

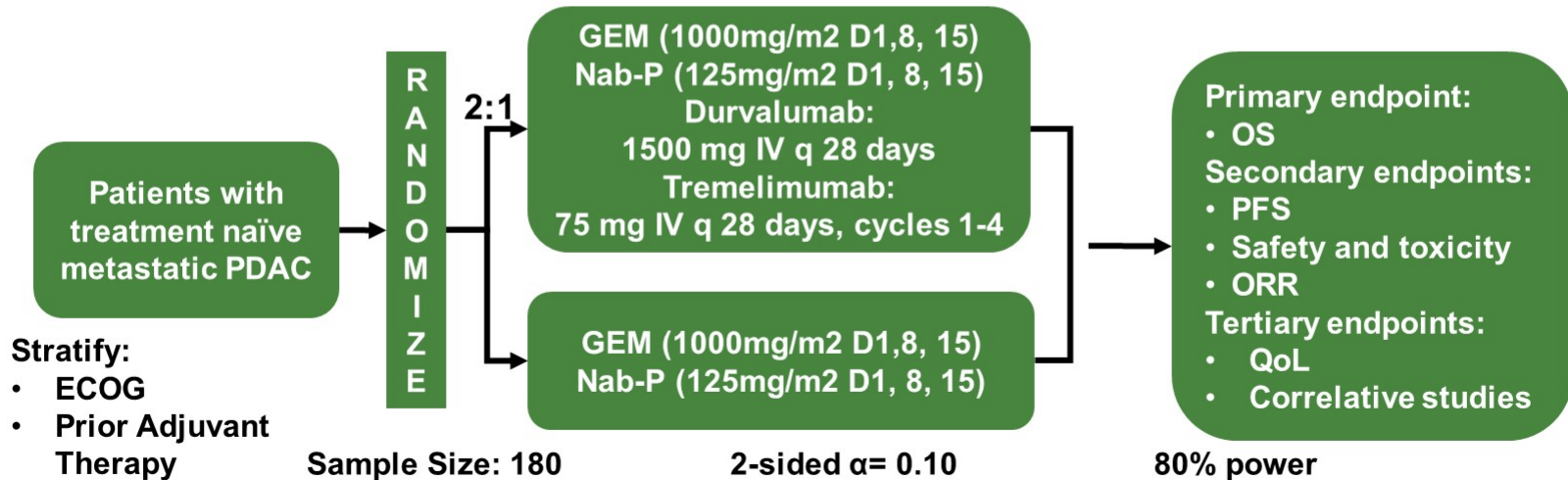
Predictive value of plasma tumor mutation burden (TMB) in the CCTG PA.7 trial: Gemcitabine (GEM) and Nab-Paclitaxel (Nab-P) vs. GEM, Nab-P, Durvalumab (D) and Tremelimumab (T) as First Line Therapy in Metastatic Pancreatic Ductal Adenocarcinoma (mPDAC)

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Background:

- The PA.7 trial assessed the efficacy of Gemcitabine + Nab-Paclitaxel given in combination with PD-L1 and CTLA-4 inhibition (Durvalumab and Tremelimumab)
- High TMB has been associated with immunotherapy sensitivity

