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

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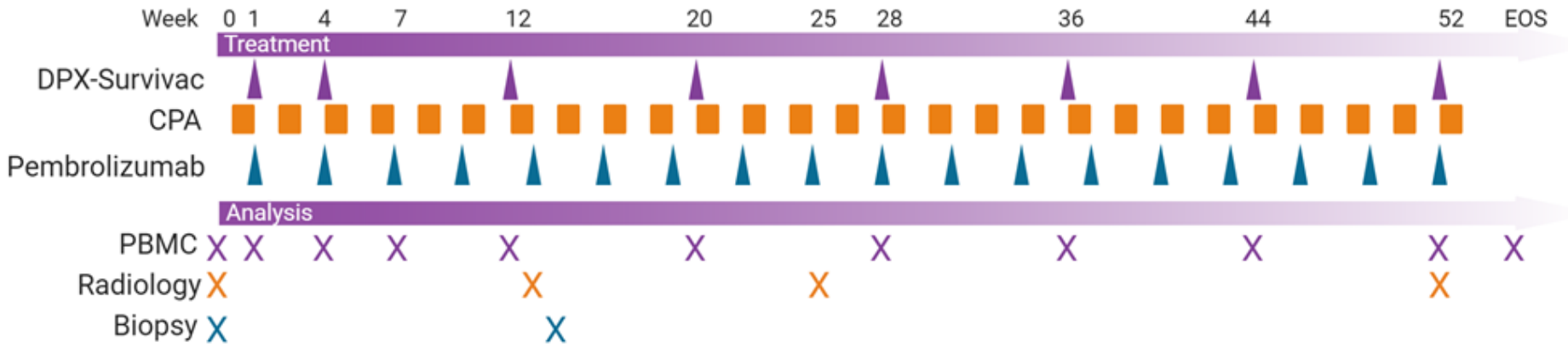
SPiReL is a Phase 2 clinical trial studying a novel immunotherapy combination:

- **DPX-Survivac:** a T cell immunotherapy against survivin-expressing tumours[3]
- **Pembrolizumab:** a potent IgG4 inhibitor of the programmed cell death receptor (PD-1)[5,6]
- **Intermittent low dose cyclophosphamide** as an immune modulator[4]



Primary Objective: to document a 24% ORR per the Modified Cheson Criteria (2007)[9]

