Molecular biology of angiosarcoma varies according to primary site.

**Head and Neck AS:**
- **IO-response markers:** 65% of cases (n=28/43; p<0.0001, q=0.0149). Figure 3B.
- **TMB-high observed in 61.3% (n=26/42; p<0.0001, q<0.0001).** Figure 2.
- **ARID1A mutation present in 33.3% (n=15/45; p=0.0578, q=1.0).** Figure 3A.

**Breast AS:**
- **Cell cycle pathway aberrations were the most common (Figure 3B) and almost entirely driven by MYC amplification present in 63.3% (n=19/30; p<0.0001, q<0.0001).** Figure 2.
- **HRAS mutations present in 16.1% (n=5/31; nsp=0.0377, q=1.0).** Figure 3A.
- **PI3KCA mutation present in 16.1% (n=5/31; nsp=0.2352, q=1.0).** Figure 3A.
- **Highest among AS subgroups.**

**Extremity AS:**
- **TP53 mutation present in 50.0% (n=21/42; p=0.0004, q=0.0716).** Figure 3A.

**Visceral AS:**
- **POU5F1 mutations present in 16.7% (n=4/24; p=0.0043, q=0.0149).** Figure 2.
- **TMB-high observed in 62.5% (n=25/40; p<0.0001, q<0.0001).** Figure 2.

**Cutaneous locations other than head and neck, breast or extremity.**

**Figure 1. Occipital for Most Frequently Altered Biomarkers.**

**Figure 2. Frequency of predictive markers of potential response to IO therapy by primary AS site.** **Doubling of V and Q value as a counter."**

**Figure 3. Frequency of biomarkers stratified by primary site. A. Specific biomarker alteration frequencies of biomarkers mutated in ≥ 3 cases were included. B. Frequencies of mutated genes grouped by pathway.**