Introduction & Background

Relapsed/refractory diffuse large B cell lymphoma is an unmet medical need. Most patients with this diagnosis are chemotherapy resistant or refractory and have failed first line chemotherapy and possibly autologous stem cell transplantation. Novel treatment approaches that target other pathways that may be driving these resistant lymphomas are important. Although CAR-T cells are a promising new treatment approach many patients will not be able to receive this therapy either because of the toxicity profile and comorbid illnesses or availability of this complex treatment approach. We have tested a novel combination immunotherapy including:

- **DPX-Survivac**: a T cell activating therapy that generates immune responses to the survivin tumor associated antigen expressed in non-Hodgkin’s lymphomas
- **Pembrolizumab**: a potent humanized mAb with high specificity of binding to PD-1
- **Intermittent, low dose cyclophosphamide**: (CPA): a potential inhibitor of regulatory T cells pathway

Trial Endpoints

The primary endpoint of this Phase II study is to document clinical activity of this treatment approach. Secondary and exploratory endpoints were aimed at documenting safety and to understand the biologic and immune effects of this treatment and to identify biomarkers that would identify patients more likely to respond clinically to this novel immune therapy.

Trial Design

Participants with recurrent/refractory DLBCL, with ECOG 0-1 and confirmed survivin expression are eligible. Participants must also be ineligible for curative therapy. The study was approved by the Ontario Cancer Research Ethics Board (OCREB), protocol number 0981.

- Study treatment includes administering two doses of 0.5 ml of DPX-Survivac, subcutaneously, 3 weeks apart followed by up to six 0.1 ml doses every 8 weeks.
- Intermittent low dose CPA is taken orally at 50 mg twice daily for 7 days followed by 7 days off.
- Pembrolizumab 200 mg IV is administered every 3 weeks.
- Study participants continue trial participation for up to one year or until disease progression, whichever occurs first.

Participants are considered evaluable when they have received 3 doses of DPX-Survivac, 4 infusions of pembrolizumab and have had an on-treatment CT scan to assess response.

Results

The SPiRel trial is being conducted at 6 Canadian centres. Recruitment began in March 2018, with a goal of 25 evaluable participants. Results presented include data from March 2018 to July 2020 from 40 screened participants, 22 of whom have been enrolled, 11 of which are evaluable.

### Baseline Tumour Infiltrates

![Image](image1.png)

#### Clinical Response and Biomarker Associations

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N = 22 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>8 (36.4)</td>
</tr>
<tr>
<td>Female</td>
<td>14 (63.6)</td>
</tr>
<tr>
<td>Age, median (range)</td>
<td>75.5 (50-82)</td>
</tr>
<tr>
<td>ECOG = 1</td>
<td>12 (54.5)</td>
</tr>
<tr>
<td>ECOG = 2</td>
<td>3 (13.6)</td>
</tr>
<tr>
<td>ECOG = 3</td>
<td>2 (8.8)</td>
</tr>
<tr>
<td>ECOG = 0</td>
<td>5 (22.7)</td>
</tr>
<tr>
<td>Time from end of last treatment to SD0 (days), median (range)</td>
<td>235.5 (21-3423)</td>
</tr>
</tbody>
</table>

#### Baseline Immune Infiltrates, ELISpot and Clinical Responses

![Image](image2.png)

#### Survivin Expression in Study Participants

![Image](image3.png)

### Analyses of Baseline PD-L1 Expression and Clinical Response

![Image](image4.png)

### Conclusions

The SPiRel clinical trial is an ongoing trial and to date results suggest:

- Higher baseline expression of PD-L1
- DPX-Survivac induced survivin-specific T cell response

Baseline CD20+ PD-L1 expression may identify patients most likely to respond to this combination immunotherapy.

The association between PD-L1 expression on B lymphoma cells and induction of survivin-specific T cell responses identifies a novel and important interactive immune mechanism of action.

References


Acknowledgements

We would like to thank IMV Inc. and Merck Canada Inc. for supporting the study.

Thank you to our clinical trial sites and Co-Investigators for participating: London Health Science Centre, McGill Health Sciences, Ottawa Health Research Institute, Sunnybrook Health Sciences Centre, Tom Baker Cancer Centre and Queen Elizabeth II Health Sciences Centre.

Thank you to our patients and families participating in our trial.

For more information about this project contact SPiRel@sunnybrook.ca