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<b>Study No:</b> TRA105120						
Title: An Open-label Study to Evaluate the Safety, Tolerability and Pharmacokinetics of Rosuvastatin when Co-administered with Eltrombopag (SB-497115-GR) in Healthy Adult Subjects						
<b>Rationale:</b> The aim of this study was to estimate the potential effects of repeat doses of eltrombopag on the pharmacokinetics (PK) of rosuvastatin.						
<b>Phase:</b> I						
<b>Study Period:</b> 18 May 2006 – 28 August 2006						
<b>Study Design:</b> This was an open-label study in healthy subjects.						
<b>Centers:</b> One center in the United States and one center in Singapore.						
<b>Indication:</b> Thrombocytopenia						
<b>Treatment:</b> Subjects received rosuvastatin and eltrombopag orally as follows: <ul style="list-style-type: none"> <li>• Day 1: rosuvastatin 10 mg once daily (<i>quaque die</i>, QD)</li> <li>• Day 6 through Day 9: eltrombopag 75 mg QD</li> <li>• Day 10: eltrombopag 75 mg QD + rosuvastatin 10 mg QD</li> </ul>						
<b>Objectives:</b> The primary objective of the study was to compare the pharmacokinetics (PK) of rosuvastatin when administered alone and with eltrombopag.						
<b>Statistical Methods:</b> The focus of the statistical analysis was to estimate the effect of repeat doses of eltrombopag on the PK of rosuvastatin. Following log <sub>e</sub> -transformation, AUC and C <sub>max</sub> were separately analyzed by analysis of variance (ANOVA), fitting terms for treatment and subject. Point estimates and 90% confidence intervals for the differences of "Day 10 – Day 1" (for rosuvastatin) were constructed using the appropriate error terms. The point estimates and associated 90% confidence intervals were then exponentially back-transformed to provide the point and 90% confidence interval estimates for the ratio "Day 10 : Day 1" as data permitted. The comparison was also made separately by Asian and Non-Asian.						
<b>Study Population:</b> Healthy adult male and female (of non-child bearing potential) subjects 18 to 64 years of age who had no clinically-significant abnormalities. Subjects were not eligible to participate if they had any clinically-relevant abnormality or a history of: Gilbert's syndrome, deep vein thrombosis or any other thromboembolic event, sensitivity to heparin or heparin induced thrombocytopenia, sensitivity to study medications or their components, thrombocytopenia or bleeding, or platelet clumping.						
<b>Number of Subjects:</b>						<b>Total</b>
Planned, N						36
Dosed, N						42
Completed, n (%)						40 (95)
Total Number Subjects Withdrawn, n (%)						2 (5)
Withdrawn Due to Adverse Events, n (%)						1 (2)
Withdrawn Due to Lack of Efficacy, n (%)						0
Withdrawn for Other Reasons, n (%)						1 (2)
<b>Demographics</b>						<b>Total</b>
N (Total)						42
Females: Males						9:33
Mean Age in Years (SD)						33.6 (7.80)
Mean Weight in Kg (SD)						73.8 (12.62)
<b>Race, n (%)</b>						<b>Total</b>
Black						12 (29)
Asian						22 (52)
White						4 (10)
American Indian or Alaska Native						4 (10)
<b>Pharmacokinetics (PK) Endpoints:</b>						
