An Oncology Simulation Model to Estimate 10-year Progression-free Survival and Overall Survival Based on the 5-Year Update from the ECHELON-2 Trial in Frontline Patients with Peripheral T-cell Lymphoma: A United States Perspective

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Background

- Peripheral T-cell lymphomas (PTCLs) are a rare and aggressive type of non-Hodgkin lymphoma (NHL) associated with a poor prognosis[1]
- Numerous PTCL subtypes have been identified,[2] including ALK-positive/negative anaplastic large cell lymphoma (ALCL)[3]
  - Systemic ALCL (sALCL) comprises approximately 2%-3% of all adult NHLs,[4-6] with at least two distinct subtypes that are characterized by hallmark cytology and uniformly strong expression of CD30[3,7,8]
- Common frontline (1L) regimens used to treat PTCL include A+CHP (brentuximab vedotin in combination with cyclophosphamide, doxorubicin, and prednisone), CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), and CHOEP (CHOP plus etoposide)[9]
- Survival rapidly declines following the first relapsed or refractory (R/R) episode in patients with PTCL; therefore, selection of an effective 1L therapy that avoids or delays a need for subsequent treatment is important[10,11]
  - Survival outcomes for patients treated with chemotherapy for R/R PTCL are reported to be only marginally better than outcomes for patients not receiving treatment[10,11]
- Results from the 5-year update of the ECHELON-2 trial[12] showed that patients with previously untreated CD30-expressing PTCL treated with A+CHP versus CHOP continued to demonstrate clinically meaningful improvements in progression-free survival (PFS) and overall survival (OS)

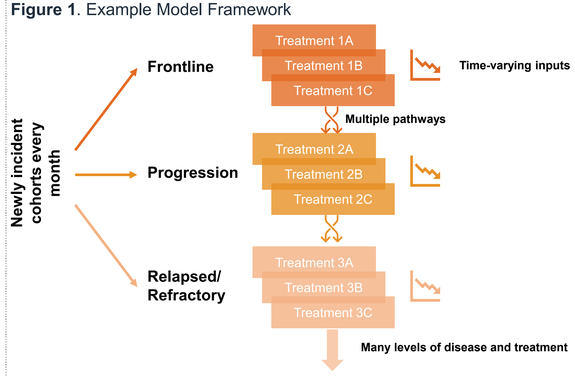
Objective

- To estimate the future annual number of patients with previously untreated PTCL alive and progression free in scenarios without and with A+CHP over 10 years, based on the 5-year follow-up results from ECHELON-2[12]

Methods

- A continuous dynamic oncology simulation model (OSM) was developed for the United States population to estimate population-level outcomes based on the annual incidence of PTCL (**Figure 1**)
  - The continuous dynamic Markov model considered disease incidence and treatment patterns for previously untreated PTCL as well as PFS and OS rates reported for commonly used therapies
  - The model assumed that all patients diagnosed with PTCL will receive 1L therapy
  - The model cycle length was 1 month

Figure 1. Example Model Framework



Methods (cont'd)

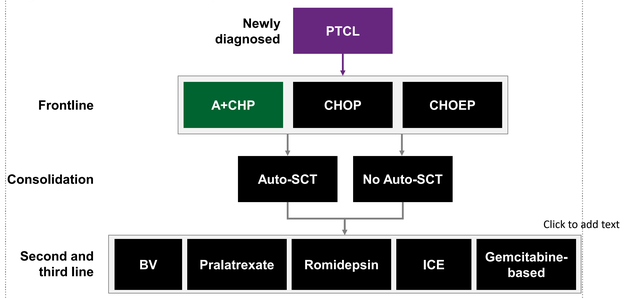
Population inputs

- The annual incidence of PTCL was derived using the incidence for NHL in 2021 (19.6 per 100,000) reported through the Surveillance, Epidemiology, and End Results (SEER) Program and applying the proportion of NHL cases that are PTCL from the Lymphoma Research Foundation (~5%) and the proportion of PTCLs that express CD30 (66%)[13,14]

Treatment patterns and utilization

- The modeled treatment pathway was informed by NCCN guidelines (v1.2021)[9] and expert clinicians' opinion on commonly used PTCL treatment regimens (**Figure 2**)
  - The model assumes that consolidation therapy is given at a single time point, after 1L treatment

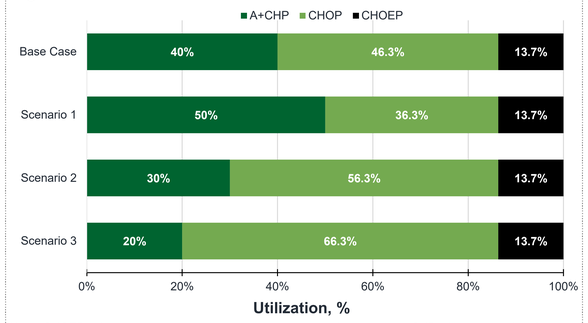
Figure 2. Modeled Pathway



Abbreviations: A+CHP, brentuximab vedotin plus cyclophosphamide, doxorubicin, and prednisone; ASCT, autologous stem cell transplant; BV, brentuximab vedotin, CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; CHOEP, cyclophosphamide, doxorubicin, vincristine, etoposide, and prednisone; ICE, ifosfamide, carboplatin, etoposide; PTCL, peripheral T-cell lymphoma

- In the scenario without A+CHP, 65% of patients were assumed to receive 1L CHOP and 35% of patients were assumed to receive 1L CHOEP
- In the scenario with A+CHP, 40% of patients were assumed to receive 1L A+CHP in the base case
- Scenario analyses were conducted for 1L A+CHP, with utilization ranging from 20% to 50%, assuming A+CHP was used instead of CHOP as recommended by clinical experts (**Figure 3**)
- Utilization of A+CHP greater than 50% was not considered as about half of PTCLs do not express CD30

