16.14) | 1.7 (7.08) | 30 | 100.2 (19.61) | -0.6 (10.36) |
| Wk 26 | 57 | 100.0 (18.46) | 2.0 (9.30) | 25 | 99.7 (18.84) | 2.9 (8.10) | 27 | 101.8 (18.73) | 0.3 (8.31) |
| End[1] | 84 | 98.5 (16.13) | 0.8 (10.77) | 82 | 105.6 (19.79) | 1.8 (8.60) | 80 | 104.6 (20.50) | 1.4 (10.38) |

[1] Last observed value while on treatment (prior to or at Week 24)

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_lb_cont.sas

21:05 Monday, June 26, 2006

Table 14-6.01
Summary Statistics for Continuous Laboratory Values

| Placebo | | | | Xanomeline Low | | | Xanomeline High | | |
|----------------------------|----|---------------|----------------------------------|----------------|---------------|----------------------------------|-----------------|---------------|----------------------------------|
| | | | Change from Bsln Mean (SD) | | | Change from Bsln Mean (SD) | | | Change from Bsln Mean (SD) |
| Visit | N | Mean (SD) | | N | Mean (SD) | | N | Mean (SD) | |
| GAMMA GLUTAMYL TRANSFERASE | | | | | | | | | |
| Bsln | 86 | 24.9 (49.75) | | 82 | 22.2 (15.57) | | 84 | 22.8 (17.71) | |
| Wk 2 | 84 | 24.2 (47.03) | -0.8 (5.52) | 80 | 22.6 (15.52) | 0.2 (9.48) | 78 | 23.7 (18.17) | 0.6 (8.96) |
| Wk 4 | 82 | 24.5 (48.68) | -0.8 (5.69) | 72 | 21.8 (13.82) | -1.1 (7.51) | 72 | 23.3 (16.08) | 0.1 (9.29) |
| Wk 6 | 75 | 19.9 (15.55) | 0.3 (6.11) | 64 | 21.9 (13.72) | -0.6 (6.88) | 67 | 21.6 (13.48) | -0.5 (6.74) |
| Wk 8 | 73 | 20.6 (16.38) | 0.1 (6.76) | 60 | 23.6 (15.55) | 1.1 (11.36) | 56 | 26.8 (29.96) | 4.0 (24.63) |
| Wk 12 | 67 | 21.4 (15.04) | 0.5 (5.70) | 52 | 21.9 (13.97) | -0.7 (8.80) | 50 | 24.7 (21.26) | 1.2 (8.19) |
| Wk 16 | 68 | 20.8 (13.00) | -0.1 (5.65) | 42 | 22.8 (14.86) | -0.1 (6.38) | 37 | 23.9 (17.79) | -1.3 (6.16) |
| Wk 20 | 66 | 20.4 (13.90) | -0.5 (5.42) | 31 | 24.1 (17.52) | -0.4 (5.90) | 31 | 22.2 (11.28) | -0.5 (5.98) |
| Wk 24 | 57 | 22.0 (16.68) | 0.5 (10.90) | 27 | 23.7 (14.75) | 0.5 (7.28) | 30 | 25.5 (22.64) | -0.9 (6.48) |
| Wk 26 | 57 | 21.4 (13.91) | -0.4 (7.08) | 25 | 22.0 (15.31) | -1.0 (8.44) | 27 | 23.4 (18.73) | -3.4 (7.97) |
| End[1] | 84 | 25.7 (48.78) | 0.7 (9.60) | 82 | 22.4 (14.03) | 0.3 (10.36) | 80 | 22.3 (15.66) | -0.6 (9.81) |
| GLUCOSE | | | | | | | | | |
| Bsln | 86 | 5.6 (2.14) | | 82 | 5.4 (0.94) | | 84 | 5.4 (1.34) | |
| Wk 2 | 83 | 5.6 (1.87) | -0.0 (1.37) | 80 | 5.6 (1.75) | 0.1 (1.50) | 78 | 6.1 (2.92) | 0.7 (2.06) |
| Wk 4 | 79 | 5.6 (1.87) | -0.0 (1.55) | 70 | 5.4 (1.41) | -0.1 (1.09) | 72 | 5.9 (1.84) | 0.4 (1.25) |
| Wk 6 | 73 | 5.7 (2.22) | 0.1 (1.37) | 62 | 5.3 (1.34) | -0.1 (1.12) | 66 | 6.0 (2.80) | 0.5 (2.20) |
| Wk 8 | 72 | 5.5 (1.35) | -0.1 (2.09) | 59 | 5.5 (1.76) | 0.1 (1.34) | 56 | 5.8 (2.15) | 0.2 (1.68) |
| Wk 12 | 67 | 6.1 (1.97) | 0.4 (1.97) | 51 | 5.9 (3.18) | 0.4 (2.78) | 49 | 6.0 (2.28) | 0.4 (1.64) |
| Wk 16 | 68 | 5.5 (1.42) | -0.2 (1.69) | 42 | 5.3 (0.83) | -0.2 (0.89) | 37 | 5.9 (2.30) | 0.2 (1.74) |
| Wk 20 | 65 | 5.8 (1.50) | 0.1 (2.08) | 30 | 5.7 (1.73) | 0.1 (1.39) | 31 | 5.8 (1.61) | 0.2 (1.47) |
| Wk 24 | 57 | 5.7 (1.83) | -0.1 (2.68) | 26 | 5.7 (1.26) | 0.2 (0.82) | 30 | 6.0 (1.92) | 0.5 (1.94) |
| Wk 26 | 57 | 5.8 (1.85) | -0.0 (1.60) | 25 | 5.5 (1.72) | 0.1 (1.35) | 27 | 5.6 (1.01) | 0.1 (1.66) |
| End[1] | 84 | 5.6 (1.61) | 0.0 (2.26) | 82 | 5.4 (1.07) | -0.1 (1.03) | 80 | 5.9 (2.15) | 0.5 (1.62) |

[1] Last observed value while on treatment (prior to or at Week 24)

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_lb_cont.sas

21:05 Monday, June 26, 2006

Table 14-6.01
Summary Statistics for Continuous Laboratory Values

| Placebo | | | | Xanomeline Low | | | | Xanomeline High | | | |
|-----------|----|-------------|--------------|----------------|-------------|--------------|----|-----------------|--------------|--|--|
| Visit | N | Mean (SD) | Change | N | Mean (SD) | Change | N | Mean (SD) | Change | | |
| | | | from Bsln | | | from Bsln | | | from Bsln | | |
| | | | Mean (SD) | | | Mean (SD) | | | Mean (SD) | | |
| PHOSPHATE | | | | | | | | | | | |
| Bsln | 86 | 1.2 (0.15) | | 81 | 1.2 (0.11) | | 83 | 1.2 (0.15) | | | |
| Wk 2 | 84 | 1.2 (0.15) | 0.0 (0.16) | 80 | 1.2 (0.15) | -0.0 (0.16) | 78 | 1.2 (0.18) | 0.0 (0.19) | | |
| Wk 4 | 82 | 1.1 (0.16) | -0.0 (0.17) | 71 | 1.1 (0.14) | -0.0 (0.14) | 72 | 1.2 (0.18) | -0.0 (0.16) | | |
| Wk 6 | 75 | 1.2 (0.15) | 0.0 (0.17) | 64 | 1.2 (0.17) | 0.0 (0.17) | 67 | 1.2 (0.15) | -0.0 (0.16) | | |
| Wk 8 | 73 | 1.1 (0.14) | 0.0 (0.13) | 60 | 1.1 (0.16) | -0.0 (0.16) | 56 | 1.2 (0.16) | -0.0 (0.18) | | |
| Wk 12 | 67 | 1.2 (0.16) | 0.0 (0.18) | 52 | 1.1 (0.14) | -0.0 (0.18) | 50 | 1.1 (0.15) | -0.0 (0.17) | | |
| Wk 16 | 68 | 1.1 (0.14) | -0.0 (0.15) | 42 | 1.1 (0.17) | -0.0 (0.19) | 37 | 1.2 (0.17) | 0.0 (0.17) | | |
| Wk 20 | 65 | 1.2 (0.17) | 0.0 (0.15) | 31 | 1.1 (0.13) | 0.0 (0.14) | 31 | 1.2 (0.15) | -0.0 (0.16) | | |
| Wk 24 | 56 | 1.2 (0.15) | 0.0 (0.16) | 27 | 1.2 (0.19) | 0.1 (0.19) | 30 | 1.1 (0.17) | -0.0 (0.17) | | |
| Wk 26 | 57 | 1.2 (0.15) | 0.0 (0.18) | 25 | 1.1 (0.17) | 0.0 (0.17) | 27 | 1.2 (0.19) | 0.0 (0.20) | | |
| End[1] | 84 | 1.2 (0.17) | 0.0 (0.18) | 82 | 1.2 (0.17) | 0.0 (0.18) | 80 | 1.2 (0.16) | 0.0 (0.17) | | |
| POTASSIUM | | | | | | | | | | | |
| Bsln | 86 | 4.3 (0.43) | | 81 | 4.3 (0.34) | | 82 | 4.3 (0.41) | | | |
| Wk 2 | 84 | 4.2 (0.41) | -0.0 (0.37) | 80 | 4.3 (0.41) | -0.0 (0.38) | 77 | 4.3 (0.40) | -0.0 (0.46) | | |
| Wk 4 | 82 | 4.2 (0.37) | -0.1 (0.38) | 71 | 4.3 (0.40) | -0.1 (0.36) | 72 | 4.2 (0.37) | -0.1 (0.46) | | |
| Wk 6 | 75 | 4.3 (0.33) | 0.0 (0.41) | 64 | 4.3 (0.39) | -0.1 (0.41) | 67 | 4.2 (0.32) | -0.1 (0.44) | | |
| Wk 8 | 73 | 4.2 (0.37) | -0.1 (0.43) | 60 | 4.3 (0.39) | -0.0 (0.38) | 56 | 4.2 (0.39) | -0.0 (0.50) | | |
| Wk 12 | 67 | 4.2 (0.41) | -0.0 (0.46) | 52 | 4.2 (0.42) | -0.2 (0.40) | 49 | 4.2 (0.26) | -0.1 (0.39) | | |
| Wk 16 | 68 | 4.2 (0.41) | -0.0 (0.46) | 42 | 4.3 (0.33) | -0.1 (0.35) | 37 | 4.3 (0.27) | 0.0 (0.35) | | |
| Wk 20 | 64 | 4.3 (0.46) | 0.0 (0.44) | 31 | 4.3 (0.36) | -0.0 (0.44) | 31 | 4.3 (0.37) | 0.0 (0.40) | | |
| Wk 24 | 56 | 4.3 (0.44) | 0.1 (0.44) | 27 | 4.3 (0.41) | -0.0 (0.35) | 30 | 4.2 (0.42) | -0.0 (0.50) | | |
| Wk 26 | 57 | 4.2 (0.38) | 0.0 (0.34) | 25 | 4.3 (0.40) | -0.0 (0.36) | 27 | 4.3 (0.39) | 0.0 (0.54) | | |
| End[1] | 84 | 4.3 (0.43) | 0.0 (0.41) | 82 | 4.3 (0.43) | -0.1 (0.39) | 80 | 4.2 (0.36) | -0.1 (0.47) | | |

[1] Last observed value while on treatment (prior to or at Week 24)

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_lb_cont.sas

21:05 Monday, June 26, 2006

Table 14-6.01
Summary Statistics for Continuous Laboratory Values

| Visit | Placebo | | | Xanomeline Low | | | Xanomeline High | | |
|---------|---------|---------------|-------------------------------|----------------|---------------|-------------------------------|-----------------|---------------|-------------------------------|
| | N | Mean (SD) | Change from Bsln Mean (SD) | N | Mean (SD) | Change from Bsln Mean (SD) | N | Mean (SD) | Change from Bsln Mean (SD) |
| PROTEIN | | | | | | | | | |
| Bsln | 86 | 70.5 (4.72) | | 82 | 70.4 (4.29) | | 84 | 71.0 (4.24) | |
| Wk 2 | 84 | 69.2 (4.93) | -1.3 (4.53) | 80 | 69.5 (4.48) | -0.9 (3.63) | 78 | 69.5 (4.31) | -1.6 (3.91) |
| Wk 4 | 82 | 69.0 (4.18) | -1.6 (3.93) | 72 | 68.8 (4.30) | -1.5 (3.97) | 72 | 69.8 (4.54) | -1.4 (3.90) |
| Wk 6 | 75 | 69.6 (3.95) | -1.2 (4.01) | 64 | 68.8 (4.33) | -1.3 (4.17) | 67 | 70.2 (4.28) | -1.1 (4.10) |
| Wk 8 | 73 | 70.5 (5.20) | -0.4 (4.35) | 60 | 69.2 (3.95) | -0.9 (3.71) | 56 | 70.6 (3.78) | -1.0 (3.57) |
| Wk 12 | 67 | 70.0 (4.28) | -0.6 (3.86) | 52 | 69.3 (4.98) | -0.8 (3.62) | 50 | 70.4 (3.83) | -1.0 (4.11) |
| Wk 16 | 68 | 71.2 (4.57) | 0.4 (4.39) | 42 | 69.3 (4.79) | -0.5 (4.27) | 37 | 70.5 (4.93) | -1.0 (4.57) |
| Wk 20 | 66 | 70.0 (4.92) | -1.1 (4.53) | 31 | 68.7 (4.82) | -1.3 (3.88) | 31 | 69.5 (4.15) | -1.8 (4.13) |
| Wk 24 | 57 | 70.1 (4.33) | -0.8 (4.81) | 27 | 70.9 (6.11) | 0.7 (4.03) | 30 | 70.7 (3.47) | -0.7 (3.83) |
| Wk 26 | 57 | 70.4 (4.48) | -0.5 (4.56) | 25 | 69.4 (5.29) | -1.1 (4.26) | 27 | 69.4 (4.89) | -2.5 (4.01) |
| End[1] | 84 | 70.2 (4.26) | -0.3 (4.35) | 82 | 70.1 (4.95) | -0.4 (3.97) | 80 | 70.4 (3.91) | -0.7 (3.63) |
| SODIUM | | | | | | | | | |
| Bsln | 86 | 140.3 (2.74) | | 82 | 140.0 (2.61) | | 83 | 140.0 (3.11) | |
| Wk 2 | 84 | 140.4 (2.62) | -0.0 (3.35) | 80 | 139.6 (2.47) | -0.3 (2.86) | 77 | 139.1 (2.74) | -0.6 (2.87) |
| Wk 4 | 82 | 139.9 (2.74) | -0.4 (3.58) | 72 | 140.1 (2.40) | 0.2 (3.16) | 72 | 139.7 (2.75) | -0.3 (3.39) |
| Wk 6 | 75 | 140.3 (2.58) | 0.0 (3.08) | 64 | 140.6 (2.69) | 0.8 (3.25) | 67 | 140.1 (2.61) | -0.2 (3.23) |
| Wk 8 | 73 | 140.7 (2.48) | 0.4 (3.33) | 60 | 140.5 (2.58) | 0.6 (3.33) | 56 | 140.5 (3.15) | 0.3 (3.79) |
| Wk 12 | 67 | 140.4 (2.39) | 0.2 (2.98) | 52 | 141.1 (2.77) | 1.1 (3.06) | 49 | 140.2 (2.39) | -0.1 (2.79) |
| Wk 16 | 68 | 141.1 (2.37) | 0.9 (3.10) | 42 | 141.0 (2.62) | 1.2 (2.93) | 37 | 141.6 (2.96) | 1.4 (3.18) |
| Wk 20 | 65 | 141.2 (2.53) | 1.1 (3.01) | 31 | 141.4 (2.53) | 1.6 (3.42) | 31 | 141.8 (3.87) | 1.2 (3.61) |
| Wk 24 | 57 | 141.7 (2.23) | 1.6 (3.27) | 27 | 141.5 (2.12) | 1.2 (3.12) | 30 | 141.6 (2.99) | 1.0 (3.10) |
| Wk 26 | 57 | 142.6 (2.25) | 2.5 (2.90) | 25 | 142.1 (2.08) | 1.9 (3.13) | 27 | 142.4 (3.07) | 1.9 (3.43) |
| End[1] | 84 | 141.5 (2.74) | 1.1 (3.51) | 82 | 141.1 (2.65) | 1.3 (3.09) | 80 | 140.5 (3.22) | 0.5 (3.50) |

[1] Last observed value while on treatment (prior to or at Week 24)

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_lb_cont.sas

21:05 Monday, June 26, 2006

Table 14-6.01
Summary Statistics for Continuous Laboratory Values

| Visit | Placebo | | | Xanomeline Low | | | Xanomeline High | | |
|---------------|---------|----------------|-------------------------------|----------------|----------------|-------------------------------|-----------------|----------------|-------------------------------|
| | N | Mean (SD) | Change from Bsln Mean (SD) | N | Mean (SD) | Change from Bsln Mean (SD) | N | Mean (SD) | Change from Bsln Mean (SD) |
| URATE | | | | | | | | | |
| Bsln | 86 | 285.0 (74.45) | | 82 | 300.7 (77.78) | | 84 | 302.2 (78.01) | |
| Wk 2 | 84 | 284.0 (68.72) | -1.8 (50.16) | 80 | 305.8 (74.25) | 1.0 (40.56) | 78 | 301.7 (81.96) | -2.7 (33.85) |
| Wk 4 | 82 | 285.6 (69.22) | -0.6 (35.59) | 72 | 299.5 (79.44) | -3.7 (38.80) | 72 | 291.4 (79.28) | -9.5 (42.17) |
| Wk 6 | 75 | 288.0 (68.73) | -1.1 (38.24) | 64 | 298.1 (74.46) | -6.2 (30.89) | 67 | 291.6 (74.82) | -9.8 (34.48) |
| Wk 8 | 73 | 285.6 (65.63) | -5.1 (36.28) | 60 | 290.9 (71.15) | -15.6 (30.49) | 56 | 291.6 (76.76) | -11.2 (35.13) |
| Wk 12 | 67 | 291.1 (70.07) | 3.2 (40.20) | 52 | 290.3 (63.20) | -11.5 (31.83) | 50 | 294.2 (78.84) | -9.0 (36.29) |
| Wk 16 | 68 | 285.8 (68.72) | -3.6 (41.33) | 42 | 288.8 (58.78) | -12.9 (39.98) | 37 | 284.1 (80.47) | -19.9 (36.13) |
| Wk 20 | 66 | 301.9 (73.43) | 12.1 (40.18) | 31 | 279.7 (58.71) | -16.5 (44.34) | 31 | 295.1 (85.89) | -9.6 (43.81) |
| Wk 24 | 57 | 293.5 (73.47) | 4.6 (42.98) | 27 | 274.9 (57.72) | -19.2 (31.26) | 30 | 288.5 (88.37) | -19.4 (50.03) |
| Wk 26 | 57 | 291.9 (74.43) | 5.1 (44.39) | 25 | 279.3 (60.01) | -13.6 (39.12) | 27 | 301.1 (86.31) | -12.6 (47.68) |
| End[1] | 84 | 290.5 (73.86) | 4.7 (46.43) | 82 | 298.3 (80.54) | -3.1 (37.11) | 80 | 292.4 (80.83) | -10.5 (42.35) |
| UREA NITROGEN | | | | | | | | | |
| Bsln | 86 | 5.5 (1.39) | | 82 | 6.4 (1.97) | | 84 | 5.8 (1.88) | |
| Wk 2 | 84 | 5.8 (1.51) | 0.3 (1.17) | 80 | 6.6 (1.82) | 0.3 (1.53) | 78 | 6.0 (2.06) | 0.3 (1.36) |
| Wk 4 | 82 | 5.9 (1.47) | 0.3 (1.11) | 72 | 6.4 (1.63) | 0.0 (1.37) | 72 | 5.9 (1.87) | 0.3 (1.30) |
| Wk 6 | 75 | 6.1 (1.42) | 0.5 (1.16) | 64 | 6.4 (1.76) | -0.1 (1.32) | 67 | 6.0 (2.06) | 0.3 (1.43) |
| Wk 8 | 73 | 5.6 (1.58) | -0.0 (1.22) | 60 | 6.3 (1.92) | -0.0 (0.95) | 56 | 5.9 (1.93) | 0.1 (1.25) |
| Wk 12 | 67 | 5.9 (1.61) | 0.2 (1.24) | 52 | 6.2 (1.49) | -0.0 (1.45) | 50 | 5.9 (1.76) | 0.1 (1.50) |
| Wk 16 | 68 | 5.8 (1.60) | 0.2 (1.28) | 42 | 6.0 (1.62) | -0.2 (1.25) | 37 | 5.7 (1.92) | 0.2 (1.29) |
| Wk 20 | 66 | 5.8 (1.53) | 0.1 (1.28) | 31 | 5.6 (1.57) | -0.6 (1.39) | 31 | 5.9 (2.25) | 0.2 (1.50) |
| Wk 24 | 57 | 5.9 (1.32) | 0.3 (1.24) | 27 | 6.0 (2.07) | -0.0 (1.37) | 30 | 5.3 (1.92) | -0.3 (1.37) |
| Wk 26 | 57 | 6.1 (1.62) | 0.4 (1.36) | 25 | 5.7 (1.93) | -0.3 (1.14) | 27 | 5.9 (2.47) | 0.3 (1.40) |
| End[1] | 84 | 5.9 (1.38) | 0.3 (1.20) | 82 | 6.6 (1.95) | 0.2 (1.37) | 80 | 5.7 (1.97) | -0.0 (1.57) |

[1] Last observed value while on treatment (prior to or at Week 24)

