Immunoprofiling of Mismatch Repair-deficient (MMRd) Endometrial Cancer (EC) patients: Immune Checkpoint Inhibitor (ICI) – Responders (R) versus Non-Responders (NR)

Background & Objectives

- MMRd status is a robust predictive biomarker for ICi in EC, however half of MMRd EC pts do not respond (Oaknin et al, 2020; Makker et al, 2022; O’Malley et al, 2022).
- We aim to describe the immune tumor microenvironment (iTME) of Responders (R) versus Non-Responders (NR) MMRd EC pts to identify new predictive biomarkers for ICi beyond MMR or TMB status.

Methods

- Clinical data and outcomes of metastatic MMRd EC patients, treated with ICi at Gustave Roussy Institute (2016-2021), were retrospectively collected.
- Pts were classified as ICi-R (CR, PR, or SD ≥ 12 months) and NR (PD or SD < 12 months).
- Immunofluorescence (IF) and Immunohistochemistry (IHC) panels were performed for CD3, CD4, CD8, CD20, CD57, FOXP3 and CD23 (quantified by number of + cells or semi-quantitative scoring).
- Non-parametric statistical tests were performed.

Results

Table 1. Study Population (n=24). Clinicopathological features.

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<thead>
<tr>
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<th>ICI-Responders n=15</th>
<th>ICI Non-Responders n=9</th>
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</thead>
<tbody>
<tr>
<td>Age (mean;years)</td>
<td>61</td>
<td>59</td>
</tr>
<tr>
<td>Histology (Endometrioid/others*)</td>
<td>73%/27%</td>
<td>89%/11%</td>
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<tr>
<td>Histopathologic grade (1-3)</td>
<td>80%/20%</td>
<td>78%/22%</td>
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<td>Lynch syndrome (LS)/ Sporadic EC</td>
<td>27%/73%</td>
<td>11%/89%</td>
</tr>
<tr>
<td>Prior lines for advanced/recurrent disease (median/range)</td>
<td>1 (0-2)</td>
<td>1 (1-2)</td>
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*Serous, clear cell and mixed carcinoma;

- As expected, 75% of MMRd EC demonstrated high intratumoral T cell infiltration.
- High T cell infiltration alone may be not sufficient to predict response to ICi, as a proportion of High T cell infiltrated EC are Non-Responders.
- Combined T and B cell infiltration was most associated with response to ICi in MMRd EC.

Conclusions

- Lynch Syndrome was associated with response to ICi: 80% (n=4/5) of LS pts were ICI-Responders.
- T cell infiltration is frequent in MMRd EC but may be not sufficient on its own to predict response to ICi.
- Immunological features strongly associated with response to ICi in MMRd EC were:
  - Combined High T and B cells infiltration,
  - The presence of mature TLS, and
  - High CD8/FOXP3 Ratio

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