Identifying Biomarkers to Select Patients with Borderline Resectable and Locally Advanced Pancreatic Ductal Adenocarcinoma (BRPC, LAPC) for Radiotherapy (RT)
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**Introduction**
- BRPC and LAPC have poor prognosis in which surgery is the only curative treatment.
- RT has a controversial role for BRPC and LAPC, with negative and positive data in recent years.
- A high biologically effective dose of RT is required to achieve tumor ablation.
- Since RT can impact the nearby gastrointestinal tract, the use of curative doses is constrained.
- Previous studies have shown that RT following chemo is associated with better overall survival (OS).

**Primary Aims**
- There is an unmet need to identify biomarkers to select subpopulations of patients with BRPC and LAPC for RT.
- Prior results indicated that CA19-9 response and lymphopenia grade associate with outcomes after RT.
- Here, we investigated these markers and other clinical factors to identify biomarkers that may aid the decision to use RT for BRPC and LAPC.
- We hypothesized that lymphopenia grade and CA19-9 normalization would show to be independent predictors of OS.

**Methods**
- Conducted a retrospective study to analyze patients who received chemotherapy followed by RT for BRPC or LAPC between 2015 and 2020.
- Patients evaluated as a subset from a larger cohort of 454 patients.
- RT dates and lowest absolute lymphocyte counts (ALC) during RT periods were extracted from medical records.
- CA19-9 normalization = minimum CA19-9 value between the start of chemo and 6 months post-chemo < 40 U/mL.
- Lymphopenia grade >2 = patient ALC fell below 0.5 K/µL during radiation.
- Associations between variables were tested using Log-rank and Wilcoxon survival analyses.
- Variables with a p value of < .2 in univariate analysis were used in a multivariate Cox Proportional Hazard analysis test to further determine significance.

**Results**
- Preliminary analysis indicated CA19-9 to be a significant variable associated with OS as predicted.
- Lymphopenia grade did not show to be significant as an independent variable.
- However, there was a significant difference in BPRC vs LAPC OS for patients with lymphopenia grades >2.
- Additional prospective trials are needed to evaluate the ability of these factors to personalize treatment and solidify stable biomarkers.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard Ratio (95% Confidence Interval)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA19-9 Normalization</td>
<td>Norm: 0.489 (0.318-0.745)</td>
<td>0.00012</td>
</tr>
<tr>
<td>Surgery or No Surgery?</td>
<td>Surgery: 0.190 (0.106-0.342)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Radiation Type</td>
<td>IMRT: 0.496 (0.279-0.883)</td>
<td>0.0032</td>
</tr>
</tbody>
</table>

**Conclusions**
- Variables with a p value of < .2 in univariate analysis were used in a multivariate Cox Proportional Hazard analysis test to further determine significance.

**References**
1) Awalpreet et al. Radiat Oncol 2017;2:323-332
3) Reynold et al. Radiat Oncol 2019;1:95
6) Venkatesulu et al. Future Oncol 2022;15:1885-1895