13% and 24% of pts, respectively. At interim PET, CRs (DS ≤ 3) were 85.5% for the $ABVD_{DD\text{-}DI}$ and 80.5% for ABVD ($p = 0.15$). At a median FU of 35 mo.s, 97 pts had a PFS event ($ABVD_{DD\text{-}DI}$ $n = 32$; ABVD $n = 65$). The 3-y PFS per ITT was 86.7% (95% CI: 81.7–90.4) for $ABVD_{DD\text{-}DI}$ and 73.2% (95% CI: 66.9–78.5) for ABVD (Δ: 13.46%; $p = 0.0001$) [HR 0.44 (95% CI 0.28–0.67; $p = 0.0002$)] (Figure 3C). A superior 3-y PFS was also achieved in pts with mediastinal bulky ($ABVD_{DD\text{-}DI}$ 87.0% vs. ABVD 71.9%) and stage IV disease ($ABVD_{DD\text{-}DI}$ 86.4% vs. ABVD 70%) (Figure 3D, E). RT was delivered to 10% of pts in $ABVD_{DD\text{-}DI}$ and 32% in ABVD. Nine pts died ($ABVD_{DD\text{-}DI}$: 3 PD, 1 COVID; ABVD: 4 PD, 1 H_1N_1). Neutropenia ≥G3 (40.8% vs. 30.4%; $p = 0.016$) and mucositis ≥G3 (3.2% vs. 0%; $p = 0.005$) occurred more frequently in $ABVD_{DD\text{-}DI}$ versus ABVD. No excess of cardiotoxicity (G2: 0.8%, G3: 0.8%) nor respiratory events (G2: 6%, G3: 2.4%, G4: 0.4%) were recorded for $ABVD_{DD\text{-}DI}$ versus ABVD (cardiac, G2: 0.4%, G3: 0.4%; respiratory, G2: 4.4%, G3: 1.2%, G4: 0.4%).

Conclusions: The study met its primary objective. $ABVD_{DD\text{-}DI}$ improved 3-year PFS by >10%, with a reduced need for RT, no PET-adaptation, and no alarming acute safety signals. It was also more active in pts with mediastinal bulk and stage IV disease.

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Keywords: chemotherapy, Hodgkin lymphoma

No conflicts of interests pertinent to the abstract.

005 | NIVOLUMAB(N)-AVD IMPROVES PROGRESSION-FREE SURVIVAL COMPARED TO BRENTUXIMAB VEDOTIN(BV)-AVD IN ADVANCED STAGE (AS) CLASSIC HODGKIN LYMPHOMA (HL): RESULTS OF SWOG S1826

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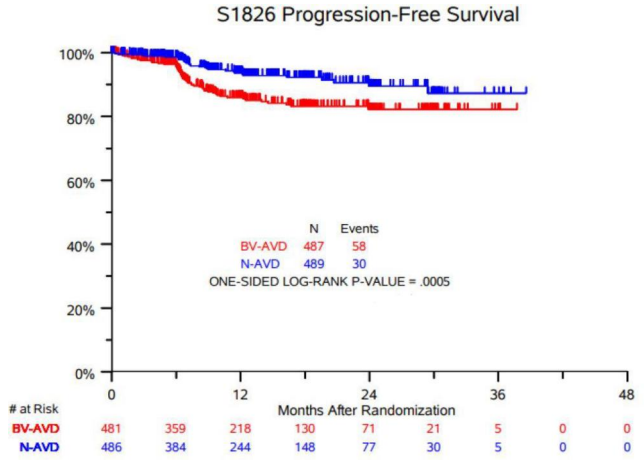
Background: The addition of BV to initial chemotherapy improves outcomes in adult and pediatric patients (pts) with AS HL. However, frontline BV adds toxicity, most pediatric pts receive radiation therapy (RT), and 7%–20% of pts still develop relapsed/refractory (RR) HL. The PD-1 pathway is central to the pathogenesis of HL and PD-1 blockade is effective in RR HL. The adult and pediatric cooperative groups of the National Clinical Trials Network (NCTN) conducted the randomized, phase 3 S1826 trial to evaluate N-AVD versus BV-AVD in pts with newly diagnosed AS HL.

Methods: Eligible pts were ≥12 years (y) with stage 3–4 HL. Pts were randomized 1:1 to either 6 cycles of N-AVD or BV-AVD. G-CSF neutropenia prophylaxis was required with BV-AVD versus optional with N-AVD. Pre-specified pts could receive RT to residually metabolically active lesions on end of treatment PET. Pts were stratified by age, international prognostic score (IPS), and intent to use RT. Response and disease progression were assessed by investigators using 2014 Lugano Classification. The primary endpoint was progression-free survival (PFS); secondary endpoints included



overall survival (OS), event-free survival, patient-reported outcomes (PROs), and safety.