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Trial Population

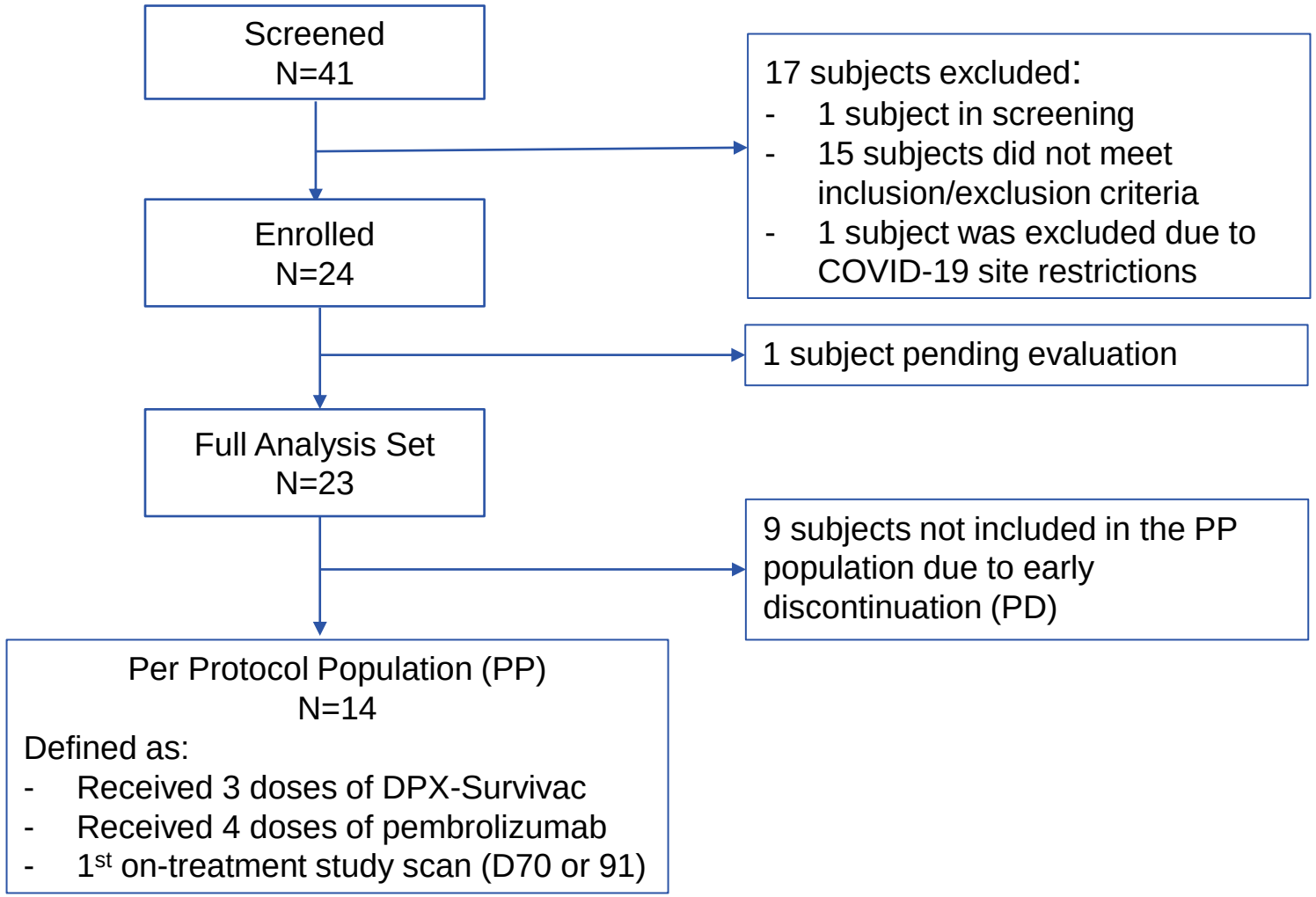

Figure 2: Consort flow diagram of 41 subjects screened and 24 subjects enrolled as of 03Nov2020

Subject Demographics

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

Table 1: 24 participants were enrolled into the study at the time of analysis. * One non-GCB sub-type is Leg-type.

