2021 ASCO ANNUAL MEETING

Canadian Cancer Trials Group
A national program of the Canadian Cancer Society

PREDICTIVE VALUE OF PLASMA ATM 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)

Renouf D, Loree J, Knox J, Kavan P, Jonker D, Welch S, Couture F, Lemay F, Tehfe M, Harb M, Aucoin N, Ko Y, Tang P, Topham J, Jia S, Du P, Schaeffer D, Gill S, Tu D, O'Callaghan C

CCTG PA.7 Study Schema:

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Patients with treatment naïve metastatic PDAC

Stratify:
- **ECOG**
- **Prior Adjuvant Therapy**

RANDOMIZE **2:1**

GEM (1000mg/m2 D1,8, 15)
Nab-P (125mg/m2 D1, 8, 15)
Durvalumab
1500 mg IV q 28 days
Tremelimumab:
75 mg IV q 28 days, cycles 1-4

GEM (1000mg/m2 D1,8, 15)
Nab-P (125mg/m2 D1, 8, 15)

Primary endpoint:
- **OS**

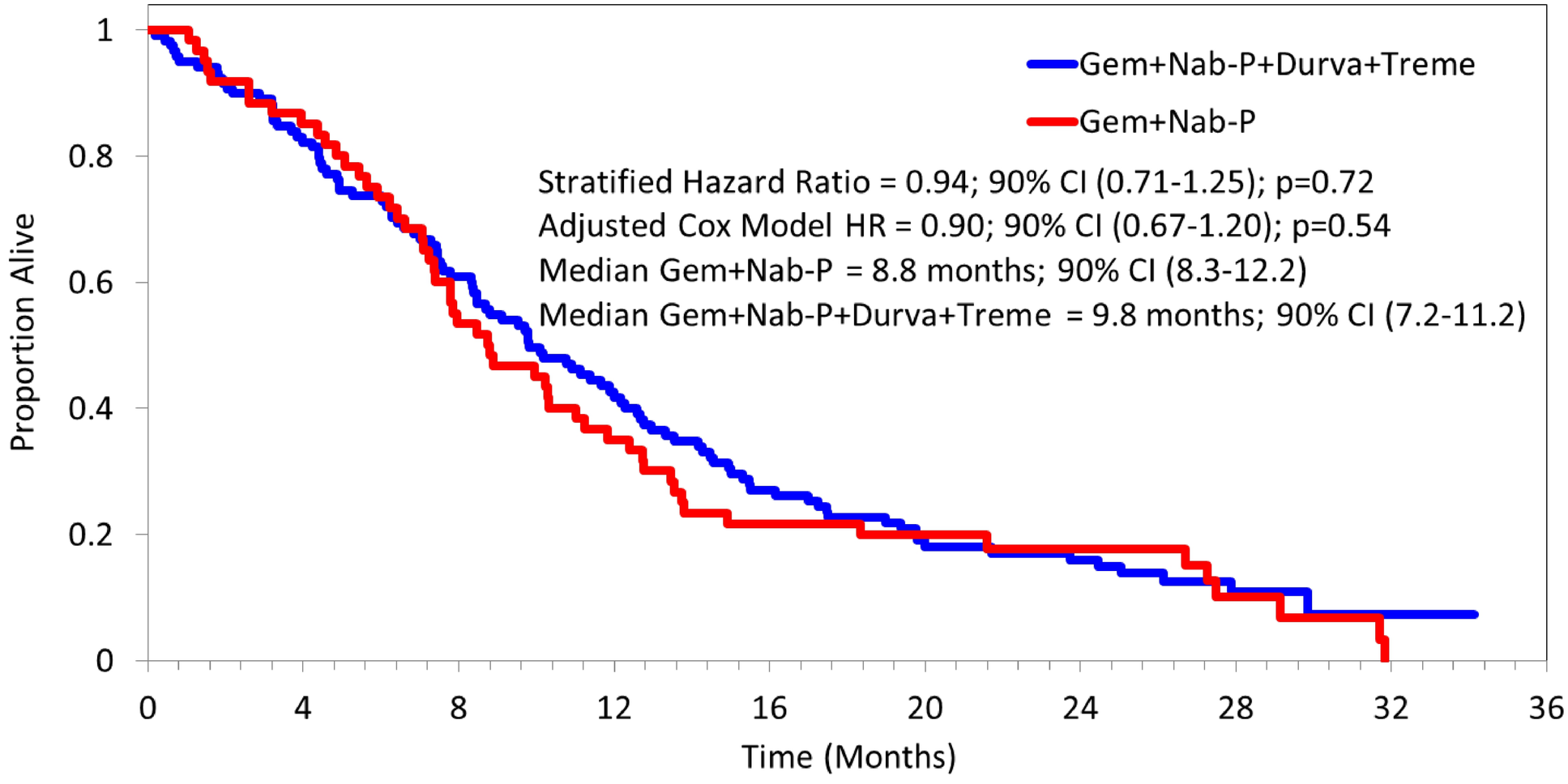
Secondary endpoints:
- **PFS**
- **Safety and toxicity**
- **ORR**

