THE COST-EFFECTIVENESS OF BRENTUXIMAB VEDOTIN IN FRONTLINE SYSTEMIC ANAPLASTIC LARGE CELL LYMPHOMA IN FRANCE

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Background

- Systemic anaplastic large cell lymphoma (sALCL) is a rare type of non-Hodgkin lymphoma and one of the most common subtypes of peripheral T-cell lymphoma (PTCL), with 12.1% of cases.
- ALK fusions are detectable in approximately 50% of cases. ALK+ sALCL is indicative of a better prognosis, with a 5-year failure-free survival (FFS) and overall survival (OS) of 60% and 70%, respectively, compared with ALK- sALCL (FFS of 49% and OS of 36%) [2].
- Based on cancer incidence and mortality estimates between 1990 and 2018, the Santé Publique France agency estimated 1 136 cases of PTCL in France in 2018[3]. From the study conducted by the French network Lymphopath[4], 8.59% and 7.86% of PTCL cases were ALK+ or ALK- sALCL, respectively - equating to 187 patients with sALCL.
- Commonly used therapies for first-line treatment of sALCL include CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisolone) in patients older than 60 years and CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, and prednisolone) in patients <60 years who can tolerate etoposide's toxicities[5,6].
- Brentuximab vedotin is a CD30-directed antibody-drug conjugate approved for several indications (EMA approval only in sALCL population), including previously untreated sALCL or other CD30-expressing PTCLs when used in combination with cyclophosphamide, doxorubicin, and prednisone (BV+CHP).

Objectives

- The objective of this study was to estimate the cost-effectiveness of brentuximab vedotin (BV) in combination with cyclophosphamide, doxorubicin and prednisone (CHP) chemotherapy versus CHOEP for patients previously untreated with sALCL. The basecase analysis focuses on CHOEP as it's the most common chemotherapy used in France for sALCL patients.

Methods

- A cost-effectiveness analysis was developed using a three-state partitioned survival model (progression-free survival [PFS], progressed disease [PD], death) over a lifetime (35-year) horizon to compare BV+CHP to chemotherapies from the French collective perspective (Figure 1).
- The proportion of patients in the PFS state over time is estimated directly from the PFS curve reported in the pivotal clinical trial ECHELON-2, and the proportion of patients in the PD state is estimated as the difference between OS and PFS.
- Standard parametric curves were fitted to the PFS and OS data to simulate the long-term outcomes from the ECHELON-2 results. Based on AIC/BIC criteria and clinical expert opinions, exponential and gamma distributions were respectively used to extrapolate OS and PFS respectively (Figure 2). After 12 years patients who are still in the progression free state are likely to not progress and follow the OS curve. Long-term OS estimates were also constrained by the general population mortality informed by the French life tables.
- The main comparator included in this analysis was CHOEP chemotherapy with relative efficacy/effectiveness and safety data derived from a network meta-analysis. The hazard ratios for CHOEP vs. CHOP are informed by the ITT population from ECHELON-2 and PTCL populations from the literature. These populations are broader than the anticipated marketing authorisation for BV+CHP in patients with untreated sALCL. However, data were insufficient to estimate relative efficacy estimates within an sALCL population.
- Unit costs (in 2020 euros) were derived from public price lists and effects measured in quality-adjusted life years (QALYs). These were evaluated with a discount rate of 2.5% and 1.5% per annum before and after 30-years, respectively, according to French guidelines.

Results

- Over a lifetime horizon, the regimen of BV+CHP versus CHOEP was associated with 3.59 QALYs gained at a total incremental cost of 43 844€, resulting in an incremental cost-effectiveness ratio (ICER) of approximately 12 211€ (Table 1).
- Table 2 and Table 3 present the disaggregated QALYs and costs that are accrued in each model arm for the sALCL population respectively. Most of the incremental cost of BV is associated with acquisition costs during treatment. According to overall survival extrapolation, BV+CHP was associated with an extension of 4.48 life years.

Figure 1. Model schematic - Partitioned survival analysis

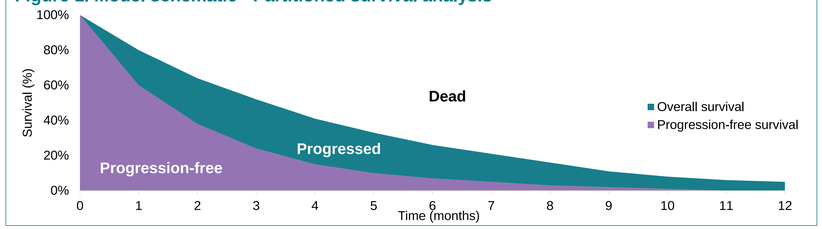
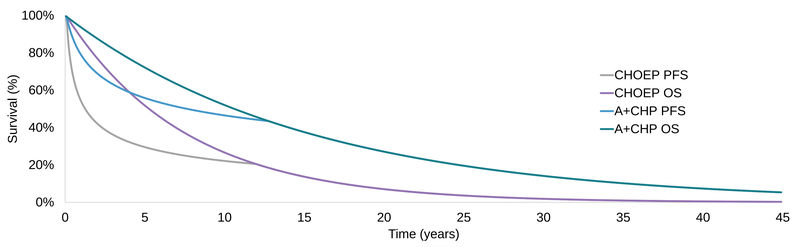


Figure 2. Standard parametric extrapolation



- The deterministic sensitivity analysis showed that the hazard ratio used for the OS and PFS and the price per pack of BV were the most impactful parameters on the results (Figure 3).
- The probabilistic sensitivity analyses generated a 95%CI of [0€ ; 40 900€] and an 80% probability of being cost-effective based on a willingness to pay (WTP) of 18 000€/QALY (Figure 4 and Figure 5).
- Sensitivity analyses identify hazard ratio used for CHOEP as the most impactful parameters on results.

