Interim PET-Adapted De-escalation Chemotherapy Regimen for Advanced Stage Classical Hodgkin Lymphoma Using Brentuximab Vedotin, Pembrolizumab, Doxorubicin, and Dacarbazine: Phase 2 Study — Updated Follow-up

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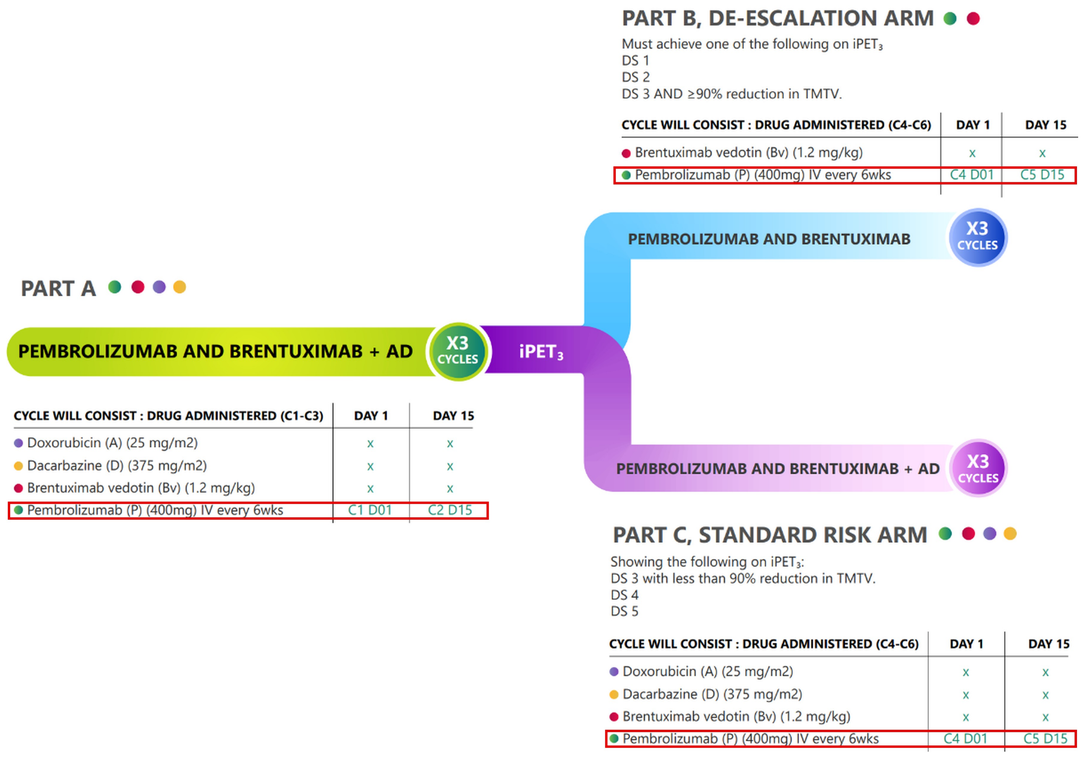
BACKGROUND

Brentuximab vedotin (Bv), nivolumab, and pembrolizumab (P) have changed frontline therapy for advanced-stage classical Hodgkin lymphoma (AS cHL).

GHSG HD18/HD21 showed PET-adapted strategies can reduce treatment without compromising efficacy.

We evaluated **BvP+AD with PET-adapted de-escalation** to reduce chemotherapy exposure.

METHODS



Study Design

Key eligibility

- Newly diagnosed cHL
- Advanced stage (III or IV) or stage II bulky (≥10 cm)

Key metrics

- 28 days per cycle
- EOT PET performed 4 weeks after last infusion
- Follow-up every 6 months with CT for the first 2 years

Primary endpoint: CR rate at EOT
Secondary endpoints: ORR, PFS, DOR

iPET3, interim PET after cycle 3; DS, Deauville score; TMTV, total metabolic tumor volume; EOT, end of therapy

RESULTS

Patient Characteristics

Patient demographics and disease characteristics	N = 25, n (%)
Age, median years (range)	30 (17–64)
Sex, female	12 (48)
Race, White	16 (64)
Disease stage at initial diagnosis	
II bulky	8 (32)
III	5 (20)
IV	12 (48)
Extranodal disease present	13 (52)
B symptoms at initial diagnosis	8 (32)
International Prognostic Score	
0–1	12 (48)
2–3	11 (44)
4–7	2 (8)

Primary Endpoint (EOT PET)

End of therapy	n	%
DS 1	5	20%
DS 2	15	60%
DS 3	2	8%
DS 4	3	12%
DS 5	0	0%
Total	**25**	**100%**

CR rate at EOT: 88% (22/25)