CCTG PA.7 Study Schema

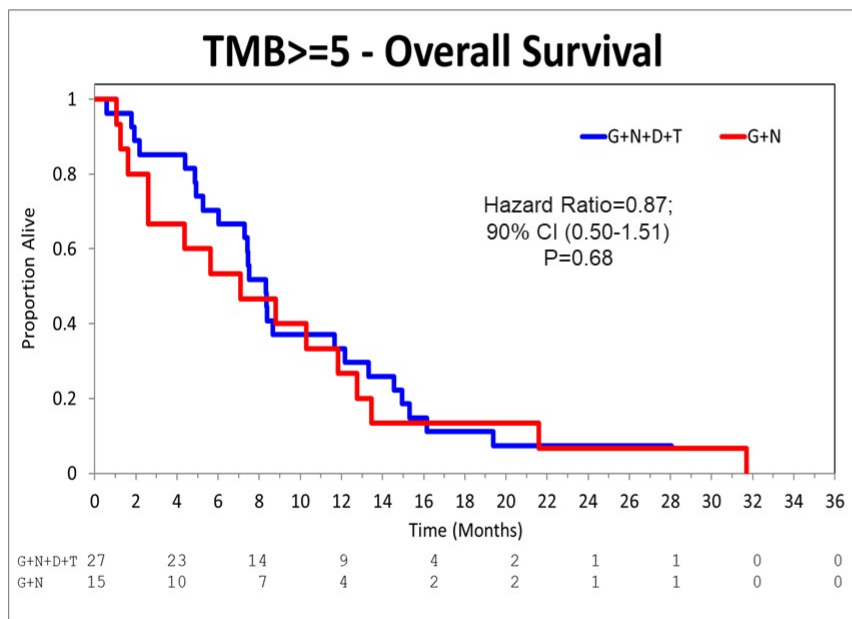


Methods:

- **cfDNA analysis performed on pre-treatment plasma samples**
 - Sequenced with PredicineATLAS™ NGS Assay
 - 600-gene, 2.4 Mb panel
 - Pre-specified cut point of 5 mut/MB selected based on distribution of TMB in the trial
 - A minimum p-value approach was used to assess other cut-points
- **Plasma TMB analysis was performed on 174/180 patients with available samples**
 - Tumor derived variants detected in 173/174 patients (99.4%)
 - 172 patients were MSS and 1 was MSI-H

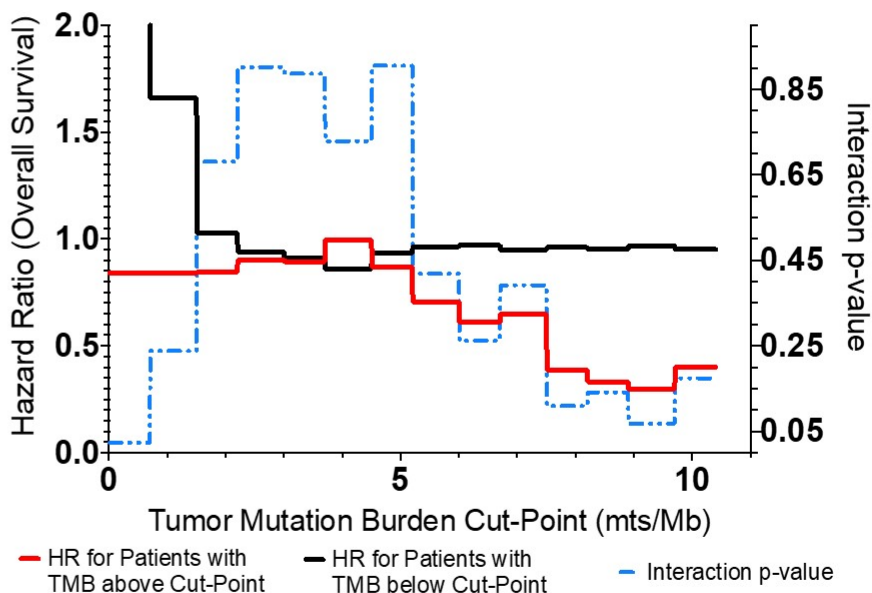
Results: Pre-specified cut-point showed no utility as a predictive biomarker but increased TMB suggests benefit

Overall Survival in Patients with TMB ≥ 5 mut/MB (27/174 (4.6%))