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_lb_cont.sas

21:05 Monday, June 26, 2006

Table 14-6.01
Summary Statistics for Continuous Laboratory Values

| Placebo | | | | Xanomeline Low | | | | Xanomeline High | | | |
|-------------|----|-------------|------------------------|----------------|-------------|------------------------|----|-----------------|------------------------|--|--|
| Visit | N | Mean (SD) | Change | N | Mean (SD) | Change | N | Mean (SD) | Change | | |
| | | | from Bsln Mean (SD) | | | from Bsln Mean (SD) | | | from Bsln Mean (SD) | | |
| HEMATOLOGY | | | | | | | | | | | |
| BASOPHILS | | | | | | | | | | | |
| Bsln | 85 | 0.1 (0.04) | | 81 | 0.1 (0.03) | | 81 | 0.1 (0.02) | | | |
| Wk 2 | 83 | 0.0 (0.02) | -0.0 (0.03) | 80 | 0.1 (0.03) | -0.0 (0.03) | 80 | 0.0 (0.03) | -0.0 (0.02) | | |
| Wk 4 | 79 | 0.0 (0.02) | -0.0 (0.03) | 71 | 0.0 (0.03) | -0.0 (0.03) | 71 | 0.0 (0.02) | -0.0 (0.02) | | |
| Wk 6 | 73 | 0.0 (0.03) | -0.0 (0.03) | 62 | 0.0 (0.03) | -0.0 (0.03) | 64 | 0.1 (0.03) | 0.0 (0.03) | | |
| Wk 8 | 72 | 0.0 (0.02) | -0.0 (0.03) | 59 | 0.1 (0.02) | -0.0 (0.04) | 56 | 0.1 (0.03) | 0.0 (0.02) | | |
| Wk 12 | 66 | 0.0 (0.02) | -0.0 (0.04) | 50 | 0.0 (0.02) | -0.0 (0.03) | 50 | 0.1 (0.03) | -0.0 (0.02) | | |
| Wk 16 | 68 | 0.0 (0.03) | -0.0 (0.04) | 42 | 0.0 (0.02) | -0.0 (0.03) | 37 | 0.1 (0.03) | -0.0 (0.02) | | |
| Wk 20 | 65 | 0.0 (0.03) | -0.0 (0.03) | 30 | 0.0 (0.02) | -0.0 (0.03) | 31 | 0.0 (0.02) | -0.0 (0.03) | | |
| Wk 24 | 58 | 0.0 (0.03) | -0.0 (0.03) | 25 | 0.0 (0.03) | -0.0 (0.02) | 30 | 0.1 (0.02) | -0.0 (0.02) | | |
| Wk 26 | 57 | 0.0 (0.02) | -0.0 (0.03) | 25 | 0.0 (0.03) | -0.0 (0.02) | 27 | 0.1 (0.03) | -0.0 (0.03) | | |
| End[1] | 84 | 0.0 (0.03) | -0.0 (0.03) | 82 | 0.0 (0.03) | -0.0 (0.03) | 81 | 0.1 (0.02) | -0.0 (0.02) | | |
| EOSINOPHILS | | | | | | | | | | | |
| Bsln | 85 | 0.1 (0.12) | | 81 | 0.1 (0.12) | | 81 | 0.1 (0.10) | | | |
| Wk 2 | 83 | 0.1 (0.10) | -0.0 (0.09) | 80 | 0.2 (0.17) | 0.0 (0.14) | 80 | 0.1 (0.11) | -0.0 (0.07) | | |
| Wk 4 | 79 | 0.1 (0.13) | -0.0 (0.09) | 71 | 0.2 (0.14) | 0.0 (0.11) | 71 | 0.2 (0.15) | 0.0 (0.13) | | |
| Wk 6 | 73 | 0.1 (0.13) | -0.0 (0.11) | 62 | 0.2 (0.21) | 0.1 (0.16) | 64 | 0.2 (0.28) | 0.1 (0.25) | | |
| Wk 8 | 72 | 0.1 (0.10) | -0.0 (0.10) | 59 | 0.3 (0.26) | 0.2 (0.23) | 56 | 0.2 (0.25) | 0.1 (0.19) | | |
| Wk 12 | 66 | 0.1 (0.09) | -0.0 (0.11) | 50 | 0.3 (0.21) | 0.1 (0.19) | 50 | 0.2 (0.17) | 0.1 (0.14) | | |
| Wk 16 | 68 | 0.1 (0.08) | -0.0 (0.10) | 42 | 0.2 (0.16) | 0.1 (0.13) | 37 | 0.2 (0.21) | 0.1 (0.17) | | |
| Wk 20 | 65 | 0.1 (0.08) | -0.0 (0.10) | 30 | 0.2 (0.19) | 0.1 (0.16) | 31 | 0.1 (0.11) | 0.0 (0.12) | | |
| Wk 24 | 58 | 0.1 (0.08) | -0.0 (0.09) | 25 | 0.2 (0.14) | 0.0 (0.12) | 30 | 0.2 (0.15) | 0.0 (0.13) | | |

[1] Last observed value while on treatment (prior to or at Week 24)

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_lb_cont.sas

21:05 Monday, June 26, 2006

Table 14-6.01
Summary Statistics for Continuous Laboratory Values

| Placebo | | | | Xanomeline Low | | | | Xanomeline High | | | |
|--|----|--------------|------------------|----------------|--------------|------------------|----|-----------------|------------------|--|--|
| | | | Change from Bsln | | | Change from Bsln | | | Change from Bsln | | |
| Visit | N | Mean (SD) | Mean (SD) | N | Mean (SD) | Mean (SD) | N | Mean (SD) | Mean (SD) | | |
| Wk 26 | 57 | 0.1 (0.10) | -0.0 (0.11) | 25 | 0.2 (0.15) | 0.0 (0.13) | 27 | 0.1 (0.10) | 0.0 (0.09) | | |
| End[1] | 84 | 0.1 (0.08) | -0.0 (0.10) | 82 | 0.2 (0.17) | 0.0 (0.14) | 81 | 0.2 (0.20) | 0.1 (0.18) | | |
| ERY. MEAN CORPUSCULAR HB CONCENTRATION | | | | | | | | | | | |
| Bsln | 85 | 20.6 (0.87) | | 80 | 20.2 (0.98) | | 80 | 20.5 (0.87) | | | |
| Wk 2 | 83 | 20.3 (0.77) | -0.3 (1.00) | 80 | 20.3 (0.85) | 0.0 (1.04) | 80 | 20.4 (0.74) | -0.0 (0.98) | | |
| Wk 4 | 77 | 20.2 (0.78) | -0.4 (1.01) | 69 | 20.2 (0.72) | -0.0 (0.94) | 70 | 20.5 (0.71) | -0.1 (0.90) | | |
| Wk 6 | 72 | 20.5 (0.77) | -0.2 (0.98) | 60 | 20.1 (0.84) | -0.2 (0.99) | 65 | 20.4 (0.89) | -0.2 (1.00) | | |
| Wk 8 | 71 | 20.3 (0.68) | -0.2 (0.85) | 56 | 20.2 (0.83) | -0.0 (0.92) | 56 | 20.5 (0.76) | -0.1 (0.93) | | |
| Wk 12 | 65 | 20.3 (0.74) | -0.3 (0.96) | 49 | 20.3 (0.68) | -0.0 (0.99) | 50 | 20.5 (0.76) | -0.1 (1.03) | | |
| Wk 16 | 68 | 20.2 (0.75) | -0.4 (1.02) | 42 | 20.0 (0.82) | -0.2 (1.02) | 37 | 20.4 (0.83) | -0.2 (1.11) | | |
| Wk 20 | 64 | 20.3 (0.80) | -0.3 (0.94) | 30 | 20.0 (0.85) | -0.4 (0.91) | 31 | 20.3 (0.88) | -0.3 (1.22) | | |
| Wk 24 | 58 | 20.1 (0.89) | -0.5 (1.01) | 25 | 20.3 (0.91) | -0.3 (0.95) | 30 | 20.4 (0.85) | -0.3 (1.29) | | |
| Wk 26 | 56 | 20.3 (0.99) | -0.4 (1.16) | 25 | 19.9 (0.94) | -0.6 (1.09) | 27 | 20.2 (0.92) | -0.6 (1.12) | | |
| End[1] | 83 | 20.2 (0.85) | -0.4 (0.99) | 82 | 20.2 (0.81) | -0.0 (0.98) | 81 | 20.4 (0.78) | -0.1 (1.08) | | |
| ERY. MEAN CORPUSCULAR HEMOGLOBIN | | | | | | | | | | | |
| Bsln | 85 | 1.9 (0.12) | | 81 | 1.9 (0.09) | | 81 | 1.9 (0.13) | | | |
| Wk 2 | 83 | 1.9 (0.11) | -0.0 (0.07) | 80 | 1.9 (0.09) | 0.0 (0.07) | 80 | 1.9 (0.13) | -0.0 (0.07) | | |
| Wk 4 | 79 | 1.9 (0.12) | -0.0 (0.07) | 71 | 1.9 (0.09) | 0.0 (0.07) | 71 | 1.9 (0.13) | -0.0 (0.06) | | |
| Wk 6 | 73 | 1.9 (0.13) | 0.0 (0.08) | 62 | 1.9 (0.08) | 0.0 (0.05) | 65 | 1.9 (0.13) | -0.0 (0.08) | | |
| Wk 8 | 72 | 1.9 (0.12) | 0.0 (0.06) | 59 | 1.9 (0.09) | 0.0 (0.06) | 56 | 1.9 (0.10) | -0.0 (0.07) | | |
| Wk 12 | 66 | 1.9 (0.12) | 0.0 (0.06) | 50 | 1.9 (0.09) | 0.0 (0.05) | 50 | 1.9 (0.09) | -0.0 (0.07) | | |
| Wk 16 | 68 | 1.9 (0.12) | -0.0 (0.05) | 42 | 1.9 (0.10) | -0.0 (0.07) | 37 | 1.9 (0.11) | -0.0 (0.08) | | |
| Wk 20 | 65 | 1.9 (0.11) | -0.0 (0.06) | 30 | 1.9 (0.08) | 0.0 (0.06) | 31 | 1.9 (0.12) | -0.0 (0.08) | | |
| Wk 24 | 58 | 1.9 (0.12) | -0.0 (0.06) | 25 | 1.9 (0.09) | -0.0 (0.06) | 30 | 1.9 (0.13) | -0.0 (0.09) | | |
| Wk 26 | 57 | 1.9 (0.12) | -0.0 (0.07) | 25 | 1.9 (0.08) | -0.0 (0.08) | 27 | 1.9 (0.12) | -0.0 (0.08) | | |

[1] Last observed value while on treatment (prior to or at Week 24)

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_lb_cont.sas

21:05 Monday, June 26, 2006

Table 14-6.01
Summary Statistics for Continuous Laboratory Values

| Placebo | | | | | Xanomeline Low | | | | | Xanomeline High | | | | |
|------------------------------|----|------------------|--------------|-----------|----------------|------------------|--------------|--|----|------------------|--------------|--|--|--|
| Visit | N | Change from Bsln | | | N | Change from Bsln | | | N | Change from Bsln | | | | |
| | | Mean (SD) | Mean (SD) | Mean (SD) | | Mean (SD) | Mean (SD) | | | | | | | |
| End[1] | 84 | 1.9 (0.12) | -0.0 (0.07) | | 82 | 1.9 (0.09) | 0.0 (0.06) | | 81 | 1.9 (0.13) | 0.0 (0.07) | | | |
| ERY. MEAN CORPUSCULAR VOLUME | | | | | | | | | | | | | | |
| Bsln | 85 | 92.9 (5.69) | | | 80 | 94.6 (4.90) | | | 80 | 93.3 (5.91) | | | | |
| Wk 2 | 83 | 94.1 (5.31) | 1.2 (3.93) | | 80 | 94.6 (4.12) | 0.2 (3.57) | | 80 | 93.4 (5.93) | 0.2 (3.91) | | | |
| Wk 4 | 77 | 94.6 (5.87) | 1.7 (3.47) | | 69 | 95.1 (4.22) | 0.6 (3.69) | | 70 | 93.0 (5.52) | 0.0 (3.69) | | | |
| Wk 6 | 72 | 94.2 (6.21) | 1.3 (3.79) | | 60 | 95.2 (4.51) | 0.7 (3.68) | | 65 | 94.0 (6.61) | 0.6 (3.99) | | | |
| Wk 8 | 71 | 94.3 (5.51) | 1.5 (3.27) | | 56 | 94.9 (3.97) | 0.6 (3.35) | | 56 | 94.4 (4.77) | 0.4 (4.03) | | | |
| Wk 12 | 65 | 94.2 (5.66) | 1.6 (3.81) | | 49 | 95.1 (4.17) | 0.9 (3.91) | | 50 | 94.9 (4.90) | 0.8 (4.20) | | | |
| Wk 16 | 68 | 94.1 (6.01) | 1.7 (4.07) | | 42 | 95.8 (5.17) | 1.2 (4.18) | | 37 | 94.7 (6.27) | 0.6 (5.05) | | | |
| Wk 20 | 64 | 93.3 (5.58) | 1.3 (4.14) | | 30 | 95.4 (5.43) | 2.0 (3.29) | | 31 | 95.1 (5.91) | 0.9 (5.12) | | | |
| Wk 24 | 58 | 93.9 (5.90) | 1.6 (3.85) | | 25 | 94.3 (3.85) | 0.8 (3.94) | | 30 | 95.0 (5.99) | 0.7 (4.97) | | | |
| Wk 26 | 56 | 93.9 (6.40) | 1.7 (4.48) | | 25 | 95.8 (4.33) | 2.6 (3.70) | | 27 | 95.4 (6.19) | 1.2 (3.93) | | | |
| End[1] | 83 | 94.4 (5.93) | 1.4 (4.07) | | 82 | 95.0 (3.98) | 0.6 (3.83) | | 81 | 93.8 (6.14) | 0.7 (4.40) | | | |
| ERYTHROCYTES | | | | | | | | | | | | | | |
| Bsln | 85 | 4.5 (0.45) | | | 81 | 4.5 (0.42) | | | 81 | 4.7 (0.47) | | | | |
| Wk 2 | 83 | 4.4 (0.40) | -0.1 (0.22) | | 80 | 4.4 (0.43) | -0.1 (0.27) | | 80 | 4.6 (0.47) | -0.1 (0.22) | | | |
| Wk 4 | 79 | 4.4 (0.45) | -0.1 (0.25) | | 71 | 4.4 (0.38) | -0.2 (0.30) | | 71 | 4.5 (0.49) | -0.1 (0.25) | | | |
| Wk 6 | 73 | 4.4 (0.37) | -0.1 (0.24) | | 62 | 4.3 (0.38) | -0.2 (0.27) | | 65 | 4.5 (0.50) | -0.1 (0.24) | | | |
| Wk 8 | 72 | 4.4 (0.41) | -0.1 (0.26) | | 59 | 4.4 (0.34) | -0.2 (0.24) | | 56 | 4.5 (0.45) | -0.1 (0.19) | | | |
| Wk 12 | 66 | 4.4 (0.44) | -0.1 (0.26) | | 50 | 4.3 (0.32) | -0.2 (0.20) | | 50 | 4.6 (0.47) | -0.1 (0.27) | | | |
| Wk 16 | 68 | 4.5 (0.41) | -0.0 (0.27) | | 42 | 4.3 (0.36) | -0.1 (0.24) | | 37 | 4.6 (0.44) | -0.2 (0.26) | | | |
| Wk 20 | 65 | 4.5 (0.41) | -0.1 (0.30) | | 30 | 4.3 (0.32) | -0.1 (0.21) | | 31 | 4.5 (0.50) | -0.2 (0.30) | | | |
| Wk 24 | 58 | 4.4 (0.45) | -0.1 (0.23) | | 25 | 4.4 (0.38) | -0.1 (0.19) | | 30 | 4.6 (0.58) | -0.1 (0.24) | | | |
| Wk 26 | 57 | 4.4 (0.42) | -0.0 (0.25) | | 25 | 4.4 (0.35) | -0.1 (0.20) | | 27 | 4.5 (0.47) | -0.2 (0.27) | | | |
| End[1] | 84 | 4.4 (0.43) | -0.1 (0.27) | | 82 | 4.4 (0.38) | -0.2 (0.25) | | 81 | 4.6 (0.49) | -0.1 (0.22) | | | |

[1] Last observed value while on treatment (prior to or at Week 24)

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_lb_cont.sas

21:05 Monday, June 26, 2006

Table 14-6.01
Summary Statistics for Continuous Laboratory Values

| Placebo | | | | Xanomeline Low | | | | Xanomeline High | | | |
|------------|----|-------------|------------------------|----------------|-------------|------------------------|----|-----------------|------------------------|--|--|
| Visit | N | Mean (SD) | Change | N | Mean (SD) | Change | N | Mean (SD) | Change | | |
| | | | from Bsln Mean (SD) | | | from Bsln Mean (SD) | | | from Bsln Mean (SD) | | |
| HEMATOCRIT | | | | | | | | | | | |
| Bsln | 85 | 0.4 (0.04) | | 80 | 0.4 (0.04) | | 80 | 0.4 (0.04) | | | |
| Wk 2 | 83 | 0.4 (0.04) | -0.0 (0.03) | 80 | 0.4 (0.04) | -0.0 (0.03) | 80 | 0.4 (0.04) | -0.0 (0.03) | | |
| Wk 4 | 77 | 0.4 (0.04) | -0.0 (0.03) | 69 | 0.4 (0.04) | -0.0 (0.03) | 70 | 0.4 (0.04) | -0.0 (0.03) | | |
| Wk 6 | 72 | 0.4 (0.04) | -0.0 (0.03) | 60 | 0.4 (0.04) | -0.0 (0.03) | 65 | 0.4 (0.04) | -0.0 (0.03) | | |
| Wk 8 | 71 | 0.4 (0.04) | -0.0 (0.03) | 56 | 0.4 (0.03) | -0.0 (0.02) | 56 | 0.4 (0.03) | -0.0 (0.03) | | |
| Wk 12 | 65 | 0.4 (0.04) | -0.0 (0.03) | 49 | 0.4 (0.03) | -0.0 (0.02) | 50 | 0.4 (0.04) | -0.0 (0.03) | | |
| Wk 16 | 68 | 0.4 (0.04) | 0.0 (0.03) | 42 | 0.4 (0.03) | -0.0 (0.03) | 37 | 0.4 (0.03) | -0.0 (0.04) | | |
| Wk 20 | 64 | 0.4 (0.04) | -0.0 (0.03) | 30 | 0.4 (0.03) | -0.0 (0.02) | 31 | 0.4 (0.04) | -0.0 (0.04) | | |
| Wk 24 | 58 | 0.4 (0.04) | 0.0 (0.03) | 25 | 0.4 (0.04) | -0.0 (0.02) | 30 | 0.4 (0.04) | -0.0 (0.04) | | |
| Wk 26 | 56 | 0.4 (0.04) | 0.0 (0.03) | 25 | 0.4 (0.04) | -0.0 (0.03) | 27 | 0.4 (0.04) | -0.0 (0.03) | | |
| End[1] | 83 | 0.4 (0.04) | -0.0 (0.03) | 82 | 0.4 (0.04) | -0.0 (0.03) | 81 | 0.4 (0.04) | -0.0 (0.03) | | |
| HEMOGLOBIN | | | | | | | | | | | |
| Bsln | 85 | 8.6 (0.83) | | 81 | 8.6 (0.77) | | 81 | 8.9 (0.78) | | | |
| Wk 2 | 83 | 8.4 (0.76) | -0.2 (0.42) | 80 | 8.4 (0.76) | -0.2 (0.46) | 80 | 8.7 (0.83) | -0.2 (0.42) | | |
| Wk 4 | 79 | 8.4 (0.82) | -0.2 (0.44) | 71 | 8.4 (0.78) | -0.3 (0.50) | 71 | 8.6 (0.78) | -0.2 (0.45) | | |
| Wk 6 | 73 | 8.4 (0.77) | -0.2 (0.44) | 62 | 8.3 (0.76) | -0.3 (0.46) | 65 | 8.6 (0.75) | -0.3 (0.44) | | |
| Wk 8 | 72 | 8.5 (0.76) | -0.2 (0.46) | 59 | 8.3 (0.71) | -0.3 (0.39) | 56 | 8.7 (0.73) | -0.3 (0.39) | | |
| Wk 12 | 66 | 8.4 (0.83) | -0.2 (0.42) | 50 | 8.3 (0.69) | -0.3 (0.34) | 50 | 8.8 (0.79) | -0.3 (0.42) | | |
| Wk 16 | 68 | 8.5 (0.73) | -0.1 (0.46) | 42 | 8.3 (0.69) | -0.2 (0.42) | 37 | 8.7 (0.70) | -0.3 (0.47) | | |
| Wk 20 | 65 | 8.4 (0.80) | -0.2 (0.51) | 30 | 8.2 (0.63) | -0.2 (0.46) | 31 | 8.7 (0.79) | -0.4 (0.46) | | |
| Wk 24 | 58 | 8.3 (0.82) | -0.2 (0.40) | 25 | 8.4 (0.69) | -0.2 (0.36) | 30 | 8.9 (0.85) | -0.3 (0.36) | | |
| Wk 26 | 57 | 8.4 (0.80) | -0.2 (0.47) | 25 | 8.3 (0.67) | -0.3 (0.39) | 27 | 8.7 (0.74) | -0.5 (0.39) | | |
| End[1] | 84 | 8.4 (0.78) | -0.2 (0.44) | 82 | 8.4 (0.69) | -0.2 (0.44) | 81 | 8.7 (0.79) | -0.2 (0.36) | | |

[1] Last observed value while on treatment (prior to or at Week 24)

