A PHASE I/II TRIAL OF BNC105P WITH EVEROLIMUS IN METASTATIC RENAL CELL CARCINOMA (mRCC): RESULTS OF THE RANDOMIZED PHASE II DISRUPTOR-1 TRIAL


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Aim: BNC105P is an inhibitor of tubulin polymerization, and preclinical studies suggest possible synergy with everolimus (EVE). In the phase I component of the current study (ASCO 2013 [Abstr 4563]), full doses of BNC105P (16 mg/m² IV on days 1 & 8 of a 21-day cycle) with EVE (10 mg po daily) were well-tolerated with no PK interactions, thus constituting the recommend phase 2 dose (RP2D). Results of a randomized phase II study evaluating this regimen are reported herein.

Methods: Pts with clear cell mRCC and 1-2 prior therapies (including ≥1 VEGF-TKI) were randomized to BNC105P + EVE (Arm A) at the RP2D or EVE alone at 10 mg po daily (Arm B). Pts were stratified by MSKCC risk factors and number of prior VEGF-TKIs. Pts with progression or intolerable toxicity on EVE could subsequently receive BNC105P alone. The primary endpoint (EP) of the study was 6-mo progression-free survival (6MPFS), with 80% power to detect an improvement from 35% to 60% with the addition of BNC105P. Secondary EPs included overall response rate (ORR), PFS, overall survival (OS) and exploratory biomarker analyses.

Results: 139 pts were randomized across 77 treatment centers (US: 63; non-US: 14), with 69 and 67 evaluable pts in Arms A and B, respectively. Baseline characteristics were balanced between treatment arms. 6MPFS was similar in the treatment arms (Arm A: 33% v Arm B: 29.8%, P = 0.66) and no difference in PFS was observed (Arm A: 4.7 mos v Arm B: 4.1 mos; P = 0.49). Unplanned subset analyses in patients with liver metastases (n = 26) showed a non-significant trend towards benefit with the addition of BNC105P (Arm A: 6.6 mos v Arm B: 2.8 mos). ORR in Arms A and B were 1.45% and 1.49%, respectively, with 1 complete response in Arm A. Most adverse events were consistent with EVE-related toxicity. Changes in several biomarkers were associated with clinical outcome with BNC105P and EVE (adiponectin [HR = 0.56, P = 0.0058], α-2-macroglobulin [HR = 0.01, P = 0.0001], β-2-microglobulin [HR= 0.39, P = 0.0013], and TNF receptor-2 [HR = 0.86, P = 0.0016]).

Conclusions: Although the primary EP was not met in an unselected population, intriguing correlative studies suggest several potentially predictive biomarkers. Further prospective assessment of BNC105P in relevant biomarker-based subsets is warranted.

Disclosure: S. Pal: has previously served at an advisory meeting for Bionomics as a consultant; G. Kremmidiotis, J. Simpson and J. Iglesias: is employed by Bionomics; T. Hutson: has previously served at an advisory board meeting for Bionomics as a consultant. All other authors have declared no conflicts of interest.