92 SAPHIRE II: PHASE 3 PLACEBO-CONTROLLED STUDY OF INTERFERON-FREE, 12-WEEK OF ABT-450/R/ABT-267, ABT-333, AND RIBAVIRIN IN 394 TREATMENT-EXPERIENCED ADULTS WITH HEPATITIS C GENOTYPE 1

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Background and aims: Efficacy in retreatment of HCV-infected patients is associated with treatment history, with the lowest responses occurring among prior peginterferon/ribavirin null-responders**.** ABT-450 is an HCV NS3/4A protease inhibitor(dosed with ritonavir 100mg, ABT-450/r) identified by AbbVie and Enanta. ABT-267 is an NS5A inhibitor; ABT-333 is an NS5B RNA polymerase inhibitor. The safety and efficacy of ABT-450/r/ABT-267+ABT-333+RBV(3D+RBV) was evaluated among non-cirrhotic peginterferon/ribavirin-experienced, HCV genotype(GT)1-infected patients in an interferon-free phase III trial. Methods: In this double-blind, placebo-controlled trial, prior peginterferon/ribavirin relapsers, partial-responders, or null-responder patients were randomized(3:1) to receive ABT-450/r/ABT-267(150mg/100mg/25mgQD)+ABT-333(250mgBID)+weight-based RBV(Arm A) or matching placebos(Arm B) for 12 weeks. Results: 297 patients received 3D+RBV; 97 received matching placebos. The Arm A(3D+RBV active regimen) SVR12 rate was 96.3%(286/297). 2.4% of patients had virologic failure. SVR12 rates in prior peginterferon/ribavirin relapsers, partial-responders, and null-responders were 95.3%, 100%, and 95.2%, respectively. SVR12 rates were comparable among genotype 1a and 1b patients (96.0% and 96.7%, respectively). The most common adverse events(AEs) in Arm A(3D+RBV active regimen) and Arm B(placebo) were headache(36.4% and 35.1%, respectively) and fatigue(33.3% and 22.7%, respectively); the frequency of these events did not differ significantly between arms(*P*>0.05). No moderate/severe AEs occurred significantly more frequently in Arm A vs. B(*P*>0.05). Rates of discontinuation due to AEs were 1.0% and 0% in Arm A(3D+RBV active regimen) and Arm B(placebo), respectively.

Conclusions: A multi-targeted antiviral approach combining ritonavir-boosted ABT-450, ABT-267, and ABT-333 with ribavirin achieves high SVR12 rates with low rates of treatment discontinuation in treatment-experienced non-cirrhotic HCV genotype 1-infected patients, including prior null-responders.

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