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_lb_cont.sas

21:05 Monday, June 26, 2006

Table 14-6.01
Summary Statistics for Continuous Laboratory Values

| Placebo | | | | Xanomeline Low | | | | Xanomeline High | | | |
|-------------|----|-------------|------------------------|----------------|-------------|------------------------|----|-----------------|------------------------|--|--|
| Visit | N | Mean (SD) | Change | N | Mean (SD) | Change | N | Mean (SD) | Change | | |
| | | | from Bsln Mean (SD) | | | from Bsln Mean (SD) | | | from Bsln Mean (SD) | | |
| LEUKOCYTES | | | | | | | | | | | |
| Bsln | 85 | 6.9 (1.76) | | 81 | 6.6 (1.95) | | 81 | 6.5 (1.54) | | | |
| Wk 2 | 83 | 6.5 (1.55) | -0.4 (1.40) | 80 | 6.9 (1.99) | 0.2 (1.37) | 80 | 6.5 (1.59) | -0.1 (1.18) | | |
| Wk 4 | 79 | 6.4 (1.63) | -0.4 (1.17) | 71 | 6.8 (2.12) | 0.1 (1.53) | 71 | 6.6 (1.42) | 0.1 (1.21) | | |
| Wk 6 | 73 | 6.5 (1.57) | -0.4 (1.36) | 62 | 6.9 (1.99) | 0.1 (1.14) | 65 | 7.0 (1.84) | 0.4 (1.65) | | |
| Wk 8 | 72 | 6.5 (1.70) | -0.3 (1.28) | 59 | 7.1 (1.88) | 0.3 (1.26) | 56 | 6.9 (1.95) | 0.4 (1.64) | | |
| Wk 12 | 66 | 6.3 (1.28) | -0.5 (1.09) | 50 | 6.8 (2.03) | 0.2 (0.97) | 50 | 6.6 (1.51) | -0.0 (1.21) | | |
| Wk 16 | 68 | 6.4 (1.50) | -0.5 (1.29) | 42 | 6.6 (2.11) | 0.2 (1.44) | 37 | 6.8 (1.72) | -0.1 (1.37) | | |
| Wk 20 | 65 | 6.5 (1.77) | -0.5 (1.40) | 30 | 6.5 (1.94) | 0.1 (1.24) | 31 | 6.6 (1.67) | -0.2 (1.21) | | |
| Wk 24 | 58 | 6.7 (1.77) | -0.2 (1.37) | 25 | 6.3 (1.84) | 0.0 (1.16) | 30 | 6.7 (1.80) | -0.1 (1.16) | | |
| Wk 26 | 57 | 6.4 (1.47) | -0.4 (1.24) | 25 | 6.1 (1.93) | -0.3 (1.15) | 27 | 6.7 (1.78) | -0.2 (1.42) | | |
| End[1] | 84 | 6.6 (1.80) | -0.2 (1.32) | 82 | 6.8 (2.17) | 0.1 (1.35) | 81 | 6.7 (1.76) | 0.2 (1.37) | | |
| LYMPHOCYTES | | | | | | | | | | | |
| Bsln | 85 | 1.8 (0.57) | | 81 | 1.8 (0.57) | | 81 | 1.7 (0.52) | | | |
| Wk 2 | 83 | 1.7 (0.50) | -0.1 (0.37) | 80 | 1.8 (0.66) | 0.0 (0.45) | 80 | 1.7 (0.50) | 0.0 (0.38) | | |
| Wk 4 | 79 | 1.7 (0.56) | -0.0 (0.38) | 71 | 1.8 (0.67) | 0.0 (0.49) | 71 | 1.7 (0.50) | -0.0 (0.44) | | |
| Wk 6 | 73 | 1.8 (0.58) | -0.0 (0.41) | 62 | 1.9 (0.64) | 0.1 (0.47) | 64 | 1.7 (0.48) | -0.0 (0.44) | | |
| Wk 8 | 72 | 1.8 (0.67) | -0.0 (0.44) | 59 | 1.9 (0.65) | 0.1 (0.45) | 56 | 1.7 (0.50) | -0.0 (0.36) | | |
| Wk 12 | 66 | 1.7 (0.58) | -0.1 (0.42) | 50 | 1.8 (0.58) | -0.1 (0.45) | 50 | 1.6 (0.47) | -0.0 (0.37) | | |
| Wk 16 | 68 | 1.7 (0.58) | -0.1 (0.42) | 42 | 1.8 (0.63) | -0.1 (0.34) | 37 | 1.7 (0.62) | 0.0 (0.41) | | |
| Wk 20 | 65 | 1.7 (0.50) | -0.1 (0.45) | 30 | 1.7 (0.59) | -0.1 (0.50) | 31 | 1.7 (0.59) | -0.0 (0.36) | | |
| Wk 24 | 58 | 1.8 (0.65) | -0.0 (0.48) | 25 | 1.8 (0.56) | -0.1 (0.37) | 30 | 1.7 (0.56) | -0.0 (0.37) | | |
| Wk 26 | 57 | 1.8 (0.59) | -0.0 (0.43) | 25 | 1.7 (0.62) | -0.1 (0.39) | 27 | 1.8 (0.61) | 0.1 (0.50) | | |
| End[1] | 84 | 1.8 (0.59) | -0.0 (0.46) | 82 | 1.8 (0.62) | -0.0 (0.46) | 81 | 1.6 (0.54) | -0.0 (0.38) | | |

[1] Last observed value while on treatment (prior to or at Week 24)

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_lb_cont.sas

21:05 Monday, June 26, 2006

Table 14-6.01
Summary Statistics for Continuous Laboratory Values

| Visit | Placebo | | | Xanomeline Low | | | Xanomeline High | | |
|-----------|---------|----------------|-------------------------------|----------------|----------------|-------------------------------|-----------------|----------------|-------------------------------|
| | N | Mean (SD) | Change from Bsln Mean (SD) | N | Mean (SD) | Change from Bsln Mean (SD) | N | Mean (SD) | Change from Bsln Mean (SD) |
| MONOCYTES | | | | | | | | | |
| Bsln | 85 | 0.4 (0.15) | | 81 | 0.5 (0.16) | | 81 | 0.4 (0.12) | |
| Wk 2 | 83 | 0.4 (0.15) | -0.0 (0.14) | 80 | 0.5 (0.16) | 0.0 (0.13) | 80 | 0.4 (0.15) | 0.0 (0.12) |
| Wk 4 | 79 | 0.4 (0.12) | 0.0 (0.11) | 71 | 0.5 (0.17) | -0.0 (0.15) | 71 | 0.4 (0.13) | 0.0 (0.13) |
| Wk 6 | 73 | 0.4 (0.15) | -0.0 (0.13) | 62 | 0.5 (0.19) | 0.0 (0.16) | 64 | 0.5 (0.15) | 0.0 (0.13) |
| Wk 8 | 72 | 0.4 (0.14) | 0.0 (0.14) | 59 | 0.5 (0.14) | 0.0 (0.14) | 56 | 0.5 (0.15) | 0.0 (0.14) |
| Wk 12 | 66 | 0.4 (0.13) | 0.0 (0.13) | 50 | 0.5 (0.15) | 0.0 (0.12) | 50 | 0.4 (0.15) | -0.0 (0.11) |
| Wk 16 | 68 | 0.5 (0.15) | 0.0 (0.17) | 42 | 0.5 (0.16) | 0.0 (0.12) | 37 | 0.5 (0.16) | 0.0 (0.14) |
| Wk 20 | 65 | 0.5 (0.16) | 0.0 (0.15) | 30 | 0.5 (0.13) | 0.0 (0.13) | 31 | 0.5 (0.17) | 0.0 (0.18) |
| Wk 24 | 58 | 0.5 (0.17) | 0.0 (0.17) | 25 | 0.5 (0.19) | 0.0 (0.11) | 30 | 0.5 (0.18) | -0.0 (0.12) |
| Wk 26 | 57 | 0.4 (0.14) | 0.0 (0.14) | 25 | 0.4 (0.17) | -0.0 (0.12) | 27 | 0.5 (0.14) | -0.0 (0.13) |
| End[1] | 84 | 0.5 (0.17) | 0.0 (0.17) | 82 | 0.5 (0.17) | 0.0 (0.13) | 81 | 0.5 (0.15) | 0.0 (0.12) |
| PLATELET | | | | | | | | | |
| Bsln | 84 | 250.3 (65.52) | | 79 | 233.8 (58.58) | | 81 | 227.7 (54.74) | |
| Wk 2 | 83 | 246.2 (57.55) | -4.4 (36.21) | 78 | 247.4 (59.37) | 9.1 (46.36) | 80 | 238.2 (59.77) | 8.4 (31.55) |
| Wk 4 | 78 | 243.8 (54.30) | -7.4 (40.04) | 70 | 239.2 (57.80) | 5.7 (39.75) | 70 | 238.3 (49.60) | 9.8 (29.21) |
| Wk 6 | 73 | 250.8 (58.97) | -3.3 (36.82) | 62 | 238.3 (55.74) | 3.5 (43.39) | 63 | 239.1 (56.79) | 9.2 (37.82) |
| Wk 8 | 72 | 246.0 (66.61) | -6.2 (42.35) | 59 | 245.4 (60.21) | 5.1 (46.18) | 55 | 236.9 (70.88) | 11.0 (48.13) |
| Wk 12 | 65 | 241.9 (53.71) | -12.8 (42.62) | 50 | 238.8 (49.49) | 1.9 (24.69) | 49 | 236.1 (53.03) | 9.1 (34.47) |
| Wk 16 | 68 | 241.8 (55.65) | -13.7 (43.45) | 41 | 244.5 (57.60) | 2.8 (32.93) | 37 | 230.9 (58.00) | 5.3 (25.87) |
| Wk 20 | 65 | 248.4 (60.70) | -8.4 (30.42) | 30 | 240.7 (64.07) | 7.3 (42.65) | 30 | 235.1 (65.46) | 2.3 (22.80) |
| Wk 24 | 57 | 238.8 (51.89) | -11.3 (35.06) | 24 | 249.7 (63.44) | 1.8 (33.48) | 29 | 238.3 (67.53) | 4.5 (26.74) |
| Wk 26 | 56 | 247.6 (60.11) | -2.7 (41.73) | 25 | 241.3 (57.16) | -1.9 (38.84) | 27 | 237.4 (67.14) | 0.3 (26.99) |
| End[1] | 84 | 241.5 (59.49) | -8.5 (35.55) | 82 | 236.7 (63.56) | 1.1 (36.31) | 81 | 233.8 (60.79) | 4.1 (35.89) |

[1] Last observed value while on treatment (prior to or at Week 24)

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_lb_cont.sas

21:05 Monday, June 26, 2006

Table 14-6.02

Frequency of Normal and Abnormal (Beyond Normal Range) Laboratory Values During Treatment

| | Placebo (N=86) | | | Xan. Low (N=84) | | | Xan. High (N=84) | | | p-val [1] | |
|------------------|----------------|-----------|-----------|-----------------|-----------|-----------|------------------|-----------|-----------|--------------|--|
| | Low | Normal | High | Low | Normal | High | Low | Normal | High | | |
| CHEMISTRY | | | | | | | | | | | |
| ----- | | | | | | | | | | | |
| ALBUMIN | 16 (19%) | 65 (77%) | 3 (4%) | 15 (18%) | 66 (80%) | 1 (1%) | 5 (6%) | 74 (93%) | 1 (1%) | 0.042 | |
| ALKALINE | 4 (5%) | 72 (86%) | 8 (10%) | 2 (2%) | 74 (90%) | 6 (7%) | 3 (4%) | 73 (91%) | 4 (5%) | 0.776 | |
| PHOSPHATASE | | | | | | | | | | | |
| ALANINE | 1 (1%) | 74 (88%) | 9 (11%) | 5 (6%) | 68 (83%) | 9 (11%) | 0 | 70 (88%) | 10 (13%) | 0.185 | |
| AMINOTRANSFERASE | | | | | | | | | | | |
| ASPARTATE | 0 | 74 (88%) | 10 (12%) | 0 | 72 (88%) | 10 (12%) | 0 | 72 (90%) | 8 (10%) | 0.907 | |
| AMINOTRANSFERASE | | | | | | | | | | | |
| BILIRUBIN | 0 | 78 (93%) | 6 (7%) | 0 | 79 (98%) | 2 (2%) | 0 | 75 (94%) | 5 (6%) | 0.402 | |
| UREA NITROGEN | 0 | 75 (89%) | 9 (11%) | 0 | 60 (73%) | 22 (27%) | 0 | 68 (85%) | 12 (15%) | 0.023 | |
| CALCIUM | 5 (6%) | 78 (93%) | 1 (1%) | 7 (9%) | 72 (88%) | 3 (4%) | 7 (9%) | 71 (89%) | 2 (3%) | 0.789 | |
| CHOLESTEROL | 5 (6%) | 73 (87%) | 6 (7%) | 6 (7%) | 72 (88%) | 4 (5%) | 6 (8%) | 70 (88%) | 4 (5%) | 0.962 | |
| CREATINE KINASE | 1 (1%) | 66 (79%) | 17 (20%) | 1 (1%) | 68 (83%) | 13 (16%) | 0 | 67 (84%) | 13 (16%) | 0.816 | |
| CHLORIDE | 0 | 74 (88%) | 10 (12%) | 0 | 74 (90%) | 8 (10%) | 0 | 78 (98%) | 2 (3%) | 0.058 | |
| CREATININE | 0 | 80 (95%) | 4 (5%) | 0 | 76 (93%) | 6 (7%) | 0 | 73 (91%) | 7 (9%) | 0.572 | |
| GAMMA GLUTAMYL | 4 (5%) | 73 (87%) | 7 (8%) | 4 (5%) | 69 (84%) | 9 (11%) | 1 (1%) | 71 (89%) | 8 (10%) | 0.689 | |
| TRANSFERASE | | | | | | | | | | | |
| GLUCOSE | 0 | 82 (98%) | 2 (2%) | 0 | 81 (99%) | 1 (1%) | 0 | 77 (96%) | 3 (4%) | 0.534 | |
| POTASSIUM | 3 (4%) | 80 (95%) | 1 (1%) | 3 (4%) | 79 (96%) | 0 | 2 (3%) | 78 (98%) | 0 | 1.000 | |
| SODIUM | 4 (5%) | 75 (89%) | 5 (6%) | 3 (4%) | 74 (90%) | 5 (6%) | 7 (9%) | 62 (78%) | 11 (14%) | 0.177 | |
| PHOSPHATE | 1 (1%) | 83 (99%) | 0 | 0 | 80 (98%) | 2 (2%) | 1 (1%) | 78 (98%) | 1 (1%) | 0.518 | |
| PROTEIN | 1 (1%) | 76 (90%) | 7 (8%) | 2 (2%) | 75 (91%) | 5 (6%) | 1 (1%) | 77 (96%) | 2 (3%) | 0.536 | |
| URATE | 3 (4%) | 77 (92%) | 4 (5%) | 1 (1%) | 75 (91%) | 6 (7%) | 4 (5%) | 69 (86%) | 7 (9%) | 0.564 | |
| HEMATOLOGY | | | | | | | | | | | |
| ----- | | | | | | | | | | | |

Note: Percentages are based on the number of subjects with non-missing assessments (i.e., the total of the subjects in the low, normal, and high categories) within each treatment group.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labnormfreq.sas

21:05 Monday, June 26, 2006

Table 14-6.02

Frequency of Normal and Abnormal (Beyond Normal Range) Laboratory Values During Treatment

| | Placebo (N=86) | | | Xan. Low (N=84) | | | Xan. High (N=84) | | | p-val [1] |
|--------------------|----------------|-----------|-----------|-----------------|-----------|-----------|------------------|-----------|-----------|--------------|
| | Low | Normal | High | Low | Normal | High | Low | Normal | High | |
| BASOPHILS | 0 | 84 (100%) | 0 | 0 | 82 (100%) | 0 | 0 | 81 (100%) | 0 | |
| EOSINOPHILS | 0 | 84 (100%) | 0 | 0 | 71 (87%) | 11 (13%) | 0 | 74 (91%) | 7 (9%) | 0.001 |
| HEMATOCRIT | 5 (6%) | 74 (89%) | 4 (5%) | 9 (11%) | 72 (88%) | 1 (1%) | 1 (1%) | 78 (96%) | 2 (2%) | 0.052 |
| HEMOGLOBIN | 14 (17%) | 68 (81%) | 2 (2%) | 10 (12%) | 72 (88%) | 0 | 5 (6%) | 73 (90%) | 3 (4%) | 0.093 |
| LYMPHOCYTES | 6 (7%) | 73 (87%) | 5 (6%) | 4 (5%) | 69 (84%) | 9 (11%) | 4 (5%) | 76 (94%) | 1 (1%) | 0.103 |
| ERY. MEAN | 0 | 81 (96%) | 3 (4%) | 0 | 81 (99%) | 1 (1%) | 1 (1%) | 75 (93%) | 5 (6%) | 0.186 |
| CORPUSCULAR | | | | | | | | | | |
| HEMOGLOBIN | | | | | | | | | | |
| ERY. MEAN | 15 (18%) | 68 (82%) | 0 | 17 (21%) | 65 (79%) | 0 | 9 (11%) | 72 (89%) | 0 | 0.231 |
| CORPUSCULAR HB | | | | | | | | | | |
| CONCENTRATION | | | | | | | | | | |
| ERY. MEAN | 1 (1%) | 53 (64%) | 29 (35%) | 0 | 64 (78%) | 18 (22%) | 1 (1%) | 64 (79%) | 16 (20%) | 0.077 |
| CORPUSCULAR VOLUME | | | | | | | | | | |
| MONOCYTES | 2 (2%) | 80 (95%) | 2 (2%) | 1 (1%) | 77 (94%) | 4 (5%) | 0 | 79 (98%) | 2 (2%) | 0.626 |
| PLATELET | 0 | 81 (96%) | 3 (4%) | 2 (2%) | 77 (94%) | 3 (4%) | 2 (2%) | 77 (95%) | 2 (2%) | 0.681 |
| ERYTHROCYTES | 13 (15%) | 71 (85%) | 0 | 18 (22%) | 64 (78%) | 0 | 11 (14%) | 68 (84%) | 2 (2%) | 0.238 |
| LEUKOCYTES | 7 (8%) | 73 (87%) | 4 (5%) | 6 (7%) | 68 (83%) | 8 (10%) | 4 (5%) | 74 (91%) | 3 (4%) | 0.462 |

Note: Percentages are based on the number of subjects with non-missing assessments (i.e., the total of the subjects in the low, normal, and high categories) within each treatment group.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labnormfreq.sas

21:05 Monday, June 26, 2006

Table 14-6.03

Frequency of Normal and Abnormal (Clinically Significant Change from Previous Visit) Laboratory Values During Treatment

| | Placebo (N=86) | | | Xan. Low (N=84) | | | Xan. High (N=84) | | | p-val [1] |
|----------------------------|----------------|-----------|-----------|-----------------|-----------|-----------|------------------|-----------|-----------|--------------|
| | Low | Normal | High | Low | Normal | High | Low | Normal | High | |
| CHEMISTRY | | | | | | | | | | |
| ----- | | | | | | | | | | |
| ALBUMIN | 10 (12%) | 71 (85%) | 3 (4%) | 6 (7%) | 72 (88%) | 4 (5%) | 5 (6%) | 66 (83%) | 9 (11%) | 0.235 |
| ALKALINE PHOSPHATASE | 1 (1%) | 78 (93%) | 5 (6%) | 0 | 79 (98%) | 2 (2%) | 0 | 77 (96%) | 3 (4%) | 0.599 |
| ALANINE AMINOTRANSFERASE | 4 (5%) | 75 (89%) | 5 (6%) | 6 (7%) | 69 (84%) | 7 (9%) | 7 (9%) | 68 (85%) | 5 (6%) | 0.820 |
| ASPARTATE AMINOTRANSFERASE | 2 (2%) | 73 (87%) | 9 (11%) | 8 (10%) | 71 (87%) | 3 (4%) | 3 (4%) | 75 (94%) | 2 (3%) | 0.045 |
| BILIRUBIN | 0 | 79 (94%) | 5 (6%) | 1 (1%) | 79 (98%) | 1 (1%) | 2 (3%) | 75 (94%) | 3 (4%) | 0.296 |
| UREA NITROGEN | 0 | 83 (99%) | 1 (1%) | 1 (1%) | 79 (96%) | 2 (2%) | 1 (1%) | 78 (98%) | 1 (1%) | 0.796 |
| CALCIUM | 6 (7%) | 76 (90%) | 2 (2%) | 4 (5%) | 76 (93%) | 2 (2%) | 0 | 77 (96%) | 3 (4%) | 0.140 |
| CHOLESTEROL | 1 (1%) | 81 (96%) | 2 (2%) | 0 | 82 (100%) | 0 | 1 (1%) | 79 (99%) | 0 | 0.500 |
| CREATINE KINASE | 8 (10%) | 64 (76%) | 12 (14%) | 6 (7%) | 71 (87%) | 5 (6%) | 7 (9%) | 65 (81%) | 8 (10%) | 0.474 |
| CHLORIDE | 3 (4%) | 78 (93%) | 3 (4%) | 0 | 80 (98%) | 2 (2%) | 2 (3%) | 77 (96%) | 1 (1%) | 0.496 |
| CREATININE | 0 | 82 (98%) | 2 (2%) | 0 | 81 (99%) | 1 (1%) | 0 | 80 (100%) | 0 | 0.775 |
| GAMMA GLUTAMYL TRANSFERASE | 1 (1%) | 81 (96%) | 2 (2%) | 4 (5%) | 72 (88%) | 6 (7%) | 2 (3%) | 74 (93%) | 4 (5%) | 0.378 |
| GLUCOSE | 1 (1%) | 81 (96%) | 2 (2%) | 1 (1%) | 81 (99%) | 0 | 3 (4%) | 74 (93%) | 3 (4%) | 0.317 |
| POTASSIUM | 2 (2%) | 82 (98%) | 0 | 2 (2%) | 78 (96%) | 1 (1%) | 3 (4%) | 74 (93%) | 3 (4%) | 0.464 |
| SODIUM | 10 (12%) | 60 (71%) | 14 (17%) | 7 (9%) | 62 (76%) | 13 (16%) | 12 (15%) | 58 (73%) | 10 (13%) | 0.728 |
| PHOSPHATE | 1 (1%) | 82 (98%) | 1 (1%) | 0 | 79 (98%) | 2 (2%) | 2 (3%) | 76 (95%) | 2 (3%) | 0.661 |
| PROTEIN | 5 (6%) | 73 (87%) | 6 (7%) | 1 (1%) | 80 (98%) | 1 (1%) | 5 (6%) | 74 (93%) | 1 (1%) | 0.062 |
| URATE | 2 (2%) | 81 (96%) | 1 (1%) | 0 | 82 (100%) | 0 | 0 | 80 (100%) | 0 | 0.331 |

