R Consortium R Submission Pilot 1 - Summary Tables and Figures

Version: Jan 18, 2022

Note: In this pilot, different open-source packages were used when generating each of the 4 analysis outputs to test wider use case scenarios. The outputs were formatted differently intentionally to cover different company specific formatting choices.

Table 14-2.01

Summary of Demographic and Baseline Characteristics

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Protocol: CDISCPILOT01
Population: Intent-to-Treat

  ----------------------------------------------------------------------------
                                    Placebo    Xanomeline Low Dose  Xanomeline High Dose
                                    (N=86)           (N=84)               (N=84)
  ----------------------------------------------------------------------------
Age
  Mean (sd)                      75.21 (8.59)     75.67 (8.29)         74.38 (7.89)
  Median                              76              77.5                  76
  Min - Max                        52 - 89          51 - 88             56 - 88
Pooled Age Group 1
  <65                                 14               8                    11
  65-80                               42              47                    55
  >80                                 30              29                    18
Race
  WHITE                               78              78                    74
  BLACK OR AFRICAN AMERICAN            8               6                     9
  AMERICAN INDIAN OR ALASKA NATIVE     0               0                     1
Baseline Height (cm)
  Mean (sd)                     162.57 (11.52)   163.43 (10.42)       165.82 (10.13)
  Median                            162.6            162.6                165.1
  Min - Max                     137.2 - 185.4    135.9 - 195.6        146.1 - 190.5
Baseline Weight (kg)
  Mean (sd)                      62.76 (12.77)    67.28 (14.12)         70 (14.65)
  Median                            60.55            64.9                 69.2
  Min - Max                       34 - 86.2      45.4 - 106.1          41.7 - 108
Baseline BMI (kg/m^2)
  Mean (sd)                      23.64 (3.67)     25.06 (4.27)         25.35 (4.16)
  Median                             23.4             24.3                 24.8
  Min - Max                      15.1 - 33.3      17.7 - 40.1          13.7 - 34.5
MMSE Total
  Mean (sd)                      18.05 (4.27)     17.87 (4.22)         18.51 (4.16)
  Median                             19.5              18                   20
  Min - Max                       10 - 23          10 - 24              10 - 24
  ----------------------------------------------------------------------------

Program: tlf_demographic.Rmd
2021-11-11 19:39:23
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Table 14-3.01

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

Table 14-3.01
Primary Endpoint Analysis: ADAS Cog (11) - Change from Baseline to Week 24 - LOCF

	Placebo (N=79)	Xanomeline High Dose (N=74)	Xanomeline Low Dose (N=81)
Baseline			
n	79	74	81
Mean (SD)	24.1 (12.19)	21.3 (11.74)	24.4 (12.92)
Median (Range)	21.0 (5;61)	18.0 (3;57)	21.0 (5;57)
Week 24			
n	79	74	81
Mean (SD)	26.7 (13.79)	22.8 (12.48)	26.4 (13.18)
Median (Range)	24.0 (5;62)	20.0 (3;62)	25.0 (6;62)
Change from Baseline			
n	79	74	81
Mean (SD)	2.5 (5.80)	1.5 (4.26)	2.0 (5.55)
Median (Range)	2.0 (-11;16)	1.0 (-7;13)	2.0 (-11;17)
p-value(Dose Response) [1][2]		0.245	
p-value(Xan - Placebo) [1][3]		0.233	0.569
Diff of LS Means (SE)		-1.0 (0.84)	-0.5 (0.82)
95% CI		(-2.7;0.7)	(-2.1;1.1)
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: <run interactively>   *16:06 Tuesday, January 18, 2022*

