Introduction

The predicted efficacy and tolerability of plamotamab in the Phase 1 study in B-cell malignancies is assessed. Plamotamab is a humanized anti-CD3 x anti-CD20 bispecific antibody designed to activate T cells with high specificity for target cell. The Phase 1 study is ongoing, with the first patients enrolled in August 2020. The study will evaluate the safety, tolerability, and anti-tumor activity of plamotamab in patients with advanced hematological malignancies. The Phase 1 study is designed to establish the optimal dosing regimen and schedule for plamotamab, which will be used to determine the maximum tolerated dose (MTD) and to select a recommended dose (RD). The secondary objectives are to evaluate the safety, tolerability, and activity of plamotamab in patients with advanced hematological malignancies.

Methods

The study is a single-center, open-label, dose-escalation study in patients with relapsed/refractory B-cell malignant lymphoma. The study design includes a weight-based dosing cohort (Part B) and a flat-dose cohort (Part C). The dosing schedule is planned weekly weight-based and flat dose. The study will include patients who have not received prior anti-CD20 therapy or who have received anti-CD20 therapy within 6 months of study entry. The study will be conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. The study is funded by ADC Therapeutics.

Results

As of data cut date, we analyzed a safety population of 50 subjects (38 DLBCL, 12 FL) for the weight-based dose cohorts (Part B) and a safety population of 14 subjects (14) for the flat-dose cohort (Part C). The safety population was 49 subjects (49). The overall response rate was 32.6% (4/12) in Part B and 28.5% (4/14) in Part C. The most common adverse events in Part B were lymphopenia (80%), neutropenia (73%), and thrombocytopenia (73%). The most common adverse events in Part C were lymphopenia (86%), neutropenia (85%), and thrombocytopenia (81%). The study is ongoing, and further analysis is needed to evaluate the long-term safety and efficacy of plamotamab.

Cytokine Release Syndrome (CRS)

The cytokine release syndrome (CRS) is a common adverse event associated with the use of bispecific antibodies. In the Phase 1 study, CRS was observed in both the weight-based and flat-dose cohorts. The CRS grade was used in the analysis. The denominator for percentages is the number of subjects (n) dosed at each dose level. The most common CRS grade was grade 1 (100%). The incidence of grade ≥3 CRS events was 14.3% in Part B and 7.1% in Part C. The study is ongoing, and further analysis is needed to evaluate the long-term safety and efficacy of plamotamab.

Table 1: Summary of SAsA

| SAsA | Rx | Response Rate: n/N (%): 3.0 | CR | 4.0 | 5.0 | 6.0 | 7.0 | 8.0 | 9.0 | 10.0 | 11.0 | 12.0 | 13.0 | 14.0 | 15.0 | 16.0 | 17.0 | 18.0 | 19.0 | 20.0 | 21.0 | 22.0 | 23.0 | 24.0 | 25.0 | 26.0 | 27.0 | 28.0 | 29.0 | 30.0 | 31.0 | 32.0 | 33.0 | 34.0 | 35.0 | 36.0 | 37.0 | 38.0 | 39.0 | 40.0 | 41.0 | 42.0 | 43.0 | 44.0 | 45.0 | 46.0 | 47.0 | 48.0 | 49.0 | 50.0 | 51.0 | 52.0 | 53.0 | 54.0 | 55.0 | 56.0 | 57.0 | 58.0 | 59.0 | 60.0 | 61.0 | 62.0 | 63.0 | 64.0 | 65.0 | 66.0 | 67.0 | 68.0 | 69.0 | 70.0 | 71.0 | 72.0 | 73.0 | 74.0 | 75.0 | 76.0 | 77.0 | 78.0 | 79.0 | 80.0 | 81.0 | 82.0 | 83.0 | 84.0 | 85.0 | 86.0 | 87.0 | 88.0 | 89.0 | 90.0 | 91.0 | 92.0 | 93.0 | 94.0 | 95.0 | 96.0 | 97.0 | 98.0 | 99.0 | 100.0 |

Table 2: Summary of Responses

<table>
<thead>
<tr>
<th>Response</th>
<th>n</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Response (CR)</td>
<td>3</td>
<td>100.0</td>
</tr>
<tr>
<td>Partial Response (PR)</td>
<td>4</td>
<td>40.0</td>
</tr>
<tr>
<td>Stable Disease (SD)</td>
<td>6</td>
<td>60.0</td>
</tr>
<tr>
<td>Progressive Disease (PD)</td>
<td>6</td>
<td>60.0</td>
</tr>
</tbody>
</table>

Cytokine Release Syndrome (CRS) Grade 1 - 3

- In the ongoing Phase 1 study in B-cell malignancies, plamotamab was generally well-tolerated.
- There were no Grade 4 or 5 CRS events in Part C, with other safety events being generally mild or moderate.
- Grade 3 CRS events were observed in both the weight-based and flat-dose cohorts.
- The study is ongoing, and further analysis is needed to evaluate the long-term safety and efficacy of plamotamab.

Footnote:


References

