Tumor mutational burden in anal cancer

Tumor mutational burden (TMB) in malignant diseases

- TMB: total **number of somatic mutations** per coding area of tumor genome
- High TMB → more **neoantigens** and potentially increased **T-cell reactivity**
- TMB cutoff unclear – Keynote 158 trial: ≥ 10 Mutations/Megabase

Marabelle et al, Lancet Oncology 2020

Tumor Mutational Burden – Keynote 158 trial

- 1066 patients with 10 different solid tumor entities
- 89 with recurrent/metastatic anal cancer
- **Overall**: Higher overall response rate (ORR) in patients with high TMB (≥ 10 Mut/Mb)
- **Anal cancer**:
  - Patients with better ORR had higher median TMB (7.57 vs. 5.04)

Marabelle et al, Lancet Oncology 2020

Tumor Mutational Burden – Head and Neck Cancer

- 126 Patients, treated with anti PD-1/L1 immune checkpoint inhibitors (ICI)
- HPV+ Pts w/ improved OS
- TMB significantly higher in HPV- patients (8.2 vs. **4.7**)
- No difference in response in HPV+ according to TMB Status

Hanna et al, JCI Insight 2019

TMB: literature overview

Author	Patients (n)	Median TMB (Mutations/MB)	% of patients w/ high TMB	Note
Shao	125	**4.4**	**13.6%**	No immunotherapy, no differences in OS
Yarchoan	32	**4.35**	**15.6%**	n.a.
Marabelle	89	**n.a.**	**15.7%**	Pts w/ better ORR to ICI had higher median TMB

- **A significant proportion of patients with anal cancer have a high TMB that was comparable to HPV+ head and neck cancers**
- **The long-term prognostic impact of TMB in anal cancer remains unclear**

Shao, JAMA Network Open 2020; Marabelle, Lancet Oncology 2020; Yarchoan, JCI Insight 2019

Summary

- Proportion of high TMB / median TMB in anal cancer comparable to other HPV-driven malignancies (cervical, vulvar, head and neck)
- Association between TMB and long-term oncological outcome after ICI in anal cancer needs to be evaluated

Shao, JAMA Network Open 2020; Marabelle, Lancet Oncology 2020; Yarchoan, JCI Insight 2019; Hanna, JCI Insight 2018;