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“Denosumab for Giant Cell Tumors of the Spine; Molecular Predictors of Clinical Response”

Giant Cell Tumors of the spine are aggressive tumors affecting the young adult population, leading to deformity, pain and paralysis. Surgery to resect these tumors is associated with high morbidity and significant recurrence rate. Denosumab, a medication targeting the cells responsible for bony resorption, has been employed in the spine either to control disease in unresectable tumors or to make the surgery easier by reducing and calcifying tumors. While it has been employed successfully, variable response rate has been observed and so far, there is not predictors of treatment response. Information is lacking on long-term use of this medication; how does this medication interact with bony formation? This is of utmost importance when a young patient might be on lifelong treatment. Hence, patient selection and an understanding of the interaction between the medication and the bone are of critical importance in this population, particularly in the spine where tumor progression/ lack of treatment response can lead to paralysis. There is an urgent need to determine which patient would benefit the most from this medication. Using our local cohort of GCTs treated with Denosumab, our primary objective is to identify markers expressed by the tumor that predict treatment response to Denosumab.

Aim 1 is to explore potential molecular biomarkers for treatment response. Using these established molecular or immunohistochemical biomarkers, we will explore their relationship with treatment response.

Aim 2 is to explore the structural and biomechanical properties of the post treatment bone. One of the two usages of denosumab is stand-alone for a long-term used. While pain has been shown to be improved with this treatment and calcifications have been observed, the structural properties are unknown. We propose to study the material nature, structure, and mechanical properties of the Denosumab treated specimen.

Ultimately, this research will provide insight about predictive factors for response with denosumab and will lead to a comprehensive knowledge of the interaction between the medication and the host. This exploratory research will promote bone health and judicious treatment selection in this young population.