

Cost-utility of idelalisib in combination with rituximab in relapsed or refractory chronic lymphocytic leukaemia

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Background

- Chronic lymphocytic leukaemia (CLL) is clinically characterized by the proliferation and accumulation of immunoincompetent lymphocytes of small size, mature appearance and B-monoclonal phenotype¹.
- CLL is the most common form of adult leukaemia in Western countries with an estimated incidence of 4.2:100,000/year².
- New oral targeted therapies represent a clinical advantage for CLL patients with a significant improvement of their outcomes, but higher costs³.
- Idelalisib, a potent and selective orally administered inhibitor of PI3K δ , has been approved, in combination with rituximab, for the treatment of adult patients with CLL who have received at least one prior therapy, or as first line treatment in the presence of 17p deletion or TP53 mutation in patients who are not eligible for any other therapies^{4,5}.

Objective

To evaluate the incremental cost-utility ratio of idelalisib in combination with rituximab versus rituximab in monotherapy in the treatment of patients with relapsed or refractory CLL, from the Spanish National Health System perspective.

Methods

Model structure

- Previously published partitioned survival model of area under the curve with three mutually exclusive health states: progression-free survival (PFS), disease progression and death⁶⁻⁹ (Figure 1).
- The model begins with initial cohort of patients (mean body surface area of 1.80 m²; mean age of 70 years; 58.8% male) with CLL receiving a second line (2L) or subsequent line (+2L) of treatment with idelalisib in combination with rituximab or rituximab in monotherapy in the pre-progression state. During a cycle, patients can be: dead; alive in the pre-progression state; or alive in the post-progression state. Those in the latter state remain there until death.
- Cycle length: one week.
- Lifetime horizon: 30 years.
- Progression-free survival was extrapolated using a Weibull distribution (function with the best fit).

Treatment alternatives⁴

- Idelalisib (150 mg b.i.d. orally; until disease progression or unacceptable toxicity) in combination with rituximab (375 mg/m² Body Surface Area infusion -BSA- on day 1 for first cycle and 500 mg/m² BSA infusion on day 1 for subsequent cycles; 8 cycles maximum).
- Rituximab (375 mg/m² BSA infusion on day 1 for first cycle and 500 mg/m² BSA infusion on day 1 for subsequent cycles; 8 cycles maximum).

Clinical data

- Survival data were based on the results of the pivotal CLL clinical trial comparing idelalisib in combination with rituximab versus rituximab in monotherapy⁴, and external sources.
- Grade 3 and 4 adverse events considered were anaemia, diarrhoea, infection, leucopenia, pneumonia, neutropenia, febrile neutropenia and thrombocytopenia.
- Frequencies for adverse events were derived from the idelalisib clinical trial⁴, and other sources¹⁰.
- Each adverse event was associated to a specific disutility.

Costs

- Spanish National Health System perspective.
- Direct medical costs (€, 2016): drugs¹¹, administration drugs¹², monitoring^{12,13}, adverse events^{12,13} and disease management^{12,13}.
- Exfactory price with mandatory deduction^{11,14}: Idelalisib (Zydelig®, 60 tablets, 150 mg), €3,885.00; Rituximab (Mabthera®, 1 vial, 500mg), €1,049.35.

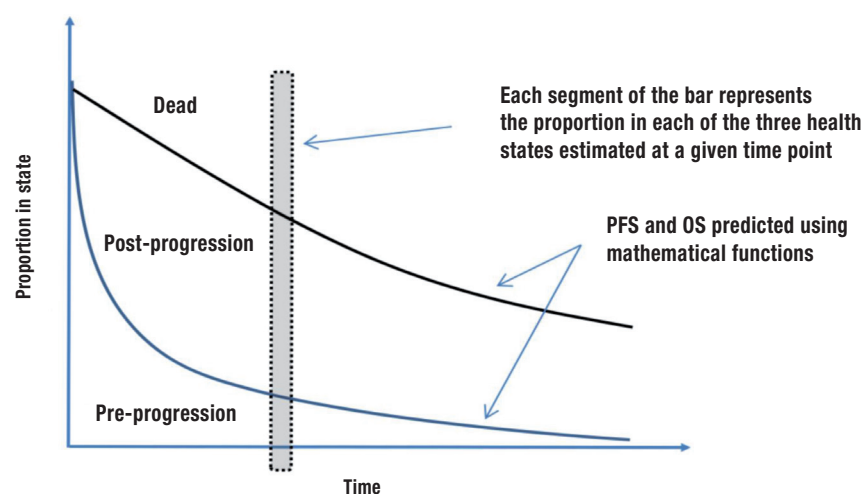
Utilities and disutilities were obtained from published literature^{15,16}.