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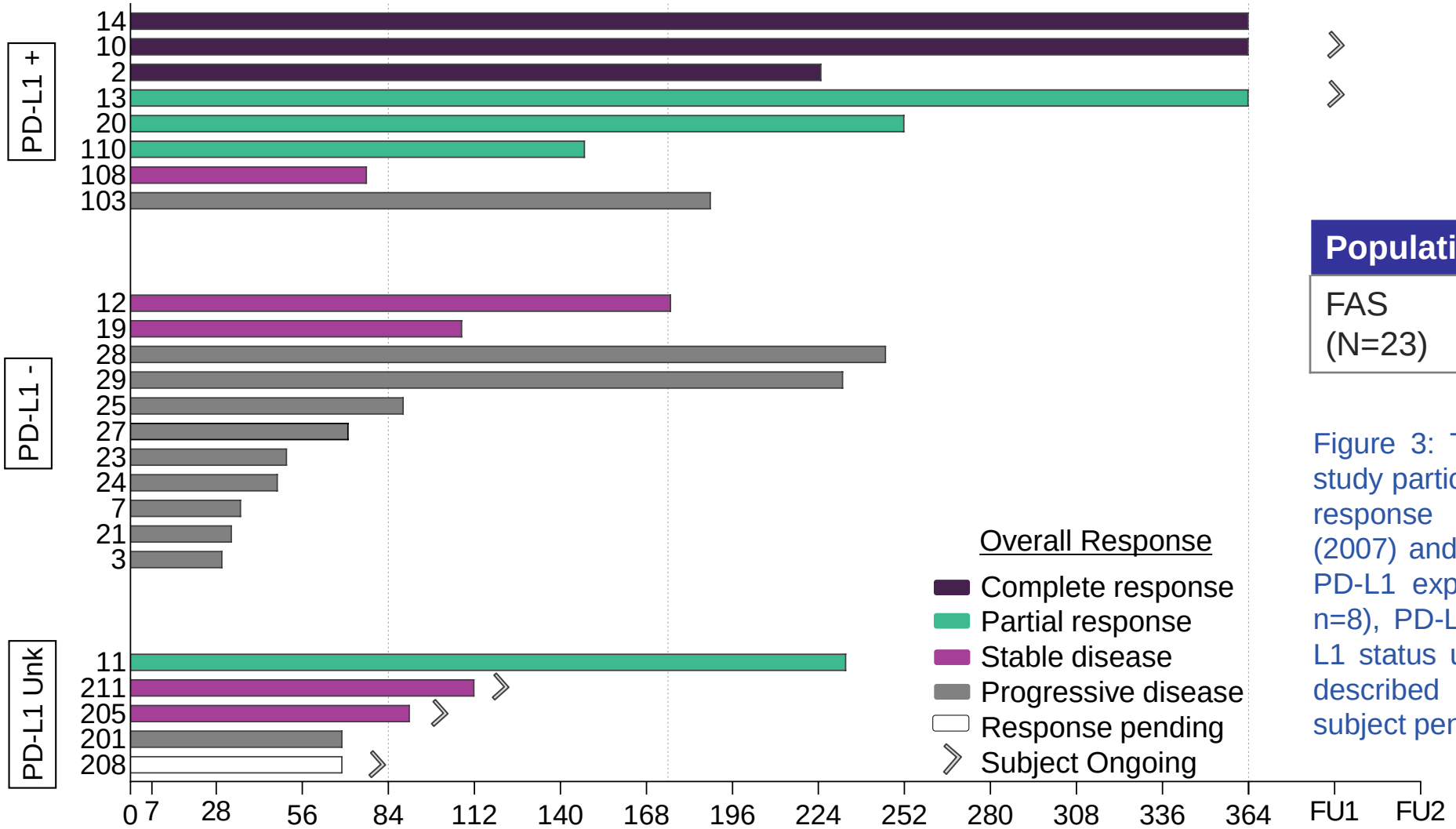
Time on Treatment



Population	ORR	DCR
FAS (N=23)	30.4%	52.2%

Figure 3: Time on treatment for all enrolled study participants (n=24) showing best overall response per Modified Cheson Criteria[4] (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).

