

**A Phase 1/2 Dose Escalation and Expansion Study of Cabiralizumab (cabira; FPA-008), an anti-CSF1R antibody, in Tenosynovial Giant Cell Tumor (TGCT, Diffuse Pigmented Villonodular Synovitis D-PVNS)**

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**Background:** TGCT is a proliferative, neoplastic joint disease that presents as single nodule (local) or multiple nodules (diffuse D-TGCT). Localized overexpression of colony stimulating factor 1 (CSF1) leads to recruitment of cells expressing the CSF1 receptor (CSF1R), formation of a tumor and inflammation of joints and tendons. Cabira is a monoclonal antibody that inhibits the interaction of the CSF1 and IL-34 ligands with their shared receptor CSF1R.

**Methods:** This Ph 1/2 study is evaluating safety and efficacy of cabira monotherapy administered IV Q 2wk for 6 mo in patients (pts) with D-TGCT. Eligible pts have inoperable D-TGCT or tumor for which resection would cause unacceptable morbidity. Response is evaluated by MRI, pt reported outcomes, and Ogilvie-Harris (O-H) score (which combines pain, synovitis, range of motion and functional capacity on a scale of 0-12).

**Results:** As of 15 Dec 2016, 22 pts received  $\geq 1$  dose of cabira at 1, 2 or 4mg/kg. Dose-related exposure increase and significant reduction in target peripheral monocytes were observed. No dose limiting toxicity was identified. 4 mg/kg was chosen for Ph2 based on efficacy, tolerability, and PK. AEs  $\geq$  Gr 2 ( $> 10\%$ ) were CK elevation 46%, rash and other skin disorders 36%, fatigue 23%, and periorbital/peripheral/face edema 18% each. Gr 3 AEs in  $\geq 2$  pt were CK elevation (n = 8) and periorbital edema (n = 2). Four drug-related SAEs were reported in 3 pts; hypertension, fever, CRP elevation, and myocarditis.

AEs of CK elevation were asymptomatic, improved to  $< 2X$  ULN after protocol mandated drug discontinuation and are a known on-target effect of CSF1R inhibition. An amendment was made during Phase 2 to allow dosing with higher CK levels

Activity at 4 mg/kg was: 1PR and 1 CK discontinuation in 3 pts in Ph1; 4 PRs in 7 evaluable pts with 6 additional ongoing in Ph2. Positive functional status improvements by O-H score were noted in objective responders (from 2 to 7).

**Conclusions:** The initial demonstration of objective and functional activity supports further development of cabiralizumab in pts with D-TGCT. Updated data from the ongoing Ph2 will be presented. [NCT02471716](#).