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PHASE II STUDY OF PAZOPANIB MONOTHERAPY FOR PATIENTS WITH RELAPSED/REFRACTORY UROTHELIAL CANCER (INT70/09, NCT01031875)

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Background: Treatment of patients (pts) with relapsed/refractory urothelial cancer (UC) is very often unsuccessful. Single agents or combination therapies (Rx) yielded thus far unsatisfactory results and investigation of novel compounds is a priority. Targeting the VEGF/PDGF axis is supported by a good pre-clinical rationale in UC. Pazopanib (PZP), a multitargeted drug with distinct anti-angiogenic activity is being investigated in an ongoing Phase II trial.

Methods: Pts with histologically documented UC unresponsive or relapsing after ≥1 CDDP-based Rx for metastatic disease were included. PZP 800 mg once daily until disease progression (PD) or unacceptable toxicity was planned. All patients were investigated with computed tomography (CT) and 18-fluorine-deoxyglucose positron-emission tomography (18FDG-PET) at baseline and q4weeks thereafter. An optimal 2-stage Simon's design is applied whereby 2 responses should be observed in 21 patients before moving to full enrollment of 41 cases. RECIST v.1.1 response-rate (RR) is the primary endpoint.

Results: 18 pts were enrolled from 02 to 07/2010. Median age is 65 yrs (43-79). Eight pts had UC of the upper urinary tract while 10 had a bladder primary tumor. 16/18 pts had multiple sites of metastases (median 2, range 1-4). Median number of prior therapies is 2 (1-4) and median number of prior platinum-based cycles is 5 (3-12). 7/18 pts had received RT.
Four (22%) pts had confirmed RECIST-defined partial response (PR), 11 had a stable disease (83% clinical benefit). Twelve pts (67%) had necrotic evolution of multiple metastases and/or a decreased SUV at PET consistent with PR (typically residual peripheral halo of uptake). Median follow-up is 3 months (1-6). G1-2 hypertension and hand-foot syndrome occurred in 3 pts, diarrhoea in 4 pts, and G2 increase of liver transaminases in 2 pts.

Conclusions: PZP is endowed of substantial antitumor activity that justifies full study enrollment in pts with pre-treated and usually unresponsive UC. Responses are best seen at CT-densitometry and PET in agreement with the mechanism of action of PZP. Results for the fully enrolled trial will be available in October 2010.

Disclosures: All authors declare no conflict of interest.