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784P PHARMACOKINETIC (PK) ACTIVITY OF CABAZITAXEL (CBZ) IN PATIENTS (PTS) WITH RENAL IMPAIRMENT (RI)

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Aim: Limited data are available on Cbz PK in pts with RI (14 with moderate RI, 1 with severe RI [Ferron, Cancer Chemother Pharmacol 2013]). This open-label, multicentre study assessed Cbz PK in pts with advanced solid tumours and normal or impaired renal function.

Methods: Pts enrolled into cohorts A (normal control, creatinine clearance [CrCL] >80 ml/min/1.73 m^2), B (moderate RI, CrCL 30– < 50 ml/min/1.73 m^2) or C (severe RI, CrCL <30 ml/min/1.73 m^2) received Cbz 25 mg/m^2 Q3W (A and B), or 20 mg/m^2, which could be increased to 25 mg/m^2 (C). The primary endpoint was Cbz PK (clearance normalised to body surface area [CL/BSA]; area under the curve normalised to dose [AUC/dose]). PK parameters were calculated by non-compartmental analysis and individual modelling using a 3-compartment open model with first-order elimination. Log PK parameters and Cbz unbound fraction (FU) were analysed using linear regression and linear mixed models, respectively. Geometric mean (GM) estimates were determined using log CrCL corresponding to the mean of each cohort's CrCL interval (moderate and severe RI: 40 and 15 ml/min/1.73 m^2, respectively). GM ratios (GMRs) were expressed vs control (90 ml/min/1.73 m^2).

Results: Pts (n = 25) received a median of 3 Cbz cycles (range 1–20: cohort A, 5 [2–13]; cohort B, 3 [1–15]; cohort C, 5 [1–20]), and 24 were eligible for PK analysis (8/cohort). For moderate and severe RI vs controls, GMR estimates were: CL/BSA 0.95 (90% CI 0.80–1.13) and 0.89 (0.61–1.32); AUC/dose 1.06 (0.88–1.27) and 1.14 (0.76–1.71); FU 0.99 (0.94–1.04) and 0.97 (0.87–1.09), respectively. Estimated slope of linear regression of log parameters vs log CrCL was: CL/BSA 0.06 (90% CI -0.15–0.28); AUC/dose -0.07 (-0.30–0.16); Cbz FU 0.02 (-0.05–0.08). Cbz safety was consistent with previous reports.

Conclusions: RI had no clinically meaningful effect on Cbz PK. Non-significant trends of increasing AUC and decreasing Cbz CL with greater RI were seen.

Table: 784P

PK parameter estimates for pts with moderate and severe renal impairment and controls

	GM estimate (90% CI)		
Control CrCL 90 ml/min/1.73 m^2	Moderate renal impairment CrCL 40 ml/min/1.73 m^2	Severe renal impairment CrCL 15 ml/min/1.73 m^2	
CL/BSA, l/h/m^2	29.81 (24.18–36.75)	28.34 (24.44–32.86)	26.66 (20.15–35.27)
AUC/dose, ng*h/ml/mg/m^2	33.23 (26.65–41.44)	35.21 (30.24–40.99)	37.75 (28.29–50.39)
Cbz FU, %	5.51 (5.08–5.96)	5.44 (5.13–5.76)	5.36 (4.95–5.80)

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