Costs and health outcomes were discounted at a rate of 3% per year¹⁷.

The willingness-to-pay thresholds considered was €45,000 per QALY gained¹⁸.

One-way deterministic and probabilistic sensitivity analyses (1,000 iterations) were performed to evaluate model robustness.

Figure 1: Overall model schematic



References

- Santos FP, et al. Small lymphocytic lymphoma and chronic lymphocytic leukemia: are they the same disease? *Cancer J* 2012;18:396-403.
- Eichhorst B, et al. Chronic lymphocytic leukaemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2015;26 Suppl 5:78-84.
- Chen Q, et al. Economic burden of chronic lymphocytic leukemia in the era of oral targeted therapies in the United States. *J Clin Oncol* 2017;35(2):166-74.
- Furman RR, et al. Idelalisib and rituximab in relapsed chronic lymphocytic leukemia. *N Engl J Med* 2014;371:1107-1117.
- Molica S. Highlights in the treatment of chronic lymphocytic leukemia from the 2014 meeting of the American Society of Hematology. *Expert Rev Hematol* 2015;8:277-81.
- Gouveia M, et al. Cost-effectiveness of idelalisib in combination with rituximab for the treatment of relapsed/refractory Chronic Lymphocytic Leukemia (CLL) in Portugal. *Value Health* 2015;18(7):A461-2.
- Kumar G, et al. A Scotland based cost-effectiveness analysis of idelalisib (Zydelig®) in combination with rituximab for the treatment of adults with Chronic Lymphocytic Leukemia (CLL). *Value Health* 2015;18(7):A455.
- Lafont H, et al. Cost-effectiveness of idelalisib plus rituximab in chronic lymphocytic leukaemia. *Value Health* 2015;18(7):A460.
- Sullivan W, et al. The cost effectiveness of idelalisib in chronic lymphocytic leukaemia in England and Wales. *Value Health* 2015;18(7):A454-5.
- Niederle N, et al. Bendamustine compared to fludarabine as second-line treatment in chronic lymphocytic leukemia. *Ann Hematol* 2013;92(5):653-60.
- Bot Plus-Consejo General de Colegios Oficiales de Farmacéuticos.
- Oblique Consulting. Base de datos de costes sanitarios eSalud [eSalud Health Cost database] [Internet]. Barcelona: Oblique Consulting; 2017 [cited 2017 Oct 16]. Available at: <http://www.oblique.com/bddcostes/>.
- Panel of experts in the haemato-oncology field to validate all data in the Spanish setting.
- RD 08/2010-Ministerio de Sanidad, Servicios Sociales e Igualdad.
- Naltes B, et al. Health state utilities for non small cell lung cancer. *Health Qual Life Outcomes* 2006;4:64.
- Beusterien KM, et al. Population preference values for treatment outcomes in chronic lymphocytic leukaemia: a cross-sectional utility study. *Health Qual Life Outcomes* 2010;8:50.
- López-Bastida J, et al. Spanish recommendations on economic evaluation of health technologies. *Eur J Health Econ* 2010;11:153-20.
- De Cook E, et al. Valor umbral del coste por de vida ganado para recomendar la adopción de tecnologías sanitarias en España: evidencias procedentes de una revisión de la literatura. *Pharmacoconomics Sp Res Art* 2007;4:97-107.

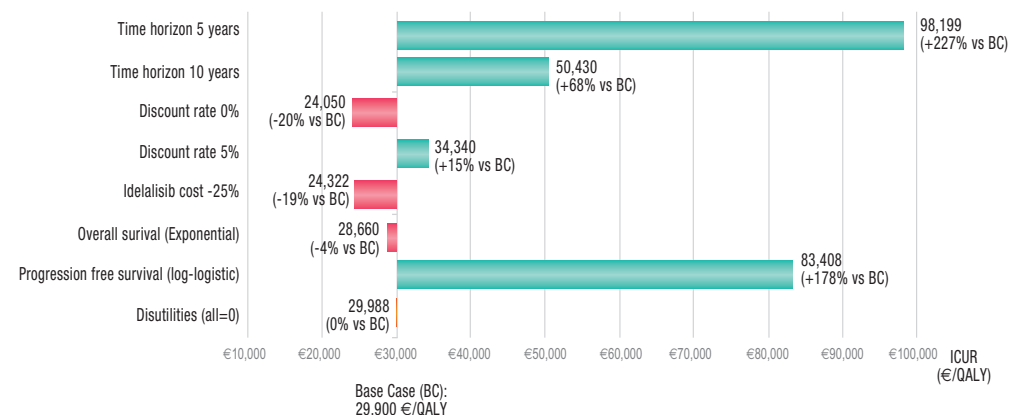
Results

Table 2. Cost-effectiveness and cost-utility analysis of idelalisib in combination with rituximab versus rituximab in monotherapy. Base-case lifetime model results