Note: Percentages are based on the number of subjects with non-missing assessments (i.e., the total of the subjects in the low, normal, and high categories) within each treatment group.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labnormfreq.sas

21:05 Monday, June 26, 2006

Table 14-6.03

Frequency of Normal and Abnormal (Clinically Significant Change from Previous Visit) Laboratory Values During Treatment

| | Placebo (N=86) | | | Xan. Low (N=84) | | | Xan. High (N=84) | | | p-val [1] |
|--------------------|----------------|-----------|---------|-----------------|-----------|----------|------------------|-----------|----------|--------------|
| | Low | Normal | High | Low | Normal | High | Low | Normal | High | |
| HEMATOLOGY | | | | | | | | | | |
| ----- | | | | | | | | | | |
| BASOPHILS | 1 (1%) | 82 (98%) | 1 (1%) | 2 (2%) | 80 (98%) | 0 | 1 (1%) | 79 (99%) | 0 | 0.948 |
| EOSINOPHILS | 4 (5%) | 80 (95%) | 0 | 3 (4%) | 70 (85%) | 9 (11%) | 4 (5%) | 68 (85%) | 8 (10%) | 0.010 |
| HEMATOCRIT | 2 (2%) | 79 (95%) | 2 (2%) | 4 (5%) | 77 (95%) | 0 | 1 (1%) | 76 (95%) | 3 (4%) | 0.351 |
| HEMOGLOBIN | 0 | 84 (100%) | 0 | 2 (2%) | 80 (98%) | 0 | 0 | 80 (100%) | 0 | 0.215 |
| LYMPHOCYTES | 4 (5%) | 76 (90%) | 4 (5%) | 2 (2%) | 79 (96%) | 1 (1%) | 2 (3%) | 77 (96%) | 1 (1%) | 0.498 |
| ERY. MEAN | 1 (1%) | 83 (99%) | 0 | 0 | 81 (99%) | 1 (1%) | 0 | 80 (100%) | 0 | 0.884 |
| CORPUSCULAR | | | | | | | | | | |
| HEMOGLOBIN | | | | | | | | | | |
| ERY. MEAN | 1 (1%) | 82 (99%) | 0 | 0 | 80 (99%) | 1 (1%) | 0 | 80 (100%) | 0 | 0.885 |
| CORPUSCULAR HB | | | | | | | | | | |
| CONCENTRATION | | | | | | | | | | |
| ERY. MEAN | 0 | 80 (96%) | 3 (4%) | 2 (2%) | 78 (96%) | 1 (1%) | 1 (1%) | 75 (94%) | 4 (5%) | 0.396 |
| CORPUSCULAR VOLUME | | | | | | | | | | |
| MONOCYTES | 5 (6%) | 74 (88%) | 5 (6%) | 1 (1%) | 80 (98%) | 1 (1%) | 1 (1%) | 78 (98%) | 1 (1%) | 0.081 |
| PLATELET | 0 | 84 (100%) | 0 | 1 (1%) | 80 (98%) | 1 (1%) | 0 | 79 (99%) | 1 (1%) | 0.546 |
| ERYTHROCYTES | 0 | 83 (99%) | 1 (1%) | 1 (1%) | 81 (99%) | 0 | 0 | 80 (100%) | 0 | 0.884 |
| LEUKOCYTES | 4 (5%) | 78 (93%) | 2 (2%) | 2 (2%) | 77 (94%) | 3 (4%) | 3 (4%) | 74 (93%) | 3 (4%) | 0.934 |

