

Baseline PD-L1 expression and tumor immune infiltration is associated with clinical response in patients with r/r DLBCL treated with DPX-Survivac, low-dose cyclophosphamide and pembrolizumab

N.L. Berinstein^{1,6}, I.A. Bence-Bruckler², N. Forward³, P. Laneuville⁴, J. Mangel⁵, D. Stewart⁶, I. Amitai¹, G. Klein⁶, N. Pennell⁶, I. Rashedi¹, K. Roos⁶, R. Conlon⁷, Y. Bramhecha⁷



¹ Sunnybrook Health Sciences Centre, ² Ottawa Hospital Research Institute, ³ Queen Elizabeth II Health Sciences Centre, ⁴ McGill University Health Centre ⁵ London Health Sciences Centre, ⁶ Tom Baker Cancer Centre, ⁶ Sunnybrook Research Institute, ⁷ IMV Inc.



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 transplantation¹. 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 approach². We have tested a novel combination immunotherapy including:

- **DPX-Survivac** a T cell activating therapy that generates immune responses to the survivin tumour associated antigen expressed in non-Hodgkin's lymphomas^{3,4}
- **Pembrolizumab**⁵ a potent humanized mAb with high specificity of binding to PD-1
- **Intermittent, low dose cyclophosphamide (CPA)**: a potential inhibitor of regulatory T cells pathway⁶

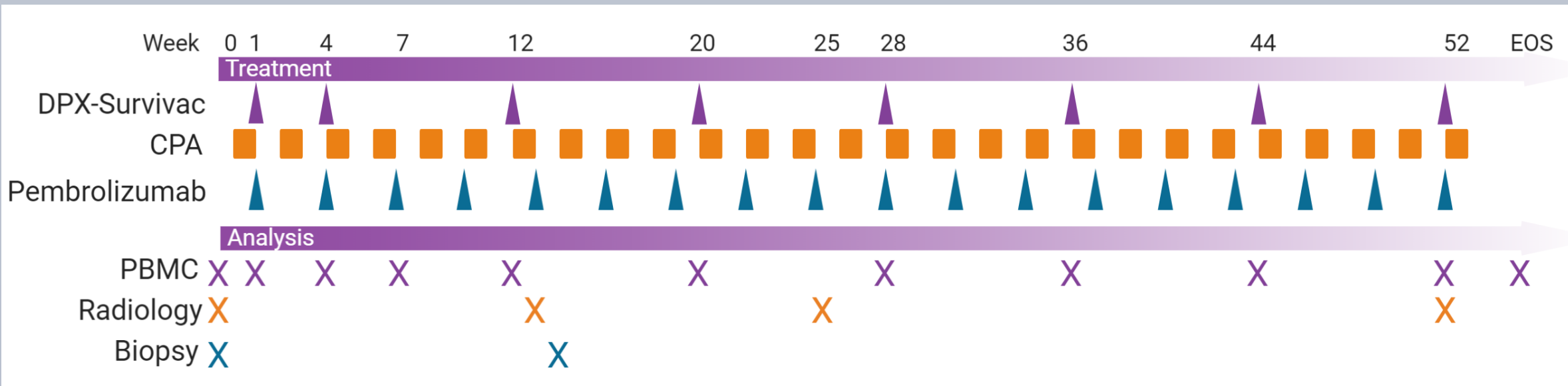
Trial Endpoints

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.