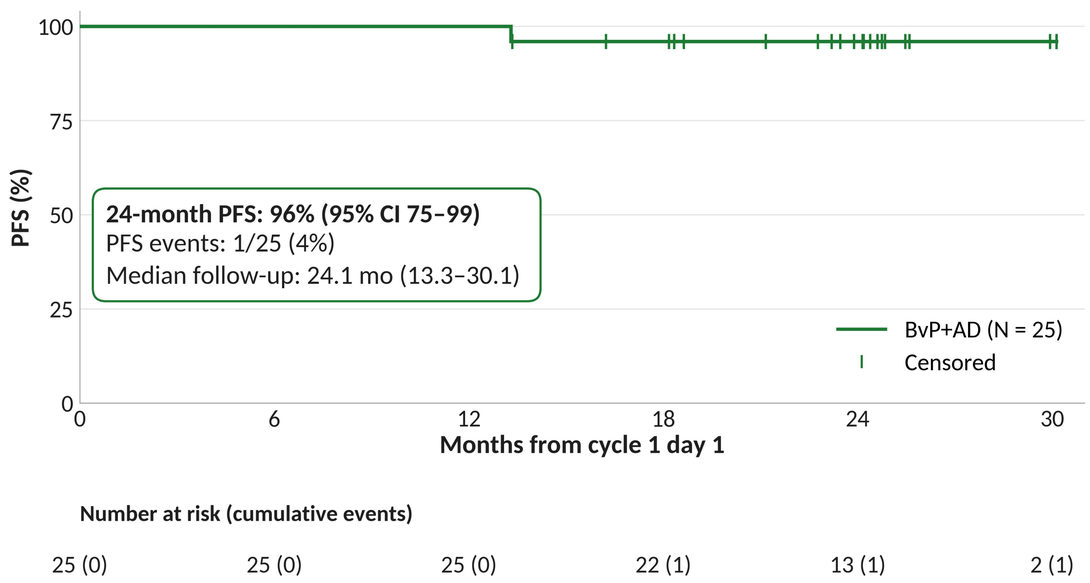
All 3 patients with DS 4 at EOT achieved CR on follow-up PET.

Interim PET (after cycle 3)

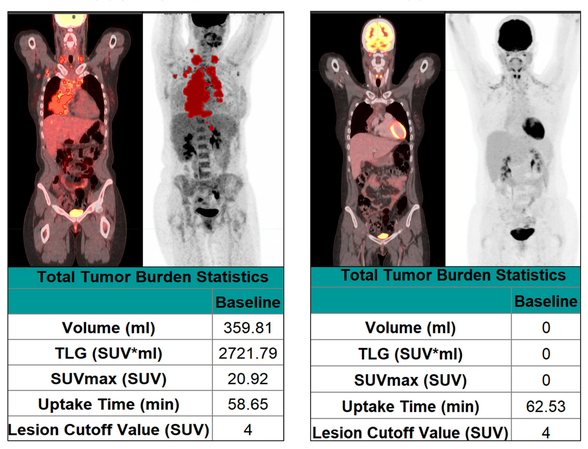
Interim PET	n	%
DS 1	2	8%
DS 2	16	64%
DS 3	7	28%
DS 4	0	0%
DS 5	0	0%
Total	**25**	**100%**

DS 3: all 7 patients had ≥90% reduction in TMTV and proceeded to Part B, the de-escalation arm.

Progression-Free Survival



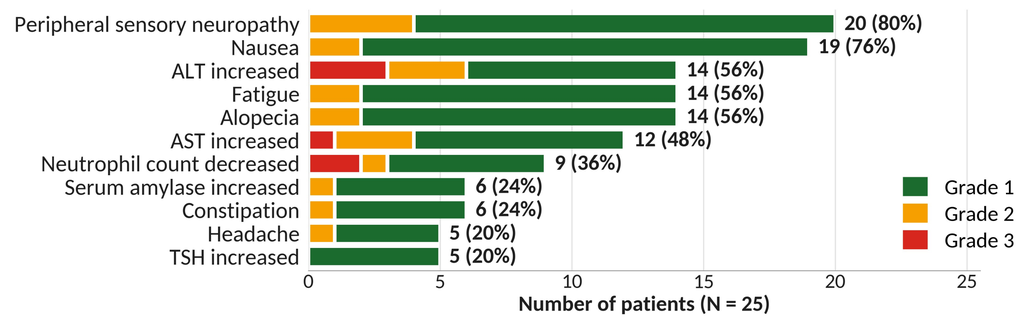
TMTV Measurement



Segmentation: MIM Software LesionID™ Pro

Adverse Events

Treatment-related AEs in ≥20% of patients (any grade; highest grade per patient)



Adverse events of special interest

- **No febrile neutropenia** was reported. Grade 3 neutropenia occurred in **2 patients (8%)**; all resolved.
- **Growth factor support** was given to **7 patients** as primary prophylaxis.
- **Peripheral neuropathy** occurred in **20 patients (80%)**: grade 1 in 16 (64%) and grade 2 in 4 (16%). **No grade 3 PN.** PN resolved in 8 of 20 (40%) by last follow-up.
- **Dose modifications:** brentuximab vedotin was reduced to 0.9 mg/kg for PN in 4 patients. Pembrolizumab was discontinued in 2 patients for grade 3 ALT elevation.
- **No grade 4 or 5** adverse events occurred.
- **Serious AEs:** 6 events in **5 patients (20%)**: fever (2), grade 3 neutropenia (1), suspected pneumonitis (1), grade 3 diarrhea requiring admission (1) and B-cell lymphoma (1).

Immune-mediated AEs of interest

- **Hepatitis:** grade 3 ALT elevation in 3 patients (12%) and grade 3 AST elevation in 1 (4%); all LFT abnormalities resolved.
- **Thyroid dysfunction** in 6 patients (24%): hyperthyroidism followed by hypothyroidism requiring thyroid replacement in 2; isolated grade 1 TSH elevation in 4.
- **No confirmed colitis:** 1 patient was admitted with grade 3 diarrhea that resolved spontaneously within 1 day, without steroids or other intervention. GI deferred colonoscopy as symptoms had resolved.
- **Pneumonitis:** 1 suspected grade 2 event, never confirmed; treated with a prednisone taper and resolved without holding pembrolizumab.

CONCLUSION

- **BvP+AD with PET-adapted de-escalation** showed favorable safety and durable efficacy in frontline advanced-stage cHL.
- All patients met de-escalation criteria, reducing anthracycline/alkylator exposure by **50%**, with **no radiotherapy**, **88% EOT CR**, and **96% PFS at 24 months** (median follow-up 24.1 months).
- Longer follow-up and larger cohorts are needed.