Note: Percentages are based on the number of subjects with non-missing assessments (i.e., the total of the subjects in the low, normal, and high categories) within each treatment group.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labnormfreq.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|--------------------------|----------|--------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| Week | Shift to | | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| CHEMISTRY | | | | | | | | |
| ----- | | | | | | | | |
| ALANINE AMINOTRANSFERASE | 2 | n | 81 | 2 | 77 | 1 | 78 | 0 |
| | | Normal | 81 (100%) | 0 | 77 (100%) | 0 | 78 (100%) | 0 |
| | | High | 0 | 2 (100%) | 0 | 1 (100%) | 0 | 0 |
| | 4 | n | 77 | 2 | 69 | 1 | 72 | 0 |
| | | Normal | 77 (100%) | 1 (50%) | 69 (100%) | 0 | 72 (100%) | 0 |
| | | High | 0 | 1 (50%) | 0 | 1 (100%) | 0 | 0 |
| | 6 | n | 72 | 1 | 59 | 1 | 66 | 0 |
| | | Normal | 71 (99%) | 1 (100%) | 59 (100%) | 0 | 66 (100%) | 0 |
| | | High | 1 (1%) | 0 | 0 | 1 (100%) | 0 | 0 |
| | 8 | n | 71 | 1 | 57 | 1 | 56 | 0 |
| | | Normal | 71 (100%) | 0 | 57 (100%) | 0 | 54 (96%) | 0 |
| | | High | 0 | 1 (100%) | 0 | 1 (100%) | 2 (4%) | 0 |
| | 12 | n | 66 | 1 | 49 | 1 | 50 | 0 |
| | | Normal | 65 (98%) | 1 (100%) | 48 (98%) | 1 (100%) | 49 (98%) | 0 |
| | | High | 1 (2%) | 0 | 1 (2%) | 0 | 1 (2%) | 0 |
| | 16 | n | 67 | 1 | 40 | 0 | 37 | 0 |
| | | Normal | 67 (100%) | 1 (100%) | 40 (100%) | 0 | 37 (100%) | 0 |
| | 20 | n | 64 | 1 | 29 | 0 | 31 | 0 |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|---------|----------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| Week | Shift to | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| | Normal | 64 (100%) | 1 (100%) | 29 (100%) | 0 | 31 (100%) | 0 |
| 24 | n | 56 | 1 | 25 | 0 | 30 | 0 |
| | Normal | 55 (98%) | 1 (100%) | 25 (100%) | 0 | 30 (100%) | 0 |
| | High | 1 (2%) | 0 | 0 | 0 | 0 | 0 |
| 26 | n | 56 | 1 | 24 | 0 | 27 | 0 |
| | Normal | 56 (100%) | 1 (100%) | 23 (96%) | 0 | 27 (100%) | 0 |
| | High | 0 | 0 | 1 (4%) | 0 | 0 | 0 |
| ALBUMIN | 2 | 83 | 0 | 78 | 0 | 78 | 0 |
| | Normal | 83 (100%) | 0 | 78 (100%) | 0 | 78 (100%) | 0 |
| 4 | n | 79 | 0 | 70 | 0 | 72 | 0 |
| | Normal | 79 (100%) | 0 | 70 (100%) | 0 | 72 (100%) | 0 |
| 6 | n | 73 | 0 | 60 | 0 | 66 | 0 |
| | Normal | 73 (100%) | 0 | 60 (100%) | 0 | 66 (100%) | 0 |
| 8 | n | 72 | 0 | 58 | 0 | 56 | 0 |
| | Normal | 72 (100%) | 0 | 58 (100%) | 0 | 56 (100%) | 0 |
| 12 | n | 67 | 0 | 50 | 0 | 50 | 0 |
| | Normal | 67 (100%) | 0 | 50 (100%) | 0 | 50 (100%) | 0 |
| 16 | n | 68 | 0 | 40 | 0 | 37 | 0 |
| | Normal | 68 (100%) | 0 | 40 (100%) | 0 | 37 (100%) | 0 |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|----------------------|----------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| Week | Shift to | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| ALKALINE PHOSPHATASE | 20 n | 65 | 0 | 29 | 0 | 31 | 0 |
| | Normal | 65 (100%) | 0 | 29 (100%) | 0 | 31 (100%) | 0 |
| | 24 n | 57 | 0 | 25 | 0 | 30 | 0 |
| | Normal | 57 (100%) | 0 | 25 (100%) | 0 | 30 (100%) | 0 |
| | 26 n | 57 | 0 | 24 | 0 | 27 | 0 |
| | Normal | 57 (100%) | 0 | 24 (100%) | 0 | 27 (100%) | 0 |
| | 2 n | 82 | 2 | 78 | 0 | 77 | 1 |
| | Normal | 82 (100%) | 0 | 78 (100%) | 0 | 77 (100%) | 0 |
| | High | 0 | 2 (100%) | 0 | 0 | 0 | 1 (100%) |
| | 4 n | 80 | 2 | 69 | 0 | 71 | 1 |
| | Normal | 80 (100%) | 0 | 69 (100%) | 0 | 71 (100%) | 0 |
| | High | 0 | 2 (100%) | 0 | 0 | 0 | 1 (100%) |
| | 6 n | 75 | 0 | 62 | 0 | 66 | 1 |
| | Normal | 75 (100%) | 0 | 62 (100%) | 0 | 66 (100%) | 0 |
| | High | 0 | 0 | 0 | 0 | 0 | 1 (100%) |
| | 8 n | 72 | 1 | 58 | 0 | 55 | 1 |
| | Normal | 72 (100%) | 0 | 57 (98%) | 0 | 55 (100%) | 0 |
| | High | 0 | 1 (100%) | 1 (2%) | 0 | 0 | 1 (100%) |
| | 12 n | 66 | 1 | 50 | 0 | 49 | 1 |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|-------------------------------|----------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| Week | Shift to | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| | Normal | 66 (100%) | 0 | 50 (100%) | 0 | 49 (100%) | 0 |
| | High | 0 | 1 (100%) | 0 | 0 | 0 | 1 (100%) |
| 16 | n | 67 | 1 | 40 | 0 | 36 | 1 |
| | Normal | 67 (100%) | 0 | 40 (100%) | 0 | 36 (100%) | 0 |
| | High | 0 | 1 (100%) | 0 | 0 | 0 | 1 (100%) |
| 20 | n | 64 | 1 | 30 | 0 | 30 | 1 |
| | Normal | 63 (98%) | 0 | 30 (100%) | 0 | 30 (100%) | 0 |
| | High | 1 (2%) | 1 (100%) | 0 | 0 | 0 | 1 (100%) |
| 24 | n | 55 | 1 | 26 | 0 | 30 | 0 |
| | Normal | 54 (98%) | 0 | 26 (100%) | 0 | 30 (100%) | 0 |
| | High | 1 (2%) | 1 (100%) | 0 | 0 | 0 | 0 |
| 26 | n | 56 | 1 | 24 | 0 | 27 | 0 |
| | Normal | 55 (98%) | 0 | 24 (100%) | 0 | 27 (100%) | 0 |
| | High | 1 (2%) | 1 (100%) | 0 | 0 | 0 | 0 |
| ASPARTATE AMINOTRANSFERASE | 2 | n | 81 | 2 | 78 | 0 | 78 |
| | | Normal | 80 (99%) | 1 (50%) | 77 (99%) | 0 | 78 (100%) |
| | | High | 1 (1%) | 1 (50%) | 1 (1%) | 0 | 0 |
| | 4 | n | 77 | 2 | 69 | 1 | 72 |
| | | Normal | 76 (99%) | 1 (50%) | 69 (100%) | 1 (100%) | 72 (100%) |
| | | High | 1 (1%) | 1 (50%) | 0 | 0 | 0 |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| Week | Shift to | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|------|----------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| | | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| 6 | n | 72 | 1 | 60 | 0 | 66 | 0 |
| | Normal | 71 (99%) | 1 (100%) | 60 (100%) | 0 | 65 (98%) | 0 |
| | High | 1 (1%) | 0 | 0 | 0 | 1 (2%) | 0 |
| 8 | n | 71 | 1 | 58 | 0 | 56 | 0 |
| | Normal | 70 (99%) | 1 (100%) | 58 (100%) | 0 | 55 (98%) | 0 |
| | High | 1 (1%) | 0 | 0 | 0 | 1 (2%) | 0 |
| 12 | n | 66 | 1 | 50 | 0 | 50 | 0 |
| | Normal | 65 (98%) | 1 (100%) | 49 (98%) | 0 | 50 (100%) | 0 |
| | High | 1 (2%) | 0 | 1 (2%) | 0 | 0 | 0 |
| 16 | n | 67 | 1 | 40 | 0 | 37 | 0 |
| | Normal | 67 (100%) | 1 (100%) | 39 (98%) | 0 | 37 (100%) | 0 |
| | High | 0 | 0 | 1 (3%) | 0 | 0 | 0 |
| 20 | n | 64 | 1 | 29 | 0 | 31 | 0 |
| | Normal | 64 (100%) | 1 (100%) | 29 (100%) | 0 | 31 (100%) | 0 |
| 24 | n | 56 | 1 | 25 | 0 | 30 | 0 |
| | Normal | 54 (96%) | 1 (100%) | 24 (96%) | 0 | 30 (100%) | 0 |
| | High | 2 (4%) | 0 | 1 (4%) | 0 | 0 | 0 |
| 26 | n | 56 | 1 | 24 | 0 | 27 | 0 |
| | Normal | 55 (98%) | 1 (100%) | 23 (96%) | 0 | 27 (100%) | 0 |
| | High | 1 (2%) | 0 | 1 (4%) | 0 | 0 | 0 |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|-----------|----------|--------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| Week | Shift to | | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| BILIRUBIN | 2 | n | 83 | 0 | 78 | 0 | 77 | 1 |
| | | Normal | 82 (99%) | 0 | 78 (100%) | 0 | 77 (100%) | 1 (100%) |
| | | High | 1 (1%) | 0 | 0 | 0 | 0 | 0 |
| | 4 | n | 79 | 0 | 70 | 0 | 71 | 1 |
| | | Normal | 78 (99%) | 0 | 70 (100%) | 0 | 71 (100%) | 0 |
| | | High | 1 (1%) | 0 | 0 | 0 | 0 | 1 (100%) |
| | 6 | n | 73 | 0 | 60 | 0 | 65 | 1 |
| | | Normal | 73 (100%) | 0 | 60 (100%) | 0 | 65 (100%) | 1 (100%) |
| | 8 | n | 72 | 0 | 58 | 0 | 55 | 1 |
| | | Normal | 72 (100%) | 0 | 58 (100%) | 0 | 55 (100%) | 1 (100%) |
| | 12 | n | 67 | 0 | 50 | 0 | 49 | 1 |
| | | Normal | 67 (100%) | 0 | 50 (100%) | 0 | 48 (98%) | 1 (100%) |
| | | High | 0 | 0 | 0 | 0 | 1 (2%) | 0 |
| | 16 | n | 68 | 0 | 40 | 0 | 36 | 1 |
| | | Normal | 68 (100%) | 0 | 40 (100%) | 0 | 36 (100%) | 1 (100%) |
| | 20 | n | 65 | 0 | 29 | 0 | 30 | 1 |
| | | Normal | 65 (100%) | 0 | 29 (100%) | 0 | 29 (97%) | 1 (100%) |
| | | High | 0 | 0 | 0 | 0 | 1 (3%) | 0 |
| | 24 | n | 57 | 0 | 25 | 0 | 29 | 1 |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|---------|----------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| Week | Shift to | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| | Normal | 57 (100%) | 0 | 25 (100%) | 0 | 29 (100%) | 1 (100%) |
| CALCIUM | 26 n | 57 | 0 | 24 | 0 | 26 | 1 |
| | Normal | 57 (100%) | 0 | 23 (96%) | 0 | 26 (100%) | 1 (100%) |
| | High | 0 | 0 | 1 (4%) | 0 | 0 | 0 |
| | 2 n | 84 | 0 | 78 | 0 | 78 | 0 |
| | Normal | 84 (100%) | 0 | 78 (100%) | 0 | 78 (100%) | 0 |
| | 4 n | 82 | 0 | 70 | 0 | 72 | 0 |
| | Normal | 82 (100%) | 0 | 70 (100%) | 0 | 72 (100%) | 0 |
| | 6 n | 75 | 0 | 62 | 0 | 67 | 0 |
| | Normal | 75 (100%) | 0 | 62 (100%) | 0 | 67 (100%) | 0 |
| | 8 n | 73 | 0 | 58 | 0 | 56 | 0 |
| | Normal | 73 (100%) | 0 | 58 (100%) | 0 | 56 (100%) | 0 |
| | 12 n | 67 | 0 | 50 | 0 | 50 | 0 |
| | Normal | 67 (100%) | 0 | 50 (100%) | 0 | 50 (100%) | 0 |
| | 16 n | 68 | 0 | 40 | 0 | 37 | 0 |
| | Normal | 68 (100%) | 0 | 40 (100%) | 0 | 37 (100%) | 0 |
| | 20 n | 66 | 0 | 30 | 0 | 31 | 0 |
| | Normal | 66 (100%) | 0 | 30 (100%) | 0 | 31 (100%) | 0 |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|----------|------|----------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| | Week | Shift to | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| CHLORIDE | 24 | n | 57 | 0 | 26 | 0 | 30 | 0 |
| | | Normal | 57 (100%) | 0 | 26 (100%) | 0 | 30 (100%) | 0 |
| | 26 | n | 57 | 0 | 24 | 0 | 27 | 0 |
| | | Normal | 57 (100%) | 0 | 24 (100%) | 0 | 27 (100%) | 0 |
| | 2 | n | 84 | 0 | 78 | 0 | 76 | 0 |
| | | Normal | 84 (100%) | 0 | 78 (100%) | 0 | 76 (100%) | 0 |
| | 4 | n | 82 | 0 | 70 | 0 | 71 | 0 |
| | | Normal | 82 (100%) | 0 | 70 (100%) | 0 | 71 (100%) | 0 |
| | 6 | n | 75 | 0 | 62 | 0 | 66 | 0 |
| | | Normal | 75 (100%) | 0 | 62 (100%) | 0 | 66 (100%) | 0 |
| | 8 | n | 73 | 0 | 58 | 0 | 56 | 0 |
| | | Normal | 73 (100%) | 0 | 58 (100%) | 0 | 56 (100%) | 0 |
| | 12 | n | 67 | 0 | 50 | 0 | 49 | 0 |
| | | Normal | 67 (100%) | 0 | 50 (100%) | 0 | 49 (100%) | 0 |
| | 16 | n | 68 | 0 | 40 | 0 | 37 | 0 |
| | | Normal | 68 (100%) | 0 | 40 (100%) | 0 | 37 (100%) | 0 |
| | 20 | n | 65 | 0 | 30 | 0 | 31 | 0 |
| | | Normal | 65 (100%) | 0 | 30 (100%) | 0 | 31 (100%) | 0 |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|-------------|------|----------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| | Week | Shift to | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| CHOLESTEROL | 24 | n | 57 | 0 | 26 | 0 | 30 | 0 |
| | | Normal | 57 (100%) | 0 | 26 (100%) | 0 | 30 (100%) | 0 |
| | 26 | n | 57 | 0 | 24 | 0 | 27 | 0 |
| | | Normal | 57 (100%) | 0 | 24 (100%) | 0 | 27 (100%) | 0 |
| | 2 | n | 84 | 0 | 78 | 0 | 78 | 0 |
| | | Normal | 84 (100%) | 0 | 78 (100%) | 0 | 78 (100%) | 0 |
| | 4 | n | 82 | 0 | 70 | 0 | 72 | 0 |
| | | Normal | 82 (100%) | 0 | 70 (100%) | 0 | 72 (100%) | 0 |
| | 6 | n | 75 | 0 | 62 | 0 | 67 | 0 |
| | | Normal | 75 (100%) | 0 | 62 (100%) | 0 | 67 (100%) | 0 |
| | 8 | n | 73 | 0 | 58 | 0 | 56 | 0 |
| | | Normal | 73 (100%) | 0 | 58 (100%) | 0 | 56 (100%) | 0 |
| | 12 | n | 67 | 0 | 50 | 0 | 50 | 0 |
| | | Normal | 67 (100%) | 0 | 50 (100%) | 0 | 50 (100%) | 0 |
| | 16 | n | 68 | 0 | 40 | 0 | 37 | 0 |
| | | Normal | 68 (100%) | 0 | 40 (100%) | 0 | 37 (100%) | 0 |
| | 20 | n | 66 | 0 | 30 | 0 | 31 | 0 |
| | | Normal | 66 (100%) | 0 | 30 (100%) | 0 | 31 (100%) | 0 |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|-----------------|--------|-----------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| | Week | Shift to | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| CREATINE KINASE | 24 | n | 57 | 0 | 26 | 0 | 30 | 0 |
| | | Normal | 57 (100%) | 0 | 26 (100%) | 0 | 30 (100%) | 0 |
| | 26 | n | 57 | 0 | 24 | 0 | 27 | 0 |
| | | Normal | 57 (100%) | 0 | 24 (100%) | 0 | 27 (100%) | 0 |
| | 2 | n | 83 | 0 | 77 | 1 | 75 | 3 |
| | | Normal | 81 (98%) | 0 | 74 (96%) | 1 (100%) | 74 (99%) | 3 (100%) |
| | | High | 2 (2%) | 0 | 3 (4%) | 0 | 1 (1%) | 0 |
| | 4 | n | 79 | 0 | 69 | 1 | 69 | 3 |
| | | Normal | 78 (99%) | 0 | 68 (99%) | 1 (100%) | 68 (99%) | 3 (100%) |
| | | High | 1 (1%) | 0 | 1 (1%) | 0 | 1 (1%) | 0 |
| | 6 | n | 73 | 0 | 59 | 1 | 63 | 3 |
| | | Normal | 73 (100%) | 0 | 58 (98%) | 1 (100%) | 61 (97%) | 2 (67%) |
| | | High | 0 | 0 | 1 (2%) | 0 | 2 (3%) | 1 (33%) |
| | 8 | n | 72 | 0 | 57 | 1 | 54 | 2 |
| | | Normal | 71 (99%) | 0 | 57 (100%) | 1 (100%) | 53 (98%) | 2 (100%) |
| | | High | 1 (1%) | 0 | 0 | 0 | 1 (2%) | 0 |
| 12 | n | 67 | 0 | 49 | 1 | 48 | 2 | |
| | Normal | 65 (97%) | 0 | 48 (98%) | 1 (100%) | 47 (98%) | 1 (50%) | |
| | High | 2 (3%) | 0 | 1 (2%) | 0 | 1 (2%) | 1 (50%) | |
| 16 | n | 68 | 0 | 39 | 1 | 36 | 1 | |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|------------|-----------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| Week | Shift to | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| CREATININE | Normal | 66 (97%) | 0 | 39 (100%) | 1 (100%) | 36 (100%) | 1 (100%) |
| | High | 2 (3%) | 0 | 0 | 0 | 0 | 0 |
| | 20 n | 65 | 0 | 29 | 0 | 30 | 1 |
| | Normal | 65 (100%) | 0 | 27 (93%) | 0 | 29 (97%) | 1 (100%) |
| | High | 0 | 0 | 2 (7%) | 0 | 1 (3%) | 0 |
| | 24 n | 57 | 0 | 25 | 0 | 29 | 1 |
| | Normal | 55 (96%) | 0 | 25 (100%) | 0 | 29 (100%) | 1 (100%) |
| | High | 2 (4%) | 0 | 0 | 0 | 0 | 0 |
| | 26 n | 57 | 0 | 24 | 0 | 26 | 1 |
| | Normal | 57 (100%) | 0 | 24 (100%) | 0 | 25 (96%) | 1 (100%) |
| | High | 0 | 0 | 0 | 0 | 1 (4%) | 0 |
| | 2 n | 84 | 0 | 78 | 0 | 78 | 0 |
| | Normal | 84 (100%) | 0 | 78 (100%) | 0 | 78 (100%) | 0 |
| | 4 n | 82 | 0 | 70 | 0 | 72 | 0 |
| | Normal | 82 (100%) | 0 | 70 (100%) | 0 | 72 (100%) | 0 |
| | 6 n | 75 | 0 | 62 | 0 | 67 | 0 |
| Normal | 75 (100%) | 0 | 62 (100%) | 0 | 67 (100%) | 0 | |
| 8 n | 73 | 0 | 58 | 0 | 56 | 0 | |
| Normal | 73 (100%) | 0 | 58 (100%) | 0 | 56 (100%) | 0 | |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|----------------------------|------|----------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| | Week | Shift to | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| GAMMA GLUTAMYL TRANSFERASE | 12 | n | 67 | 0 | 50 | 0 | 50 | 0 |
| | | Normal | 67 (100%) | 0 | 50 (100%) | 0 | 50 (100%) | 0 |
| | 16 | n | 68 | 0 | 40 | 0 | 37 | 0 |
| | | Normal | 68 (100%) | 0 | 40 (100%) | 0 | 37 (100%) | 0 |
| | 20 | n | 66 | 0 | 30 | 0 | 31 | 0 |
| | | Normal | 66 (100%) | 0 | 30 (100%) | 0 | 31 (100%) | 0 |
| | 24 | n | 57 | 0 | 26 | 0 | 30 | 0 |
| | | Normal | 57 (100%) | 0 | 26 (100%) | 0 | 30 (100%) | 0 |
| | 26 | n | 57 | 0 | 24 | 0 | 27 | 0 |
| | | Normal | 57 (100%) | 0 | 24 (100%) | 0 | 27 (100%) | 0 |
| | 2 | n | 82 | 2 | 76 | 2 | 76 | 2 |
| | | Normal | 82 (100%) | 1 (50%) | 75 (99%) | 1 (50%) | 75 (99%) | 1 (50%) |
| | | High | 0 | 1 (50%) | 1 (1%) | 1 (50%) | 1 (1%) | 1 (50%) |
| | 4 | n | 80 | 2 | 68 | 2 | 70 | 2 |
| | | Normal | 80 (100%) | 1 (50%) | 68 (100%) | 1 (50%) | 70 (100%) | 1 (50%) |
| | | High | 0 | 1 (50%) | 0 | 1 (50%) | 0 | 1 (50%) |
| | 6 | n | 74 | 1 | 61 | 1 | 66 | 1 |
| | | Normal | 74 (100%) | 0 | 61 (100%) | 1 (100%) | 66 (100%) | 0 |
| | High | 0 | 1 (100%) | 0 | 0 | 0 | 1 (100%) | |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|---------|----------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| Week | Shift to | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| 8 | n | 72 | 1 | 57 | 1 | 55 | 1 |
| | Normal | 72 (100%) | 0 | 56 (98%) | 1 (100%) | 54 (98%) | 0 |
| | High | 0 | 1 (100%) | 1 (2%) | 0 | 1 (2%) | 1 (100%) |
| 12 | n | 66 | 1 | 49 | 1 | 49 | 1 |
| | Normal | 66 (100%) | 0 | 49 (100%) | 1 (100%) | 49 (100%) | 0 |
| | High | 0 | 1 (100%) | 0 | 0 | 0 | 1 (100%) |
| 16 | n | 67 | 1 | 39 | 1 | 36 | 1 |
| | Normal | 67 (100%) | 1 (100%) | 39 (100%) | 1 (100%) | 36 (100%) | 0 |
| | High | 0 | 0 | 0 | 0 | 0 | 1 (100%) |
| 20 | n | 65 | 1 | 29 | 1 | 31 | 0 |
| | Normal | 65 (100%) | 0 | 29 (100%) | 0 | 31 (100%) | 0 |
| | High | 0 | 1 (100%) | 0 | 1 (100%) | 0 | 0 |
| 24 | n | 56 | 1 | 26 | 0 | 29 | 1 |
| | Normal | 54 (96%) | 1 (100%) | 25 (96%) | 0 | 29 (100%) | 0 |
| | High | 2 (4%) | 0 | 1 (4%) | 0 | 0 | 1 (100%) |
| 26 | n | 56 | 1 | 24 | 0 | 26 | 1 |
| | Normal | 55 (98%) | 1 (100%) | 23 (96%) | 0 | 26 (100%) | 0 |
| | High | 1 (2%) | 0 | 1 (4%) | 0 | 0 | 1 (100%) |
| GLUCOSE | 2 n | 82 | 1 | 78 | 0 | 78 | 0 |
| | Normal | 82 (100%) | 1 (100%) | 78 (100%) | 0 | 77 (99%) | 0 |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| Week | Shift to | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|------|----------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| | | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| | High | 0 | 0 | 0 | 0 | 1 (1%) | 0 |
| 4 | n | 78 | 1 | 69 | 0 | 72 | 0 |
| | Normal | 78 (100%) | 1 (100%) | 69 (100%) | 0 | 72 (100%) | 0 |
| 6 | n | 72 | 1 | 60 | 0 | 66 | 0 |
| | Normal | 72 (100%) | 1 (100%) | 60 (100%) | 0 | 65 (98%) | 0 |
| | High | 0 | 0 | 0 | 0 | 1 (2%) | 0 |
| 8 | n | 71 | 1 | 57 | 0 | 56 | 0 |
| | Normal | 71 (100%) | 1 (100%) | 57 (100%) | 0 | 56 (100%) | 0 |
| 12 | n | 66 | 1 | 50 | 0 | 49 | 0 |
| | Normal | 66 (100%) | 1 (100%) | 49 (98%) | 0 | 49 (100%) | 0 |
| | High | 0 | 0 | 1 (2%) | 0 | 0 | 0 |
| 16 | n | 67 | 1 | 40 | 0 | 37 | 0 |
| | Normal | 67 (100%) | 1 (100%) | 40 (100%) | 0 | 37 (100%) | 0 |
| 20 | n | 64 | 1 | 29 | 0 | 31 | 0 |
| | Normal | 64 (100%) | 1 (100%) | 29 (100%) | 0 | 31 (100%) | 0 |
| 24 | n | 56 | 1 | 25 | 0 | 30 | 0 |
| | Normal | 56 (100%) | 1 (100%) | 25 (100%) | 0 | 30 (100%) | 0 |
| 26 | n | 56 | 1 | 24 | 0 | 27 | 0 |
| | Normal | 56 (100%) | 1 (100%) | 24 (100%) | 0 | 27 (100%) | 0 |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|-----------|----------|--------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| Week | Shift to | | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| PHOSPHATE | 2 | n | 84 | 0 | 78 | 0 | 78 | 0 |
| | | Normal | 84 (100%) | 0 | 78 (100%) | 0 | 78 (100%) | 0 |
| | 4 | n | 82 | 0 | 68 | 0 | 72 | 0 |
| | | Normal | 82 (100%) | 0 | 68 (100%) | 0 | 72 (100%) | 0 |
| | 6 | n | 75 | 0 | 62 | 0 | 67 | 0 |
| | | Normal | 75 (100%) | 0 | 62 (100%) | 0 | 67 (100%) | 0 |
| | 8 | n | 73 | 0 | 58 | 0 | 56 | 0 |
| | | Normal | 73 (100%) | 0 | 58 (100%) | 0 | 56 (100%) | 0 |
| | 12 | n | 67 | 0 | 50 | 0 | 50 | 0 |
| | | Normal | 67 (100%) | 0 | 50 (100%) | 0 | 50 (100%) | 0 |
| | 16 | n | 68 | 0 | 40 | 0 | 37 | 0 |
| | | Normal | 68 (100%) | 0 | 40 (100%) | 0 | 37 (100%) | 0 |
| | 20 | n | 65 | 0 | 30 | 0 | 31 | 0 |
| | | Normal | 65 (100%) | 0 | 30 (100%) | 0 | 31 (100%) | 0 |
| | 24 | n | 56 | 0 | 26 | 0 | 30 | 0 |
| | | Normal | 56 (100%) | 0 | 26 (100%) | 0 | 30 (100%) | 0 |
| | 26 | n | 57 | 0 | 24 | 0 | 27 | 0 |
| | | Normal | 57 (100%) | 0 | 24 (100%) | 0 | 27 (100%) | 0 |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|-----------|----------|--------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| Week | Shift to | | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| POTASSIUM | 2 | n | 84 | 0 | 78 | 0 | 76 | 0 |
| | | Normal | 84 (100%) | 0 | 78 (100%) | 0 | 76 (100%) | 0 |
| | 4 | n | 82 | 0 | 68 | 0 | 71 | 0 |
| | | Normal | 82 (100%) | 0 | 68 (100%) | 0 | 71 (100%) | 0 |
| | 6 | n | 75 | 0 | 62 | 0 | 66 | 0 |
| | | Normal | 75 (100%) | 0 | 62 (100%) | 0 | 66 (100%) | 0 |
| | 8 | n | 73 | 0 | 58 | 0 | 56 | 0 |
| | | Normal | 73 (100%) | 0 | 58 (100%) | 0 | 56 (100%) | 0 |
| | 12 | n | 67 | 0 | 50 | 0 | 49 | 0 |
| | | Normal | 67 (100%) | 0 | 50 (100%) | 0 | 49 (100%) | 0 |
| | 16 | n | 68 | 0 | 40 | 0 | 37 | 0 |
| | | Normal | 68 (100%) | 0 | 40 (100%) | 0 | 37 (100%) | 0 |
| | 20 | n | 64 | 0 | 30 | 0 | 31 | 0 |
| | | Normal | 64 (100%) | 0 | 30 (100%) | 0 | 31 (100%) | 0 |
| | 24 | n | 56 | 0 | 26 | 0 | 30 | 0 |
| | | Normal | 56 (100%) | 0 | 26 (100%) | 0 | 30 (100%) | 0 |
| | 26 | n | 57 | 0 | 24 | 0 | 27 | 0 |
| | | Normal | 57 (100%) | 0 | 24 (100%) | 0 | 27 (100%) | 0 |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|---------|------|----------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| | Week | Shift to | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| PROTEIN | 2 | n | 84 | 0 | 78 | 0 | 78 | 0 |
| | | Normal | 84 (100%) | 0 | 78 (100%) | 0 | 78 (100%) | 0 |
| | 4 | n | 82 | 0 | 70 | 0 | 72 | 0 |
| | | Normal | 82 (100%) | 0 | 70 (100%) | 0 | 72 (100%) | 0 |
| | 6 | n | 75 | 0 | 62 | 0 | 67 | 0 |
| | | Normal | 75 (100%) | 0 | 62 (100%) | 0 | 67 (100%) | 0 |
| | 8 | n | 73 | 0 | 58 | 0 | 56 | 0 |
| | | Normal | 73 (100%) | 0 | 58 (100%) | 0 | 56 (100%) | 0 |
| | 12 | n | 67 | 0 | 50 | 0 | 50 | 0 |
| | | Normal | 67 (100%) | 0 | 50 (100%) | 0 | 50 (100%) | 0 |
| | 16 | n | 68 | 0 | 40 | 0 | 37 | 0 |
| | | Normal | 68 (100%) | 0 | 40 (100%) | 0 | 37 (100%) | 0 |
| | 20 | n | 66 | 0 | 30 | 0 | 31 | 0 |
| | | Normal | 66 (100%) | 0 | 30 (100%) | 0 | 31 (100%) | 0 |
| | 24 | n | 57 | 0 | 26 | 0 | 30 | 0 |
| | | Normal | 57 (100%) | 0 | 26 (100%) | 0 | 30 (100%) | 0 |
| | 26 | n | 57 | 0 | 24 | 0 | 27 | 0 |
| | | Normal | 57 (100%) | 0 | 24 (100%) | 0 | 27 (100%) | 0 |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|--------|------|----------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| | Week | Shift to | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| SODIUM | 2 | n | 84 | 0 | 78 | 0 | 76 | 0 |
| | | Normal | 84 (100%) | 0 | 78 (100%) | 0 | 76 (100%) | 0 |
| | 4 | n | 82 | 0 | 70 | 0 | 71 | 0 |
| | | Normal | 82 (100%) | 0 | 70 (100%) | 0 | 71 (100%) | 0 |
| | 6 | n | 75 | 0 | 62 | 0 | 66 | 0 |
| | | Normal | 75 (100%) | 0 | 62 (100%) | 0 | 66 (100%) | 0 |
| | 8 | n | 73 | 0 | 58 | 0 | 56 | 0 |
| | | Normal | 73 (100%) | 0 | 58 (100%) | 0 | 56 (100%) | 0 |
| | 12 | n | 67 | 0 | 50 | 0 | 49 | 0 |
| | | Normal | 67 (100%) | 0 | 50 (100%) | 0 | 49 (100%) | 0 |
| | 16 | n | 68 | 0 | 40 | 0 | 37 | 0 |
| | | Normal | 68 (100%) | 0 | 40 (100%) | 0 | 37 (100%) | 0 |
| | 20 | n | 65 | 0 | 30 | 0 | 31 | 0 |
| | | Normal | 65 (100%) | 0 | 30 (100%) | 0 | 31 (100%) | 0 |
| | 24 | n | 57 | 0 | 26 | 0 | 30 | 0 |
| | | Normal | 57 (100%) | 0 | 26 (100%) | 0 | 30 (100%) | 0 |
| | 26 | n | 57 | 0 | 24 | 0 | 27 | 0 |
| | | Normal | 57 (100%) | 0 | 24 (100%) | 0 | 27 (100%) | 0 |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|-------|----------|--------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| Week | Shift to | | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| URATE | 2 | n | 84 | 0 | 78 | 0 | 78 | 0 |
| | | Normal | 84 (100%) | 0 | 78 (100%) | 0 | 78 (100%) | 0 |
| | 4 | n | 82 | 0 | 70 | 0 | 72 | 0 |
| | | Normal | 82 (100%) | 0 | 70 (100%) | 0 | 72 (100%) | 0 |
| | 6 | n | 75 | 0 | 62 | 0 | 67 | 0 |
| | | Normal | 75 (100%) | 0 | 62 (100%) | 0 | 67 (100%) | 0 |
| | 8 | n | 73 | 0 | 58 | 0 | 56 | 0 |
| | | Normal | 73 (100%) | 0 | 58 (100%) | 0 | 56 (100%) | 0 |
| | 12 | n | 67 | 0 | 50 | 0 | 50 | 0 |
| | | Normal | 67 (100%) | 0 | 50 (100%) | 0 | 50 (100%) | 0 |
| | 16 | n | 68 | 0 | 40 | 0 | 37 | 0 |
| | | Normal | 68 (100%) | 0 | 40 (100%) | 0 | 37 (100%) | 0 |
| | 20 | n | 66 | 0 | 30 | 0 | 31 | 0 |
| | | Normal | 66 (100%) | 0 | 30 (100%) | 0 | 31 (100%) | 0 |
| | 24 | n | 57 | 0 | 26 | 0 | 30 | 0 |
| | | Normal | 57 (100%) | 0 | 26 (100%) | 0 | 30 (100%) | 0 |
| | 26 | n | 57 | 0 | 24 | 0 | 27 | 0 |
| | | Normal | 57 (100%) | 0 | 24 (100%) | 0 | 27 (100%) | 0 |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|---------------|----------|--------|----------------|----------|-----------------|----------|------------------|----------|
| | | | Normal at | High at | Normal at | High at | Normal at | High at |
| | | | Baseline | Baseline | Baseline | Baseline | Baseline | Baseline |
| Week | Shift to | | | | | | | |
| UREA NITROGEN | 2 | n | 84 | 0 | 76 | 2 | 78 | 0 |
| | | Normal | 84 (100%) | 0 | 76 (100%) | 2 (100%) | 77 (99%) | 0 |
| | | High | 0 | 0 | 0 | 0 | 1 (1%) | 0 |
| | 4 | n | 82 | 0 | 68 | 2 | 72 | 0 |
| | | Normal | 82 (100%) | 0 | 68 (100%) | 2 (100%) | 72 (100%) | 0 |
| | 6 | n | 75 | 0 | 60 | 2 | 67 | 0 |
| | | Normal | 75 (100%) | 0 | 60 (100%) | 2 (100%) | 67 (100%) | 0 |
| | 8 | n | 73 | 0 | 56 | 2 | 56 | 0 |
| | | Normal | 73 (100%) | 0 | 56 (100%) | 2 (100%) | 56 (100%) | 0 |
| | 12 | n | 67 | 0 | 49 | 1 | 50 | 0 |
| | | Normal | 67 (100%) | 0 | 49 (100%) | 1 (100%) | 50 (100%) | 0 |
| | 16 | n | 68 | 0 | 39 | 1 | 37 | 0 |
| | | Normal | 68 (100%) | 0 | 39 (100%) | 1 (100%) | 37 (100%) | 0 |
| | 20 | n | 66 | 0 | 29 | 1 | 31 | 0 |
| | | Normal | 66 (100%) | 0 | 29 (100%) | 1 (100%) | 31 (100%) | 0 |
| | 24 | n | 57 | 0 | 25 | 1 | 30 | 0 |
| | | Normal | 57 (100%) | 0 | 25 (100%) | 1 (100%) | 30 (100%) | 0 |
| | 26 | n | 57 | 0 | 23 | 1 | 27 | 0 |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|------------|----------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| Week | Shift to | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| | Normal | 57 (100%) | 0 | 23 (100%) | 1 (100%) | 26 (96%) | 0 |
| | High | 0 | 0 | 0 | 0 | 1 (4%) | 0 |
| HEMATOLOGY | | | | | | | |
| ----- | | | | | | | |
| BASOPHILS | | | | | | | |
| 2 | n | 82 | 0 | 77 | 0 | 77 | 0 |
| | Normal | 82 (100%) | 0 | 77 (100%) | 0 | 77 (100%) | 0 |
| 4 | n | 78 | 0 | 69 | 0 | 69 | 0 |
| | Normal | 78 (100%) | 0 | 69 (100%) | 0 | 69 (100%) | 0 |
| 6 | n | 72 | 0 | 59 | 0 | 62 | 0 |
| | Normal | 72 (100%) | 0 | 59 (100%) | 0 | 62 (100%) | 0 |
| 8 | n | 71 | 0 | 56 | 0 | 55 | 0 |
| | Normal | 71 (100%) | 0 | 56 (100%) | 0 | 55 (100%) | 0 |
| 12 | n | 65 | 0 | 48 | 0 | 49 | 0 |
| | Normal | 65 (100%) | 0 | 48 (100%) | 0 | 49 (100%) | 0 |
| 16 | n | 67 | 0 | 39 | 0 | 36 | 0 |
| | Normal | 67 (100%) | 0 | 39 (100%) | 0 | 36 (100%) | 0 |
| 20 | n | 64 | 0 | 29 | 0 | 31 | 0 |
| | Normal | 64 (100%) | 0 | 29 (100%) | 0 | 31 (100%) | 0 |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|-------------|--------|-----------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| | Week | Shift to | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| EOSINOPHILS | 24 | n | 57 | 0 | 24 | 0 | 29 | 0 |
| | | Normal | 57 (100%) | 0 | 24 (100%) | 0 | 29 (100%) | 0 |
| | 26 | n | 56 | 0 | 24 | 0 | 26 | 0 |
| | | Normal | 56 (100%) | 0 | 24 (100%) | 0 | 26 (100%) | 0 |
| | 2 | n | 82 | 0 | 76 | 1 | 77 | 0 |
| | | Normal | 82 (100%) | 0 | 74 (97%) | 1 (100%) | 77 (100%) | 0 |
| | | High | 0 | 0 | 2 (3%) | 0 | 0 | 0 |
| | 4 | n | 78 | 0 | 69 | 0 | 69 | 0 |
| | | Normal | 78 (100%) | 0 | 69 (100%) | 0 | 68 (99%) | 0 |
| | | High | 0 | 0 | 0 | 0 | 1 (1%) | 0 |
| | 6 | n | 72 | 0 | 59 | 0 | 62 | 0 |
| | | Normal | 72 (100%) | 0 | 59 (100%) | 0 | 58 (94%) | 0 |
| | | High | 0 | 0 | 0 | 0 | 4 (6%) | 0 |
| | 8 | n | 71 | 0 | 56 | 0 | 55 | 0 |
| | | Normal | 71 (100%) | 0 | 53 (95%) | 0 | 52 (95%) | 0 |
| | | High | 0 | 0 | 3 (5%) | 0 | 3 (5%) | 0 |
| 12 | n | 65 | 0 | 48 | 0 | 49 | 0 | |
| | Normal | 65 (100%) | 0 | 46 (96%) | 0 | 49 (100%) | 0 | |
| | High | 0 | 0 | 2 (4%) | 0 | 0 | 0 | |
| 16 | n | 67 | 0 | 39 | 0 | 36 | 0 | |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | | |
|--|--------|----------------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| | Week | Shift to | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| ERY. MEAN CORPUSCULAR HB CONCENTRATION | | Normal | 67 (100%) | 0 | 39 (100%) | 0 | 35 (97%) | 0 |
| | | High | 0 | 0 | 0 | 0 | 1 (3%) | 0 |
| | 20 | n | 64 | 0 | 29 | 0 | 31 | 0 |
| | | Normal | 64 (100%) | 0 | 29 (100%) | 0 | 31 (100%) | 0 |
| | 24 | n | 57 | 0 | 24 | 0 | 29 | 0 |
| | | Normal | 57 (100%) | 0 | 24 (100%) | 0 | 29 (100%) | 0 |
| | 26 | n | 56 | 0 | 24 | 0 | 26 | 0 |
| | | Normal | 56 (100%) | 0 | 24 (100%) | 0 | 26 (100%) | 0 |
| | 2 | n | 82 | 0 | 76 | 0 | 76 | 0 |
| | | Normal | 82 (100%) | 0 | 76 (100%) | 0 | 76 (100%) | 0 |
| | 4 | n | 76 | 0 | 67 | 0 | 67 | 0 |
| | | Normal | 76 (100%) | 0 | 67 (100%) | 0 | 67 (100%) | 0 |
| | 6 | n | 71 | 0 | 57 | 0 | 63 | 0 |
| | | Normal | 71 (100%) | 0 | 57 (100%) | 0 | 63 (100%) | 0 |
| | 8 | n | 70 | 0 | 53 | 0 | 55 | 0 |
| | | Normal | 70 (100%) | 0 | 53 (100%) | 0 | 55 (100%) | 0 |
| 12 | n | 64 | 0 | 47 | 0 | 49 | 0 | |
| | Normal | 64 (100%) | 0 | 47 (100%) | 0 | 49 (100%) | 0 | |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04
Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|-------------------------------------|----------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| Week | Shift to | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| ERY. MEAN CORPUSCULAR HEMOGLOBIN | 16 n | 67 | 0 | 39 | 0 | 36 | 0 |
| | Normal | 67 (100%) | 0 | 39 (100%) | 0 | 36 (100%) | 0 |
| | 20 n | 63 | 0 | 29 | 0 | 31 | 0 |
| | Normal | 63 (100%) | 0 | 29 (100%) | 0 | 31 (100%) | 0 |
| | 24 n | 57 | 0 | 24 | 0 | 29 | 0 |
| | Normal | 57 (100%) | 0 | 24 (100%) | 0 | 29 (100%) | 0 |
| | 26 n | 55 | 0 | 24 | 0 | 26 | 0 |
| | Normal | 55 (100%) | 0 | 24 (100%) | 0 | 26 (100%) | 0 |
| | 2 n | 82 | 0 | 77 | 0 | 77 | 0 |
| | Normal | 82 (100%) | 0 | 77 (100%) | 0 | 77 (100%) | 0 |
| | 4 n | 78 | 0 | 69 | 0 | 69 | 0 |
| | Normal | 78 (100%) | 0 | 69 (100%) | 0 | 69 (100%) | 0 |
| | 6 n | 72 | 0 | 59 | 0 | 63 | 0 |
| | Normal | 72 (100%) | 0 | 59 (100%) | 0 | 63 (100%) | 0 |
| | 8 n | 71 | 0 | 56 | 0 | 55 | 0 |
| | Normal | 71 (100%) | 0 | 56 (100%) | 0 | 55 (100%) | 0 |
| | 12 n | 65 | 0 | 48 | 0 | 49 | 0 |

