TPS4612 Poster Session

STARLITE 2: Phase 2 study of nivolumab plus ^{177}lutetium-labeled anti–carbonic anhydrase IX (CAIX) monoclonal antibody girentuximab (^{177}Lu-girentuximab) in patients with advanced clear cell renal cell carcinoma (ccRCC).

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Background: CAIX is a cell surface glycoprotein expressed in > 95% of ccRCC but rarely in normal tissues. Radiolabeling girentuximab, a CAIX-targeting monoclonal antibody, with ^{177}Lu has shown promise as a therapeutic agent in ccRCC. Targeted delivery of radiation to ccRCC cells may prime the immune response, providing rationale for combining ^{177}Lu-girentuximab with nivolumab. This phase 2, open-label, single arm study will evaluate ^{177}Lu-girentuximab in combination with nivolumab in patients with previously treated ccRCC. **Methods:** Eligible patients have locally advanced unresectable or metastatic ccRCC, ≥1 prior line of therapy (including ≥1 anti-PD-1 or anti-PD-L1 antibody), adequate organ function, and ≥1 evaluable lesion as defined by RECIST 1.1 on ^{89}Zr-girentuximab PET/CT. Patients will receive ^{177}Lu-girentuximab (max 3 cycles; IV on day 1 of cycles 1, 4, and 7) and nivolumab (240mg IV q2 weeks starting cycle 1 day 15) until disease progression or unacceptable toxicity. FDG-PET and CT CAP will be performed prior to cycles 1, 4, and 7, and then q12 weeks. All cycles are 28 days. Patients will be evaluated in a 24-week safety lead-in phase followed by an expansion phase. In the safety lead-in phase, the primary endpoint of maximum tolerated dose (MTD) of ^{177}Lu-girentuximab in combination with nivolumab will be determined with a 3+3 design using a starting dose of 1804 MBq/m^2 (75% of single agent MTD). Based on dose limiting toxicities (DLTs), the starting ^{177}Lu-girentuximab dose will be either escalated to 2405 MBq/m^2 (cohort 2; single agent MTD) or de-escalated to 1353 MBq/m^2 (cohort -1) for the next cohort. Due to expected cumulative myelosuppression, each subsequent ^{177}Lu-girentuximab dose given to the same patient will be reduced by 25% (dose 2 = 75% of dose 1; dose 3 = 75% of dose 2). In the expansion phase, a Simon 2-stage optimal design will be used to evaluate the primary endpoint of best objective response rate by RECIST 1.1 within 24 weeks. With ≥1 response in the first Simon stage of 10 patients (includes patients treated at MTD during safety lead-in), a second stage will open (n = 19) for a total of 29 patients. The regimen will be considered worthy of further study if there are ≥4 responses in the 29 patients. Secondary endpoints include PFS, OS, and safety. Exploratory imaging with ^{89}Zr-girentuximab PET/CT will be performed at baseline and before each ^{177}Lu-girentuximab dose with results correlated with RECIST response on conventional imaging. In addition, whole body planar and SPECT imaging will be performed after each ^{177}Lu-girentuximab dose to evaluate distribution, lesion uptake, and dosimetry. The prespecified number of DLTs was exceeded in cohort 2 such that dosing reverted back to 1804 MBq/m^2, in which accrual is ongoing. Clinical trial information: NCT05239533. Research Sponsor: Telix Pharmaceuticals.