An Oncology Simulation Model to Estimate 10-Year Overall Survival, Progression-Free Survival, and Stem Cell Transplantation for Frontline, Stage III or IV Classic Hodgkin Lymphoma Based on the Overall Survival Update of the ECHELON-1 Trial: A United States Perspective

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Background

- Stage III or IV classic Hodgkin lymphoma (cHL) is primarily treated with multi-agent chemotherapy regimens, including[1]
  - ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine)
  - A+AVD (brentuximab vedotin, doxorubicin, vinblastine, and dacarbazine)
  - eBEACOPP (escalated dosing regimen of bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone)
- In ECHELON-1, after a median follow-up of approximately 6 years[2]
  - Patients with stage III or IV cHL on 1L A+AVD continued to demonstrate a robust and durable improvement in progression-free survival (PFS) vs ABVD, with a 32% reduction in the risk of progression or death (hazard ratio [HR]: 0.68, 95% CI: 0.53-0.86, nominal $P = 0.002$)
  - Patients receiving A+AVD vs ABVD demonstrated an improvement in overall survival (OS), with a 41% reduction in the risk of death (HR: 0.59; 95% CI: 0.40-0.88; $P = 0.009$)
- A+AVD is the first regimen to show an improvement in OS versus classic ABVD in patients with previously untreated stage III or IV cHL[2]

Objective

- To estimate the impact of treatment scenarios without and with 1L A+AVD on the population of US patients with cHL, we developed an oncology simulation model that incorporated data from the 6-year ECHELON-1 update

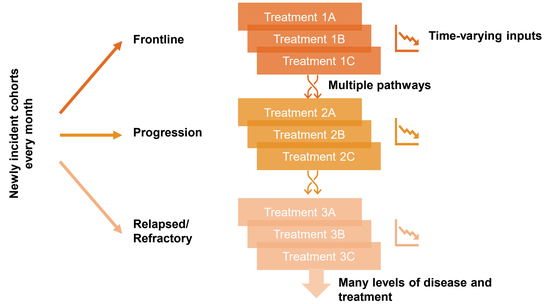
Methods

- A dynamic cohort Markov model was developed from a US perspective to estimate population-level outcomes based on the annual prevalence of cHL (**Figure 1**)

Population inputs

- Incidence of cHL was derived from the 2019 Surveillance, Epidemiology, and End Results (SEER) Program, assuming that 95% of HL cases are cHL and 42% of cHL cases are stage III or IV[3]

Figure 1. Example Model Framework

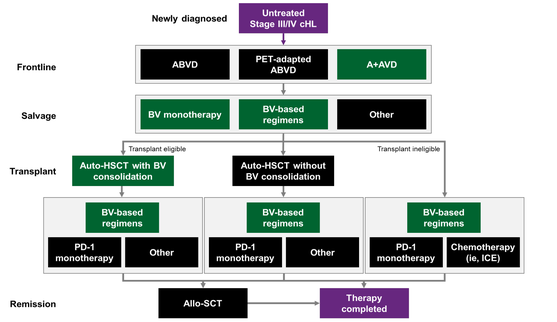


Methods (cont'd)

Treatment patterns and utilization

- The modeled treatment pathway was informed by NCCN guidelines (v2.2020)[4] and expert clinicians' opinion on commonly used regimens for stage III or IV cHL (**Figure 2**)
- The model assumed stem cell transplantation (SCT) was available at a single time point, after salvage therapy
- For each 1-month cycle, patients with progressive disease switched to second-line (2L) therapy

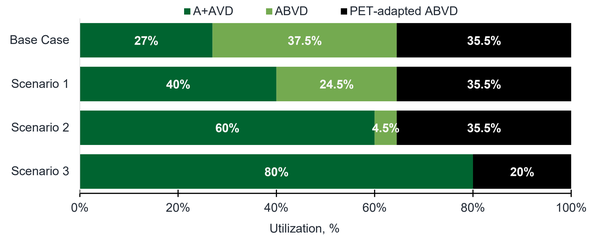
Figure 2. Modeled Pathway



Abbreviations: ABVD, doxorubicin, bleomycin, vinblastine, dacarbazine; Allo-SCT, allogenic stem cell transplantation; Auto-HSCT, autologous hematopoietic stem cell transplantation; AVD, doxorubicin, vinblastine, dacarbazine; BV, brentuximab vedotin; cHL, classical Hodgkin lymphoma; ICE, ifosfamide, carboplatin, etoposide; PD-1, programmed cell death protein 1; PET, positron emission tomography

- In the base case, a scenario without A+AVD (ABVD: 64.5%; PET-adapted therapy: 35.5%) was compared to a scenario with A+AVD (ABVD: 37.5%, PET-adapted therapy: 35.5%, A+AVD: 27%)
- Scenario analyses varied A+AVD utilization from 40% to 80% as recommended by expert clinicians' opinion (**Figure 3**)

Figure 3. Base Case and Sensitivity Analyses: Utilization Assumptions



Abbreviations: A+AVD, brentuximab vedotin in combination with doxorubicin, vinblastine, dacarbazine; ABVD, doxorubicin, bleomycin, vinblastine, dacarbazine; PET, positron emission tomography

Methods (cont'd)