NOTES: Only subjects with baseline results are included in the summary.
There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | | |
|------------------------------|----------|--------------------|------------------|--------------------|------------------|--------------------|------------------|---|
| Week | Shift to | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | |
| | Normal | 65 (100%) | 0 | 48 (100%) | 0 | 49 (100%) | 0 | |
| 16 | n | 67 | 0 | 39 | 0 | 36 | 0 | |
| | Normal | 67 (100%) | 0 | 39 (100%) | 0 | 36 (100%) | 0 | |
| 20 | n | 64 | 0 | 29 | 0 | 31 | 0 | |
| | Normal | 64 (100%) | 0 | 29 (100%) | 0 | 31 (100%) | 0 | |
| 24 | n | 57 | 0 | 24 | 0 | 29 | 0 | |
| | Normal | 57 (100%) | 0 | 24 (100%) | 0 | 29 (100%) | 0 | |
| 26 | n | 56 | 0 | 24 | 0 | 26 | 0 | |
| | Normal | 56 (100%) | 0 | 24 (100%) | 0 | 26 (100%) | 0 | |
| ERY. MEAN CORPUSCULAR VOLUME | 2 | n | 82 | 0 | 76 | 0 | 76 | 0 |
| | | Normal | 82 (100%) | 0 | 76 (100%) | 0 | 76 (100%) | 0 |
| 4 | n | 76 | 0 | 67 | 0 | 67 | 0 | |
| | Normal | 76 (100%) | 0 | 67 (100%) | 0 | 67 (100%) | 0 | |
| 6 | n | 71 | 0 | 57 | 0 | 63 | 0 | |
| | Normal | 71 (100%) | 0 | 57 (100%) | 0 | 63 (100%) | 0 | |
| 8 | n | 70 | 0 | 53 | 0 | 55 | 0 | |
| | Normal | 70 (100%) | 0 | 53 (100%) | 0 | 55 (100%) | 0 | |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | | |
|--------------|------|----------------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| | Week | Shift to | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| ERYTHROCYTES | 12 | n | 64 | 0 | 47 | 0 | 49 | 0 |
| | | Normal | 64 (100%) | 0 | 47 (100%) | 0 | 49 (100%) | 0 |
| | 16 | n | 67 | 0 | 39 | 0 | 36 | 0 |
| | | Normal | 67 (100%) | 0 | 39 (100%) | 0 | 36 (100%) | 0 |
| | 20 | n | 63 | 0 | 29 | 0 | 31 | 0 |
| | | Normal | 63 (100%) | 0 | 29 (100%) | 0 | 31 (100%) | 0 |
| | 24 | n | 57 | 0 | 24 | 0 | 29 | 0 |
| | | Normal | 57 (100%) | 0 | 24 (100%) | 0 | 29 (100%) | 0 |
| | 26 | n | 55 | 0 | 24 | 0 | 26 | 0 |
| | | Normal | 55 (100%) | 0 | 24 (100%) | 0 | 26 (100%) | 0 |
| | 2 | n | 82 | 0 | 77 | 0 | 77 | 0 |
| | | Normal | 82 (100%) | 0 | 77 (100%) | 0 | 77 (100%) | 0 |
| | 4 | n | 78 | 0 | 69 | 0 | 69 | 0 |
| | | Normal | 78 (100%) | 0 | 69 (100%) | 0 | 69 (100%) | 0 |
| | 6 | n | 72 | 0 | 59 | 0 | 63 | 0 |
| | | Normal | 72 (100%) | 0 | 59 (100%) | 0 | 63 (100%) | 0 |
| | 8 | n | 71 | 0 | 56 | 0 | 55 | 0 |
| | | Normal | 71 (100%) | 0 | 56 (100%) | 0 | 55 (100%) | 0 |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|------------|------|----------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| | Week | Shift to | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| HEMATOCRIT | 12 | n | 65 | 0 | 48 | 0 | 49 | 0 |
| | | Normal | 65 (100%) | 0 | 48 (100%) | 0 | 49 (100%) | 0 |
| | 16 | n | 67 | 0 | 39 | 0 | 36 | 0 |
| | | Normal | 67 (100%) | 0 | 39 (100%) | 0 | 36 (100%) | 0 |
| | 20 | n | 64 | 0 | 29 | 0 | 31 | 0 |
| | | Normal | 64 (100%) | 0 | 29 (100%) | 0 | 31 (100%) | 0 |
| | 24 | n | 57 | 0 | 24 | 0 | 29 | 0 |
| | | Normal | 57 (100%) | 0 | 24 (100%) | 0 | 29 (100%) | 0 |
| | 26 | n | 56 | 0 | 24 | 0 | 26 | 0 |
| | | Normal | 56 (100%) | 0 | 24 (100%) | 0 | 26 (100%) | 0 |
| | 2 | n | 82 | 0 | 76 | 0 | 76 | 0 |
| | | Normal | 82 (100%) | 0 | 76 (100%) | 0 | 76 (100%) | 0 |
| | 4 | n | 76 | 0 | 67 | 0 | 67 | 0 |
| | | Normal | 76 (100%) | 0 | 67 (100%) | 0 | 67 (100%) | 0 |
| | 6 | n | 71 | 0 | 57 | 0 | 63 | 0 |
| | | Normal | 71 (100%) | 0 | 57 (100%) | 0 | 63 (100%) | 0 |
| | 8 | n | 70 | 0 | 53 | 0 | 55 | 0 |
| | | Normal | 70 (100%) | 0 | 53 (100%) | 0 | 55 (100%) | 0 |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|------------|------|----------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| | Week | Shift to | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| HEMOGLOBIN | 12 | n | 64 | 0 | 47 | 0 | 49 | 0 |
| | | Normal | 64 (100%) | 0 | 47 (100%) | 0 | 49 (100%) | 0 |
| | 16 | n | 67 | 0 | 39 | 0 | 36 | 0 |
| | | Normal | 67 (100%) | 0 | 39 (100%) | 0 | 36 (100%) | 0 |
| | 20 | n | 63 | 0 | 29 | 0 | 31 | 0 |
| | | Normal | 63 (100%) | 0 | 29 (100%) | 0 | 31 (100%) | 0 |
| | 24 | n | 57 | 0 | 24 | 0 | 29 | 0 |
| | | Normal | 57 (100%) | 0 | 24 (100%) | 0 | 29 (100%) | 0 |
| | 26 | n | 55 | 0 | 24 | 0 | 26 | 0 |
| | | Normal | 55 (100%) | 0 | 24 (100%) | 0 | 26 (100%) | 0 |
| | 2 | n | 82 | 0 | 77 | 0 | 77 | 0 |
| | | Normal | 82 (100%) | 0 | 77 (100%) | 0 | 77 (100%) | 0 |
| | 4 | n | 78 | 0 | 69 | 0 | 69 | 0 |
| | | Normal | 78 (100%) | 0 | 69 (100%) | 0 | 69 (100%) | 0 |
| | 6 | n | 72 | 0 | 59 | 0 | 63 | 0 |
| | | Normal | 72 (100%) | 0 | 59 (100%) | 0 | 63 (100%) | 0 |
| | 8 | n | 71 | 0 | 56 | 0 | 55 | 0 |
| | | Normal | 71 (100%) | 0 | 56 (100%) | 0 | 55 (100%) | 0 |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|------------|------|----------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| | Week | Shift to | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| LEUKOCYTES | 12 | n | 65 | 0 | 48 | 0 | 49 | 0 |
| | | Normal | 65 (100%) | 0 | 48 (100%) | 0 | 49 (100%) | 0 |
| | 16 | n | 67 | 0 | 39 | 0 | 36 | 0 |
| | | Normal | 67 (100%) | 0 | 39 (100%) | 0 | 36 (100%) | 0 |
| | 20 | n | 64 | 0 | 29 | 0 | 31 | 0 |
| | | Normal | 64 (100%) | 0 | 29 (100%) | 0 | 31 (100%) | 0 |
| | 24 | n | 57 | 0 | 24 | 0 | 29 | 0 |
| | | Normal | 57 (100%) | 0 | 24 (100%) | 0 | 29 (100%) | 0 |
| | 26 | n | 56 | 0 | 24 | 0 | 26 | 0 |
| | | Normal | 56 (100%) | 0 | 24 (100%) | 0 | 26 (100%) | 0 |
| | 2 | n | 82 | 0 | 77 | 0 | 77 | 0 |
| | | Normal | 82 (100%) | 0 | 77 (100%) | 0 | 77 (100%) | 0 |
| | 4 | n | 78 | 0 | 69 | 0 | 69 | 0 |
| | | Normal | 78 (100%) | 0 | 69 (100%) | 0 | 69 (100%) | 0 |
| | 6 | n | 72 | 0 | 59 | 0 | 63 | 0 |
| | | Normal | 72 (100%) | 0 | 59 (100%) | 0 | 63 (100%) | 0 |
| | 8 | n | 71 | 0 | 56 | 0 | 55 | 0 |
| | | Normal | 71 (100%) | 0 | 56 (100%) | 0 | 55 (100%) | 0 |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|-------------|----------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| Week | Shift to | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| LYMPHOCYTES | 12 n | 65 | 0 | 48 | 0 | 49 | 0 |
| | Normal | 65 (100%) | 0 | 48 (100%) | 0 | 49 (100%) | 0 |
| | 16 n | 67 | 0 | 39 | 0 | 36 | 0 |
| | Normal | 67 (100%) | 0 | 39 (100%) | 0 | 36 (100%) | 0 |
| | 20 n | 64 | 0 | 29 | 0 | 31 | 0 |
| | Normal | 64 (100%) | 0 | 29 (100%) | 0 | 31 (100%) | 0 |
| | 24 n | 57 | 0 | 24 | 0 | 29 | 0 |
| | Normal | 57 (100%) | 0 | 24 (100%) | 0 | 29 (100%) | 0 |
| | 26 n | 56 | 0 | 24 | 0 | 26 | 0 |
| | Normal | 56 (100%) | 0 | 24 (100%) | 0 | 26 (100%) | 0 |
| | 2 n | 82 | 0 | 77 | 0 | 77 | 0 |
| | Normal | 82 (100%) | 0 | 77 (100%) | 0 | 77 (100%) | 0 |
| | 4 n | 78 | 0 | 69 | 0 | 69 | 0 |
| | Normal | 78 (100%) | 0 | 69 (100%) | 0 | 69 (100%) | 0 |
| | 6 n | 72 | 0 | 59 | 0 | 62 | 0 |
| | Normal | 72 (100%) | 0 | 59 (100%) | 0 | 62 (100%) | 0 |
| | 8 n | 71 | 0 | 56 | 0 | 55 | 0 |
| | Normal | 70 (99%) | 0 | 56 (100%) | 0 | 55 (100%) | 0 |
| | High | 1 (1%) | 0 | 0 | 0 | 0 | 0 |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04
Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|-----------|----------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| Week | Shift to | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| MONOCYTES | 12 n | 65 | 0 | 48 | 0 | 49 | 0 |
| | Normal | 64 (98%) | 0 | 48 (100%) | 0 | 49 (100%) | 0 |
| | High | 1 (2%) | 0 | 0 | 0 | 0 | 0 |
| | 16 n | 67 | 0 | 39 | 0 | 36 | 0 |
| | Normal | 67 (100%) | 0 | 39 (100%) | 0 | 36 (100%) | 0 |
| | 20 n | 64 | 0 | 29 | 0 | 31 | 0 |
| | Normal | 64 (100%) | 0 | 29 (100%) | 0 | 31 (100%) | 0 |
| | 24 n | 57 | 0 | 24 | 0 | 29 | 0 |
| | Normal | 57 (100%) | 0 | 24 (100%) | 0 | 29 (100%) | 0 |
| | 26 n | 56 | 0 | 24 | 0 | 26 | 0 |
| | Normal | 56 (100%) | 0 | 24 (100%) | 0 | 26 (100%) | 0 |
| | 2 n | 82 | 0 | 77 | 0 | 77 | 0 |
| | Normal | 82 (100%) | 0 | 77 (100%) | 0 | 77 (100%) | 0 |
| | 4 n | 78 | 0 | 69 | 0 | 69 | 0 |
| | Normal | 78 (100%) | 0 | 69 (100%) | 0 | 69 (100%) | 0 |
| | 6 n | 72 | 0 | 59 | 0 | 62 | 0 |
| | Normal | 71 (99%) | 0 | 59 (100%) | 0 | 62 (100%) | 0 |
| | Low | 1 (1%) | 0 | 0 | 0 | 0 | 0 |

NOTES: Only subjects with baseline results are included in the summary.
There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|----------|----------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| Week | Shift to | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| 8 | n | 71 | 0 | 56 | 0 | 55 | 0 |
| | Normal | 71 (100%) | 0 | 56 (100%) | 0 | 55 (100%) | 0 |
| 12 | n | 65 | 0 | 48 | 0 | 49 | 0 |
| | Normal | 65 (100%) | 0 | 48 (100%) | 0 | 49 (100%) | 0 |
| 16 | n | 67 | 0 | 39 | 0 | 36 | 0 |
| | Normal | 66 (99%) | 0 | 39 (100%) | 0 | 36 (100%) | 0 |
| | Low | 1 (1%) | 0 | 0 | 0 | 0 | 0 |
| 20 | n | 64 | 0 | 29 | 0 | 31 | 0 |
| | Normal | 64 (100%) | 0 | 29 (100%) | 0 | 31 (100%) | 0 |
| 24 | n | 57 | 0 | 24 | 0 | 29 | 0 |
| | Normal | 57 (100%) | 0 | 24 (100%) | 0 | 29 (100%) | 0 |
| 26 | n | 56 | 0 | 24 | 0 | 26 | 0 |
| | Normal | 56 (100%) | 0 | 24 (100%) | 0 | 26 (100%) | 0 |
| PLATELET | n | 82 | 0 | 74 | 0 | 77 | 0 |
| | Normal | 82 (100%) | 0 | 74 (100%) | 0 | 77 (100%) | 0 |
| 4 | n | 77 | 0 | 67 | 0 | 68 | 0 |
| | Normal | 77 (100%) | 0 | 67 (100%) | 0 | 68 (100%) | 0 |
| 6 | n | 72 | 0 | 57 | 0 | 61 | 0 |
| | Normal | 72 (100%) | 0 | 57 (100%) | 0 | 61 (100%) | 0 |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.04

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges, by Visit

| Week | Shift to | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | |
|------|----------|--------------------|------------------|--------------------|------------------|--------------------|------------------|
| | | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline |
| 8 | n | 71 | 0 | 55 | 0 | 54 | 0 |
| | Normal | 71 (100%) | 0 | 55 (100%) | 0 | 54 (100%) | 0 |
| 12 | n | 64 | 0 | 47 | 0 | 48 | 0 |
| | Normal | 64 (100%) | 0 | 47 (100%) | 0 | 48 (100%) | 0 |
| 16 | n | 67 | 0 | 37 | 0 | 36 | 0 |
| | Normal | 67 (100%) | 0 | 37 (100%) | 0 | 36 (100%) | 0 |
| 20 | n | 64 | 0 | 28 | 0 | 30 | 0 |
| | Normal | 64 (100%) | 0 | 28 (100%) | 0 | 30 (100%) | 0 |
| 24 | n | 56 | 0 | 22 | 0 | 28 | 0 |
| | Normal | 56 (100%) | 0 | 22 (100%) | 0 | 28 (100%) | 0 |
| 26 | n | 55 | 0 | 23 | 0 | 26 | 0 |
| | Normal | 55 (100%) | 0 | 23 (100%) | 0 | 26 (100%) | 0 |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshiftweek.sas

21:05 Monday, June 26, 2006

Table 14-6.05

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges

| | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | | | |
|----------------------------|--------|----------------|-----------|-----------------|-----------|------------------|-----------|----------|-------|
| | | Shift | Normal at | High at | Normal at | High at | Normal at | High at | p- |
| | | [1] | Baseline | Baseline | Baseline | Baseline | Baseline | Baseline | value |
| | | | | | | | | | |
| CHEMISTRY | | | | | | | | | |
| ----- | | | | | | | | | |
| ALANINE AMINOTRANSFERASE | n | | 82 | 2 | 79 | 1 | 80 | 0 | 0.828 |
| | Normal | | 80 (98%) | 0 | 78 (99%) | 0 | 78 (98%) | 0 | |
| | High | | 2 (2%) | 2 (100%) | 1 (1%) | 1 (100%) | 2 (3%) | 0 | |
| ALBUMIN | n | | 84 | 0 | 80 | 0 | 80 | 0 | |
| | Normal | | 84 (100%) | 0 | 80 (100%) | 0 | 80 (100%) | 0 | |
| | | | | | | | | | |
| ALKALINE PHOSPHATASE | n | | 82 | 2 | 79 | 0 | 79 | 1 | 0.611 |
| | Normal | | 81 (99%) | 0 | 78 (99%) | 0 | 79 (100%) | 0 | |
| | High | | 1 (1%) | 2 (100%) | 1 (1%) | 0 | 0 | 1 (100%) | |
| ASPARTATE AMINOTRANSFERASE | n | | 82 | 2 | 79 | 1 | 80 | 0 | 0.770 |
| | Normal | | 79 (96%) | 1 (50%) | 77 (97%) | 1 (100%) | 78 (98%) | 0 | |
| | High | | 3 (4%) | 1 (50%) | 2 (3%) | 0 | 2 (3%) | 0 | |
| BILIRUBIN | n | | 84 | 0 | 80 | 0 | 79 | 1 | 0.353 |
| | Normal | | 83 (99%) | 0 | 80 (100%) | 0 | 77 (97%) | 0 | |
| | | | | | | | | | |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

[1] A subject is counted only once for each analyte. A change will be considered shifting from normal at baseline to abnormal or from abnormal at baseline to normal at any visit during the treatment. The treatment period is defined as any planned visit after Week 0 (Visit 3), up to and including Week 24 (Visit 12).