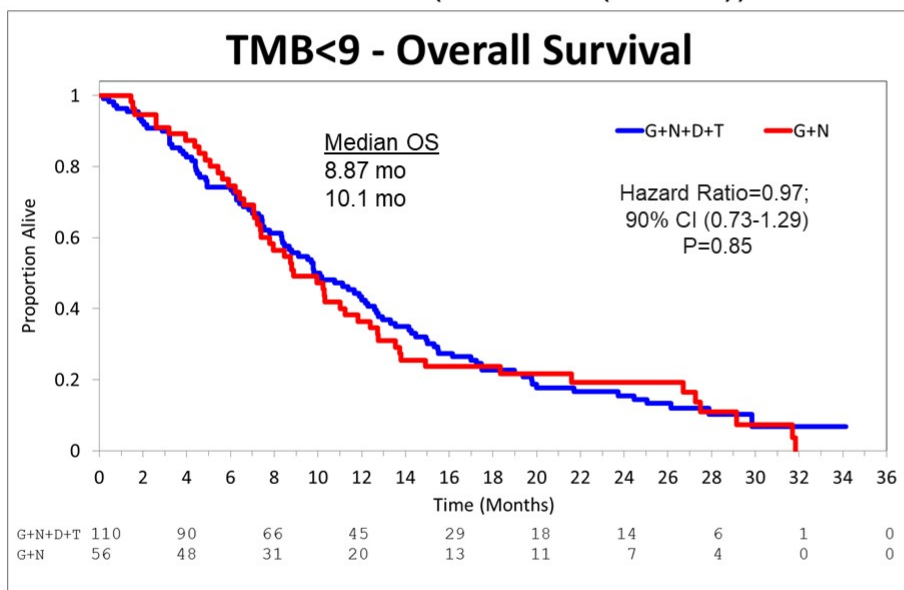
P-interaction = 0.91

Explorative analysis showed a trend for decreasing HR favoring the immunotherapy arm above the selected cut point, with no benefit in the low TMB group

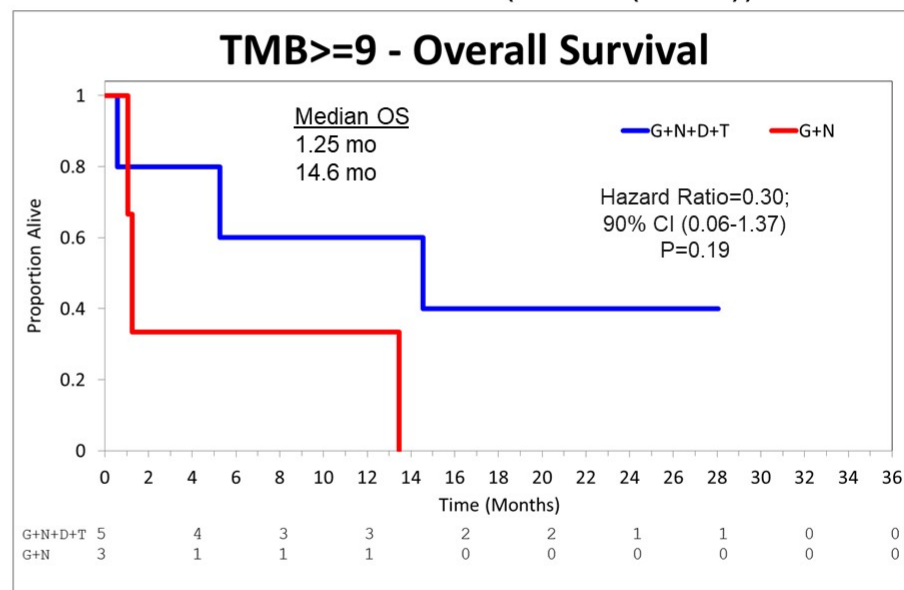


Results: A cut-point of 9 mut/MB appeared predictive of benefit in the immunotherapy arm

Overall Survival in Patients with TMB <9 mut/MB (166/174 (95.4%))



Overall Survival in Patients with TMB ≥9 mut/MB (8/174 (4.6%))



P-interaction = 0.064 (significant at pre-specified p=0.1)

Conclusions:

- Plasma TBM analysis was successful in over 99% of patients with available samples
- Plasma TMB ≥ 9 mut/Mb may predict benefit from the addition of dual immune checkpoint inhibitors (D and T) to Gem and Nab-P.
- While only present in a subgroup of pts (4.6%), this data defines a group beyond MSI-H PDAC that should be investigated further for the benefit of immunotherapy.
- **A clinical trial specifically assessing the role of chemotherapy combined with immune checkpoint inhibition in high TMB mPDAC is warranted.**