Background

Frontline treatment for advanced pancreatic ductal adenocarcinoma (PDAC) has been either 5-fluorouracil, oxaliplatin and irinotecan (FOLFIRINOX) or gemcitabine and nab-paclitaxel (GP) for the past decade. While the NAPOLI-3 trial, utilizing liposomal irinotecan, highlighted the superiority of a triplet regimen over platinum chemotherapy and confered KRAS variants in PDAC, the sample size is small and needs validation in additional datasets.

Methods

PDAC samples were tested using whole transcriptome sequencing (WTS; Illumina NovaSeq) and NextGen DNA sequencing (NextSeq, AZ). Significance was determined by X² and Fisher-Exact and p values adjusted for multiple comparisons (q). Real-world overall survival (rwOS) was obtained from insurance claims data and calculated from first of treatment to last contact with comparison done by Kaplan-Meier test.

Table 1: patient demographics

<table>
<thead>
<tr>
<th></th>
<th>G12C</th>
<th>G12V</th>
<th>G12D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Count (N)</td>
<td>621</td>
<td>1294</td>
<td>746</td>
</tr>
<tr>
<td>Median Age</td>
<td>68.0 (37 - 92.0)</td>
<td>67.0 (37 - 92.0)</td>
<td>67.0 (37 - 92.0)</td>
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<tr>
<td>Male</td>
<td>592 (95.4%)</td>
<td>1196 (92.3%)</td>
<td>600 (81.1%)</td>
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<tr>
<td>Female</td>
<td>193 (15.1%)</td>
<td>352 (27.7%)</td>
<td>146 (20.9%)</td>
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</table>

Results

Figure 1 – Median OS comparison for patients treated with FOLFIRINOX vs Gemcitabine/nab-paclitaxel (GP) by KRAS variant.

A. G12C

Median difference=230 days

B. G12D

Median difference=95 days

C. G12V

Median difference=144 days

D. G12R

Median difference=78 days

Conclusions

In patients with advanced PDAC and a G12C mutation, median overall survival appears significantly longer in those treated with GP compared to FOLFIRINOX.

The positive trend was seen in patients with other KRAS variants including G12D and G12V, consistent with the recently presented NAPOLI-3 trial.

PD-L1 staining was also highest in the KRAS G12C cohort.

While this is the largest reported analysis of outcomes to frontline chemotherapy in KRAS G12C-mutated PDAC, the sample size is small and needs validation in additional datasets.

References