Aim: Palbociclib (P), a selective oral cyclin-dependent kinase 4/6 inhibitor that blocks G1/S cell cycle progression, is in phase 2 and 3 clinical trials across multiple oncology indications. P has low solubility and high permeability. This completed phase 1 study estimated the effect of food on P bioavailability.

Methods: This randomized, open-label, 4-sequence, 4-period crossover study (NCT01904747) in 28 healthy adult volunteers estimated the relative bioavailability of single-dose P 125 mg (free base capsule) administered 30 min after a high fat/calorie meal, 30 min after a low fat/calorie meal, or between 2 moderate fat/standard calorie meals (1 h after/2 h before) versus after fasting ≥10 h overnight (washout: ≥10 d). Pharmacokinetic (PK) samples were collected predose and serially up to 144 h postdose; P concentrations were measured using validated high-performance liquid chromatography tandem mass spectrometry. PK data were analyzed using a non-compartmental approach based on a mixed effects model.

Results: Time to maximum P concentration (Tmax) and terminal plasma half-life (t1/2) values were similar across fed and fasted conditions (median Tmax: 8 h, all; mean t1/2: 22.03–23.90 h). Relative to the fasted condition, ratios of adjusted geometric means for high fat, low fat, and moderate fat conditions were 121%, 112%, and 113%, respectively, for AUCinf and 138%, 127%, and 124%, respectively, for Cmax; the slight increase in exposure in the fed versus fasted conditions was driven mainly by a subgroup of subjects (n = 3) with significantly lower exposure in the fasted condition. PK variability (% coefficient of variation) was reduced in the fed (AUCinf, 23%–27%; Cmax, 21%–24%) versus fasted (AUCinf, 39%; Cmax, 73%) conditions. In a supplemental analysis excluding the 3 subjects with significantly lower exposure in the fasted condition, food intake did not affect P exposure, and PK variability was similar across fed and fasted conditions.

Conclusions: Overall, P exposure was marginally affected, but PK variability was greatly reduced, in the fed versus the fasted condition. Thus, P should be administered with food.