5-HT3 ANTAGONISTS

Pharmacokinetic/Pharmacodynamic (PK/PD) Model for the Safety of Tigecycline

Results

Results were derived from data obtained in 928 patients enrolled in one Phase 2 trial and two Phase 3 trials, receiving tigecycline as a 100-mg loading dose and 50-mg every 12 hours. The mean age was 46 years, and 56% of patients were women. 53% of patients were enrolled in North America, 21% in Europe, and 26% in Latin America. The mean weight was 73 kg, with a range of 39 to 157 kg. 64% of patients were men and 24%, 36%, and 18% were enrolled in North America, Europe, and Latin America, respectively. Baseline nausea or vomiting was reported in 47% and 35%, respectively.

50% of patients reported nausea, and 33% of patients reported vomiting, however most (62%; 67%) of first nausea and vomiting events occurred in 18% of patients in women. More men had N (23%; 17%) than men (15%; 11%) and North American patients were lower (10%) than in other regions. AUCSS(0-12) and Cmax were not predictive of nausea or vomiting events for tigecycline. The final nausea model would predict: nausea to be less in men, Europeans, and in the absence of baseline nausea. The final vomiting model would predict: heavier and heavier women have less vomiting.

CONCLUSIONS

• The Kaplan-Meier plot of estimated probability of first vomiting occurrence was 0.155, 0.146, and 0.036 for Latin America, North America and Other regions, respectively.

• The Hosmer-Lemeshow goodness-of-fit statistic was 2.85 with 8 degrees of freedom (p = 0.9435).

• The under the ROC curve statistic was 0.981, indicating an adequate fit and predicting probability of first vomiting occurrence.

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• As shown in Table 2, the final logistic regression model included weight, sex, region of treatment, baseline nausea, and the interaction of weight and region as significant predictors of the probability of first nausea occurrence (p = 0.0227).

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• The prediction for first vomiting occurrence was based on weight, sex, region of treatment, and baseline nausea.

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