Paper #58

SAFETY AND EFFICACY OF DENOSUMAB FOR GIANT CELL TUMOR OF BONE

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Objective: Giant cell tumor of bone (GCTB) is a rare, aggressive tumor. Currently, no definitive therapy exists for patients (pts) with unresectable or metastatic GCTB. Surgery for resectable GCTB may be effective, but aggressive and morbid procedures are often required to reduce the risk of recurrence. Denosumab is a fully human monoclonal antibody against RANKL. In a previous phase 2 study, denosumab reduced the number of giant cells by ≥ 90% in the majority of GCTB pts. We report safety and efficacy results from a prespecified interim analysis of a second open-label phase 2 study of denosumab in GCTB pts.

Methods: Pts with surgically unsalvageable GCTB (Cohort 1), resectable GCTB with planned surgery (Cohort 2), or who transferred from a previous phase 2 study (Cohort 3) received SC denosumab (120 mg, Q4W). Investigator-determined disease status was assessed at each visit. Investigator-determined assessments were based on clinical status, radiologic assessments, or pathological response. For Cohort 2 pts, the timing and type of surgical intervention were also recorded and compared with the planned surgery at baseline.

Results: Enrolled pts (N = 282) were 58% female; median age 33 (range, 13-83) yrs; 47% had recurrent unresectable disease; median time on study 10 (range, 0-29) months. Adverse events were reported in 236 pts (84%); most frequently arthralgia 20%; headache 18%; nausea 17%; fatigue 16%; back pain 15%, and extremity pain 15%. Osteonecrosis of the jaw was reported in 3 pts (1%); 2 of 3 cases resolved by the analysis cut-off date with conservative therapy. One pt died of respiratory failure, not denosumab-related. Non-serious hypocalcemia was reported in 15 pts (5%). Based on investigator's assessment of disease status, 163 of 169 evaluable pts (96%) in Cohort 1 had no disease progression at any time on study. Based on best response, 158 of 159 (99%) had achieved stable disease or better. Among 100 Cohort 2 pts who had planned surgery at baseline, 64 of 71 eligible pts (90%) had not undergone their planned surgery by month 6. At the analysis cut-off date, 74 (74%) had no surgery and 16 (16%) underwent less morbid surgery than initially planned.

Conclusion: In the largest study of GCTB therapy to date, denosumab appeared to be well tolerated and delayed disease progression in the majority of pts. Denosumab also prolonged the time to surgery and reduced the need for morbid surgery in many pts. Denosumab continues to be studied as a potential treatment for GCTB.