Table 1. Base-case results

	CHOEP	BV+CHP	Incremental
Total costs	42 766€	86 609€	43 844€
Total QALYs	4.48	8.07	3.59
ICER	-	-	12 211€

Abbreviations: BV+CHP, brentuximab vedotin and cyclophosphamide, doxorubicin, and prednisone; CHOEP, cyclophosphamide, doxorubicin, vincristine, prednisone and etoposide; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

Table 2. Disaggregated QALYs and discounted life years

	CHOEP	BV+CHP	Incremental
QALYs in progression-free state	3.35	7.23	3.87
QALYs in progressed state	1.09	0.71	-0.37
QALY gain due to SCT	0.05	0.13	0.09
QALY loss due to Aes	-0.0056	-0.0065	-0.0009
Total QALYs	**4.48**	**8.07**	**3.59**
LYs in progression-free state	4.40	9.47	5.07
LYs in progressed state	1.93	1.27	-0.66
Total LYs	**6.33**	**10.74**	**4.41**

Abbreviations: BV+CHP, brentuximab vedotin and cyclophosphamide, doxorubicin, and prednisone; CHOEP, cyclophosphamide, doxorubicin, vincristine, prednisone and etoposide; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; LY, life year; SCT, stem cell transplant; AE, adverse event.

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Conflict of Interest

IB has no conflict of interest. AN, OS, ACT, HC, and CC are full-time employees of Takeda. OC and JC are full-time employees of Vyoo Agency, a consultancy company paid by Takeda to realize the data analyses.

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Table 3. Disaggregated costs

	CHOEP	BV+CHP	Incremental
Drug acquisition	0.00€	53 765.81€	53 765.81€
Drug administration	3 071.60€	3 071.60€	0.00€
Medical resource use	737.63€	1 057.85€	320.22€
Adverse events	3 915.50€	4 261.36€	345.85€
Total subsequent treatment	31 569.03€	19 173.45€	-12 395.58€
Subsequent BV+CHP	13 171.94€	4 953.24€	-8 218.70€
Salvage radiotherapy	15 381.90€	13 175.32€	-2 206.58€
Consolidative radiotherapy	41.69€	138.71€	97.02€
Consolidative SCT (alloSCT and ASCT)	2 464.58€	4 334.31€	1 869.73€
Salvage SCT	3 015.20€	1 044.89€	-1 970.31€
Mortality	965.48€	806.19€	-159.29€

Abbreviations: BV+CHP, brentuximab vedotin and cyclophosphamide, doxorubicin, and prednisone; CHOEP, cyclophosphamide, doxorubicin, vincristine, prednisone and etoposide; SCT, stem cell transplant; ASCT, autologous stem cell transplant.

Figure 3. Tornado diagram

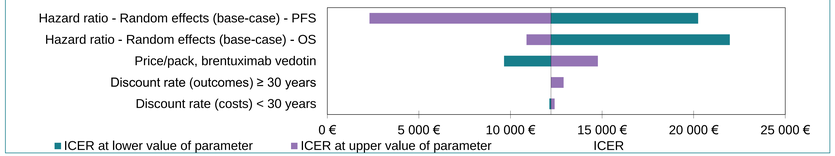


Figure 4. Willingness-to-pay

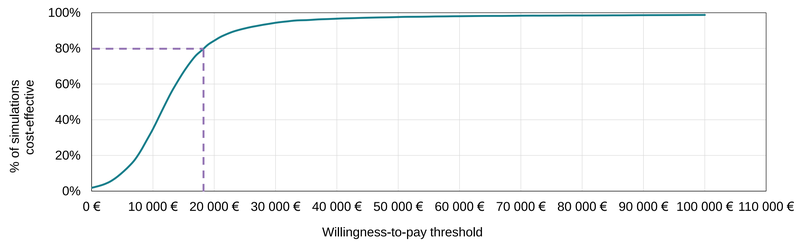
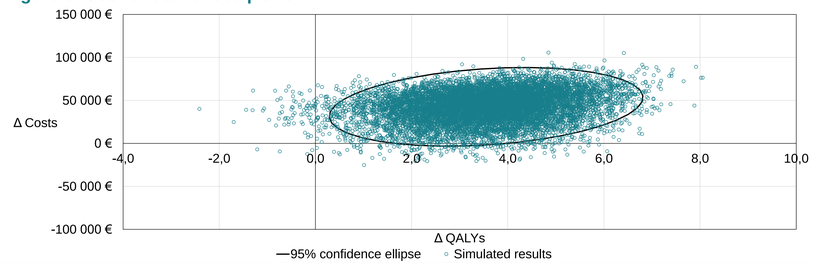


Figure 5. Cost-effectiveness plane



Conclusions

Results from this cost-effectiveness analysis suggest that BV+CHP versus CHOEP is likely to be cost-effective in France (with an ICER of 12 211€/QALY gained) based on conventional WTP threshold in adults with previously untreated sALCL. By comparison, the ICER was 21 012€/QALY gained versus the CHOP chemotherapy.

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