TREHALOSE STABILIZED FREEZE DRIED HUMAN PLATELETS, THROMBOSOMES® PERSIST IN CIRCULATION 24 HOURS AFTER INFUSION AND ARE NON-IMMUNOGENIC IN NEW ZEALAND WHITE RABBITS

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ABSTRACT

Thrombosomes®, a human platelet derived homologous agent, (PDHA) is a platelet derived variant of a critical plasma medical tool, or a self- PDHA that requires no transfusions in patients with a compatibility fre- quency not required to standard transfusions. Evaluations in regulatory agencies for approval requires analyzing the pharmacokinetics of this PDHA concerning the clearance characteristics in comparison to storage platelets (3 days old) and determining their safety and immunogenicity.

MATERIALS AND METHODS

• Thrombosomes® is produced by a proprietary process that includes trehalose and other carbohydrates and a custom (phospholipid) glycop.
• The PK, Pharmacokinetics studies involved the injection of 111-I labeled fresh rabbit platelets, human stored platelets (3 days old), human Thrombosomes®, and autologous or allogeneic rabbit-fresh damaged platelets (DFP).
• Assisted rabbits were infused with 2-10x10^11 (10x) 111-I labeled cells

BIODISTRIBUTION

• Gamma Camera image 4 hours after infusion
• Fetal Autologous Rabbit Platelets
• Thrombosomes®
• Autologous Rabbit DFP

• Heart
• Liver
• Spleen

• Ph1 (0 min)
• Ph2 (1 hr)

• Circulation kinetics of 111-I labeled preparations in rabbits. 111-I labeled Thrombosomes® preparations were infused into the circulatory system of rabbits. The radioactivity counts were normalized to the baseline counts measured in the initial sample. An identical randomization of rabbits was completed.

PHARMACOKINETIC STUDIES

• A large percentage of Thrombosomes® in rabbit DFP 60% to 75% are rapidly removed from circulation. The remaining 30% to 40% demonstrate a half-life of about 24 hrs.
• The biodistribution and circulation data suggest that the origin of platelets used in Thrombosomes® preparations does not affect their circulation persistence, but the biodegradation process significantly increases the clearance of platelets from circulation and uptake in liver, kidney and spleen.
• Safety studies in NZW rabbits at 72 times dose administered during the PK and biodistribution experiments failed to observe any host protein associated AE or SAE including hemopathological changes in the liver, kidney and spleen. POSTED 10/2014