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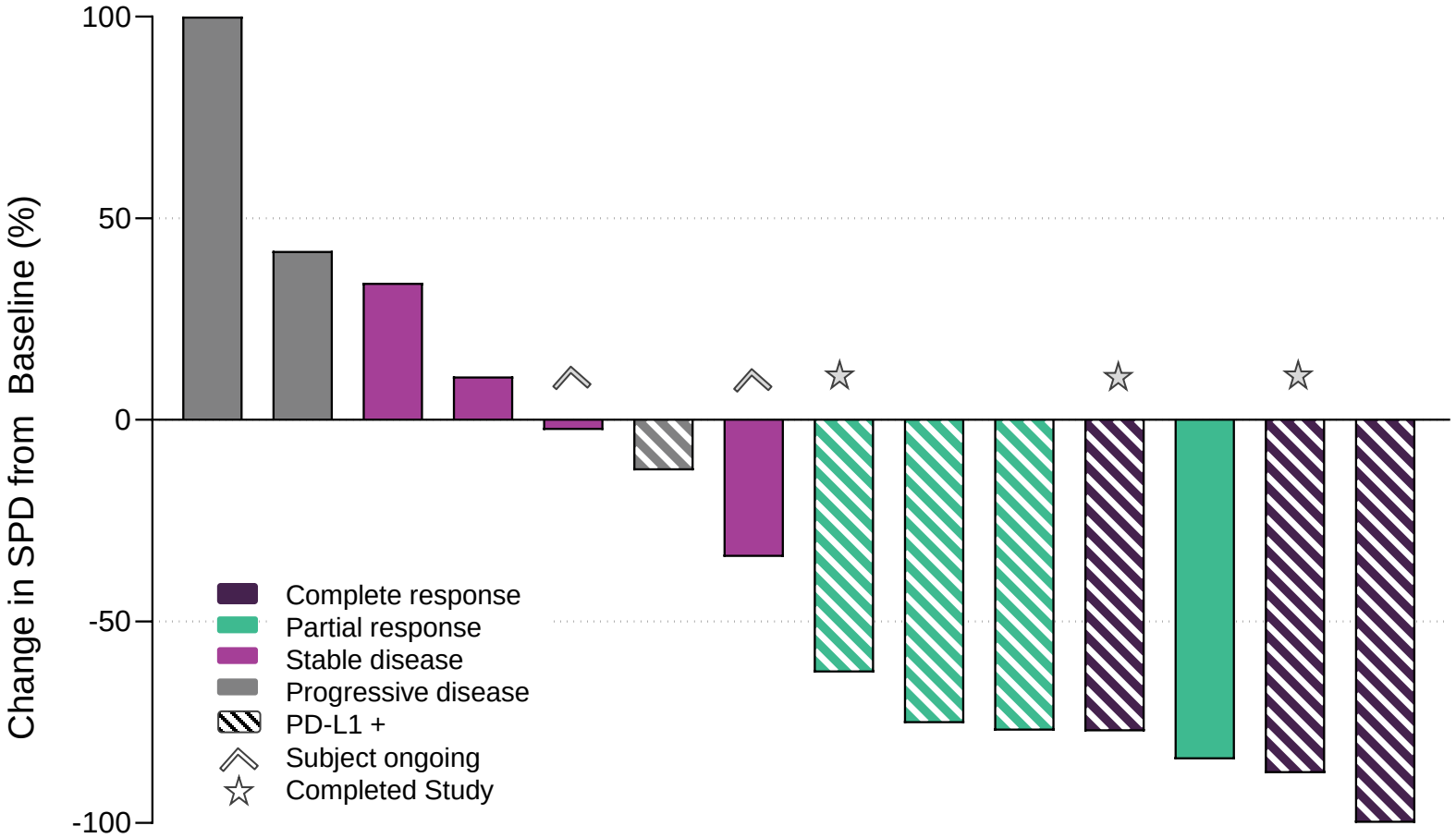
Best Overall Response (PP)



Population	ORR	DCR
Per Protocol (N=14)	50%	78.6%
PD-L1 + (N=7)	85.7%	85.7%

Figure 4: Best Overall Response, using the Modified Cheson CritIeria[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.

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Progression Free Survival

PFS in FAS (N=24)

