BACKGROUND The ABSORB III Pharmacokinetic (PK) study is a prospective, open-label, non-randomized sub-study of the ABSORB III randomized trial designed to determine the PK of everolimus delivered by the Absorb bioresorbable vascular scaffold (BVS) in subjects who only receive Absorb BVS with a minimum treatment of two de novo coronary artery lesions. The pharmacokinetic profile of Absorb BVS has not previously been described.

METHODS Twelve subjects were enrolled at two sites in the United States. Subjects received one (n=8) or two (n=4) Absorb BVS with diameters of 2.5, 3.0 or 3.5 mm and lengths of 8, 12, 18 or 28 mm. The total everolimus dose received ranged from 181 to 443 μg. Blood samples (arterial or venous) were collected from the subjects pre-procedure and at fifteen time points post-procedure (10 and 30 minutes, 1, 2, 4, 6, 12, 24, 48, 72, 96, 120 (day 5), 168 (day 7), 336 (day 14), and 792 hours after the last scaffold implantation). The concentration of everolimus in the blood was determined by Liquid Chromatography-Mass Spectrometry/Mass Spectrometry assay. The lower limit of quantification was 0.1 ng/mL. The blood concentration-time data were subjected to non-compartmental methods to determine PK parameters (Cmax, tmax, AUC, t1/2).

RESULTS Everolimus blood concentrations increased rapidly after Absorb BVS deployment, reaching maximum concentration between 0.17 and 2.37 hours (tmax), declining thereafter with a terminal half-life ranging between 45.9 and 115 hours. By 4 hours, everolimus blood concentrations were below 3 ng/ml (the chronic therapeutic level necessary to prevent organ rejection in transplant patients) in all subjects. Everolimus blood concentrations were low but measurable for up to 168 hours (7 days) after last scaffold deployment. The maximum observed everolimus concentration (Cmax) increased with dose and ranged from 1.085 to 4.460 ng/ml across the dose range studied. Similarly, individual AUC (AUC(0-12h): 12.09 to 44.22 ng/ml; AUC(0-12h): 25.37 to 104.6 ng/ml; AUC(0-12h): 33.15 to 120.8 ng/ml) increased proportionally with total scaffold dose.

CONCLUSIONS The local arterial delivery of everolimus and systemic exposure increased proportionally with dose and rapidly declined thereafter. The everolimus PK profiles seen with Absorb BVS are safe, and are similar to previously reported profiles for the cobalt chromium everolimus-eluting XIENCE stent.

CATEGORIES CORONARY: Bioresorbable Vascular Scaffolds

KEYWORDS Bioabsorbable, Bioabsorbable scaffolds