

13. DISCUSSION OF STUDY RESULTS AND CONCLUSIONS

A statistically significantly higher proportion of subjects in the active treatment groups withdrew prematurely from the study as compared to the placebo group. This is largely due to the higher proportion of subjects in the active treatment groups experiencing a dermatologic event and subsequently resulting in premature withdrawal from the study. This further hindered the study's ability to demonstrate efficacy.

A statistically significant dose response was not seen for both of the primary efficacy endpoints, change from baseline in ADAS-Cog (11) at Week 24 and CIBIC+ at Week 24, and for the secondary efficacy endpoint, mean NPI-X values from Week 4 to Week 24. Adjusted means for all 3 endpoints were similar across all treatment groups.

There were an increased number of dermatologic adverse events reported in the active treatment groups as compared to the placebo group. There were 3 serious adverse events. In addition, there were 3 deaths that were deemed unrelated to treatment.

For the laboratory data, subjects in both the xanomeline low and high dose groups showed more observations above normal range than the placebo group. Albumin was more often lower than the normal range for subjects in the placebo and xanomeline low dose group. Subjects in the xanomeline treatment groups had statistically significantly more values above the normal range than subjects in the placebo group for both urea nitrogen and eosinophils. There was a statistically significant association between clinically significant changes from the previous visit and treatment group for aspartate aminotransferase and eosinophils. Shifts from baseline for eosinophils were statistically significant with both xanomeline treatment groups showing more changes from normal to above normal than the placebo group. There was no significant association with treatment group in the Hy's law analysis examining shifts in liver function tests between baseline values and values while on treatment.

There were only minor changes from baseline in vital signs and weight at Week 24.

14. SUMMARY TABLES AND FIGURES