[2] CMH test for general association, controlling for status at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshift.sas

21:05 Monday, June 26, 2006

Table 14-6.05

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges

| | Shift [1] | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | | p- value [2] |
|-------------------------------|--------------|-----------------------|---------------------|-----------------------|---------------------|-----------------------|---------------------|--------------------|
| | | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | |
| | High | 1 (1%) | 0 | 0 | 0 | 2 (3%) | 1 (100%) | |
| CALCIUM | n | 84 | 0 | 80 | 0 | 80 | 0 | |
| | Normal | 84 (100%) | 0 | 80 (100%) | 0 | 80 (100%) | 0 | |
| CHLORIDE | n | 84 | 0 | 80 | 0 | 79 | 0 | |
| | Normal | 84 (100%) | 0 | 80 (100%) | 0 | 79 (100%) | 0 | |
| CHOLESTEROL | n | 84 | 0 | 80 | 0 | 80 | 0 | |
| | Normal | 84 (100%) | 0 | 80 (100%) | 0 | 80 (100%) | 0 | |
| CREATINE KINASE | n | 84 | 0 | 79 | 1 | 77 | 3 | 0.811 |
| | Normal | 77 (92%) | 0 | 74 (94%) | 1 (100%) | 72 (94%) | 1 (33%) | |
| | High | 7 (8%) | 0 | 5 (6%) | 0 | 5 (6%) | 2 (67%) | |
| CREATININE | n | 84 | 0 | 80 | 0 | 80 | 0 | |
| | Normal | 84 (100%) | 0 | 80 (100%) | 0 | 80 (100%) | 0 | |
| GAMMA GLUTAMYL TRANSFERASE | n | 82 | 2 | 78 | 2 | 78 | 2 | 0.898 |
| | Normal | 80 (98%) | 0 | 75 (96%) | 1 (50%) | 76 (97%) | 1 (50%) | |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

[1] A subject is counted only once for each analyte. A change will be considered shifting from normal at baseline to abnormal or from abnormal at baseline to normal at any visit during the treatment. The treatment period is defined as any planned visit after Week 0 (Visit 3), up to and including Week 24 (Visit 12).

[2] CMH test for general association, controlling for status at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshift.sas

21:05 Monday, June 26, 2006

Table 14-6.05

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges

| | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | | p-value [2] |
|-----------|--------------|-----------------------|---------------------|-----------------------|---------------------|-----------------------|---------------------|----------------|
| | Shift [1] | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | |
| | High | 2 (2%) | 2 (100%) | 3 (4%) | 1 (50%) | 2 (3%) | 1 (50%) | |
| GLUCOSE | n | 83 | 1 | 80 | 0 | 80 | 0 | 0.354 |
| | Normal | 83 (100%) | 1 (100%) | 79 (99%) | 0 | 78 (98%) | 0 | |
| | High | 0 | 0 | 1 (1%) | 0 | 2 (3%) | 0 | |
| PHOSPHATE | n | 84 | 0 | 79 | 0 | 80 | 0 | |
| | Normal | 84 (100%) | 0 | 79 (100%) | 0 | 80 (100%) | 0 | |
| POTASSIUM | n | 84 | 0 | 79 | 0 | 79 | 0 | |
| | Normal | 84 (100%) | 0 | 79 (100%) | 0 | 79 (100%) | 0 | |
| PROTEIN | n | 84 | 0 | 80 | 0 | 80 | 0 | |
| | Normal | 84 (100%) | 0 | 80 (100%) | 0 | 80 (100%) | 0 | |
| SODIUM | n | 84 | 0 | 80 | 0 | 79 | 0 | |
| | Normal | 84 (100%) | 0 | 80 (100%) | 0 | 79 (100%) | 0 | |
| URATE | n | 84 | 0 | 80 | 0 | 80 | 0 | |
| | Normal | 84 (100%) | 0 | 80 (100%) | 0 | 80 (100%) | 0 | |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

[1] A subject is counted only once for each analyte. A change will be considered shifting from normal at baseline to abnormal or from abnormal at baseline to normal at any visit during the treatment. The treatment period is defined as any planned visit after Week 0 (Visit 3), up to and including Week 24 (Visit 12).

[2] CMH test for general association, controlling for status at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshift.sas

21:05 Monday, June 26, 2006

Table 14-6.05

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges

| | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | | |
|---|-----------|--------------------|------------------|--------------------|------------------|--------------------|------------------|-------------|
| | Shift [1] | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | p-value [2] |
| UREA NITROGEN | n | 84 | 0 | 78 | 2 | 80 | 0 | 0.363 |
| | Normal | 84 (100%) | 0 | 78 (100%) | 2 (100%) | 79 (99%) | 0 | |
| | High | 0 | 0 | 0 | 0 | 1 (1%) | 0 | |
| HEMATOLOGY | | | | | | | | |
| ----- | | | | | | | | |
| BASOPHILS | n | 83 | 0 | 79 | 0 | 78 | 0 | 0.044 |
| | Normal | 83 (100%) | 0 | 79 (100%) | 0 | 78 (100%) | 0 | |
| EOSINOPHILS | n | 83 | 0 | 78 | 1 | 78 | 0 | |
| | Normal | 83 (100%) | 0 | 73 (94%) | 1 (100%) | 72 (92%) | 0 | |
| | High | 0 | 0 | 5 (6%) | 0 | 6 (8%) | 0 | |
| ERY. MEAN CORPUSCULAR HBn CONCENTRATION | n | 82 | 0 | 78 | 0 | 77 | 0 | |
| | Normal | 82 (100%) | 0 | 78 (100%) | 0 | 77 (100%) | 0 | |
| ERY. MEAN CORPUSCULAR HEMOGLOBIN | n | 83 | 0 | 79 | 0 | 78 | 0 | |
| | Normal | 83 (100%) | 0 | 79 (100%) | 0 | 78 (100%) | 0 | |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

[1] A subject is counted only once for each analyte. A change will be considered shifting from normal at baseline to abnormal or from abnormal at baseline to normal at any visit during the treatment. The treatment period is defined as any planned visit after Week 0 (Visit 3), up to and including Week 24 (Visit 12).

[2] CMH test for general association, controlling for status at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshift.sas

21:05 Monday, June 26, 2006

Table 14-6.05

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges

| | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | | p-value [2] |
|---------------------------------|--------------|-----------------------|---------------------|-----------------------|---------------------|-----------------------|---------------------|----------------|
| | Shift [1] | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | |
| ERY. MEAN CORPUSCULAR VOLUME | n | 82 | 0 | 78 | 0 | 77 | 0 | 0.388 |
| | Normal | 82 (100%) | 0 | 78 (100%) | 0 | 77 (100%) | 0 | |
| ERYTHROCYTES | n | 83 | 0 | 79 | 0 | 78 | 0 | |
| | Normal | 83 (100%) | 0 | 79 (100%) | 0 | 78 (100%) | 0 | |
| HEMATOCRIT | n | 82 | 0 | 78 | 0 | 77 | 0 | |
| | Normal | 82 (100%) | 0 | 78 (100%) | 0 | 77 (100%) | 0 | |
| HEMOGLOBIN | n | 83 | 0 | 79 | 0 | 78 | 0 | |
| | Normal | 83 (100%) | 0 | 79 (100%) | 0 | 78 (100%) | 0 | |
| LEUKOCYTES | n | 83 | 0 | 79 | 0 | 78 | 0 | |
| | Normal | 83 (100%) | 0 | 79 (100%) | 0 | 78 (100%) | 0 | |
| LYMPHOCYTES | n | 83 | 0 | 79 | 0 | 78 | 0 | |
| | Normal | 82 (99%) | 0 | 79 (100%) | 0 | 78 (100%) | 0 | |
| | High | 1 (1%) | 0 | 0 | 0 | 0 | 0 | |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

[1] A subject is counted only once for each analyte. A change will be considered shifting from normal at baseline to abnormal or from abnormal at baseline to normal at any visit during the treatment. The treatment period is defined as any planned visit after Week 0 (Visit 3), up to and including Week 24 (Visit 12).

[2] CMH test for general association, controlling for status at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshift.sas

21:05 Monday, June 26, 2006

Table 14-6.05

Shifts of Laboratory Values During Treatment, Categorized Based on Threshold Ranges

| | Shift [1] | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | | p- value [2] |
|-----------|--------------|-----------------------|---------------------|-----------------------|---------------------|-----------------------|---------------------|--------------------|
| | | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | |
| MONOCYTES | n | 83 | 0 | 79 | 0 | 78 | 0 | 0.150 |
| | Normal | 81 (98%) | 0 | 79 (100%) | 0 | 78 (100%) | 0 | |
| | Low | 2 (2%) | 0 | 0 | 0 | 0 | 0 | |
| PLATELET | n | 83 | 0 | 77 | 0 | 78 | 0 | |
| | Normal | 83 (100%) | 0 | 77 (100%) | 0 | 78 (100%) | 0 | |

NOTES: Only subjects with baseline results are included in the summary.

There were no subjects with abnormal low values at baseline.

[1] A subject is counted only once for each analyte. A change will be considered shifting from normal at baseline to abnormal or from abnormal at baseline to normal at any visit during the treatment. The treatment period is defined as any planned visit after Week 0 (Visit 3), up to and including Week 24 (Visit 12).

[2] CMH test for general association, controlling for status at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_labshift.sas

21:05 Monday, June 26, 2006

Table 14-6.06
Shifts of Hy's Law Values During Treatment

| | | Placebo (N=86) | | Xan. Low (N=84) | | Xan. High (N=84) | | p-value [2] |
|--|--------------|-----------------------|---------------------|-----------------------|---------------------|-----------------------|---------------------|----------------|
| | Shift [1] | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | Normal at Baseline | High at Baseline | |
| Transaminase 1.5 x ULN | n | 82 | 2 | 80 | 2 | 80 | 0 | 0.392 |
| | Normal | 79 (96%) | 0 | 79 (99%) | 1 (50%) | 77 (96%) | 0 | |
| | High | 3 (4%) | 2 (100%) | 1 (1%) | 1 (50%) | 3 (4%) | 0 | |
| Total Bili 1.5 x ULN and Transaminase 1.5 x ULN | n | 84 | 0 | 82 | 0 | 80 | 0 | 0.381 |
| | Normal | 83 (99%) | 0 | 82 (100%) | 0 | 80 (100%) | 0 | |
| | High | 1 (1%) | 0 | 0 | 0 | 0 | 0 | |

NOTES: Only subjects with baseline results are included in the summary.

The single subject with elevated transaminase and elevated bilirubin also had elevated alk phos (>3xULN).

[1] A subject is counted only once for each analyte. A change will be considered shifting from normal at baseline to abnormal or from abnormal at baseline to normal at any visit during the treatment. The treatment period is defined as any planned visit after Week 0 (Visit 3), up to and including Week 24 (Visit 12).

[2] CMH test for general association, controlling for status at baseline.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rt_hyslaw.sas

21:03 Monday, June 26, 2006

Table 14-7.01
Summary of Vital Signs at Baseline and End of Treatment

| Measure | Position | Treatment | N | Planned Relative Time | n | Mean | SD | Median | Min. | Max. |
|--------------------------------|-----------------------------------|-----------|----|-----------------------------|----|-------|-------|--------|-------|-------|
| Systolic Blood Pressure (mmHg) | AFTER LYING DOWN FOR 5 MINUTES | Placebo | 86 | Baseline | 85 | 138.6 | 16.75 | 140.0 | 90.0 | 180.0 |
| | | | | Week 24 | 59 | 135.8 | 17.30 | 131.0 | 100.0 | 180.0 |
| | | | | End of Trt. | 84 | 136.7 | 18.30 | 134.0 | 100.0 | 180.0 |
| | | Xan.Low | 84 | Baseline | 84 | 138.8 | 16.55 | 138.0 | 100.0 | 178.0 |
| | | | | Week 24 | 27 | 134.1 | 16.74 | 136.0 | 100.0 | 173.0 |
| | | | | End of Trt. | 84 | 135.7 | 17.17 | 134.0 | 100.0 | 190.0 |
| | AFTER STANDING FOR 1 MINUTE | Placebo | 86 | Baseline | 85 | 135.3 | 17.89 | 134.0 | 90.0 | 180.0 |
| | | | | Week 24 | 59 | 133.5 | 19.23 | 130.0 | 90.0 | 199.0 |
| | | | | End of Trt. | 84 | 133.9 | 18.68 | 130.5 | 90.0 | 199.0 |
| | | Xan.Low | 84 | Baseline | 84 | 135.6 | 18.04 | 136.0 | 100.0 | 186.0 |
| | | | | Week 24 | 27 | 131.0 | 17.82 | 130.0 | 92.0 | 168.0 |
| | | | | End of Trt. | 84 | 132.8 | 17.53 | 130.0 | 92.0 | 180.0 |
| | AFTER STANDING FOR 3 MINUTES | Placebo | 86 | Baseline | 85 | 136.5 | 18.77 | 136.0 | 80.0 | 184.0 |
| | | | | Week 24 | 30 | 130.4 | 20.83 | 128.0 | 96.0 | 198.0 |
| | | | | End of Trt. | 82 | 130.4 | 20.37 | 128.0 | 90.0 | 198.0 |
| | | Xan.High | 84 | Baseline | 84 | 140.1 | 17.82 | 141.0 | 100.0 | 188.0 |
| | | | | Week 24 | 30 | 132.2 | 18.18 | 130.0 | 101.0 | 178.0 |
| | | | | End of Trt. | 82 | 134.0 | 17.86 | 130.0 | 101.0 | 178.0 |

End of treatment is the last on-treatment assessment of the specified vital sign (on or before the Week 24 visit).

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rtvs.sas

21:06 Monday, June 26, 2006

Table 14-7.01
Summary of Vital Signs at Baseline and End of Treatment

| Measure | Position | Treatment | N | Planned Relative Time | n | Mean | SD | Median | Min. | Max. |
|---------------------------------|--------------------------------|-----------|----|-----------------------------|----|----------|-------|--------|-------|-------|
| Diastolic Blood Pressure (mmHg) | AFTER LYING DOWN FOR 5 MINUTES | Placebo | 86 | Week 24 | 59 | 134.8 | 17.35 | 131.0 | 100.0 | 190.0 |
| | | | | End of Trt. | 84 | 134.1 | 18.01 | 130.0 | 90.0 | 190.0 |
| | | | | Xan.Low | 84 | Baseline | 84 | 136.4 | 18.11 | 134.5 |
| | | | | Week 24 | 27 | 131.0 | 17.92 | 130.0 | 100.0 | 168.0 |
| | | | | End of Trt. | 83 | 133.1 | 17.80 | 130.0 | 98.0 | 200.0 |
| | | | | Xan.High | 84 | Baseline | 84 | 138.8 | 18.75 | 138.0 |
| | | | | Week 24 | 30 | 129.2 | 16.95 | 126.0 | 90.0 | 172.0 |
| | | | | End of Trt. | 81 | 130.4 | 17.77 | 130.0 | 88.0 | 184.0 |
| | | Placebo | 86 | Baseline | 85 | 75.7 | 11.09 | 76.0 | 40.0 | 99.0 |
| | | | | Week 24 | 59 | 72.9 | 11.32 | 74.0 | 44.0 | 109.0 |
| | | | | End of Trt. | 84 | 74.5 | 11.11 | 76.0 | 44.0 | 109.0 |
| | | | | Xan.Low | 84 | Baseline | 84 | 76.3 | 9.77 | 76.0 |
| | | | | Week 24 | 27 | 76.1 | 9.14 | 76.0 | 60.0 | 90.0 |
| | | | | End of Trt. | 84 | 74.3 | 8.88 | 74.0 | 45.0 | 90.0 |
| | | | | Xan.High | 84 | Baseline | 84 | 77.2 | 9.80 | 78.0 |
| | | | | Week 24 | 30 | 73.9 | 9.23 | 74.0 | 60.0 | 92.0 |
| | | | | End of Trt. | 82 | 74.1 | 9.27 | 74.0 | 56.0 | 94.0 |
| | AFTER STANDING FOR 1 MINUTE | Placebo | 86 | Baseline | 85 | 77.9 | 10.63 | 78.0 | 51.0 | 104.0 |
| | | | | Week 24 | 59 | 74.2 | 12.89 | 74.0 | 45.0 | 117.0 |
| | | | | End of Trt. | 84 | 74.9 | 12.16 | 76.0 | 45.0 | 117.0 |

End of treatment is the last on-treatment assessment of the specified vital sign (on or before the Week 24 visit).

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rtvs.sas

21:06 Monday, June 26, 2006

Table 14-7.01
Summary of Vital Signs at Baseline and End of Treatment

| Measure | Position | Treatment | N | Planned Relative Time | n | Mean | SD | Median | Min. | Max. |
|-------------|-----------------------------------|-----------|----|-----------------------------|----|------|-------|--------|------|-------|
| Pulse (bpm) | | Xan.Low | 84 | Baseline | 84 | 76.2 | 10.14 | 78.0 | 54.0 | 98.0 |
| | | | | Week 24 | 27 | 76.3 | 10.28 | 78.0 | 60.0 | 98.0 |
| | | | | End of Trt. | 84 | 75.0 | 9.34 | 75.0 | 51.0 | 98.0 |
| | | Xan.High | 84 | Baseline | 84 | 78.1 | 10.77 | 78.0 | 56.0 | 108.0 |
| | | | | Week 24 | 30 | 74.9 | 11.00 | 76.0 | 50.0 | 97.0 |
| | | | | End of Trt. | 82 | 75.9 | 11.77 | 76.5 | 48.0 | 112.0 |
| | | Placebo | 86 | Baseline | 85 | 77.7 | 11.00 | 78.0 | 46.0 | 110.0 |
| | | | | Week 24 | 59 | 74.3 | 11.38 | 74.0 | 51.0 | 110.0 |
| | | | | End of Trt. | 84 | 75.0 | 11.19 | 74.5 | 51.0 | 110.0 |
| | AFTER STANDING FOR 3 MINUTES | Xan.Low | 84 | Baseline | 84 | 76.6 | 10.93 | 76.0 | 48.0 | 108.0 |
| | | | | Week 24 | 27 | 76.2 | 10.18 | 76.0 | 57.0 | 98.0 |
| | | | | End of Trt. | 83 | 74.9 | 9.66 | 74.0 | 57.0 | 102.0 |
| | | Xan.High | 84 | Baseline | 84 | 79.6 | 10.19 | 80.0 | 51.0 | 104.0 |
| | | | | Week 24 | 30 | 76.0 | 10.63 | 78.5 | 50.0 | 98.0 |
| | | | | End of Trt. | 81 | 76.8 | 11.71 | 78.0 | 50.0 | 118.0 |
| | AFTER LYING DOWN FOR 5 MINUTES | Placebo | 86 | Baseline | 85 | 70.4 | 10.46 | 70.0 | 51.0 | 100.0 |
| | | | | Week 24 | 59 | 69.1 | 9.46 | 68.0 | 50.0 | 92.0 |
| | | | | End of Trt. | 84 | 69.3 | 9.42 | 68.5 | 50.0 | 92.0 |
| | | Xan.Low | 84 | Baseline | 84 | 68.8 | 9.52 | 68.0 | 50.0 | 88.0 |

End of treatment is the last on-treatment assessment of the specified vital sign (on or before the Week 24 visit).

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rtvs.sas

21:06 Monday, June 26, 2006

Table 14-7.01
Summary of Vital Signs at Baseline and End of Treatment

| Measure | Position | Treatment | N | Planned Relative Time | n | Mean | SD | Median | Min. | Max. |
|---------------------------------|----------|-----------|----|-----------------------------|----|------|-------|--------|------|-------|
| AFTER STANDING FOR 1 MINUTE | | | | Week 24 | 27 | 68.1 | 9.28 | 68.0 | 52.0 | 90.0 |
| | | | | End of Trt. | 84 | 67.8 | 10.55 | 68.0 | 48.0 | 100.0 |
| | | | | | | | | | | |
| | | Xan.High | 84 | Baseline | 84 | 70.1 | 9.27 | 68.0 | 52.0 | 98.0 |
| | | | | Week 24 | 30 | 69.3 | 11.88 | 68.0 | 47.0 | 96.0 |
| | | | | End of Trt. | 82 | 68.1 | 11.27 | 68.0 | 47.0 | 100.0 |
| | | Placebo | 86 | Baseline | 85 | 75.5 | 12.68 | 76.0 | 56.0 | 133.0 |
| | | | | Week 24 | 59 | 72.8 | 8.98 | 74.0 | 52.0 | 88.0 |
| | | | | End of Trt. | 84 | 73.5 | 9.09 | 74.0 | 52.0 | 96.0 |
| | | Xan.Low | 84 | Baseline | 84 | 73.5 | 10.59 | 72.0 | 53.0 | 100.0 |
| | | | | Week 24 | 27 | 72.1 | 9.53 | 74.0 | 52.0 | 88.0 |
| | | | | End of Trt. | 84 | 73.0 | 10.84 | 73.0 | 51.0 | 104.0 |
| | | Xan.High | 84 | Baseline | 84 | 75.0 | 10.89 | 72.0 | 56.0 | 104.0 |
| | | | | Week 24 | 30 | 73.4 | 11.93 | 72.0 | 54.0 | 98.0 |
| | | | | End of Trt. | 82 | 72.6 | 11.11 | 71.0 | 52.0 | 100.0 |
| AFTER STANDING FOR 3 MINUTES | | Placebo | 86 | Baseline | 85 | 74.6 | 11.94 | 74.0 | 54.0 | 134.0 |
| | | | | Week 24 | 59 | 72.8 | 8.73 | 74.0 | 56.0 | 88.0 |
| | | | | End of Trt. | 84 | 73.4 | 9.08 | 74.0 | 56.0 | 98.0 |
| | | Xan.Low | 84 | Baseline | 84 | 72.3 | 10.99 | 70.0 | 51.0 | 104.0 |
| | | | | Week 24 | 27 | 70.7 | 10.78 | 72.0 | 52.0 | 96.0 |
| | | | | End of Trt. | 83 | 71.6 | 10.42 | 72.0 | 52.0 | 97.0 |
| | | | | | | | | | | |
| | | | | | | | | | | |
| | | | | | | | | | | |

End of treatment is the last on-treatment assessment of the specified vital sign (on or before the Week 24 visit).