<b>Summary of Plasma Rosuvastatin PK Parameters and Comparisons by Race (N=39)</b>						
Plasma Rosuvastatin PK parameter	Rosuvastatin (Treatment A)			Rosuvastatin + Eltrombopag (Treatment C)		
	Asian (n=21)	Non-Asian (n=18)	Asian vs. Non-Asian	Asian (n=21)	Non-Asian (n=18)	Asian vs. Non-Asian

AUC (0-∞) (ng.hr/mL)	87.0 (58)	41.6 (58)	2.09 (1.60, 2.72)	114 (47)	78.2 (45)	1.46 (1.12, 1.91)
Cmax (ng/mL)	8.93 (63)	3.74 (59)	2.39 (1.81, 3.16)	14.4 (51)	9.91 (47)	1.45 (1.10, 1.92)
geometric mean (CVb%) for PK summary and GLS mean (90% CI) for treatment comparisons Treatment A: 10 mg rosuvastatin single dose Treatment C: 10 mg rosuvastatin single dose + 75 mg Eltrombopag (QD) x 5 days						
<b>Summary of Plasma Rosuvastatin PK Parameters and Treatment Comparisons (N=39)</b>						
<b>Plasma Rosuvastatin PK parameter</b>	<b>Rosuvastatin + Eltrombopag (Treatment C)</b>		<b>Rosuvastatin (Treatment A)</b>	<b>Rosuvastatin + Eltrombopag vs Rosuvastatin</b>		
AUC (0-∞) (ng.hr/mL)	96.0 (50)		61.9 (72)	1.55 (1.42, 1.69)		
Cmax (ng/mL)	12.1 (53)		5.97 (81)	2.03 (1.82, 2.26)		
geometric mean (CVb%) for PK summary and GLS mean (90% CI) for treatment comparisons Treatment A: 10 mg rosuvastatin single dose Treatment C: 10 mg rosuvastatin single dose + 75 mg Eltrombopag (QD) x 5 days						
<b>Summary of Eltrombopag-Rosuvastatin Drug Interaction Results by Race (N=39)</b>						
<b>Plasma Rosuvastatin PK parameter</b>	<b>Rosuvastatin+Eltrombopag vs. Rosuvastatin</b>					
	<b>Asian (n=21)</b>			<b>Non-Asian (n=18)</b>		
AUC (0-∞) (ng.hr/mL)	1.32 (1.19, 1.46)			1.88 (1.68, 2.10)		
Cmax (ng/mL)	1.61 (1.44, 1.80)			2.65 (2.35, 3.00)		
GLS mean (90% CI) for treatment comparisons Treatment A: 10 mg rosuvastatin single dose Treatment C: 10 mg rosuvastatin single dose + 75 mg Eltrombopag (QD) x 5 days						
Safety results: An adverse event (AE) was defined as an AE that occurred after screening through the end of the study or early withdrawal.						
	<b>Treatment A (n=42)</b>	<b>Treatment B (n=41)</b>	<b>Treatment C (n=41)</b>			
<b>Adverse Events</b>	<b>n (%)</b>	<b>n (%)</b>	<b>n (%)</b>			
Number of Subjects With Any AE	9 (21)	4 (10)	5 (12)			
Upper respiratory tract infection	3 (7)	0	0			
Gastroenteritis	2 (5)	0	1 (2)			
Headache	2 (5)	0	1 (2)			
Viral upper respiratory tract infection	1 (2)	0	0			
Abdominal pain	1 (2)	0	0			
Gastritis	1 (2)	0	0			
Nausea	1 (2)	0	0			
Rash pustular	0	1 (2)	0			
Flatulence	0	1 (2)	0			
Vision blurred	0	1 (2)	0			
Musculoskeletal pain	0	1 (2)	0			
Herpes zoster	0	0	1 (2)			
Hordeolum	0	0	1 (2)			
Pharyngitis streptococcal	0	0	1 (2)			
Diarrhea	0	0	1 (2)			
Excoriation	0	0	1 (2)			
<b>Serious Adverse Events, n (%) [n considered by the investigator to be related, possibly related, or probably related to study medication]:</b>	<b>Treatment A (N=42)</b>	<b>Treatment B (N=41)</b>	<b>Treatment C (N=41)</b>			
	<b>n (%)</b>	<b>n (%)</b>	<b>n (%)</b>			
Subjects with Non-fatal/Fatal SAEs	0	0	0			
Treatment A: 10 mg rosuvastatin single dose Treatment B: mg Eltrombopag (QD) x 5 days Treatment C: 10 mg rosuvastatin single dose + 75 mg Eltrombopag (QD) x 5 days						

Publications: None