A097 Molecular Profiling of Two Unclassified Primary Bone and Soft Tissue Tumors

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Introduction: Next generation sequencing (NGS) has become the standard of practice for evaluation of solid tumors and the basis for precision medicine initiatives. There is significant data for profiling of many tumor types that can complement traditional diagnostic and prognostic tests and can lead to better therapeutic selection. Here we present NGS data on two unclassified bone and soft tissue tumors and discuss the clinical implications of these profiles. **Methods:** DNA/RNA were extracted from FFPE tissue using the Qiagen AllPrep kit. Libraries were prepared with an Illumina TruSight Tumor 170 automated method on the Biomek NXp span-8 liquid handler (Beckman Coulter), then sequenced on the NextSeq® 500 System. DNA and RNA Alignment and variant calling was preformed using TruSight Tumor 170 v1.0 Local App (Illumina). Non-synonymous single nucleotide variants and indels in coding regions, with a variant allele frequency greater than 5%, coverage greater than 250x, and a gnomAD population frequency less than 5% were retained and reviewed in Integrative Genomics Viewer (Broad Institute). High confidence fusions and amplifications with a copy number greater than 5 were also retained. **Results:** We identified one iliac bone high-grade undifferentiated sarcoma with epithelioid features and one high grade malignant neoplasm of uncertain lineage of the lower leg. The former harbored two fusions, one involving exon 8 of MSH2 and intron 1 of SUCLG1 and one involving exon 2 of MET and WNT2. Copy number gene amplifications in FGF23 (5.5), FGF6 (5.4) and KRAS (7.3) were also identified. The mutated genes with the highest variant allele frequency (VF) were KRAS (0.8894), ATR (0.8375 and 0.8296) and BRCA2 (0.7425). Point mutations in other genes such as FANCI, TP53, SMO, FGF3, MSH2, ARID1A, GNAS, FGFR2, RICTOR and JAK3 were also identified. The second tumor only harbored point mutations in PIK3CG (0.5976), CDK6 (0.5346), MSH3 (0.5192), NRG1 (0.4983), NOTCH3 (0.4948), BRCA2 (0.4746), BRCA1 (0.4341), MUTYH (0.4328), MRE11A (0.4294), CARD11 (0.3274) and ROS1 (0.194). **Conclusions:** NGS is a powerful tool for investigating genetic profiles of challenging bone and soft tissue tumors. Even in tumors, which remain unclassified with no pathognomonic driver genetic events, it can still provide useful potentially clinical actionable data.