Monalizumab in combination with cetuximab in patients (pts) with recurrent or metastatic (R/M) head and neck cancer (SCCHN) previously treated or not with PD-L1 inhibitors (IO): 1-year survival data.


1 Center for Head and Neck Cancer, Abramson Cancer Center, Philadelphia, PA, USA; Medical Oncology, Centre Oscar Lambret, Lille, France; 2 Head and Neck Oncology Center, Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, NY, New York, USA; 3 Head and Neck and Thoracic Oncology, FoS Cancer Center, Philadelphia, PA, USA; Medical Oncology, Ag-hum, Marseille, France; 4 Medical Oncology, Institut Curie, Paris, France; 5 Medical Oncology, Institut Gustave Roussy, Villejuif, France; 6 Medical Oncology, Hopital Laennec, Marseille, France; 7 Medical Oncology, Centre Léon Bérard, Lyon, France.

Background

Monalizumab is a first-in-class humanized IgG4 checkpoint inhibitor targeting NKG2A receptors expressed on subsets of CD8+ T cells and NK cells.

Cetuximab inhibits epidermal growth factor receptor (EGFR) signaling and binds to CD16/Fc receptor (RIII) to promote antibody-dependent cell-mediated cytotoxicity (ADCC).

Background HIV-2 in combination with monalizumab may enhance ADCC induced by monalizumab and thereby provide greater antitumor activity than cetuximab alone.8

Blinding HIV-2 and triggering CD123 constitutes a novel form of dual immunotherapy that includes blockade of a novel immune checkpoint.

Study Design

Monalizumab and cetuximab have 2 trials to evaluate the combination of monalizumab and cetuximab in patients with recurrent and metastatic squamous cell carcinoma of the head and neck cancer (R/M SCCHN) (NCT02404359).

Primary objective Objective Response Rate (ORR) RECIST 1.1

Secondary objectives Durable Response Rate (DOR), Progression-Free Survival (PFS), Overall Survival (OS), Safety

Exploratory objectives Translational analysis

Key eligibility criteria

• R/M SCCHN histologically confirmed, HPV (+) or HPV (-)
• Prior cetuximab allowed if for locally advanced disease with no PD
• Maximum of 2 prior systemic treatment regimens for R/M disease

Patient and disease characteristics

Table: Patient and disease characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All (n=40)</th>
<th>IO Naïve (n=22)</th>
<th>IO Pretreated (n=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range)</td>
<td>64 (27-74)</td>
<td>64 (24-74)</td>
<td>64 (25-73)</td>
</tr>
<tr>
<td>Sex</td>
<td>Female 12 (30%)</td>
<td>5 (23%)</td>
<td>7 (39%)</td>
</tr>
<tr>
<td>Risk</td>
<td>High 24 (60%)</td>
<td>13 (59%)</td>
<td>11 (61%)</td>
</tr>
<tr>
<td>SCCHN site</td>
<td>Nasopharynx 13 (33%)</td>
<td>6 (27%)</td>
<td>7 (39%)</td>
</tr>
<tr>
<td>HPV status</td>
<td>Positive 30 (75%)</td>
<td>19 (86%)</td>
<td>11 (61%)</td>
</tr>
<tr>
<td>Prior cetuximab allowed</td>
<td>Yes 26 (65%)</td>
<td>14 (64%)</td>
<td>12 (55%)</td>
</tr>
<tr>
<td>Maximum of 2 prior systemic treatment regimens for R/M disease</td>
<td>Yes 26 (65%)</td>
<td>14 (64%)</td>
<td>12 (55%)</td>
</tr>
</tbody>
</table>

Efficacy results

Table: Efficacy results

<table>
<thead>
<tr>
<th>Primary endpoints</th>
<th>All (n=40)</th>
<th>IO Naïve (n=22)</th>
<th>IO Pretreated (n=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Response Rate</td>
<td>44%</td>
<td>45%</td>
<td>43%</td>
</tr>
<tr>
<td>Overall Survival</td>
<td>Median 14.1 months [8.0-.NR]</td>
<td>14.1 months [8.0-.NR]</td>
<td>14.1 months [8.0-.NR]</td>
</tr>
<tr>
<td>Progression-Free Survival</td>
<td>Median 7.8 months [3.5-6.9]</td>
<td>7.8 months [3.5-6.9]</td>
<td>7.8 months [3.5-6.9]</td>
</tr>
</tbody>
</table>

Conclusions

• In a cohort of 40 patients of heavily pretreated SCCHN patients, monalizumab and cetuximab combination demonstrated an acceptable safety profile, a high response rate (27.5%), and promising OS (median 8.5 mo and 12 mo survival rate 44%).

• An additional cohort of 40 patients with R/M SCCHN who have received both platinum-based chemotherapy and anti-PD-L1 is being enrolled in this study to confirm the preliminary results seen in this subgroup, a population with a continued high unmet medical need.

The study is sponsored by Inna Phar and supported by AstaZeneca.

Corresponding author : Roger B. Cohen, MD. Roger.Cohen@pennmedicine.upenn.edu

Abbreviations

ID: 1134P

References

5. André, Vivier et al., Cell 2018