Giant Cell Tumor of Bone: Initial Results of Anti-Sclerostin Therapy

Jonah Mitchell Liwag[1], Tyler Y Shimabukuro, Lee-Ann Murata, wendy kurata, Sean P Kelly
[1]Orthopaedic Surgery

INTRODUCTION: Giant Cell Tumor of Bone (GCTB) is a rare, locally aggressive skeletal neoplasm associated with significant patient morbidity. Recurrence rates have been shown to be as high as 50% following resection or curettage alone. While anti-RANKL therapy (denosumab) is commonly used as an adjuvant treatment, recurrence remains a concern after cessation. As neoadjuvant treatment, denosumab has also been shown make the surgical margins less clear complicating curettage. Sclerostin (SOST), a negative regulator of bone formation, has been identified in the neoplastic stromal cells of GCTB and anti-SOST therapies, such as blosozumab and romosozumab, have been safely used to treat recalcitrant osteoporosis. This study explores the potential of anti-SOST therapy to treat GCTB in a cell culture model.

METHODS:

A de novo cell line and two commercially available cell lines were cultured and tested for the characteristic H3F3A (G34W) mutation to confirm the diagnosis and identification of the neoplastic cells. Cells were treated with either blosozumab (anti-SOST), romosozumab (anti-SOST), denosumab (anti-RANKL), or a control group with no medication. Cell counts were recorded pre and post treatment and percent growth rate compared to control was recorded. Statistical analysis was performed including paired t-test for the primary comparisons of blosozumab to control and denosumab with $p<0.05$. Additionally Type II ANOVA, Tukey's HSD, Cohen's d tests were performed.

RESULTS:

All three cell lines were successfully cultured and confirmed to harbor the H3F3A (G34W) mutation. Compared to control, the overall growth rate for denosumab was 130.9%. For the anti-SOST treatments, blosozumab and romosozumab, showed 81.13% and 121.3% growth rates when compared to control, respectively. With comparison to control, there was no statistical difference for blosozumab. When compared to denosumab, blosozumab had a statistically significant difference in cell growth ($p=.0046$). ANOVA testing including Tukey were not statistically significant. Finally, the results of the Cohen's d test revealed that blosozumab had a moderate inhibition of cell growth compared to control ($d=0.772$) while denosumab and romosozumab had moderate acceleration of cell growth compared to control ($d=0.508$ and $d=0.356$).

DISCUSSION AND CONCLUSION:

Our results suggest blosozumab (anti-SOST) inhibits GCTB growth when compared to denosumab (RANKL) and exhibits moderate treatment effect compared to control. Differences may exist in the efficacy of anti-SOST treatments, blosozumab and romosozumab, and may stem from variations in antibody isotope (IgG2 vs IgG4) or binding epitope specificity. Further research is required to determine the clinical translatability of these findings but may indicate a role for anti-SOST treatment in GCTB.