THE EFFECTS OF CO-ADMINISTERING A MONOCLONAL ANTIBODY TO PROPROTEIN CONVERTASE SUBTILISIN/KEXIN TYPE 9 SERINE PROTEASE, REGN727/SAR236553, WITH 10 AND 80 MG ATORVASTATIN COMPARED TO 80 MG ATORVASTATIN ALONE IN PATIENTS WITH PRIMARY HYPERCHOLESTEROLEMIA (NCT: 01288469)

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**Background:** Low-density lipoprotein cholesterol (LDL-C) reduction significantly lowers cardiovascular risk in at-risk patients. Atorvastatin 80 mg/day (A80) is a proven and highly efficacious LDL-C-lowering treatment. However, many patients do not achieve goals with maximal dose of statin. Proprotein convertase subtilisin/kexin 9 (PCSK9) binds to LDL receptors (LDLRs), increasing LDLR degradation and reducing the rate of LDL-C removal from the circulation. REGN727/SAR236553, a fully human monoclonal antibody, binds to PCSK9, enhances LDLR expression, and further reduces LDL-C levels in statin-treated patients. The primary objective of this study was to assess the LDL-C efficacy of high dose of A (A80) alone compared to both A 10 mg/day (A10) and A80 combined with subcutaneously (sc) administered REGN727/SAR236553.

**Methods:** This was a multicenter, double-blind, placebo-controlled study conducted in patients with hypercholesterolemia and LDL-C ≥100 mg/dL on A10 for ≥6 weeks prior to randomization to 3 parallel treatment groups: A80 + placebo (n=29), A80 + REGN727/SAR236553 sc every 2 weeks (q2w) (n=30), or A10 + REGN727/SAR236553 sc q2w (n=29). All patients were treated for 8 weeks and then followed for an additional 8 weeks.

**Results:** After 8 weeks of treatment, A10 + REGN727/SAR236553 patients had an additional [mean (SD)] LDL-C reduction of 66.7% (12.5), and those on A80 + REGN727/SAR236553 achieved a 72.3% (14.4) reduction, compared to a 17.7% (27.2) reduction in patients on A80 + placebo (p<0.0001). Significant reductions were also observed in apolipoprotein B, non-high density lipoprotein cholesterol and lipoprotein(a) with A80 + REGN727/SAR236553 versus A80 alone. Statistical comparisons with A10 were not performed. There was one serious adverse event of dehydration in the A80 + REGN727/SAR236553 group, which was deemed not treatment related. No other significant safety concern was observed.

**Conclusions:** Co-administration of REGN727/SAR236553 with A10 or A80 resulted in a significant and substantial decrease in LDL-C and was well tolerated.