

The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

Study No: TRA102861	
Title: An Open-Label Mass Balance Study to Investigate the Metabolic Disposition of a Single Oral Dose of ¹⁴ C SB-497115-GR in Healthy Male Subjects.	
Rationale: This study was designed to investigate the absorption and excretion of SB-497115 (eltrombopag) in humans using [¹⁴ C] radiolabelled drug substance administered orally.	
Phase: I	
Study Period: 15 September 2005 – 01 October 2005	
Study Design: An open-label, single dose, non-randomized, mass balance study in healthy male subjects	
Center: One center in the United States	
Indication: Thrombocytopenia	
Treatment: Subjects received the equivalent of a 75 mg dose of eltrombopag as an oral solution containing approximately 100 μ Ci (0.70 mSv) of radioactivity.	
<p>Objectives: The primary objectives of this study were as follows:</p> <ul style="list-style-type: none"> • To determine the total recovery and relative excretion of radiocarbon in urine and feces after a single, oral dose of [¹⁴C]eltrombopag 75 mg (100 μCi) in healthy male subjects. • To generate samples (for a separate study) with which to characterize and quantify the metabolic profile of SB-497115 in plasma, urine, and feces following administration of [¹⁴C]eltrombopag to healthy male subjects. • To compare total radiocarbon (drug-related material) in blood and plasma relative to parent plasma concentration. 	
<p>Statistical Methods: Six evaluable subjects were enrolled into the study. To be considered evaluable, a subject must have completed all 96 h PK sampling of blood, urine, and feces. Plasma eltromboag PK parameters include AUC (0-t), AUC (0-∞), C_{max}, t_{max} and t_{1/2}.</p> <p>PK parameters for plasma and whole blood radiocarbon concentrations were calculated and described for eltrombopag. The blood:plasma ratio of [¹⁴C]eltrombopag related material was calculated at each time point. Plasma concentration-time profiles for eltrombopag were compared with those for total radiocarbon to estimate how much of the total measured radiocarbon was due to metabolites.</p> <p>The total radiocarbon excreted in urine and feces per unit time was calculated, in addition to the cumulative percentage of the total radiocarbon administered. The cumulative total amounts of eltrombopag excreted in urine and feces per unit time were calculated if sufficient radioactivity was present. The percent of the dose attributable to eltrombopag was compared to the total radiocarbon recovered, to determine how much of the recovered dose was due to metabolites.</p> <p>No statistical analyses of the PK data were planned. PK data were listed and summarized.</p> <p>Safety analyses included extent of exposure, AEs, clinical laboratory evaluations, vital signs and ECGs. All safety data was listed and summarized by treatment.</p>	
Study Population: The study population was comprised of healthy adult males 30 to 55 years of age who had no clinically significant abnormalities identified by a physician by evaluation of medical history, physical examination, clinical laboratory tests or electrocardiogram. Subjects with previous history of deep vein thrombosis, any other thromboembolic event, sensitivity to heparin, or heparin induced thrombocytopenia were not eligible to participate in the study.	
Number of Subjects:	Total
Planned N	6
Dosed N	6
Completed n (%)	6 (100)
Total Number Subjects Withdrawn, n (%)	0

Withdrawn Due to Adverse Events, n (%)	0	
Withdrawn Due to Lack of Efficacy, n (%)	0	
Withdrawn for Other Reasons, n (%)	0	
Demographics		
N (Safety)	6	
Females: Males	0:6	
Mean Age in Years (SD)	35.8 (6.85)	
Not Hispanic or Latino, n (%)	6 (100)	
Pharmacokinetics (PK) Endpoints:		
Geometric Mean (CVb%) SB-497115 Plasma PK Parameters	Plasma Concentration	
AUC (0-∞), ng.h/mL	144739 (35.5)	
AUC (0-t), ng.h/mL	142289 (34.7)	
Cmax, ng/mL	10851 (21.5)	
tmax, h (Median [Range])	2.50 (2.00-4.02)	
t1/2, h	32.3 (18.3)	
Geometric Mean (CVb%) SB-497115 Radiocarbon PK Parameters	Plasma Concentration	Blood Concentration
AUC (0-∞), ng.h/mL	240492 (38.1)	135178 (36.8)
AUC (0-t), ng.h/mL	223577 (37.2)	123780 (36.5)
Cmax, ng/mL	10019 (25.5)	5290 (27.4)
tmax, h (Median [Range])	2.50 (1.50-4.00)	2.50 (2.00-4.00)
t1/2, h	49.3 (28.7)	51.9 (41.0)
Cumulative Recovery of SB-497115 Radiocarbon		
Urine - Collection Interval in Hours	Mean (SD)	
0 - 12	4.12 (2.20)	
0 - 24	11.9 (5.45)	
0 - 48	22.6 (7.48)	
0 - 72	26.5 (7.72)	
0 - 96	28.5 (7.99)	
0 - 120	29.6 (8.13)	
0 - 144	30.2 (8.24)	
0 - 168	30.7 (8.32)	
Feces - Collection Interval in Hours	Mean (SD)	
0 - 12	0	
0 - 24	0.02 (0.03)	
0 - 48	9.50 (13.9)	
0 - 72	24.4 (5.99)	
0 - 96	36.0 (13.5)	
0 - 120	48.7 (14.5)	
0 - 144	58.0 (9.02)	
0 - 168	58.9 (9.74)	
Toilet Tissue - Collection Interval in Hours	Mean (SD)	
0 - 24	0	
0 - 48	0.01 (0.02)	
0 - 72	0.02 (0.02)	
0 - 96	0.02 (0.03)	
0 - 120	0.03 (0.03)	
0 - 144	0.03 (0.03)	
0 - 168	0.03 (0.03)	
Total Recovery (Urine + Feces), Mean (SD)	89.6 (3.73)	
Safety results: An adverse event (AE) was defined as an AE that occurred starting on Day 1 through the end of the confinement period or early withdrawal		

	Total
Adverse Events:	n (%)
Number of Subjects With Any AE	2 (33)
Stomach discomfort	1 (17)
Urinary incontinence	1 (17)
Serious Adverse Events, n (%) [# considered by the investigator to be related, possibly related, or probably related to study medication]:	Total
	n (%)
Subjects with Non-fatal/Fatal SAEs	0

Publications: None
