PHARMACOKINETICS OF SUBCUTANEOUSLY ADMINISTERED CB2679D/ISU304 IN WILD-TYPE AND HEMOPHILIA B MICE

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INTRODUCTION

The rapid clearance of FIX necessitates frequent intravenous (IV) administrations to achieve effective prophylaxis for patients with hemophilia B (HB). Subcutaneous (SC) administration would be a preferred route of administration but has been limited by low bioavailability and potency of the marketed FIX products. CB2679d/ISU304 has enhanced biological properties including resistance to inhibition by ATIII, increased affinity for FVIIIa, and increased catalytic activity compared with wild-type FIX. The variant has three mutations: R316Y/R338E/T343R that were introduced using rational design. A single dose subcutaneous injection of Hemophilia B mice

METHODS

Blood levels of FIX antigen and predicted activity after IV or subcutaneous FIX administration in normal mice

BLOOD LEVELS OF FIX ANTIGEN AND ACTIVITY AFTER DAILY SUBCUTANEOUS ADMINISTRATION OF CB2679D/ISU304 IN HEMOPHILIA B MICE

DISCUSSION

A single dose subcutaneous injection in Hemophilia B mice

PHARMACOKINETICS OF NORMAL MICE

BLOOD LEVELS OF FIX ANTIGEN AND ACTIVITY AFTER SINGLE DOSE SUBCUTANEOUS ADMINISTRATION OF CB2679D/ISU304 IN HEMOPHILIA B MICE

SUMMARY

Dose dependent increase in antigen and activity levels

Dose dependent increase in antigen and activity levels

Dose dependent increase in antigen and measured activity levels

Daily subcutaneous dosing of CB2679d/ISU304 demonstrated the effects of the bioavailability, potency, time to maximal concentration, and half-life by reaching a steady-state activity sufficient to correct severe hemophilia to mild hemophilia, in hemophilia B mice, after three days.