Tertiary endpoints:
- **QoL**
- **Correlative studies**

Sample Size: 180

DNA repair pathway aberrations beyond MMR have been associated with potential immune sensitivity

Results: Overall Survival



Correlative Analysis

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•cfDNA analysis performed on pre-treatment plasma samples

- Sequenced with PredicineATLAS™ NGS Assay
  - 600-gene, 2.4 Mb panel

•Plasma DNA repair 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: *ATM* mutations appeared predictive of benefit in the immunotherapy arm

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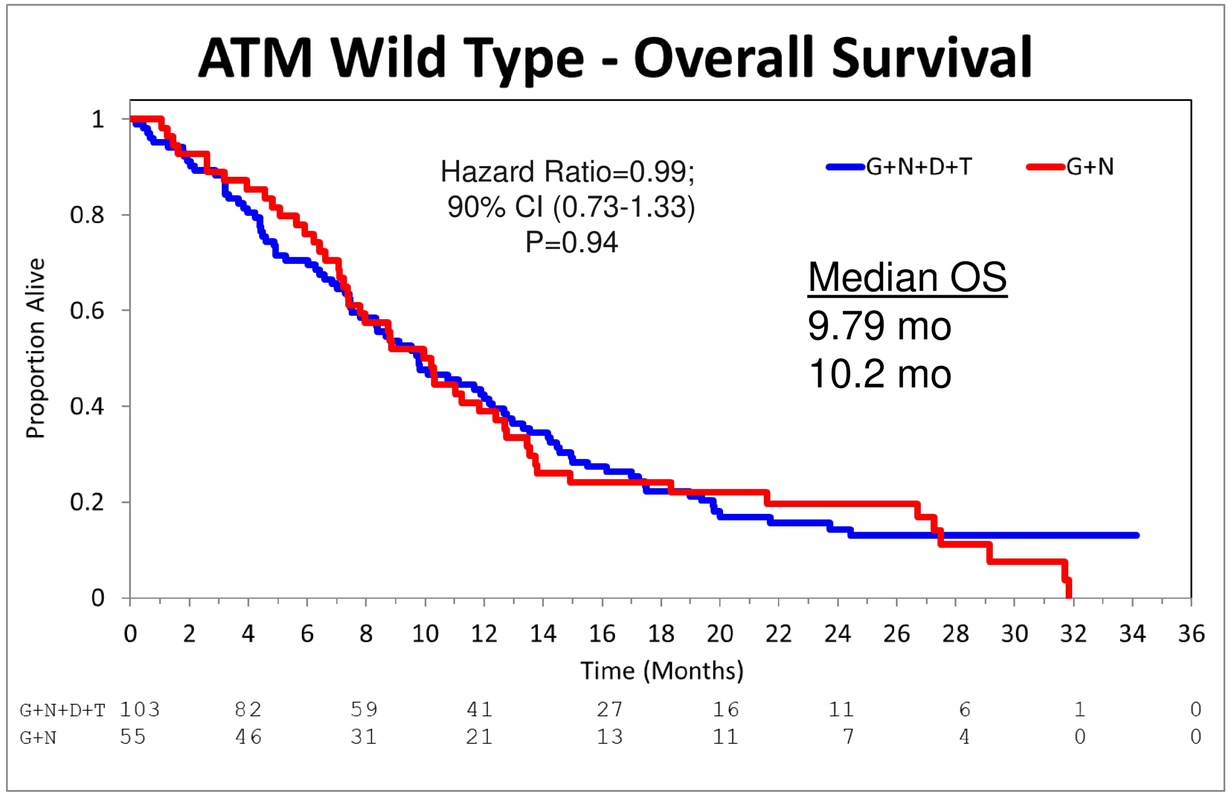
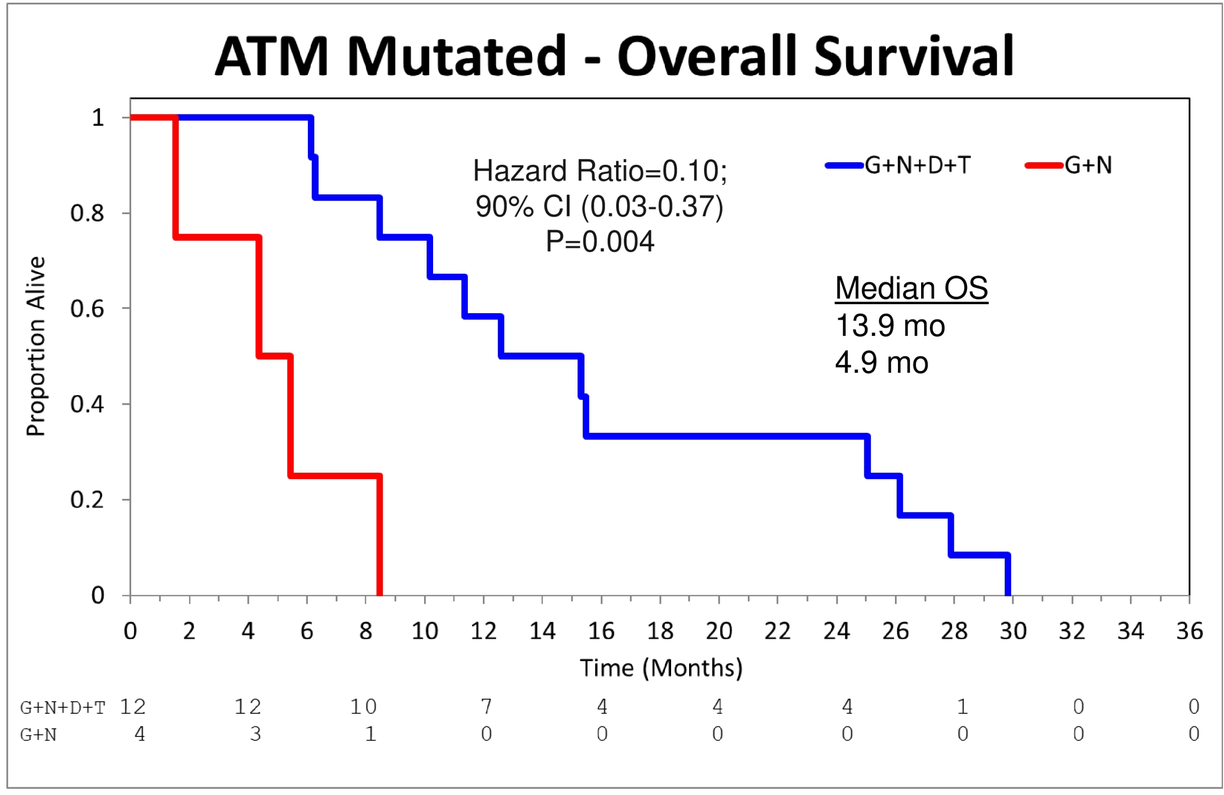
Overall Survival in Patients with germline *ATM* Wild Type (158/174 (90.8 %))



Overall Survival in Patients with germline *ATM* mutations (16/174 (9.2%))



P-interaction = 0.014 (significant at pre-specified p=0.1)

Conclusions:

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- The addition of durvalumab and tremelimumab to gemcitabine and nab-paclitaxel did not result in a significant improvement in OS, PFS or ORR

- Plasma cfDNA analysis was successful in over 99% of patients with available samples

- Plasma germline *ATM* mutations may predict benefit from the addition of dual immune checkpoint inhibitors (D and T) to Gem and Nab-P

- This data supports that there may be groups beyond dMMR that should be investigated further for benefit of immunotherapy in PDAC