Table 14-3.02

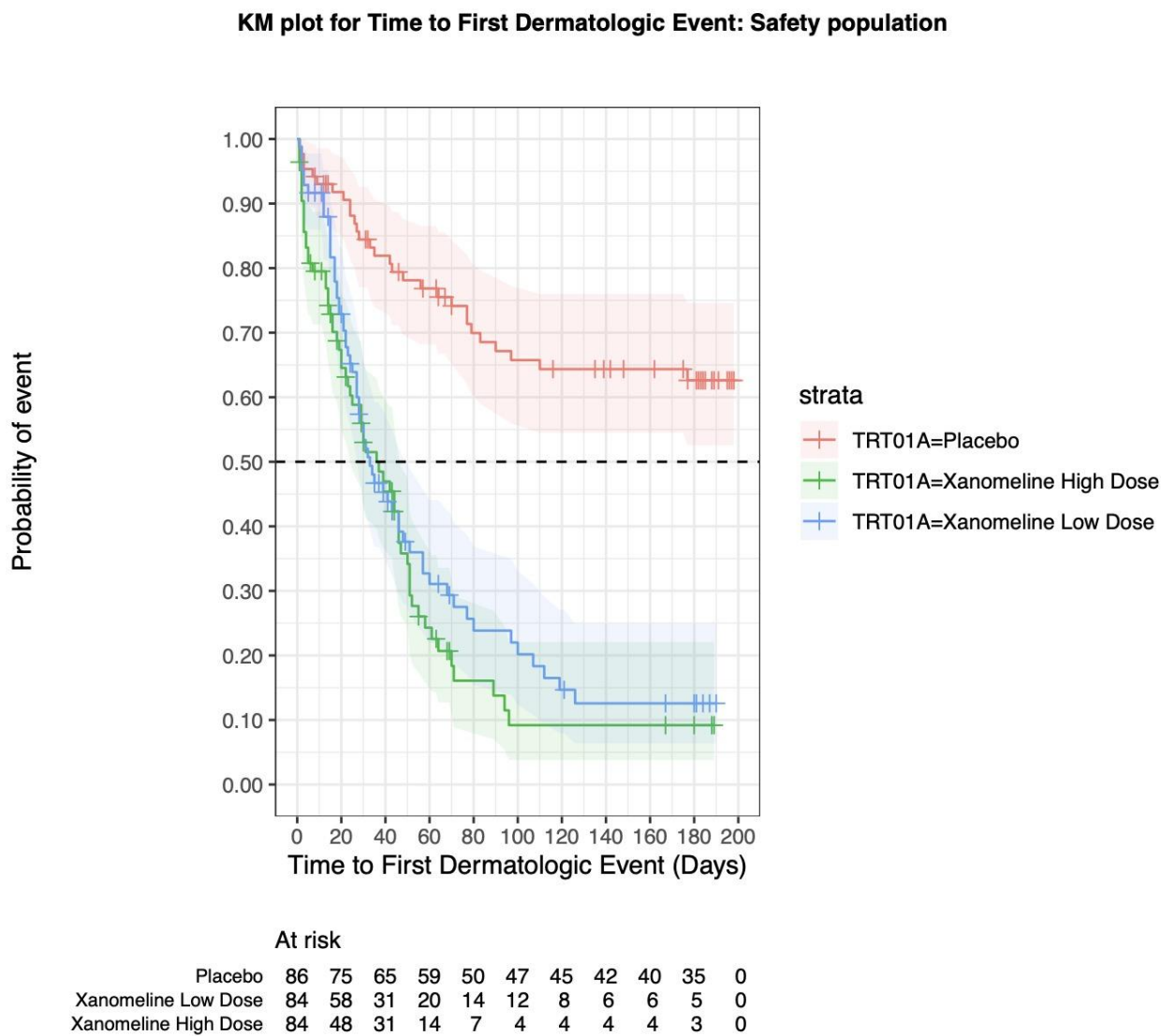**Primary Endpoint Analysis: CIBIC+ - Summary at Week 24 - LOCF**

ANCOVA of Change from Baseline at Week 20

Treatment	Baseline[a]		Week 20		Change from Baseline		
	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	LS Mean (95% CI)[b]
Study Drug	84	5.4 (1.34)	31	5.8 (1.61)	31	0.2 (1.47)	0.16 (-0.31, 0.63)
Placebo	86	5.6 (2.14)	65	5.8 (1.50)	65	0.1 (2.08)	0.09 (-0.23, 0.42)
Pairwise Comparison			Difference in LS Mean (95% CI)[b]				p-Value
Study Drug vs. Placebo			0.07 (-0.50, 0.63)				0.822
Root Mean Squared Error of Change = 1.31							
[a] Table is based on participants who have observable data at Baseline and Week 20. [b] Based on an Analysis of covariance (ANCOVA) model with treatment and baseline value as covariates CI = Confidence Interval, LS = Least Squares, SD = Standard Deviation							

Source: [pilot1wrappers: adam-adlbc]

Figure 14-1

Time to Dermatologic Event by Treatment Group

KM plot for Time to First Dermatologic Event: Safety population

At risk

Placebo	86	75	65	59	50	47	45	42	40	35	0
Xanomeline Low Dose	84	58	31	20	14	12	8	6	6	5	0
Xanomeline High Dose	84	48	31	14	7	4	4	4	4	3	0

Program: tlf_kmplot.Rmd [2021−11−11 19:30:38]