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418PD NCI-MATCH Arms N & P: Phase II study of PI3K beta inhibitor GSK2636771 in patients (pts) with cancers (ca) with PTEN mutation/ deletion (mut/del) or PTEN protein loss

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Background: The NCI-MATCH trial is the largest national study (1173 sites) for pts with relapsed/ refractory solid tumors, lymphomas and myeloma, which assigns targeted therapies based on individual tumor molecular alterations detected using the adapted Oncomine AmpliSeq panel (143 genes) and immunohistochemistry (IHC). We hypothesized that patients with PTEN-deficient cancers enrolled to Arms N and P may benefit from treatment with the PI3K beta-selective inhibitor GSK2636771.

Methods: Eligibility: relapsed/refractory ca, good end-organ function, and ECOG PS $\leq$ 1. Pts were screened for molecular alterations by centralized testing on fresh tumor biopsy and had deleterious PTEN mut/del without loss of expression (Arm N) or complete loss of cytoplasmic and nuclear PTEN staining on IHC (Arm P), and no other aberrations activating the PI3K/MTOR and MAPK pathways (mut in PIK3CA, PIK3R1, BRAF, KRAS, AKT1, TSC1/2, mTOR, RHEB, NF2, NRAS, HRAS). Pts received GSK2636771 400mg/day (28-days cycles). RECIST 1.1 overall response rate (ORR) was the primary endpoint.

Results: Of 59 enrolled pts, 56 were eligible and received treatment. Of 22 pts with PTEN mut/del (Arm N: 6 uterine, 2 breast, 2 prostate, 2 head/neck ca, 10 other), all are off treatment as of analysis (14 disease progression, 4 for adverse events [AEs], 4 other). One pt (4.5%) with prostate ca (PTEN deletion, MPRSS2-ERG fusion) attained a partial response (-42%). Of 7 (32%) pts with stable disease (SD), 2 had SD $>$ 6 months (uterine leiomyosarcoma; endometrial carcinoma). Of 34 pts with loss of PTEN protein by IHC (Arm P: 7 prostate, 6 breast, 3 squamous anal ca, 2 cholangiocarcinoma, 16 other), all are off treatment as of analysis (26 disease progression, 4 for AE, 4 other). Of 9 (37.5%) pts with SD, 3 had SD $>$ 6 months (prostate cancer; squamous bladder cancer, squamous anal cancer). Median progression-free survival was 1.8 months for both arms. Gr $\geq$ 3 treatment-related (tr) reversible toxicities were experienced by 30% (7) and 20% (7) of pts in arms N and P, respectively. No tr Gr 5 toxicities were observed in either arm.

Conclusions: Single agent GSK2636771 has very modest activity in ca with PTEN gene mutation/deletion and/or PTEN protein loss.

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