# LOW-DOSE NIVOLUMAB COMBINED WITH AVD CHEMOTHERAPY (NIVO40-AVD) FOR ADVANCED-STAGE HODGKIN LYMPHOMA: INTERIM RESULTS OF A PHASE 2 TRIAL

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## INTRODUCTION

The SWOG S1826 trial demonstrated high efficacy and low toxicity of first-line nivolumab combined with doxorubicin, vinblastine and dacarbazine (N-AVD) in newly diagnosed advanced-stage classic Hodgkin lymphoma (cHL), with a two-year progression-free survival (PFS) of 92%. This regimen has already changed the frontline treatment of advanced-stage cHL.

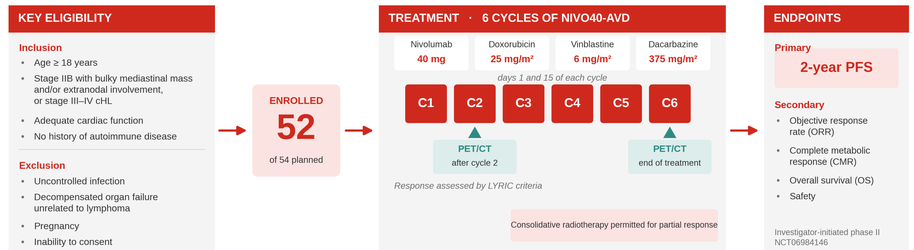
Because of the unique mechanism of PD-1 blockade, nivolumab doses as low as 0.1–0.3 mg/kg achieve 70–90% receptor occupancy and clinically meaningful responses[1]. A recent systematic review and meta-analysis confirmed the high efficacy and acceptable toxicity of low-dose PD-1 inhibition in relapsed or refractory cHL[2].

This is an interim analysis of an investigator-initiated phase II trial (NCT06984146) of low-dose nivolumab combined with AVD (Nivo40-AVD) for advanced-stage cHL.

## MATERIALS AND METHODS

The trial was approved by the institutional ethics committee and all patients provided written informed consent (NCT06984146). Study schema is represented in Figure 1.

**Figure 1. Study design.**




## RESULTS

At data cutoff, 52 of the 54 planned patients were enrolled (Table 1).

**Table 1. Baseline characteristics of enrolled patients.**

| Baseline characteristics | Nivo40-AVD (n=52) |
|---|---|
| Age, median (range) | 36 years (range 19–73) |
| 18-30 years<br>31-60 years<br>>60 years | 16 (31%)<br>30 (58%)<br>6 (12%) |
| Male<br>Female | 21 (40%)<br>31 (60%) |
| Weight, median (range) | 72.5 (48–130) |
| Nivolumab dose per kg, median (range) | 0.56 (0.31–0.83) |
| Nodular sclerosis<br>Mixed cellularity<br>Lymphocyte-depleted | 50 (96%)<br>1 (2%)<br>1 (2%) |
| Stage IIB<br>Stage III<br>Stage IV | 17 (33%)<br>12 (24%)<br>23 (44%) |
| B-symptoms | 42 (81%) |
| Bulky mediastinal disease | 20 (39%) |
| Extranodal disease | 28 (54%) |
| Bone marrow involvement | 5 (10%) |
| EBV+ | 7 (13%) |
| IPS 0-3<br>IPS 4-7 | 34 (65%)<br>18 (35%) |

Of the 52 enrolled patients, 48 (92%) completed 2 cycles and underwent interim assessment, and 30 (58%) completed all 6 cycles and underwent end-of-treatment evaluation (Figure 2).

After 2 cycles, ORR in evaluable patients was 95.8%, with a CMR rate of 77.1%, PMR of 18.8%, and indeterminate response (IR) of 4.1% (Figure 3). The corresponding rates in the 30 patients assessed after 6 cycles were 86.7%, 83.3%, 3.3% and 13.3%, respectively. The lower ORR at the end of treatment reflects reclassification of LYRIC indeterminate responses rather than loss of response — CMR increased from 77.1% to 83.3%. One patient with IR received consolidative radiation.

At a median follow-up of 11 months (range 6-22) only 1 progression event was registered (at 11 months).

**Figure 2. Swimmer plot of individual patients trajectories (n=52)**

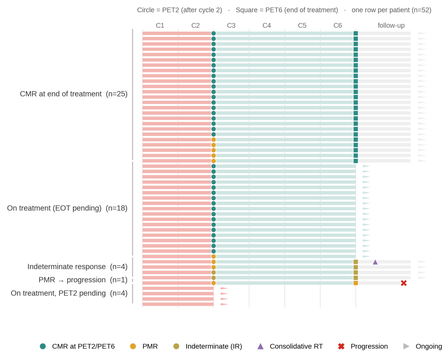
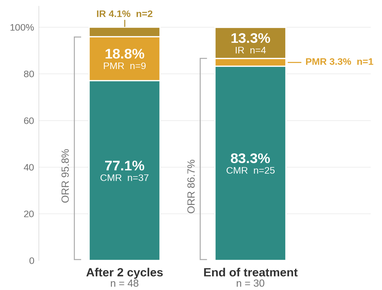



**Figure 3. Response rates at interim and end of treatment assessment**




Grade 3–4 adverse events included neutropenia (46.7%), and transaminitis (6.7%). All patients with severe neutropenia received G-CSF support and the median number of cycles requiring support was 3 (range 1-6). Nivolumab discontinuation due to immune-related adverse events occurred in 2 patients.

The cost of treatment was reduced by 75% as compared to conventional nivolumab first-line strategy.

## CONCLUSIONS

Nivo40-AVD is active in advanced-stage cHL: CMR 77.1% after 2 cycles and 83.3% at end of treatment, which is similar to conventional dosing.

Early disease control is preserved: 1 progression among 52 patients at a median follow-up of 11 months.

Drug cost fell by 75%, which could make frontline PD-1 immunochemotherapy feasible in resource-limited settings.

Follow-up is immature against primary endpoint (2 year PFS), enrollment is continued, further data is warranted.

## CONTACT INFORMATION

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## REFERENCES

1. Gandhi KA, Shirsat A, Kumar HJS, et al. Pharmacokinetics and clinical outcomes of low-dose nivolumab relative to conventional dose in patients with advanced cancer. Cancer Chemother Pharmacol 2024;94:659–668.

2. Akhmedov M, Zeynalova P, Fedenko A, Kaprin A. Low-dose PD-1 inhibition in relapsed/refractory classic Hodgkin lymphoma: systematic review and meta-analysis. Invest New Drugs 2025;43:1013–1021.

**Nivolumab 40 mg + AVD: similar to conventional dosing response patterns at one-quarter of the drug cost**