	Idelalisib + rituximab (IR)	Rituximab (R)	Incremental IR versus R
Total costs (€, 2016)	118,254	23,874	94,380
<i>Disease management costs</i>	35,614	14,555	21,059
<i>Treatment costs</i>	82,640	9,319	73,321
Life-years gained (LYG)	9.998	3.592	6.406
Quality adjusted life years (QALY)	4.965	1.818	3.147
Incremental cost-effectiveness ratio of IR versus R (ICER, €/LYG)		14,733	
Incremental cost-utility ratio of IR versus R (ICUR, €/QALY)		29,990	

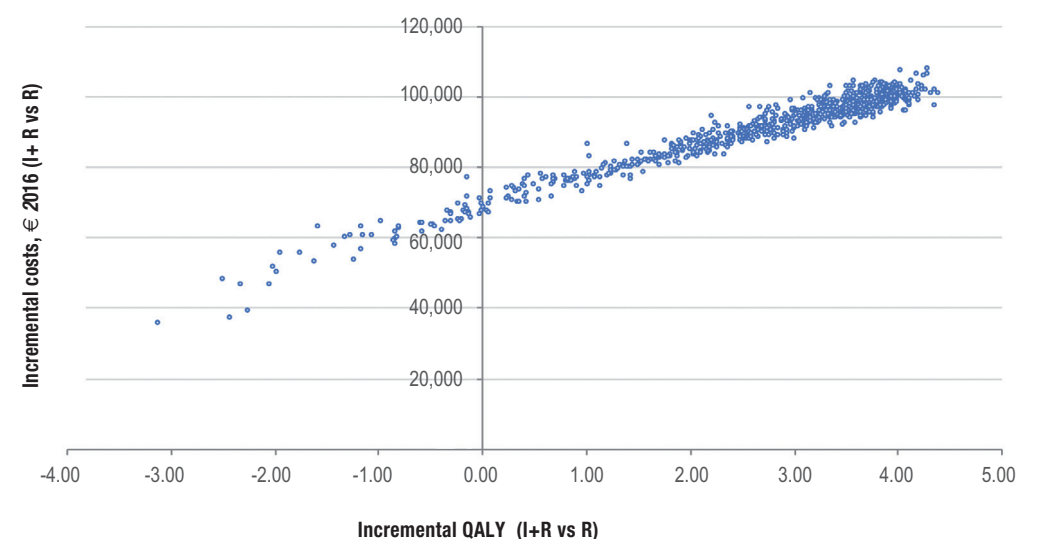
- Compared to rituximab in monotherapy, idelalisib in combination with rituximab increases 6.4 LYG or 3.1 QALY, with higher costs per patient, €94,380 (Table 2).
- This resulted in an ICER of €14,733 per LYG and an ICUR of €29,990 per QALY gained with idelalisib in combination with rituximab compared to rituximab in monotherapy (Table 2).

Figure 2. Cost-utility analysis of idelalisib in combination with rituximab versus rituximab in monotherapy. Deterministic sensitivity analysis results, as Tornado diagram



- Results were sensitive to the time horizon and the distribution that adjusts the progression-free data (log-logistic distribution) (Figure 2).

Figure 3. Cost-utility analysis plane: cost per QALY gained with idelalisib in combination with rituximab (I+R) versus rituximab in monotherapy (R)



- In the probabilistic sensitivity analysis, idelalisib in combination with rituximab is cost-effective in 78% of iterations, using the referenced threshold of €45,000 per QALY gained in Spain¹⁴ (Figure 3).

Conclusions

- In previously treated adult patients with relapsed or refractory chronic lymphocytic leukaemia (who have received at least one prior therapy), idelalisib in combination with rituximab in comparison with rituximab in monotherapy:
 - Increases survival and survival adjusted by quality of life.
 - Is a cost-effective treatment, from the perspective of the Spanish National Health System.
- To date, idelalisib in combination with rituximab is the only oral targeted therapy showing its efficiency, versus rituximab in monotherapy, in Spain.



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