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Oral CSF1-receptor inhibition with PLX3397 for tenosynovial giant cell tumor/pigmented villonodular synovitis: MRI assessment using novel modified RECIST, tumor volume scoring, and tissue damage scoring

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Introduction: Tenosynovial giant cell tumor (TGCT) is a rare locally aggressive neoplasm of the synovium sometimes requiring joint replacement or amputation. Measuring treatment response with Response Evaluation Criteria In Solid Tumors (RECIST 1.1) in clinical trials of TGCT is challenging and doesn't consider local tissue damage, a major cause of morbidity. We compared conventional RECIST to two novel methods, modified RECIST (mRECIST) and tumor volume scoring (TVS), and added a scoring method for local tissue damage (TDS) in a longitudinal trial of PLX3397, an oral inhibitor of colony stimulating factor (CSF)1 receptor kinase.

Methods: Fourteen patients with progressive or relapsing TGCT from an ongoing, single-arm, multi-center phase 1 trial of PLX3397 (1000 mg daily total dose) had MRI at baseline and every 2 months for up to 24 months. Two patients also had serial FDG-PET. Images were assessed centrally, blinded to visit order, by two independent radiologists using RECIST (based on longest tumor dimensions), mRECIST (short-axis dimensions), and TVS (10% increments of maximally distended normal synovial cavity or tendon sheath). For TVS, Partial Response (PR) was ≥ 50% decrease, and Progressive Disease (PD) was ≥ 30% increase over the lowest score. TDS, adapted from Whole-Organ MRI Score (WORMS) for osteoarthritis, assessed multiple features, including bone erosion, marrow edema and joint effusion. Baseline CSF1 expression was assayed by in situ hybridization staining and reviewed by an expert pathologist.

Results: CSF1 expression was confirmed in all (n=12) qualified samples. Conventional RECIST showed a majority of the patients as responders (64% PR, 36% stable disease (SD), none progressed) and median tumor decrease of 39%. mRECIST and TVS showed higher proportions of responders (both 79% PR, 21% SD, none progressed) and greater median tumor decrease (48%, 61%). Both patients with FDG-PET showed response to treatment. TDS showed 71% had bone erosions; none progressed; 71% had marrow edema; 80% improved. 78% had joint effusion; 57% improved.

Conclusions: Treatment with PLX3397 resulted in sustained tumor regression in the majority of patients based on conventional RECIST. mRECIST, TVS and TDS provided superior assessment of TGCT than RECIST did, will be studied further in a Phase 3 TGCT trial.