Clinical inputs

- Clinical inputs for PFS and OS in all lines of therapy were informed by real-world treatment utilization and published treatment-specific clinical trial data[2,5-17]
- Evidence from the 6-year ECHELON-1 update provided inputs for ABVD and A+AVD[2]
  - PFS: A+AVD, 82.3% (95% CI: 79.1–85.0); ABVD, 74.5% (70.8–77.7); HR, 0.678 (0.532–0.863)
  - OS: A+AVD, 93.9% (91.6–95.5); ABVD, 89.4% (86.6–91.7); HR, 0.590 (0.396-0.879)

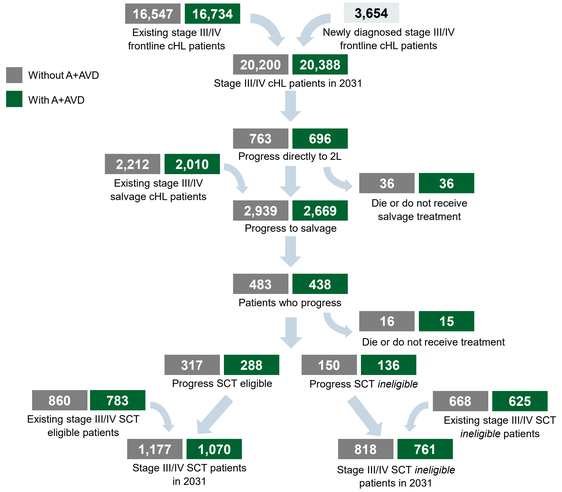
Results

- The number of patients newly diagnosed with stage III or IV cHL in 2031 was estimated at 3,654

Base-case analysis

- The number of patients with cHL alive and progression free following 1L therapy was estimated at 20,200 in a setting without A+AVD and 20,388 in a setting with A+AVD (A+AVD utilization = 27%; Δ+188, 0.93%) in 2031 (**Figure 4**)
- Over 10 years, the estimated total number of deaths was 2,650 without and 2,290 with A+AVD (Δ-360, 14% fewer deaths), the estimated number of SCTs was 3,200 without and 2,900 with A+AVD (Δ-300, 9.4% fewer SCTs), and the estimated number of second cancers was 1,418 without and 1,308 with A+AVD (Δ-110, 8%)

Figure 4. Patient Flow in 2031 for the Base Case Without and With A+AVD (27%)



Abbreviations: 2L, second-line therapy; A+AVD, brentuximab vedotin, doxorubicin, vinblastine, dacarbazine; cHL, classical Hodgkin lymphoma; SCT, stem cell transplantation

Results (cont'd)

- The model predicted that, annually for every 100 patients prescribed A+AVD, 3.7 more deaths would be avoided, 6.7 more patients would achieve ≥5 years' PFS, 2.9 fewer patients would require an SCT, and 1.1 more second cancers would be avoided

Scenario analyses

- Varying 1L A+AVD utilization from 40%-80% avoided 530-840 deaths (20%-32% decrease), added 278-517 more patients (1.4%-2.6% increase) with cHL remaining 1L progression-free, avoided 440-780 SCTs (13.8%-24.4% decrease), and avoided 163-319 (12%-22% increase) second cancers vs the scenario without A+AVD (**Table 1**)

Table 1. No. of Patients With Stage III or IV cHL Progression-Free and Deaths, SCTs, and Second Cancers Avoided Over 10 Years With Varying 1L A+AVD Utilization, Base Case and Scenario Analyses

	No. of patients							
	Total 1L progression-free	Additional 1L progression-free[a]	Total deaths over 10 yrs	Deaths avoided over 10 yrs[a]	Total SCT over 10 yrs	SCT avoided over 10 yrs[a]	Total second cancers over 10 yrs	Second cancers avoided over 10 yrs[a]
No A+AVD	20,200	-	2,650	-	3,200	-	1,418	-
A+AVD at 27% (base case)	20,388	188	2,290	360	2,900	300	1,308	110
A+AVD at 40%	20,478	278	2,120	530	2,760	440	1,255	163
A+AVD at 60%	20,617	417	1,850	800	2,590	610	1,173	245
A+AVD at 80%	20,717	517	1,810	840	2,420	780	1,099	319

[a] Compared with a scenario without frontline A+AVD
Abbreviations: 1L, frontline; A+AVD, brentuximab vedotin, doxorubicin, vinblastine, dacarbazine; cHL, classic Hodgkin lymphoma; SCT, stem cell transplantation

Limitations

- This model was streamlined by combining treatment regimens; mean PFS and OS values for various regimens were calculated to represent the broader treatment groups
- SCT was included only at one time point (post 2L therapy in remission); in clinical practice, SCT is utilized beyond 2L therapy and for disease in partial remission
- The assumption of constant hazards for PFS and OS was not tested

Conclusion

- Over 10 years, varying 1L A+AVD utilization from 27%-80% in the United States resulted in an estimated 360-840 deaths avoided (14%-32% decrease)
- The significant improvement in OS and observed improvement in PFS in the ECHELON-1 trial, the first to show an improvement in OS versus classic ABVD in stage III or IV cHL, may translate to more patients with stage III or IV cHL alive and progression-free, more deaths avoided, fewer patients developing primary refractory/relapsed disease, fewer patients needing additional therapies including SCT, and more second cancers avoided in scenarios with vs without A+AVD

References

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