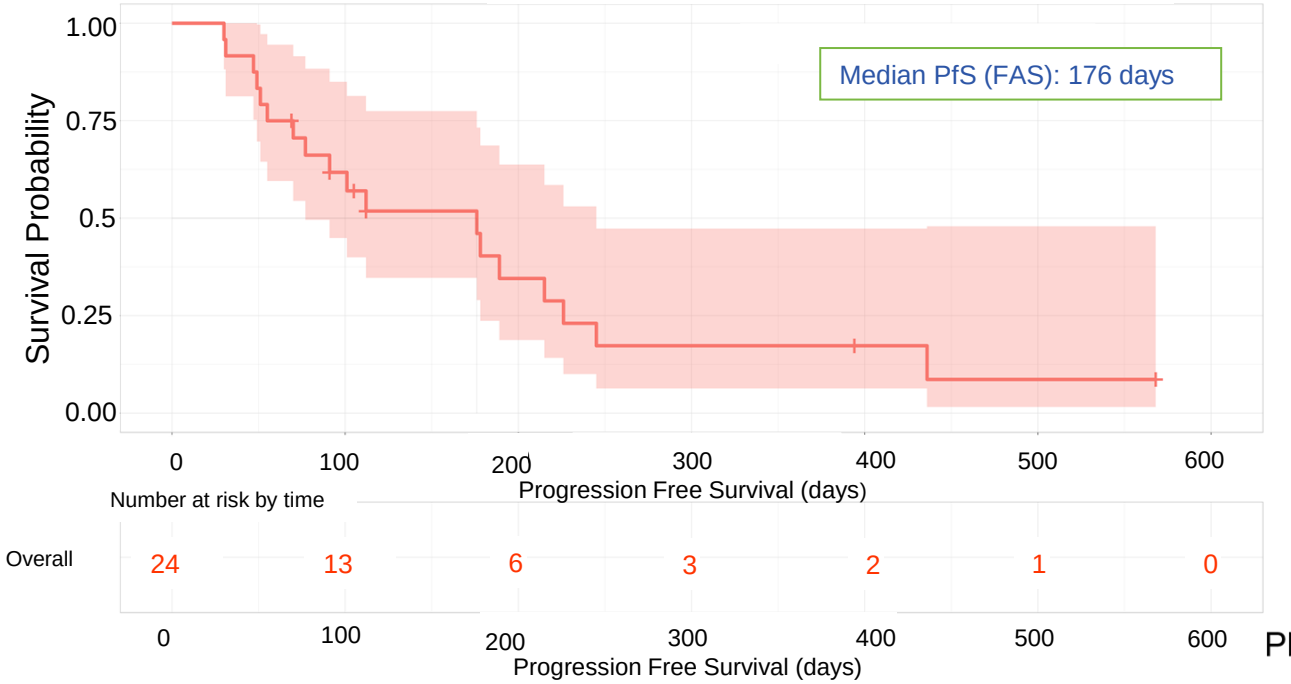
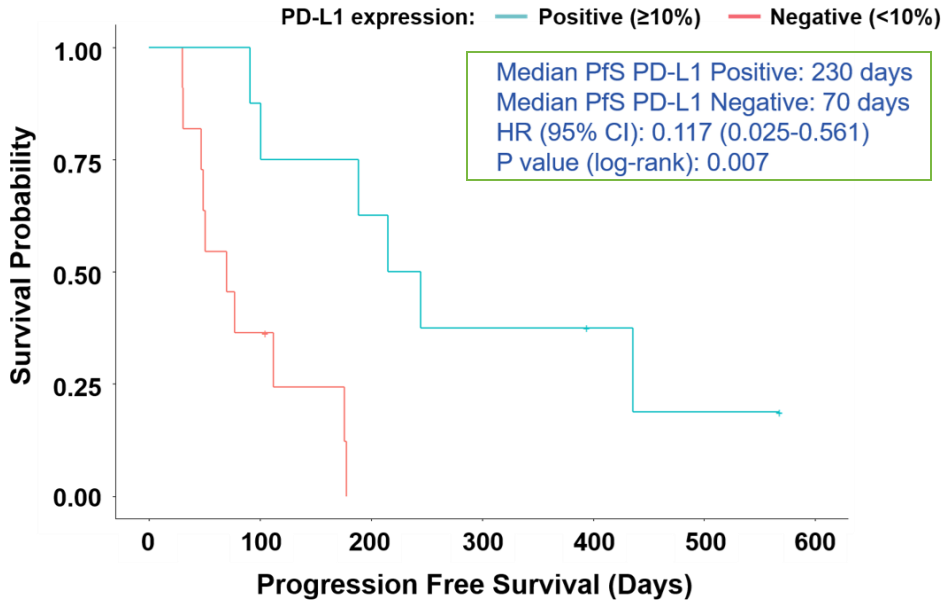


Figure 5: Kaplan Meier curve demonstrating PFS in the FAS (N=24), as of 03Nov2020.

PFS by Baseline PD-L1 Expression (N=19)



PD-L1 Expression:	Number at risk by time						
Positive (≥10%)	8	7	5	3	2	1	0
Negative (<10%)	11	4	0	0	0	0	0

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.