Figure 3. A+CHP Utilization for the Base Case and for Scenario Analyses



Note: CHOEP utilization was assumed to remain constant; the increase in A+CHP utilization is taken from CHOP utilization. **Abbreviations:** A+CHP, brentuximab vedotin in combination with cyclophosphamide, doxorubicin, and prednisone; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; CHOEP, cyclophosphamide, doxorubicin, vincristine, etoposide, and prednisone

Methods (cont'd)

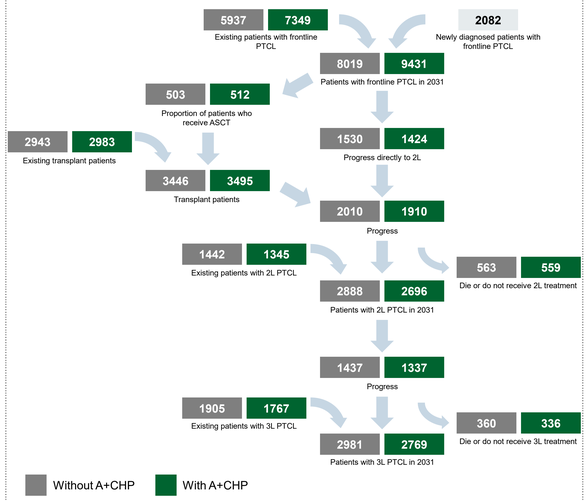
Clinical inputs

- Clinical inputs for PFS and OS in all lines of therapy, including consolidation, were primarily derived from the published literature[15-22]
  - Evidence from the 5-year ECHELON-2 trial[12] update provided inputs for A+CHP and CHOP that showed statistically significant and clinically meaningful improvements with A+CHP vs CHOP in patients with previously untreated PTCL including a
    - 30% reduction in progression events: PFS, 51.4% (95% CI: 42.8% - 59.4%) vs 43.0% (35.8% - 50.0%); hazard ratio (HR), 0.70 (0.53 - 0.91), *P*=0.0077
    - 28% lower risk of death: OS, 70.1% (63.3% - 75.9%) vs 61.0% (54.0 - 67.3); HR: 0.72 (0.53 - 0.99), *P*=0.0424
  - Brentuximab vedotin, romidepsin, pralatrexate, ICE (ifosfamide, carboplatin, etoposide), and gemcitabine-based regimens were included in the model as second and later lines of therapy
- The model also allowed for a portion of patients in remission on 1L treatment who were eligible to receive stem cell transplantation (SCT)
- The annual prevalence of patients living progression free with PTCL in the 1L setting with each prescribed scenario was estimated for 10 years (year 2031) without and with the availability of A+CHP

Results

- The estimated annual number of patients with newly diagnosed PTCL in 2031 was 2082
- The estimated number of patients alive and progression free in 2031 based on 1L treatment was 8019 in a scenario without A+CHP and 9431 in the scenario with A+CHP (Δ+1412, 17.6% increase) (**Figure 4**)
- As compared with 1L CHOP, 1L A+CHP would reduce the number of patients requiring 2L therapy by 2031 from 1530 to 1424 (Δ-106, 7.0% decrease)

Figure 4. Annual Patient Flow in 2031 for Patients with Previously Untreated PTCL



Abbreviations: 2L, second line; 3L, third line; A+CHP, brentuximab vedotin in combination with cyclophosphamide, doxorubicin, and prednisone; ASCT, autologous stem cell transplant; PTCL, peripheral T-cell lymphoma

Results (cont'd)

- Results from scenario analyses that varied 1L A+CHP uptake from 20% to 50% estimated an additional 732 (9.1% increase) to 1752 (21.8% increase) patients with PTCL alive and progression free in the year 2031.

Table 1. Scenario Analysis, Number of Patients Progression Free in 2031 with Varying A+CHP Utilization

Utilization	No. of patients		
	1L PTCL patients in 2031	Deaths avoided by 2031	Additional patients progression free in 2031[a]
A+CHP at 50%	9771	1505	1752
A+CHP at 40% (base case)	9431	1216	1412
A+CHP at 30%	9091	927	1072
A+CHP at 20%	8751	638	732

[a] Compared to a scenario without frontline A+CHP. **Abbreviations:** 1L, frontline; A+CHP, brentuximab vedotin in combination with cyclophosphamide, doxorubicin, and prednisone; PTCL, peripheral T-cell lymphoma.

Limitations

- No trial directly compared CHOEP and A+CHP, therefore, the model assumed CHOEP and CHOP had comparable efficacy
- Due to a lack of published data, the model assumed utilization was similar for second- and third-line therapies
- Additionally, there were limited data on the efficacy of second- and third-line therapies in patients with PTCL
- Although the model includes consolidation with autologous SCT, SCT was modeled at one time point only, as part of 1L therapy. In practice, patients may receive an allogeneic SCT in the R/R setting, though the number of patients is limited
- Most clinical trials enrolling patients with PTCL do not stratify results by PTCL subtypes and/or CD30 expression due to the rare nature of the disease and small study sample sizes
- Results from clinical trials and consultations with clinical experts indicate patients with ALCL have more favorable outcomes compared with patients with non-ALCL subtypes. As the ECHELON-2 trial enrolled a majority of patients with sALCL, results from this model may not be generalizable across other PTCL subtypes

Conclusions

- When incorporated into an OSM, the durable and significant improvements in PFS and OS seen with A+CHP vs CHOP in the 5-year follow-up data from ECHELON-2, translated into an estimated increase in the number of 1L PTCL patients who remain alive and progression free for greater than 10 years in scenarios with compared to those without A+CHP

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