First Report of SVR12 for a NS5A Replication Complex Inhibitor, BMS-790052, in Combination With PegIFNα-2a and RBV: Phase IIa Trial in Treatment-Naïve HCV 1 Subjects

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Poster 1373


BACKGROUND

- BMS-790052 is a potent, first-in-class, highly selective HCV NS5A Replication Complex Inhibitor with pan-oculengy and broad-genotype coverage in vitro
- IC50 values of 0.01 and 0.02 against genotype (Gt) 1a and 1b replicons
- BMS-790052 inhibits HCV RNA replication through the NS5A protein, as essential component of the HCV replication complex
- BMS-790052 has a pharmacokinetic profile supportive of once daily dosing
- BMS-790052 plus pegylated interferon alfa-2a (PEG-IFNα) and deoxyribonucleic acid (DNA) has shown high rates of early HCV RNA suppression (both HCV and HCV alone), when associated with peginterferon
- This poster presents the first sustained virologic response (SVR) data obtained for a NS5A Replication Complex Inhibitor

OBJECTIVES

- Assess the efficacy and safety of BMS-790052 in combination with pegIFNα-2a in treatment-naïve subjects infected with HCV GT1

METHODS

- Randomized, open-label, safety and efficacy study with 3:1 randomization: 3 mg BMS-790052: n = 12; 10 mg BMS-790052: n = 12; Placebo: n = 12
- BMS-790052 HCV GT1a, 3 mg and 10 mg are administered once-daily as monotherapy (M) or in combination with pegIFNα-2a/RBV (C)
- Early HCV RNA responses were evaluated in the 3 mg and 10 mg treatment groups, with treatment durations of 12 weeks (Wk 12) for patients treated with BMS-790052 plus pegIFNα-2a (B/C)
- Virologic breakthroughs and relapse were observed in the 10 mg treatment group
- In an exploratory analysis evaluating the effect of the RS12979860 (rs5880) SNP genotype on treatment outcomes, 12 patients were treated with BMS-790052 plus pegIFNα-2a (B/C) for 12 weeks
- This small, non-stratified study was consistent with that of pegIFNα-2a/RBV alone

RESULTS

- Summary of Safety Results
  - No serious adverse events (SAEs) were reported beyond study week 24
  - The BMS-790052 dosing groups were comparable to the placebo group for both clinical and laboratory parameters
- Summary of Efficacy Results
  - Higher rates of SVR12 were observed in all BMS-790052 dose groups compared with placebo (P = 0.001; Table 1)
  - BMS-790052 3 mg and 10 mg in both early and late responses rated significantly higher than placebo at Wk 12 (P = 0.001; Table 1)
- Table 2. Summary of Key Safety Data
- Table 3. Baseline Demographics and Disease Characteristics

CONCLUSIONS

- BMS-790052 is a potent HCV NS5A Replication Complex Inhibitor with pan-oculengy and broad-genotype coverage
- The AI444014 Week 12 SVR results support further development of BMS-790052 in combination with pegIFNα-2a/RBV
- BMS-790052 plus pegIFNα-2a/RBV was generally well tolerated with a safety profile consistent with that of pegIFNα-2a/RBV

REFERENCES


46th EASL Congress, Berlin, Germany, March 30-April 3, 2011