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Survivin-specific ELISpot Responses

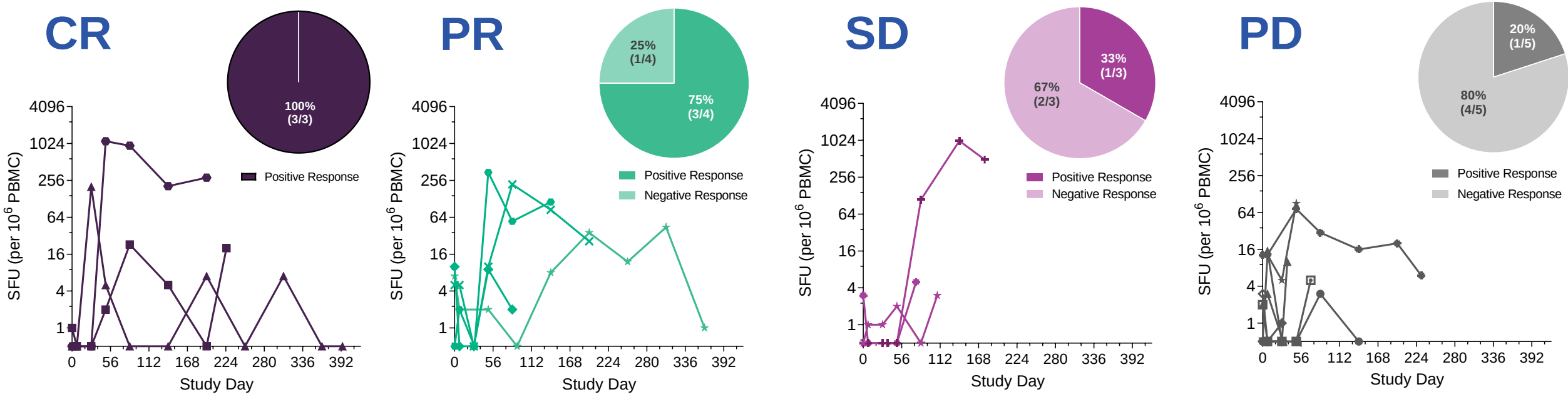

Figure 7: Treatment induced Survivin T cell responses: IFN-y ELISpot responses represented as Spot Forming Units (SFU) per 10^6cells collected at baseline and on-treatment for subjects with CR, PR, SD and PD (per Modified Cheson Criteria[9] (2007)). The pie-charts demonstrate the percentage of subjects 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).

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Treatment-Related Adverse Events

TRAE Reported in ≥ 10% of Subjects (N=24)

