#11539: Deciphering the molecular landscape and the tumor microenvironment of Perivascular Epithelioid Cell Neoplasm (=PEComa)

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Background & Aim:
- PEComa is a rare mesenchymal neoplasm composed of perivascular epithelioid cells. Due to its rarity, diagnosis is challenging, and no standardized treatment guidelines have been established.
- A part of PEComas showed a benefit upon nab-sirolimus treatment (Wagner AJ et al, ASCO 2019)
- A subgroup of PEComas are characterized by a loss of function mutation in TSC1/2.
- In the majority the molecular landscape and the composition of the tumor microenvironment (TME) remain largely unclear.
- We conducted this study to elucidate the genetic landscape of PEComas.

Patients & Methods:
- Thirty-five PEComa specimens were centrally analyzed at the Caris Life Sciences laboratory.
- NextGen DNA sequencing (NextSeq, 592 gene panel or NovaSeq, whole-exome-sequencing), whole-transcriptome RNA sequencing (NovaSeq) and immunohistochemistry (Caris Life Sciences, Phoenix, AZ) were performed.
- Gene expression profiling (GEP) was performed by unsupervised hierarchical clustering.
- RNA deconvolution analysis was performed using the Microenvironment Cell Populations (MCP)-counter method to quantify immune cell populations.

Results:

1) Most common mutations detected were TP53 (47%), ATRX (32%), TSC1/2 (11%/29%) and MSH3 (17%). TP53 mutations occurred less frequently (25 vs 60%, p=0.055) in TSC1/2-mutated (TSC1/2-mt) compared to TSC1/2-wildtype (TSC1/2-wt) tumors.

2) Thirty-five PEComa specimens were centrally analyzed at the Caris Life Sciences laboratory.

3) This might explain why not all patients showed a benefit when using mTOR inhibitors.

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CONCLUSIONS:
1) PEComas are characterized by a heterogeneous molecular landscape with a high prevalence of TSC1/2 mutations.
2) Only a subset of TSC1/2-mt PEComas were associated with an up-regulation of the PI3K-Akt-mTOR pathway.
3) This might explain why not all patients showed a benefit when using mTOR inhibitors.