MSMilan2023
9th Joint ECTRIMS-ACTRIMS Meeting
11–13 October 2023 | Milan, Italy

Abstract Number: 1071/P289

A Phase 1 Study of the Safety, Pharmacokinetics and Pharmacodynamics of BMS-986196, an Oral CNS-penetrant BTK Inhibitor, in Healthy Adults

Nathalie Goletiani [1],Vineet Goti [1],Ramakrishna Boyanapalli [1],Ahad Sabet [2],Angela Mirzac [1],Mary Syto [1],Mark Thomas [1],**Marc Gleichmann * [1]**,

[1] BMS, Lawrenceville, United States, [2] Icon plc, Salt Lake City, United States

Introduction:

BMS-986196 is an orally administered, potent, selective, CNS-penetrant, irreversible Bruton's tyrosine kinase (BTK) inhibitor in clinical development for multiple sclerosis.

Objectives/Aims:

To determine the safety, pharmacokinetics, and target engagement levels of BMS-986196.

Methods:

BMS-986196 was evaluated in a Phase 1 clinical study in healthy adults. The study consisted of Parts A - C. Parts A and B were designed as randomised, double-blind, placebo-controlled single and multiple ascending dose studies, respectively. In Part A, single doses ranging from 1 mg to 90 mg were evaluated across 6 panels, each panel consisting of 6 participants receiving BMS-986196 and 2 participants receiving placebo. In Part B, 14 daily doses with dose levels ranging from 20 mg to 90 mg once daily (QD) were evaluated across 4 panels, each panel consisting of 8 participants receiving BMS-986196 and 2 participants receiving placebo. Part C was an exploratory evaluation of food and formulation effects on BMS-986196 pharmacokinetics; it was an open-label, 4-way cross-over study with participants randomised to 4 treatment sequences evaluating 25 mg BMS-986196.

Results:

In total, 102 participants were randomised. BMS-986196 was safe and tolerated at all dose levels across Parts A - C. No serious adverse events (SAE) were reported, and all adverse events (AE) were of mild or moderate intensity. No participants discontinued study drug due to AE.

BMS-986196 plasma concentration and pharmacokinetic parameters, including peak plasma concentration (Cmax) and area under the plasma concentration time curve (AUC) increased dose-dependently. Formulation effects on Cmax and AUC were observed. Relative to BMS-986196 administration in the fasted state, administration of BMS-986916 after food intake increased AUC. Doses ≥ 20 mg QD resulted in near maximal BTK occupancy in whole blood.

Conclusion:

BMS-986196 was safe and tolerated at all dose levels in this study. Taken together, the safety, pharmacokinetic and BTK occupancy results support future clinical studies of BMS-986196.

Disclosures:

NG, VG, RB, AM, MS, MT, and MG are employees of BMS AS is an employee of Icon plc.