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rtvs.sas

21:06 Monday, June 26, 2006

Table 14-7.01
Summary of Vital Signs at Baseline and End of Treatment

| Measure | Position | Treatment | N | Planned Relative Time | n | Mean | SD | Median | Min. | Max. |
|---------|----------|-----------|----|-----------------------------|----|------|-------|--------|------|-------|
| | | Xan.High | 84 | Baseline | 84 | 74.0 | 10.76 | 72.0 | 52.0 | 100.0 |
| | | | | Week 24 | 30 | 72.4 | 11.92 | 71.5 | 54.0 | 96.0 |
| | | | | End of Trt. | 81 | 71.8 | 10.76 | 70.0 | 54.0 | 106.0 |

End of treatment is the last on-treatment assessment of the specified vital sign (on or before the Week 24 visit).

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rtvs.sas

21:06 Monday, June 26, 2006

Table 14-7.02
Summary of Vital Signs Change from Baseline at End of Treatment

| Measure | Position | Treatment | N | Planned Relative Time | n | Mean | SD | Median | Min. | Max. |
|--------------------------------|-----------------------------------|-----------|----|-----------------------------|----|------|-------|--------|-------|------|
| Systolic Blood Pressure (mmHg) | AFTER LYING DOWN FOR 5 MINUTES | Placebo | 86 | Week 24 | 58 | -2.1 | 14.73 | -4.0 | -28.0 | 50.0 |
| | | | | End of Trt. | 83 | -2.0 | 16.76 | -4.0 | -32.0 | 50.0 |
| | | Xan.Low | 84 | Week 24 | 27 | -0.3 | 17.19 | 2.0 | -48.0 | 30.0 |
| | | | | End of Trt. | 84 | -3.1 | 16.57 | -2.0 | -48.0 | 34.0 |
| | | Xan.High | 84 | Week 24 | 30 | -5.6 | 17.18 | -7.0 | -36.0 | 26.0 |
| | | | | End of Trt. | 82 | -5.8 | 14.48 | -8.0 | -36.0 | 29.0 |
| | AFTER STANDING FOR 1 MINUTE | Placebo | 86 | Week 24 | 58 | -1.7 | 16.87 | 0.0 | -32.0 | 40.0 |
| | | | | End of Trt. | 83 | -1.6 | 17.76 | 0.0 | -46.0 | 48.0 |
| | | Xan.Low | 84 | Week 24 | 27 | -0.1 | 17.73 | -1.0 | -30.0 | 48.0 |
| | | | | End of Trt. | 84 | -2.8 | 17.40 | -1.5 | -52.0 | 48.0 |
| | | Xan.High | 84 | Week 24 | 30 | -6.3 | 19.49 | -9.0 | -36.0 | 42.0 |
| | | | | End of Trt. | 82 | -6.7 | 16.98 | -8.0 | -44.0 | 42.0 |
| | AFTER STANDING FOR 3 MINUTES | Placebo | 86 | Week 24 | 58 | -1.0 | 15.80 | -3.5 | -36.0 | 38.0 |
| | | | | End of Trt. | 83 | -2.5 | 16.61 | -4.0 | -40.0 | 48.0 |
| | | Xan.Low | 84 | Week 24 | 27 | -0.1 | 16.20 | 0.0 | -30.0 | 30.0 |
| | | | | End of Trt. | 83 | -3.5 | 16.51 | -4.0 | -52.0 | 60.0 |
| | | Xan.High | 84 | Week 24 | 30 | -9.0 | 16.88 | -8.0 | -40.0 | 30.0 |
| | | | | | | | | | | |

End of treatment is the last on-treatment assessment of the specified vital sign (on or before the Week 24 visit).

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rtvs.sas

21:06 Monday, June 26, 2006

Table 14-7.02
Summary of Vital Signs Change from Baseline at End of Treatment

| Measure | Position | Treatment | N | Planned Relative Time | n | Mean | SD | Median | Min. | Max. |
|---------------------------------|-----------------------------------|-----------|----|-----------------------------|----|------|-------|--------|-------|------|
| | | | | End of Trt. | 81 | -8.3 | 15.21 | -8.0 | -40.0 | 30.0 |
| Diastolic Blood Pressure (mmHg) | AFTER LYING DOWN FOR 5 MINUTES | Placebo | 86 | Week 24 | 58 | -0.8 | 10.82 | -0.5 | -18.0 | 41.0 |
| | | | | End of Trt. | 83 | -1.0 | 10.99 | 0.0 | -34.0 | 41.0 |
| | | Xan.Low | 84 | Week 24 | 27 | -0.9 | 7.71 | -2.0 | -20.0 | 16.0 |
| | | | | End of Trt. | 84 | -2.0 | 8.80 | -2.0 | -30.0 | 18.0 |
| | | Xan.High | 84 | Week 24 | 30 | -2.2 | 9.20 | -1.0 | -20.0 | 21.0 |
| | | | | End of Trt. | 82 | -3.1 | 8.79 | -4.0 | -24.0 | 21.0 |
| | AFTER STANDING FOR 1 MINUTE | Placebo | 86 | Week 24 | 58 | -2.3 | 10.08 | -4.0 | -23.0 | 24.0 |
| | | | | End of Trt. | 83 | -2.8 | 10.17 | -2.0 | -34.0 | 24.0 |
| | | Xan.Low | 84 | Week 24 | 27 | 1.0 | 7.30 | 2.0 | -20.0 | 18.0 |
| | | | | End of Trt. | 84 | -1.2 | 8.93 | 0.0 | -30.0 | 20.0 |
| | | Xan.High | 84 | Week 24 | 30 | -2.3 | 10.85 | -7.0 | -18.0 | 22.0 |
| | | | | End of Trt. | 82 | -2.1 | 12.10 | -2.0 | -34.0 | 28.0 |
| | AFTER STANDING FOR 3 MINUTES | Placebo | 86 | Week 24 | 58 | -2.3 | 9.56 | -3.5 | -22.0 | 20.0 |
| | | | | End of Trt. | 83 | -2.7 | 9.36 | -2.0 | -30.0 | 20.0 |
| | | Xan.Low | 84 | Week 24 | 27 | -1.6 | 8.29 | 0.0 | -20.0 | 10.0 |
| | | | | End of Trt. | 83 | -1.8 | 9.69 | -1.0 | -24.0 | 38.0 |

End of treatment is the last on-treatment assessment of the specified vital sign (on or before the Week 24 visit).

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rtvs.sas

21:06 Monday, June 26, 2006

Table 14-7.02
Summary of Vital Signs Change from Baseline at End of Treatment

| Measure | Position | Treatment | N | Planned Relative Time | n | Mean | SD | Median | Min. | Max. |
|-------------|-----------------------------------|-----------|----|-----------------------------|----|------|-------|--------|-------|------|
| Pulse (bpm) | AFTER LYING DOWN FOR 5 MINUTES | Xan.High | 84 | Week 24 | 30 | -2.1 | 9.77 | -3.5 | -20.0 | 16.0 |
| | | | | End of Trt. | 81 | -2.6 | 10.81 | -2.0 | -40.0 | 27.0 |
| | | Placebo | 86 | Week 24 | 58 | -0.3 | 8.77 | -1.0 | -24.0 | 24.0 |
| | | | | End of Trt. | 83 | -0.9 | 8.69 | -1.0 | -24.0 | 24.0 |
| | | Xan.Low | 84 | Week 24 | 27 | -1.6 | 10.53 | 0.0 | -24.0 | 25.0 |
| | | | | End of Trt. | 84 | -1.0 | 11.12 | -0.5 | -24.0 | 32.0 |
| | AFTER STANDING FOR 1 MINUTE | Xan.High | 84 | Week 24 | 30 | -2.0 | 11.16 | -2.0 | -34.0 | 20.0 |
| | | | | End of Trt. | 82 | -1.7 | 8.95 | -2.0 | -34.0 | 20.0 |
| | | Placebo | 86 | Week 24 | 58 | -1.7 | 11.72 | 0.5 | -53.0 | 18.0 |
| | | | | End of Trt. | 83 | -1.8 | 11.05 | -1.0 | -53.0 | 20.0 |
| | | Xan.Low | 84 | Week 24 | 27 | -1.3 | 9.05 | 0.0 | -20.0 | 12.0 |
| | | | | End of Trt. | 84 | -0.5 | 11.69 | 0.0 | -24.0 | 34.0 |
| | AFTER STANDING FOR 3 MINUTES | Xan.High | 84 | Week 24 | 30 | -1.8 | 13.41 | -3.0 | -36.0 | 20.0 |
| | | | | End of Trt. | 82 | -2.1 | 10.43 | -1.5 | -36.0 | 22.0 |
| | | Placebo | 86 | Week 24 | 58 | -1.5 | 10.47 | 0.0 | -46.0 | 14.0 |
| | | | | End of Trt. | 83 | -1.0 | 9.89 | 0.0 | -46.0 | 18.0 |

End of treatment is the last on-treatment assessment of the specified vital sign (on or before the Week 24 visit).

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rtvs.sas

21:06 Monday, June 26, 2006

Table 14-7.02
Summary of Vital Signs Change from Baseline at End of Treatment

| Measure | Position | Treatment | N | Planned Relative Time | n | Mean | SD | Median | Min. | Max. |
|----------|----------|-----------|---|-----------------------------|----|------|-------|--------|-------|------|
| | | | | | | | | | | |
| Xan.Low | | 84 | | Week 24 | 27 | -2.1 | 8.77 | -2.0 | -20.0 | 16.0 |
| | | | | End of Trt. | 83 | -0.7 | 10.73 | -1.0 | -22.0 | 29.0 |
| Xan.High | | 84 | | Week 24 | 30 | -2.7 | 11.12 | -2.0 | -40.0 | 14.0 |
| | | | | End of Trt. | 81 | -1.9 | 9.49 | -1.0 | -40.0 | 20.0 |

End of treatment is the last on-treatment assessment of the specified vital sign (on or before the Week 24 visit).

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rtvs.sas

21:06 Monday, June 26, 2006

Table 14-7.03
Summary of Weight Change from Baseline at End of Treatment

| Measure | Treatment | N | Planned Relative | n | Mean | SD | Median | Min. | Max. |
|--------------------------------|-----------|----|---------------------|----|------|-------|--------|-------|-------|
| | | | Time | | | | | | |
| Weight (kg) | Placebo | 86 | Baseline | 86 | 62.8 | 12.77 | 60.6 | 34.0 | 86.2 |
| | | | Week 24 | 59 | 63.2 | 12.58 | 63.5 | 34.0 | 86.6 |
| | | | End of Trt. | 84 | 63.3 | 12.66 | 64.0 | 34.0 | 86.6 |
| | Xan.Low | 84 | Baseline | 83 | 67.3 | 14.13 | 64.9 | 45.4 | 106.1 |
| | | | Week 24 | 27 | 67.4 | 14.07 | 62.6 | 45.5 | 106.1 |
| | | | End of Trt. | 84 | 66.7 | 14.32 | 65.9 | 41.7 | 106.1 |
| | Xan.High | 84 | Baseline | 84 | 70.0 | 14.65 | 69.2 | 41.7 | 108.0 |
| | | | Week 24 | 30 | 71.1 | 15.82 | 68.7 | 49.9 | 105.7 |
| | | | End of Trt. | 81 | 69.7 | 14.00 | 70.3 | 42.2 | 105.7 |
| Weight Change from Baseline | Placebo | 86 | Week 24 | 59 | 0.1 | 2.30 | 0.0 | -4.5 | 8.2 |
| | | | End of Trt. | 84 | 0.2 | 2.05 | 0.0 | -4.5 | 8.2 |
| | Xan.Low | 84 | Week 24 | 27 | -0.3 | 2.04 | 0.0 | -5.4 | 3.2 |
| | | | End of Trt. | 83 | -0.4 | 2.41 | 0.0 | -14.5 | 5.9 |
| | Xan.High | 84 | Week 24 | 30 | 1.0 | 6.47 | -0.2 | -4.5 | 33.3 |
| | | | End of Trt. | 81 | 0.1 | 4.19 | -0.4 | -5.5 | 33.3 |

End of treatment is the last on-treatment assessment of weight (on or before the Week 24 visit).

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\rtvs.sas

21:06 Monday, June 26, 2006

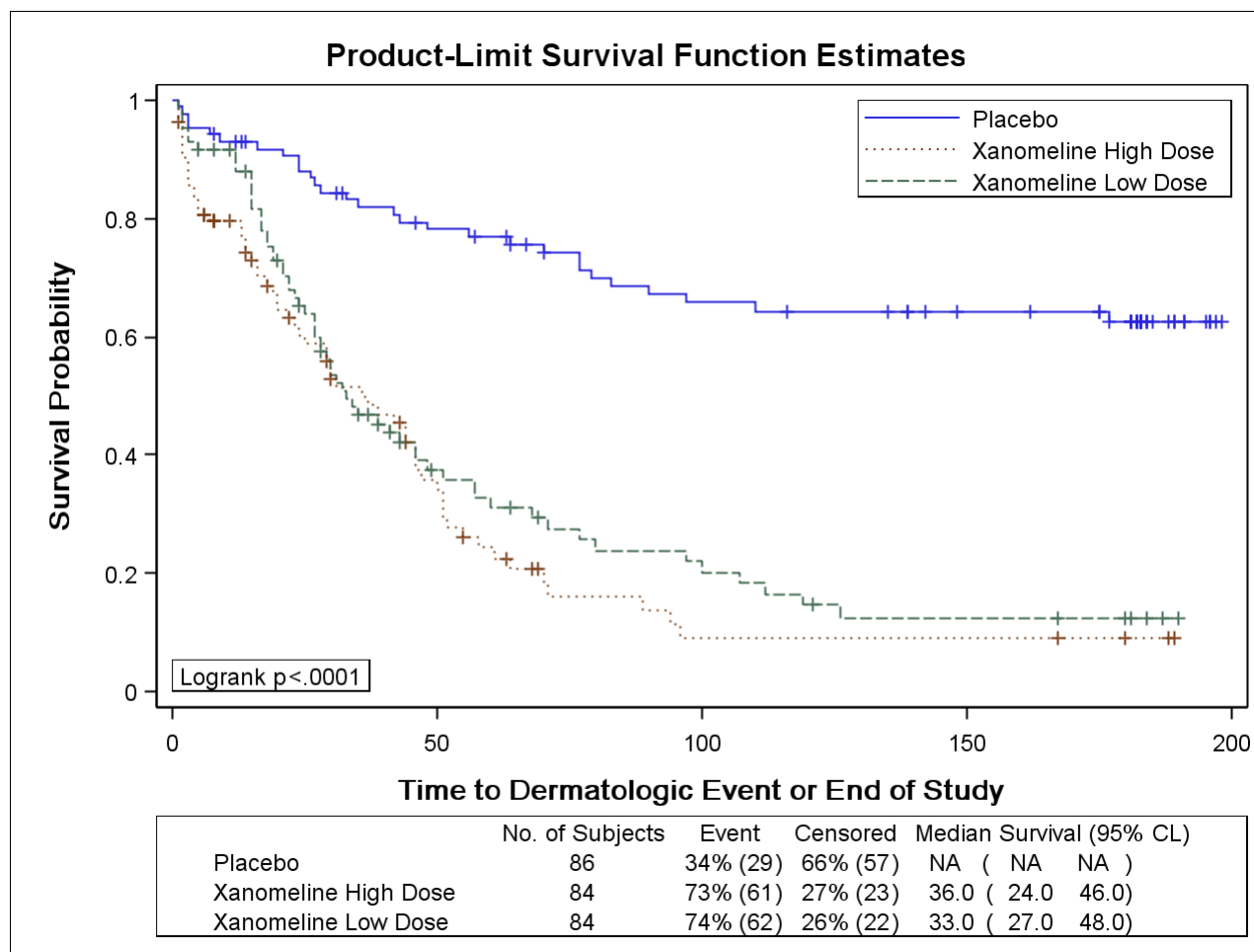
Table 14-7.04
Summary of Concomitant Medications (Number of Subjects)

| Therapeutic class, n (%) | Placebo (N=86) | Xanomeline Low Dose (N=84) | Xanomeline High Dose (N=84) |
|--|-------------------|----------------------------------|-----------------------------------|
| Patients receiving at least one concomitant medication | 77 (90%) | 74 (88%) | 78 (93%) |
| ALIMENTARY TRACT AND METABOLISM | 12 (14%) | 11 (13%) | 9 (11%) |
| CALCIUM | 7 (8%) | 6 (7%) | 3 (4%) |
| ALGELDRATE | 2 (2%) | 0 | 2 (2%) |
| LOPERAMIDE HYDROCHLORIDE | 1 (1%) | 1 (1%) | 1 (1%) |
| METFORMIN HYDROCHLORIDE | 1 (1%) | 1 (1%) | 0 |
| NIZATIDINE | 1 (1%) | 1 (1%) | 4 (5%) |
| CALCIUM CARBONATE | 0 | 0 | 1 (1%) |
| CIMETIDINE | 0 | 1 (1%) | 0 |
| SIMETICONE | 0 | 2 (2%) | 0 |
| ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS | 1 (1%) | 0 | 1 (1%) |
| LEUPRORELIN ACETATE | 1 (1%) | 0 | 1 (1%) |
| BLOOD AND BLOOD FORMING ORGANS | 0 | 1 (1%) | 0 |
| FERROUS SULFATE | 0 | 1 (1%) | 0 |
| CARDIOVASCULAR SYSTEM | 12 (14%) | 12 (14%) | 7 (8%) |
| AMLODIPINE | 8 (9%) | 1 (1%) | 2 (2%) |
| FUROSEMIDE | 2 (2%) | 2 (2%) | 1 (1%) |
| NIFEDIPINE | 2 (2%) | 0 | 0 |
| DOXAZOSIN MESILATE | 1 (1%) | 2 (2%) | 1 (1%) |
| DIGOXIN | 0 | 3 (4%) | 2 (2%) |
| DILTIAZEM HYDROCHLORIDE | 0 | 0 | 1 (1%) |
| FELODIPINE | 0 | 1 (1%) | 0 |
| FLUVASTATIN | 0 | 2 (2%) | 0 |
| LOSARTAN POTASSIUM | 0 | 2 (2%) | 0 |
| DERMATOLOGICALS | 0 | 0 | 1 (1%) |

Table 14-7.04
Summary of Concomitant Medications (Number of Subjects)

| Therapeutic class, n (%) | Placebo (N=86) | Xanomeline Low Dose (N=84) | Xanomeline High Dose (N=84) |
|--|-------------------|----------------------------------|-----------------------------------|
| CLOBETASOL PROPIONATE | 0 | 0 | 1 (1%) |
| GENITO URINARY SYSTEM AND SEX HORMONES | 6 (7%) | 10 (12%) | 5 (6%) |
| ESTROGENS CONJUGATED | 6 (7%) | 10 (12%) | 5 (6%) |
| NERVOUS SYSTEM | 23 (27%) | 14 (17%) | 8 (10%) |
| ACETYLSALICYLIC ACID | 21 (24%) | 11 (13%) | 6 (7%) |
| ALPRAZOLAM | 1 (1%) | 0 | 0 |
| DONEPEZIL HYDROCHLORIDE | 1 (1%) | 2 (2%) | 2 (2%) |
| SUMATRIPTAN | 1 (1%) | 0 | 0 |
| HALOPERIDOL | 0 | 1 (1%) | 0 |
| PAROXETINE HYDROCHLORIDE | 0 | 1 (1%) | 0 |
| RESPIRATORY SYSTEM | 4 (5%) | 1 (1%) | 4 (5%) |
| SALBUTAMOL SULFATE | 2 (2%) | 1 (1%) | 0 |
| GUAIFENESIN | 1 (1%) | 0 | 0 |
| IPRATROPIUM BROMIDE | 1 (1%) | 0 | 0 |
| NAPROXEN SODIUM | 1 (1%) | 0 | 3 (4%) |
| BUDESONIDE | 0 | 0 | 1 (1%) |
| SYSTEMIC HORMONAL PREPARATIONS, EXCL. | 2 (2%) | 13 (15%) | 8 (10%) |
| HYDROCORTISONE | 2 (2%) | 13 (15%) | 8 (10%) |
| UNCODED | 74 (86%) | 70 (83%) | 77 (92%) |
| UNCODED | 74 (86%) | 70 (83%) | 77 (92%) |

Figure 14-1
Time to Dermatologic Event by Treatment Group



Note: Dermatologic events were identified as adverse events associated with skin conditions such as rash, pruritus, dermatitis. A full list of adverse event terms is presented in the final study report.

Source: C:\cdisc_pilot\PROGRAMS\DRAFT\TFLs\kmfigure.sas

21:45 Monday, June 26, 2006