Deleterious effect of baseline steroids on efficacy of PD-(L)1 blockade in patients with NSCLC.

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Steroids and PD-(L)1 Blockade

- Steroids are the mainstay of treatment for immune related adverse events (irAEs)
  - Use of steroids to treat irAEs does not appear to diminish efficacy of PD-(L)1 blockade
- Efficacy in patients receiving baseline steroids is unknown
  - Patients on baseline steroids (prednisone ≥10 mg) were not eligible for clinical trials of PD-(L)1 inhibitors
  - Mechanism of action of PD-(L)1 blockade may include "proliferative burst" of CD8+ T-cells
**Methods**

- **Memorial Sloan Kettering Cancer Center** (n=455)
  - Retrospective Review
  - Patients with advanced NSCLC treated with single-agent PD-(L)1 inhibitor
  - Medical records reviewed to identify steroid use on Day 1 of treatment (≥10mg prednisone)

- **Gustave Roussy Cancer Center** (n=185)
  - ORR by RECIST
  - PFS
  - OS from start of treatment

Cohorts analyzed independently

Pooled subgroup and multivariate analysis
Impact of Baseline Steroids on PD-(L)1 Efficacy: Progression-free Survival

MSKCC Cohort

- No steroids (n=402)
- Steroids (n=53)

HR 1.7, p<0.0001

GRCC Cohort

- No steroids (n=148)
- Steroids (n=37)

HR 1.5, p<0.0001
Impact of Baseline Steroids on PD-(L)1 Efficacy: Overall Survival

MSKCC Cohort

- No steroids (n=402)
- Steroids (n=53)

HR 2.1, p<0.0001

GRCC Cohort

- No steroids (n=148)
- Steroids (n=37)

HR 2.0, p<0.001
# Impact of Baseline Steroids on PD-(L)1 Efficacy: Multivariate Analysis

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>ORR Odds Ratio (95% CI)</th>
<th>p-value</th>
<th>PFS Hazard Ratio (95% CI)</th>
<th>p-value</th>
<th>OS Hazard Ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking status (never vs ever)</td>
<td>0.33 (0.15-0.74)</td>
<td>0.007</td>
<td>1.64 (1.30-2.04)</td>
<td>&lt;0.001</td>
<td>1.03 (0.81-1.33)</td>
<td>0.78</td>
</tr>
<tr>
<td>Performance status (ECOG ≥2 vs 0/1)</td>
<td>0.29 (0.11-0.75)</td>
<td>0.11</td>
<td>1.97 (1.55-2.50)</td>
<td>&lt;0.001</td>
<td>2.29 (1.75-2.98)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of brain metastases (yes vs no)</td>
<td>0.88 (0.52-1.49)</td>
<td>0.6</td>
<td>1.16 (0.96-1.41)</td>
<td>0.1</td>
<td>1.37 (1.11-1.7)</td>
<td>0.003</td>
</tr>
<tr>
<td>Steroid use (yes vs no)</td>
<td>0.42 (0.17-1.01)</td>
<td>0.053</td>
<td>1.31 (1.03-1.67)</td>
<td>0.03</td>
<td>1.66 (1.28-2.16)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Baseline steroids and PD-(L)1 Efficacy: Conclusions

- Baseline steroid use when starting PD-(L)1 blockade is associated with inferior outcomes (PFS and OS)
  - Effect may be predictive and/or prognostic
- Prudent use of steroids in patients for whom PD-(L)1 blockade is planned should be considered
  - Consideration of non-steroid alternatives for management of cancer symptoms
  - Medically necessary steroids (e.g. brain metastases) should NOT be avoided
- Implications for patients receiving chemo + PD-(L)1 is uncertain