Introduction

MEDI8852 is a human IgG1 kappa mAb that binds to the conserved stalk region of the influenza HA protein (Figure 1). MEDI8852 inhibits biological processes that contribute to the pathogenesis of influenza – MEDI8852 directly neutralizes type A influenza viruses, blocking viral cell entry, HA maturation, and cell-to-cell spread – MEDI8852 also exhibits FC receptor-mediated viral clearance through antibody-dependent cell-mediated cytotoxicity (ADCC), antibody-dependent cellular phagocytosis, and complement-dependent cytotoxicity.

Methods

Healthy subjects aged 18 to 65 years were enrolled in this study. Subjects were randomized to receive a single intravenous (IV) dose of either MEDI8852 or placebo on Day 1. Dose escalation was based on review of Day 8 safety data. Subjects were followed through Day 29 for adverse events (AEs), and through Day 101 for serious AEs (SAEs), PK, and antidrug antibody (ADA) responses. MEDI8852 is being developed to treat patients hospitalized with type A influenza. The primary objective of the present study was to evaluate the safety and pharmacokinetics (PK) of MEDI8852.

Results

Subjects

A total of 40 subjects (32 MEDI8852 and 8 placebo) were enrolled in the study. All were Grade 1 or 2 in severity. The most frequently reported AEs were comparable across treatment groups (MEDI8852 37.5% and placebo 37.5%); no AEs of special interest, including allergic reactions, infusion-related reactions, hepatic function abnormalities, and immune complex disease (vasculitis, anaphylaxis] were reported (Table 2).

Safety

Overall AE rates were similar between the total MEDI8852 group and the placebo group and were not dose dependent (Table 2). Subjects received a single IV dose of MEDI8852 on Day 1 and were followed for safety through Day 101. Safety data gathered through Day 8 after dosing were reviewed to ensure enhanced activity over the agent alone.

Pharmacokinetics

MEDI8852 demonstrated linear PK, with dose-proportional increases in serum concentrations (Figure 3).

Conclusions

MEDI8852 demonstrated an acceptable safety profile in healthy adults, with no major safety findings, no SAEs, and no deaths. MEDI8852 exhibited linear PK characteristics. MEDI8852 supports continued development for treatment of individuals who are hospitalized with influenza A virus infection.

Reference

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