Integration of Somatic Molecular Profiling for Rare Epithelial Gynecologic Cancer Patients

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Background

Rare gynecologic malignancies (R-GYN):

• Defined as <6/100,000/year\(^1\)
• Represent >50% of gynecologic cancers\(^2\)
• Involve >30 histologic subtypes\(^2\)

### Rare Epithelial Gynecologic Cancers
- Cervical adenocarcinoma
- Ovarian low grade
- Ovarian transitional cell/Brenner tumor
- Ovarian squamous
- Endometrial papillary serous/squamous
- Vulvar and Vaginal cancers
- Clear cell cancers
- Carcinosarcomas
- Mucinous cancers
- Small cell cancers

### Rare Non-epithelial Gynecologic Cancers
- Gynecologic sarcomas
- Sex cord tumors
- Germ cell tumors
- Gestational trophoblastic tumors

1. http://www.rarecare.eu

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**Patient Characteristics**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th># Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical Adenocarcinoma/Adenosquamous</td>
<td>11</td>
</tr>
<tr>
<td>Vulvar</td>
<td>12</td>
</tr>
<tr>
<td>Mucinous</td>
<td>17</td>
</tr>
<tr>
<td>Uterine Serous</td>
<td>24</td>
</tr>
<tr>
<td>Carcinosarcoma</td>
<td>32</td>
</tr>
<tr>
<td>Clear Cell</td>
<td>38</td>
</tr>
<tr>
<td>Low Grade</td>
<td>54</td>
</tr>
<tr>
<td>Others$</td>
<td>6</td>
</tr>
</tbody>
</table>

* Others: Vaginal, Transitional/ Brenner Ovarian, Small Cell, Ovarian squamous

**Patients Profiled**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age (range)</td>
<td>59.5 (21-88)</td>
</tr>
<tr>
<td>Median Lines of Prior Treatments (range)</td>
<td>1 (0-4)</td>
</tr>
<tr>
<td>ECOG Performance Status (0/1)</td>
<td>69% / 31%</td>
</tr>
</tbody>
</table>

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Molecular Profiling Results

Patients Profiled | N=194
--- | ---
≥ 1 somatic mutation, n (%) | 139 (72%) (range 1-4)
Archival sample from primary tumor vs metastatic archival sample for profiling | 132 (68%) vs 62 (31%)
Median time from diagnosis to profiling | 18 months (range 1-361)

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Best Tumor Reduction in Therapeutic Trials

Genotype-Unmatched
RECIST v1.1  ORR 7/28 evaluable (25%)

Median tumor size reduction -7% (-60 to +31)

Genotype-Matched
RECIST v1.1  ORR 8/27 evaluable (30%)

Median tumor size reduction -18% (-70 to +36)

* Progression on non-target lesions
^ p=0.16

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TTP on Genotype-Matched Trials vs Genotype-Unmatched vs Standard Therapy

<table>
<thead>
<tr>
<th></th>
<th>TTP</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TTP Genotype-Matched (N=24)</td>
<td>5.5 months (1.2-22)</td>
<td>0.03</td>
</tr>
<tr>
<td>TTP Genotype-Unmatched (N=25)</td>
<td>2.7 months (0.7-18.9)</td>
<td></td>
</tr>
<tr>
<td>TTP Standard therapy post-Profiling (N=26)</td>
<td>2.7 months (0.3-14.6)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

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Conclusions

- Somatic molecular profiling frequently identifies actionable molecular alterations in R-GYN cancer patients.
- Somatic molecular profiling can be integrated into the routine care of R-GYN cancer patients, expanding the spectrum of therapeutic approaches in a population with limited standard options.
- Clinical activity was seen in genotype-matched and unmatched patients on trials.
- Median TTP was longer with genotype-matched targeted trials compared to unmatched trials and standard therapy post-profiling.
- Prospective randomized trials are needed with integrated somatic genotyping.