Presentation Title:

A phase 4, multicenter, global clinical study to evaluate discontinuation and rechallenge of pexidartinib in patients with tenosynovial giant cell tumor (TGCT) previously treated with pexidartinib

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ABSTRACT:

Objective: Pexidartinib demonstrated a robust tumor response with manageable safety in patients with TGCT in the phase 3 ENLIVEN study; however, data are needed to understand whether intermittent dosing may be a viable treatment strategy for patients free from progression while on therapy. This phase 4, open-label, nonrandomized study (NCT04526704) evaluated outcomes in patients with TGCT following pexidartinib discontinuation/rechallenge.

Methods: Patients with TGCT from prior studies (NCT02371369; NCT01004861; NCT02734433; NCT03291288) were enrolled after the prior study's end-of-treatment visit. Patients chose to continue (Treatment Continuation Cohort [TCC]; same dose from prior study) or discontinue pexidartinib with option to re-initiate (Treatment-free/Re-treatment Cohort [TF/RTC]) at the investigator's/patient's discretion. The primary endpoint was proportion of patients remaining treatment-free at 12- and 24-months after entering the TF period. Secondary endpoints included proportion of patients with progressive disease (PD) by RECIST v1.1, patient-reported outcomes (PROMIS physical function, health-related quality of life [EQ-5D 5L]), and safety.

Results: From October 2020 to April 2021, 32 patients enrolled (21 in TCC, 11 in TF/RTC). Median age was 47.5 (range: 21-81) years, 50% were female, and the knee was the most common tumor site (84%). 15 (47%) patients had received pexidartinib at 800 mg/day, 9 (28%) at 400 mg/day, and 8 (25%) at 600 mg/day. 4 patients (TCC) discontinued early due to adverse event (n=1), physician decision (n=1), or patient withdrawal (n=2). No PD was reported in the TCC; 6/11 (55%) patients in the TF/RTC had PD in the TF period. 3/11 (27%) patients in the TF/RTC resumed pexidartinib due to progression per RECIST (n=1), symptomatic progression (n=1), or both symptomatic and RECIST progression (n=1). Probability of remaining TF (ie, primary endpoint) was 73% (95% CI: 37%, 90%) at both 12- and 24-months. All 3 patients who restarted pexidartinib experienced tumor growth arrest by 1-month (n=2) or 6-months (n=1) after pexidartinib rechallenge. Overall, PROMIS physical function and EQ-5D-5L were stable for both Cohorts over 24 months. There were no grade 5 TEAEs/TEAEs of special interest; grade 4 CPK increase occurred in 1/21 (TCC) and 1/3 (TF/RTC) patients.

Conclusion: In this phase 4 study, no progression was observed in patients who continued pexidartinib, while PD occurred in 55% who discontinued treatment. Tumor progression stopped within 1-6 months in the 3 patients who resumed pexidartinib; no new safety signals emerged. These results suggest intermittent dosing may be safe and effective for patients who have TGCT disease control with pexidartinib.