Clinical Effectiveness of Combination Immunotherapy DPX-Survivac, Low Dose Cyclophosphamide, and Pembrolizumab in Recurrent/Refractory DLBCL: The SPiReL Study

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SPiReL is a Phase 2 clinical trial studying a novel immunotherapy combination:

- **DPX-Survivac**: a T cell immunotherapy against survivin-expressing tumours
- **Pembrolizumab**: a potent IgG4 inhibitor of the programmed cell death receptor (PD-1)
- **Intermittent low dose cyclophosphamide** as an immune modulator

Primary Objective: to document a 24% ORR per the Modified Cheson Criteria (2007)
Trial Population

Screened
N=41

Enrolled
N=24

17 subjects excluded:
- 1 subject in screening
- 15 subjects did not meet inclusion/exclusion criteria
- 1 subject was excluded due to COVID-19 site restrictions

Full Analysis Set
N=23

1 subject pending evaluation

9 subjects not included in the PP population due to early discontinuation (PD)

Per Protocol Population (PP)
N=14

Defined as:
- Received 3 doses of DPX-Survivac
- Received 4 doses of pembrolizumab
- 1st on-treatment study scan (D70 or 91)

Figure 2: Consort flow diagram of 41 subjects screened and 24 subjects enrolled as of 03Nov2020
## Subject Demographics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N = 24 (%)</th>
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<tbody>
<tr>
<td>Male</td>
<td>9 (37.5)</td>
</tr>
<tr>
<td>Female</td>
<td>15 (62.5)</td>
</tr>
<tr>
<td><strong>Age, median (range)</strong></td>
<td>74.5 (50-82)</td>
</tr>
<tr>
<td>ECOG = 0</td>
<td>11 (45.8)</td>
</tr>
<tr>
<td>ECOG = 1</td>
<td>13 (54.2)</td>
</tr>
<tr>
<td><strong>LDH, median (range)</strong></td>
<td>248.5 (154-730)</td>
</tr>
<tr>
<td>GCB</td>
<td>14 (58.3)</td>
</tr>
<tr>
<td>Non-GCB*</td>
<td>10 (41.7)</td>
</tr>
<tr>
<td><strong>Stage III/IV</strong></td>
<td>18 (75)</td>
</tr>
<tr>
<td>Transformed</td>
<td>6 (25)</td>
</tr>
<tr>
<td>Relapsed DLBCL</td>
<td>17 (70.8)</td>
</tr>
<tr>
<td>Refractory DLBCL</td>
<td>7 (29.2)</td>
</tr>
<tr>
<td><strong>Number of previous treatments, median (range)</strong></td>
<td>2 (1-7)</td>
</tr>
<tr>
<td>Previous ASCT</td>
<td>4 (16.7)</td>
</tr>
<tr>
<td><strong>Time from end of last treatment to SD0 (days), median (range)</strong></td>
<td>250.5 (21-3423)</td>
</tr>
<tr>
<td><strong>Time from diagnosis until SD0 (days), median (range)</strong></td>
<td>1511 (226-5827)</td>
</tr>
</tbody>
</table>

Table 1: 24 participants were enrolled into the study at the time of analysis. * One non-GCB sub-type is Leg-type.
Figure 3: Time on treatment for all enrolled study participants (n=24) showing best overall response per Modified Cheson Criteria (2007) and separated as PD-L1+ (defined as PD-L1 expression ≥ 10% by central mIHC, n=8), PD-L1 negative and subjects with PD-L1 status unknown. The ORR and DCR are described in Table 2 for the FAS (n=23, 1 subject pending response).
Figure 4: Best Overall Response, using the Modified Cheson Criteria\(^9\), for evaluable Per Protocol (PP) subjects (N=14). PD-L1 positive subjects are shown, defined as PD-L1 expression of ≥ 10% as assessed by central mIHC. Table 3 (above) demonstrates the ORR and DCR of the PP and in PD-L1+ subjects. One subject with a PR (11) did not have sufficient tissue to assess PD-L1 expression.
Figure 5: Kaplan Meier curve demonstrating PFS in the FAS (N=24), as of 03Nov2020.

Figure 6: Kaplan Meier curve demonstrating PFS in subjects with positive baseline PD-L1 expression (blue) versus negative PD-L1 expression. PD-L1 positive is defined as expression ≥ 10% by central mIHC.
Survivin-specific ELISpot Responses

Figure 7: Treatment induced Survivin T cell responses: IFN-γ ELISpot responses represented as Spot Forming Units (SFU) per 10^6 cells collected at baseline and on-treatment for subjects with CR, PR, SD and PD (per Modified Cheson Criteria^9 (2007)). The pie-charts demonstrate the percentage of subjects with positive ELISpot responses within each of the clinical responders sub-groups. Subjects with a baseline sample and > 2 different on-treatment samples are included for analysis (N=15).
Figure 8: Treatment-related adverse events (TRAE) in enrolled subjects (n=24) reported in $>10\%$ of enrolled subjects. Events are counted once per subject, at the highest reported grade per CTCAE 4.03. TRAEs were reported by 17 of 24 (70.8\%) enrolled subjects.

Figure 9: All treatment-related adverse events (TRAE) assessed as $>\text{Grade } 3$ by CTCAE 4.03. Events assessed as $>\text{Grade } 3$ were experienced by 5 (20.8\%) of enrolled subjects. Only 1 Serious TRAE was reported (pancreatitis).
Conclusion

- DPX-Survivac, pembrolizumab and low dose CPA is a promising treatment combination in subjects with aggressive relapsed/refractory DLBCL:
  - 50% ORR and 78.6% DCR in evaluable subjects
  - 85.7% ORR and 85.7% DCR in PD-L1+ subjects

- This treatment combination is well-tolerated in this population:
  - Median age of 74.5 years
  - Most common reported events are Grade 1 and 2 injection site reactions
  - Only 5 (20.8%) subjects reported TRAE $\geq$ Grade 3

- Baseline level of PD-L1 expression is a potential predictor of response to this treatment combination and is associated with a longer progression free survival
  - PDL1 may be an important biomarker for patient selection for future development of this treatment combination

- Positive ELISpot response is associated with objective response and clinical benefit supporting the contribution of DPX-Survivac to this treatment combination
Disclosures

Bence-Bruckler: Merck: Membership on an entity's Board of Directors or advisory committees.
Forward: Seattle Genetics: Research Funding; IMV: Research Funding; Merck: Research Funding; Astellas: Research Funding; Servier: Membership on an entity's Board of Directors or advisory committees; Roche: Membership on an entity's Board of Directors or advisory committees; IMV: Membership on an entity's Board of Directors or advisory committees; Janssen: Membership on an entity's Board of Directors or advisory committees; Calgene: Membership on an entity's Board of Directors or advisory committees; AbbVie: Membership on an entity's Board of Directors or advisory committees; Pfizer: Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; AstraZeneca: Membership on an entity's Board of Directors or advisory committees.
Stewart: Roche: Honoraria; Janssen: Honoraria; Abbvie: Honoraria; Gilead: Honoraria; Celgene: Honoraria; Amgen: Honoraria; Sandoz: Honoraria; Novartis: Honoraria; AstraZeneca: Honoraria; Teva: Honoraria.
Bramhecha: IMV Inc.: Current Employment.
Conlon: IMV Inc.: Current Employment.

References