A RANDOMIZED STUDY OF THE RELATIVE BIOAVAILABILITY, PHARMACODYNAMICS, AND SAFETY OF ALIROCUMAB, A FULLY HUMAN MONOCLONAL ANTIBODY TO PROPROTEIN CONVERTASE SUBTILISIN/KEXIN TYPE 9, AFTER SINGLE SUBCUTANEOUS ADMINISTRATION AT THREE DIFFERENT INJECTION SITES IN HEALTHY SUBJECTS

Poster Contributions
Hall C
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Background: Alirocumab administered subcutaneously (SC) in the abdomen significantly reduced low-density lipoprotein cholesterol (LDL-C) in Phase 1 and 2 trials of up to 12 weeks duration. As patients may use different injection sites, the bioavailability of a single dose of alirocumab was compared after injection in the abdomen, upper arm, and thigh.

Methods: This single-center, open-label, randomized Phase 1 study (NCT01785329) was conducted in healthy subjects (18-45 years) in 3 parallel groups receiving a single 75 mg dose of alirocumab SC at 3 distinct sites: abdomen, upper arm, and thigh. Subjects were followed for 85 days ± 2 days after study drug administration. Pharmacokinetic (PK) parameters for the systemic exposure of alirocumab were calculated. LDL-C % changes resulting from different injection sites were estimated using linear mixed effects models.

Results: Sixty subjects (20/group) were randomized (39 male, 21 female; 20-45 years). Mean (SEM) LDL-C baseline levels were comparable in the 3 groups: 3.39 (0.159), 3.34 (0.154), and 3.13 (0.097) mmol/L in the abdomen, upper arm, and thigh groups, respectively (mean levels in mg/dL: 131.1, 129.2 and 121.0, respectively). On Day 15, the % decrease in LDL-C was 48.4% in the abdomen group, 39.5% in the upper arm group and 45.6% in the thigh group. Overall there was no effect of injection site on LDL-C levels across the entire time course (p-value of the interaction between days and injection site groups = 0.453). PK profiles were similar among the 3 injection sites, with a non-statistically significant trend for lower exposure to alirocumab for thigh or upper arm vs abdomen group. There were no serious adverse events (AEs). Treatment emergent AEs were experienced in 8/20, 11/20, and 13/20 subjects in the abdomen, upper arm, and thigh groups, respectively. Most common AEs in all groups were nasopharyngitis and headache.

Conclusions: A single administration of alirocumab 75 mg by SC route in subjects presented similar PK and pharmacodynamic profiles regardless of injection site.