Monalizumab in combination with cetuximab post platinum and anti-PD-(L)1 in patients with recurrent/metastatic squamous cell carcinoma of the head and neck (R/M SCCHN): updated results from a phase 2 trial


Background

- Monalizumab is a first-in-class, humanized IgG4-κ-domain blocking the NKG2A receptor, which is expressed in CD8+ and NK cells.
- Cetuximab inhibits oncogenic EGFR signaling and binds to EGF/EGFR to promote TKI/DC.
- NK cell stimulation with monalizumab may enhance ADCC induced by cetuximab and thereby provide greater antitumor activity than cetuximab alone.
- Blocking NKG2A and triggering CD16+ cells normalizes a state of cellular immunosuppression that includes blockade of a normal immune checkpoint.
- We previously reported the clinical activity and safety of monalizumab in combination with cetuximab in R/M SCCHN after platinum-based chemotherapy.
- Cetuximab single agent was approved in the US in R/M SCCHN progressing after platinum-based therapy with ORR 12.6%, median PFS of 2.3 months, median OS of 11.5 months, 6 months OS < 50%, and 12 months OS < 25%.
- Very recently, two studies [1, 2], Wendling and Pimentel-Carbone, were approved as single agent in R/M SCCHN with disease progression on or after platinum-containing chemotherapy with ORR 10%, median PFS 2.2 months, and median OS of 7.6 months [2].
- To date, no treatment options are currently approved in patients progressing after platinum and post-anti-PD-(L)1.
- This is a multicenter, single arm, phase Ib-II trial with different cohorts to evaluate the combination of monalizumab and cetuximab in patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck (R/M SCCHN) (NCT02643550). Dose escalation and cohort 1 in patients post platinum (anti-PD-(L)1 naïve or pretreated) were previously presented. 8-9. Cohort 2 enrolled patients the head and neck (R/M SCCHN) after platinum-based chemotherapy. 8-9
- To date, no treatment options are currently approved in patients progressing after platinum and post-anti-PD-(L)1.

Main results

- As of August 31, 2020, 40 patients with R/M SCCHN post platinum and anti-PD-(L)1 were included in cohort 2 in US and France (Table 1). Median duration of follow-up (FU) was 11.1 months (range 7.9-15.9).
- Figure 1 shows responses, PFS and OS of patients enrolled in Cohort 2.
- In cohort 1 of the study, 19 patients received platinum and post anti-PD-(L)1, and were enrolled with the same selection criteria and similar characteristics than cohort 2. Thus an exploratory analysis combining these patients to those enrolled in Cohort 2 is provided in Figure 2.

Study Design

- This is a multicenter, single arm, phase Ib-II trial with different cohorts to evaluate the combination of monalizumab and cetuximab in patients with recurrent or metastatic squamous cell carcinoma of the head and neck (R/M SCCHN) (NCT02643550). Dose escalation and cohort 1 in patients post platinum (anti-PD-(L)1 naïve or pretreated) were previously presented 8-9. Cohort 2 enrolled patients post-platinum and post anti-PD-(L)1.

Key eligibility criteria in cohort 2

- R/M SCCHN histologically confirmed.
- HPV+ or HPV-.
- Progression (PD) after platinum-based chemotherapy and prior anti-PD-(L)1.
- Maximum 2 prior systemic treatment regimens for R/M disease.
- Prior radiationallowed to have the locally advanced disease with RT and PD for at least 4 months.

Treatment

- Monalizumab (750 mg Q2W) +
- Cetuximab

Table 1: Patients demographic and disease characteristics

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Cohort 2</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range)</td>
<td>62 (43-81)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>Male 5/21</td>
<td>25%</td>
</tr>
<tr>
<td>Prior anti-PD-(L)1</td>
<td>Sensitive 12/23 52%</td>
<td>25%</td>
</tr>
<tr>
<td>Prior anti-PD-(L)1</td>
<td>Resistant 5/23 22%</td>
<td>25%</td>
</tr>
<tr>
<td>Prior platinum therapy</td>
<td>Sensitive 13/25 52%</td>
<td>25%</td>
</tr>
<tr>
<td>Prior platinum therapy</td>
<td>Resistant 5/23 22%</td>
<td>25%</td>
</tr>
<tr>
<td>Prior cetuximab therapy</td>
<td>Yes 22/25 88%</td>
<td>25%</td>
</tr>
<tr>
<td>Prior cetuximab therapy</td>
<td>No 3/25 12%</td>
<td>25%</td>
</tr>
<tr>
<td>Prior VIN therapy</td>
<td>No 22/25 88%</td>
<td>25%</td>
</tr>
<tr>
<td>Prior VIN therapy</td>
<td>Yes 3/25 12%</td>
<td>25%</td>
</tr>
<tr>
<td>Prior HPV+ / HPV- therapy</td>
<td>HPV+ 13/23 52%</td>
<td>25%</td>
</tr>
<tr>
<td>Prior HPV+ / HPV- therapy</td>
<td>HPV- 12/23 52%</td>
<td>25%</td>
</tr>
</tbody>
</table>

Patient Characteristics

- Cohort 2 included patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck (R/M SCCHN) (NCT02643550). Dose escalation and cohort 1 in patients post-platinum and post anti-PD-(L)1.
- There was no fatal AE nor AE leading to treatment discontinuation (of note, one patient left the study after the first administration of cetuximab and did not receive monalizumab; he was replaced and is not included in the analysis).

Safety results

- All 40 patients had at least one adverse event.
- 10 patients (25%) had Grade 3-4 AEs regarding of causality, and only 4 patients (10%) had Grade 4 AE related to any study drug.
- The most common (> 10%) AEs related to monalizumab or cetuximab were dermatitis acneiforme (72%), dry skin (35%), pruritus (22%), fatigue (10%), hyponatremia (20%), skin fissures (20%), inflammation related rash (18%), mucosal inflammation (18%), nausea (18%), paronychia (18%), rash (5%), and diarrhea (2%).
- Only 1 patient (2%) had Grade 4 AE 3-4 related to monalizumab: peripheral sensory neuropathy.

Conclusion

- The monalizumab and cetuximab combination therapy demonstrates good safety profile and promising activity in R/M SCCHN post platinum and post anti-PD-(L)1, where no treatment options are currently approved.

- In this population with a high medical need, we observed a high response rate and long durations of response.

Acknowledgments

- We thank the patients who participated in the 2021-2023 study and their families, the investigators, co-ordinated and clinical study site staff of the participating institutions.

References


- Poster 81P

- Abstract 235

- Current

- Former

- Current

- Former

- Current

- Former

- Current

- Former

- Current

- Former

- Former