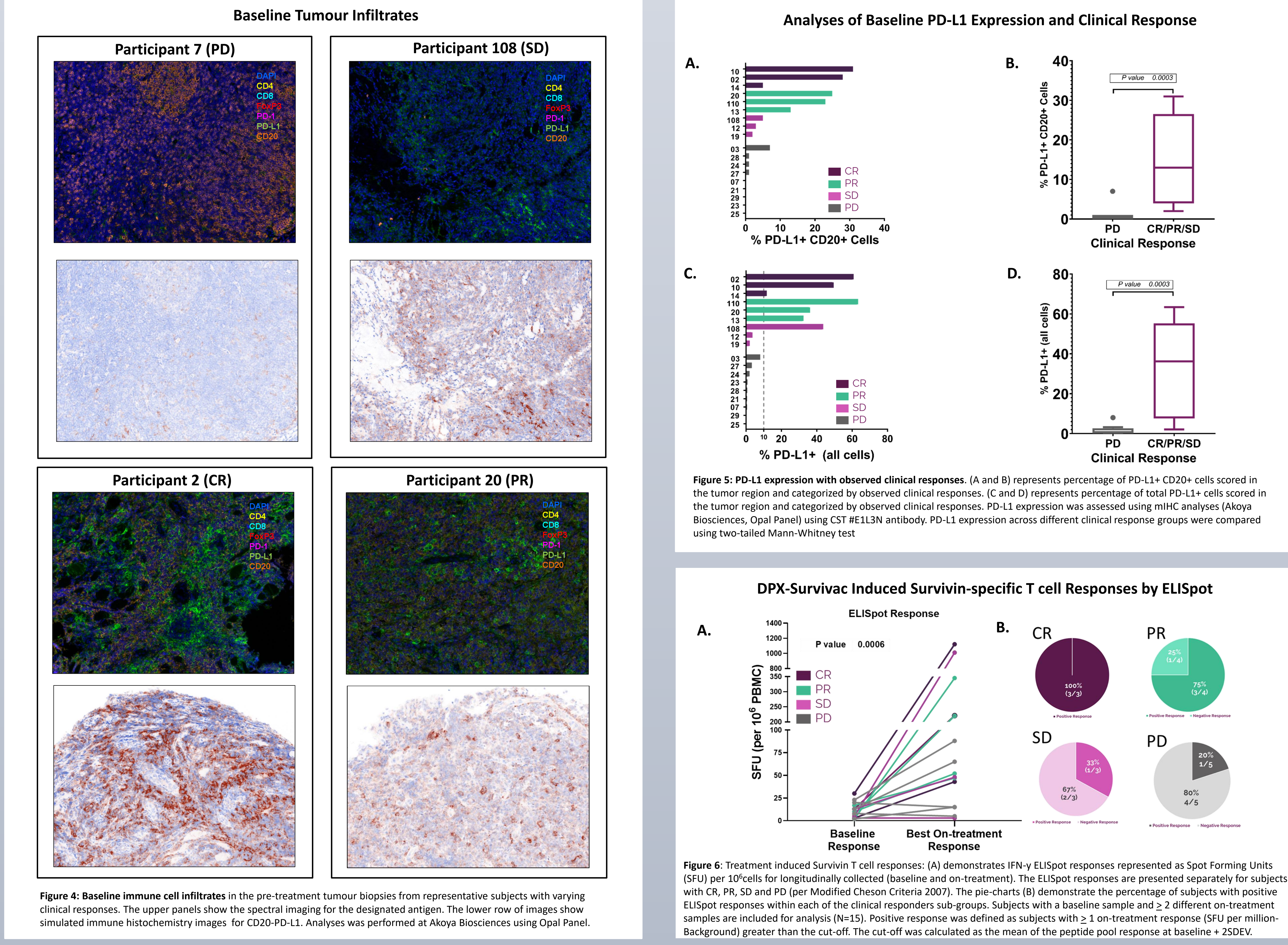
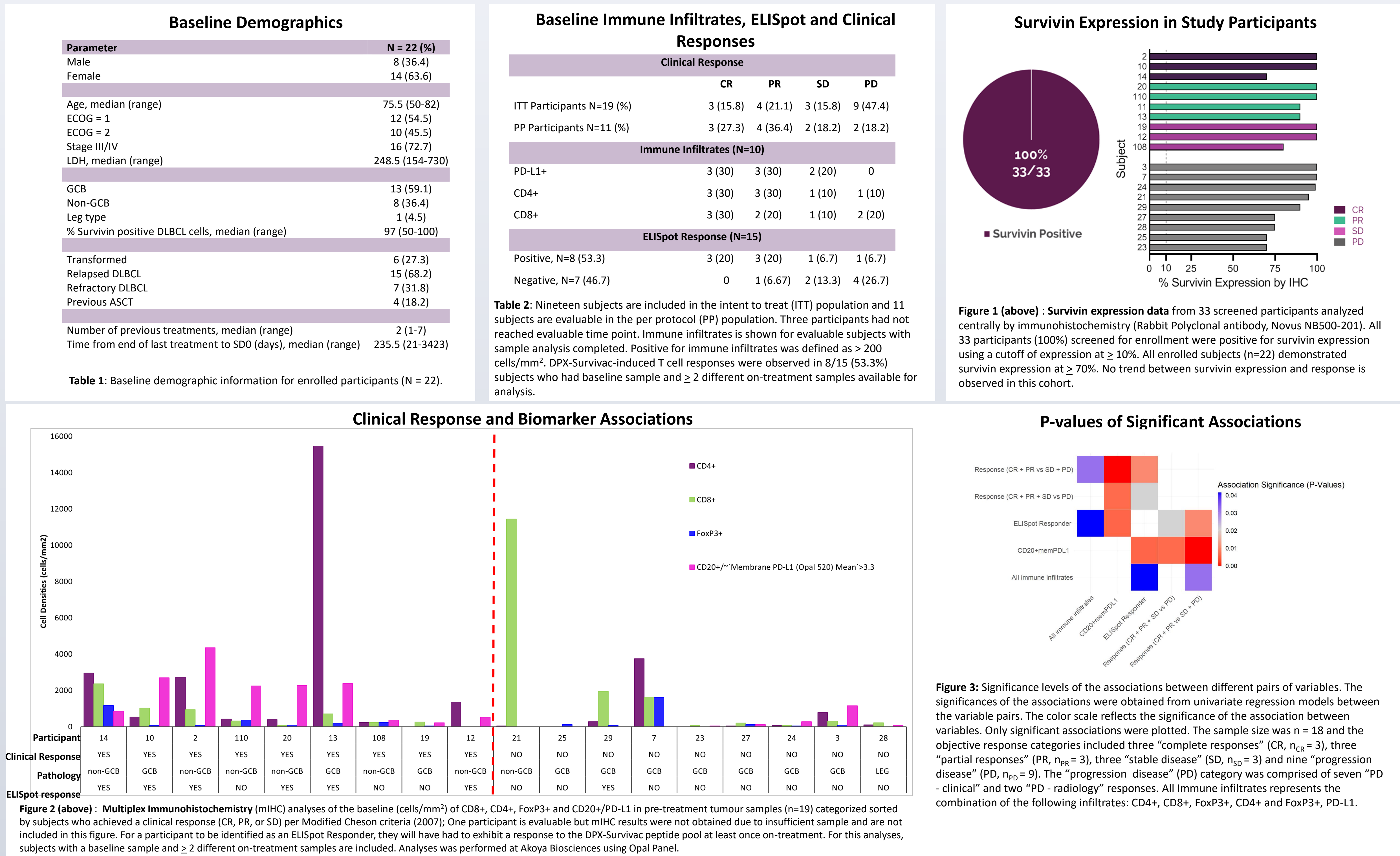
- Study treatment includes administering two doses of 0.5 mL of DPX-Survivac, subcutaneously, 3 weeks apart followed by up to six 0.1 mL doses every 8 weeks.
- Intermittent low dose CPA is taken orally at 50 mg twice daily for 7 days followed by 7 days off.
- Pembrolizumab 200 mg IV is administered every 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.



Conclusions

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

Combination immunotherapy with DPX-Survivac, pembrolizumab and intermittent, low dose cyclophosphamide can induce clinical response and disease control in patients with R/R DLBCL.

- Clinical responses are associated with:
- 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

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