Results: 994 pts were enrolled from 7/9/19 to 10/5/22; 976 were eligible and randomized to N-AVD (n = 489) or BV-AVD (n = 487). Median age was 27y (range 12–83y), 56% of pts were male, 76% were white, 12% were black, and 13% were Hispanic. 24% of pts were <18y, 10% were > 60y, and 32% had IPS 4–7. To date, <1% of pts received RT. At the planned 2nd interim analysis (50% of total PFS events) the SWOG Data and Safety Monitoring Committee recommended to report the primary results because the primary PFS endpoint crossed the protocol-specified conservative statistical boundary. 30 PFS events occurred after N-AVD versus 58 events after BV-AVD. With a median follow-up of 12.1 months, PFS was superior in the N-AVD arm (HR 0.48, 99% CI 0.27–0.87, one-sided p = 0.0005); 1y PFS: N-AVD, 94%, BV-AVD, 86% (Figure). 11 deaths (7 due to adverse events, AE) were observed after BV-AVD compared to 4 after N-AVD (3 due to AE). The rate of grade (gr) ≥3 hematologic AE was 48.4% (45.1% gr ≥3 neutropenia) after N-AVD compared to 30.5% (23.9% gr ≥3 neutropenia) after BV-AVD. Rates (any gr) of febrile neutropenia (5.6% N vs. 6.4% BV), pneumonitis (2.0% N vs. 3.2% BV), ALT elevation (30.7% N vs. 39.8% BV), and colitis (1% N vs. 1.3% BV) were similar. Hypo/hyperthyroidism was more frequent after N-AVD (7%/3% N vs. <1% BV) while peripheral neuropathy was more common after BV-AVD (sensory: 28.1%, 1.2% gr ≥ 3 N vs. 54.2%,7.8% gr ≥ 3 BV; motor: 4% N vs. 6.8% BV).

Conclusions: N-AVD improved PFS versus BV-AVD in pts with AS HL. Few immune AEs were observed and < 1% of pts received RT. Longer follow-up is needed to assess OS and PROs. S1826, the largest HL study in NCTN history, is an important step towards advancing and harmonizing the pediatric and adult treatment of AS HL.

Encore Abstract—previously submitted to ASCO 2023

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Keywords: Hodgkin lymphoma, immunotherapy, targeting the tumor microenvironment

Conflicts of interests pertinent to the abstract

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006 | FOURTH GENERATION HUCART19-IL18 PRODUCES DURABLE RESPONSES IN LYMPHOMA PATIENTS PREVIOUSLY RELAPSED/REFRACTORY TO ANTI-CD19 CAR T-CELL THERAPY

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Introduction: Lymphoma (NHL) patients (pts) relapsing/refractory (R/R) to anti-CD19 chimeric antigen receptor T-cells (CART) represent a challenging group in need of effective therapies. HuCART19-IL18 is a 4th generation 4-1BB CART product designed to express humanized anti-CD19 CAR and secrete interleukin 18, a pro-inflammatory cytokine shown to enhance CART efficacy in pre-clinical models. Its humanized scFv may allow for better persistence, and the additional use of a novel expedited 3-day manufacturing protocol may improve the product's potency.

Methods: We are conducting a first-in-human trial of huCART19-IL18 in pts ≥18 years old with CD19+ R/R B-cell NHL or CLL, who have had at least 2 prior lines of therapy including failure of prior CART. Using a modified Bayesian optimal interval dose titration design, we are exploring doses between 3 and 300 million huCART19-IL18+ cells. The product is administered as a single IV infusion following lymphodepleting (LD) chemotherapy. Bridging therapy is optional and huCART19-IL18 re-treatment is permitted for pts not achieving complete response (CR). Responses are assessed at 3, 6, 9, and 12 months (mo) using Lugano criteria for NHL and revised iwCLL criteria for CLL.

Results: As of 3 March 2023, 16 pts have enrolled. 15 pts had huCART19-IL18 manufactured and all achieved a minimum protocol-defined dose. The 13 pts infused to date include 5 DLBCL, 4 FL, 2 MCL, 1 HGBCL, 1 THRBCL pts. The median age is 65 years (53–74), 77% male, 92% had prior anti-CD19 CART (axi-cel 6, tisa-cel 4, brex-cel 1, tisa-cel+liso-cel 1) with 67% relapsed and 33% refractory to prior CART. The median number of prior therapies was 8 (4–14); 11 (85%) pts received bridging therapy. LD