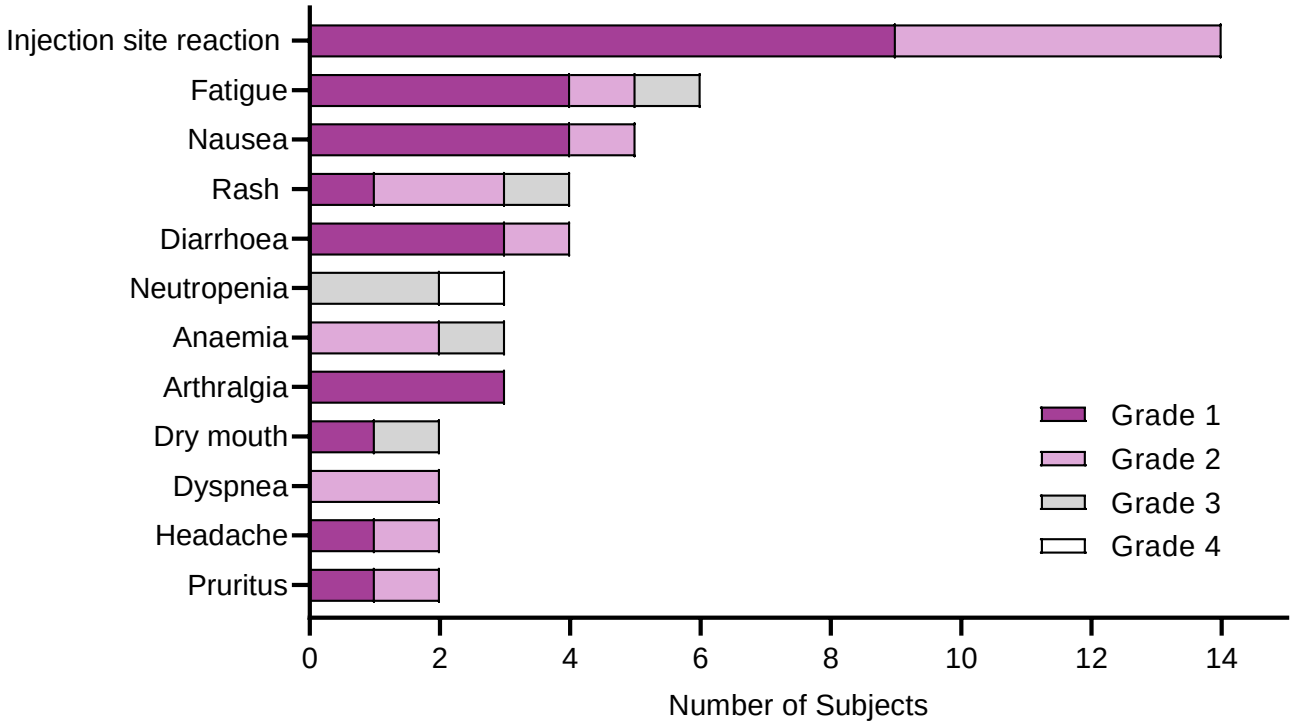

Figure 8: Treatment-related adverse events (TRAE) in enrolled subjects (n=24) reported in ≥ 10% of enrolled subjects. Events are counted once per subject, at the highest reported grade per CTCAE 4.03. TRAEs were reported by 17 of 24 (70.8%) enrolled subjects.

All TRAE Assessed as ≥ Grade 3

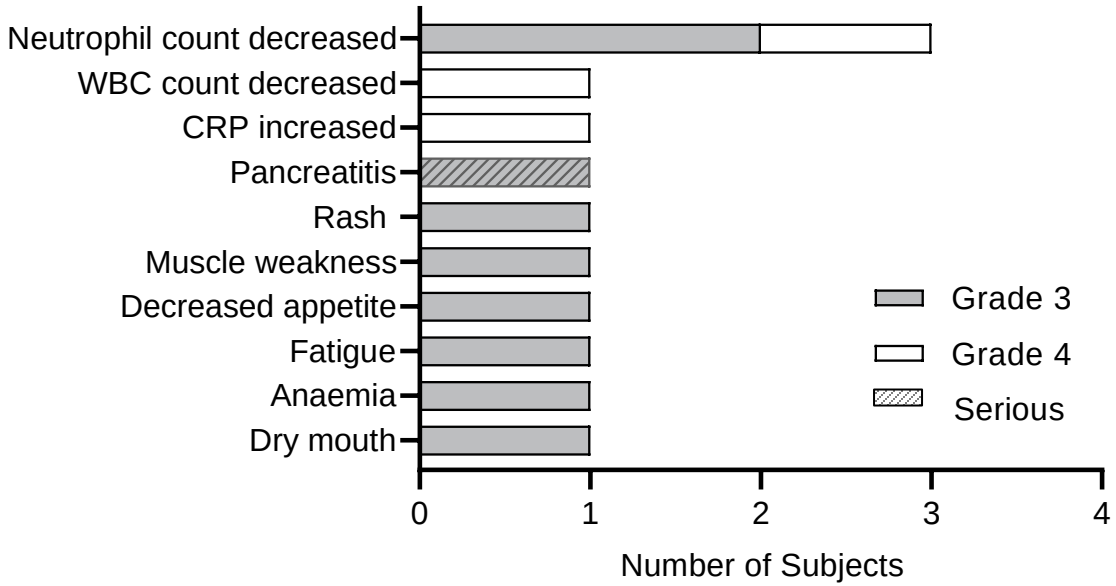

Figure 9: All treatment-related adverse events (TRAE) assessed as ≥ Grade 3 by CTCAE 4.03. Events assessed as ≥ Grade 3 were experienced by 5 (20.8%) of enrolled subjects. Only 1 Serious TRAE was reported (pancreatitis).

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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

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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; *Janssen:* Membership on an entity's Board of Directors or advisory committees; *IMV:* 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.

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