

#G121

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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PRESENTED AT: Gastrointestinal Cancers Symposium

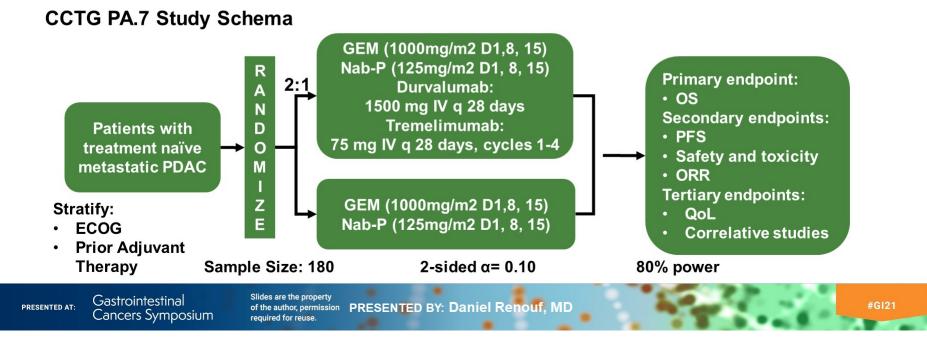
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Background:



- 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



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%))

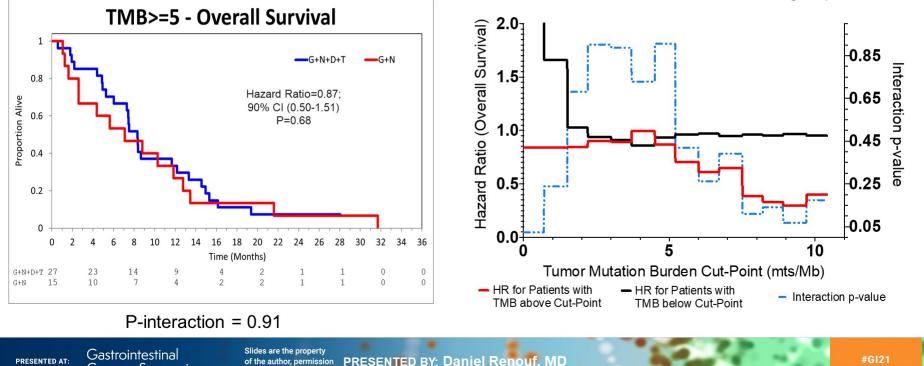
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Explorative analysis showed a trend for decreasing HR favoring the immunotherapy arm above the selected cut point, with no benefit in the low TMB group



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

Overall Survival in Patients with Overall Survival in Patients with TMB <9 mut/MB (166/174 (95.4%)) TMB ≥9 mut/MB (8/174 (4.6%)) TMB<9 - Overall Survival TMB>=9 - Overall Survival 1 Median OS G+N+D+T G+N G+N+D+1 G+N Median OS 1.25 mo 0.8 0.8 8.87 mo 14.6 mo Hazard Ratio=0.97; Hazard Ratio=0.30; 10.1 mo Proportion Alive Proportion Alive 90% CI (0.73-1.29) 90% CI (0.06-1.37) 0.6 0.6 P=0.85 P=0.19 0.4 0.4 0.2 0.2 22 24 26 28 30 32 34 10 12 14 16 18 20 36 8 10 12 14 16 18 20 22 24 26 28 30 32 34 Time (Months) Time (Months) G+N+D+T 110 90 66 45 29 18 0 G+N+D+T 5 2 2 14 6 1 3 3 0 0 0 0 G+N 56 48 31 20 13 11 7 0 0 G+N 1 0 0 0 0

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.

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