S-380.

TREATMENT EFFECT MAY BE EASIER TO DETECT IN A HIGH ENROLLING SINGLE CENTER THAN IN A MORE HETEROGENEOUS MULTICENTER ENVIRONMENT: CASE STUDY IN PONV

AUTHORS: N. K. Singla,[1] T. J. Gan,[2] C. C. Apfel[3]

AFFILIATION: [1]Lotus Clinical Research, Inc., Pasadena, CA; [2]Duke University Medical Center, Durham, NC; 3UCSF Medical Center, San Francisco, CA

INTRODUCTION: When performing efficacy trials great care is taken to minimize variability in order to maximize the standardized treatment effect. We hypothesized that the exclusive use of high quality, high enrolling sites in a multicenter trial may significantly reduce variability. We extracted our site specific data from a multicenter trial to compare our treatment effect with the aggregate data generated by the remaining 28 sites.

METHODS: A total of 733 patients from 29 centers were included in the MITT analysis of a 3 arm, double blind, RCT.[1] Patients were randomized to receive prophylactic antiemetic therapy of aprepitant 40 mg, aprepitant 125 mg or ondansetron 4 mg with the primary endpoint of complete response (no vomiting and no use of rescue medication) over 24 h. In order to determine if the observed treatment effect was greater in our single center as compared to a multicenter environment, a post-hoc analysis was performed of (a) patients enrolled by our site and (b) of the remaining patients enrolled by the remaining 28 sites. For each group, we then calculated the odds ratio for the comparison of the two aprepitant doses versus ondansetron and calculated the number of patients necessary to demonstrate a significant difference compared to ondansetron, the active control (using standard type I error of 0.05 and type II error of 0.2, i.e. 80% power).

RESULTS: Our site enrolled 95 subjects while the 28 other sites collectively enrolled 638 subjects. When the odds ratio of complete response for aprepitant (both doses) compared to ondansetron was calculated utilizing our site data exclusively, the result was significantly greater than the odds ratios calculated utilizing aggregate data from the 28 remaining sites. Because study n has an inverse non-linear relationship with the odds ratio, large differences in the calculated value of the required patients per group are apparent (table 1).

DISCUSSION: Even though all centers in this analysis adhered to a standardized protocol, superiority of aprepitant versus ondansetron becomes apparent only in a highly controlled single center environment and not in a more heterogeneous multicenter setting. This may be a spurious finding; however we observed a similar effect in another other clinical trial.[2] If this is not due to chance, underlying reasons may be (a) that a single center may in general provide a more homogeneous environment and/or (b) that outcome data collected in this particular setting were of greater consistency.

REFERENCES:

1. Anesth Analg 104 (2007):1082
2. J Clin Pharmacol 2010; 50:1068

	Treatment Assignment)	Complete response (yes/total)	Complete response (%)	Odds ratio compared to ondansetron	Patients per group needed to demonstrate difference versus ondansetron
Single High Enrolling Site	Aprepitant 125 mg	19/31	61.3	**1.39**	**626**
	Aprepitant 40 mg	24/34	70.6	**2.1**	**134**
	Ondansetron 4 mg	16/30	53.3	-	-
Multicenter Aggregate Data	Aprepitant 125 mg	84/208	40.9	**0.99**	**298,973**
	Aprepitant 40 mg	87/214	40.7	**1.00**	**5,061,615**
	Ondansetron 4 mg	88/216	40.7	-	-