Annals of Oncology 25 (Supplement 4): iv146–iv164, 2014
doi:10.1093/annonc/mdu331.23

developmental therapeutics

463P EFFECT OF FOOD ON THE BIOAVAILABILITY OF PALBOCICLIB 125 MG CAPSULES IN HEALTHY VOLUNTEERS

A. Ruiz-Garcia[1], A. Plotka[2], S. Pawlak[3], M. O'Gorman[4], M. Kosa[5], S. Nidadavolu[3], S. Phillips[6], D.D. Wang[7]

[1]*Clinical Pharmacology, Pfizer Inc, San Diego, CA, USA*
[2]*Biostatistics, Pfizer Inc, Collegeville, PA, USA*
[3]*Clinical Research and Precision Medicine, Pfizer Inc, New Haven, CT, USA*
[4]*Global Clinical Pharmacology, Pfizer Inc, Groton, CT, USA*
[5]*Clinical Assay Specialist Contracted Through Atrium Services, Pfizer Inc, San Diego, CA, USA*
[6]*Development Operations, Pfizer Inc, Groton, CT, USA*
[7]*Oncology Business Unit, Pfizer Inc, San Diego, CA, USA*

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 between study periods). No food was allowed ≥4 h postdose (all conditions except moderate fat meal). 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 (T_{max}) and terminal plasma half-life ($t_{1/2}$) values were similar across fed and fasted conditions (median T_{max}: 8 h, all; mean $t_{1/2}$: 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 AUC_{inf} and 138%, 127%, and 124%, respectively, for C_{max}; 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 (AUC_{inf}, 23%–27%; C_{max}, 21%–24%) versus fasted (AUC_{inf}, 39%; C_{max}, 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.

Disclosure: A. Ruiz-Garcia: Employment: Pfizer Inc Stock ownership: Pfizer Inc.; A. Plotka: Employment: Pfizer Stock ownership: Pfizer; S. Pawlak: Speakers' bureau: Pfizer Employment: Pfizer Stock ownership: Pfizer; M. O'Gorman, S. Nidadavolu and S. Phillips: Employment: Pfizer; M. Kosa: Employment: Contractor at Pfizer (Clinical Assay Group) through Atrium Services. D.D. Wang: Employment: Pfizer Stock ownership: Pfizer.