

Cost-effectiveness of gemtuzumab ozogamicin in combination with standard of care chemotherapy for first-line treatment of patients with CD33-positive acute myeloid leukemia in Spain

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Background

- Acute Myeloid Leukemia (AML), with a yearly incidence estimated in 3.7 cases per 100,000 individuals in Europe¹ is characterized by an uncontrolled clonal expansion of hematopoietic progenitor cells. Age adjusted 5-year survival for AML patients in Spain is estimated to be around 20%².
- Based on phase III ALFA 0701 (NCT00927498) trial³, the European Medicines Agency approved gemtuzumab ozogamicin (GO; Mylotarg[®]) – an anti-CD33 antibody-drug conjugate – in combination with standard of care (SOC) chemotherapy (daunorubicin-cytarabine) for the treatment of ≥15 years old newly diagnosed patients with de novo CD33+ AML, excluding acute promyelocytic leukaemia (APL)⁴.

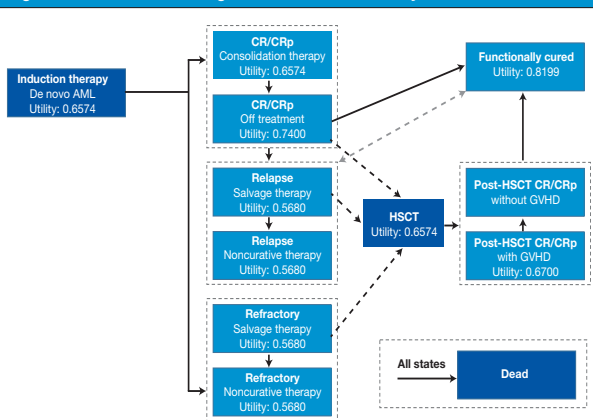
Objective

- To assess the cost-effectiveness of GO+SOC vs SOC alone for the treatment of de novo AML patients in Spain.

Methods

- A cohort state-transition model, with 12 health states (Figure 1), was used to estimate in monthly cycles the lifetime accumulated cost and benefits in terms of life years gained (LYG) and quality-adjusted-life-years (QALYs) in a hypothetical cohort of AML patients with favorable (3.30%), intermediate (66.40%) and unknown (9.23%) cytogenetic profiles⁵.

Figure 1. Model structure diagram and health state utility values



AML, acute myeloid leukemia; CR, complete remission; CRp, complete remission with incomplete platelet recovery; GVHD, graft versus host disease; HSCT, hematopoietic stem-cell transplant

Methods

- Patient profile was defined based on characteristics of the patients included in ALFA 0701 trial³.
- Patients were randomized to receive SOC+GO during induction (GO+SOC arm) or SOC alone (SOC arm). Patients in remission following induction therapy received up to 2 courses of consolidation therapy with SOC alone or with GO, according to their initial randomization.
- Therapeutic regimens were defined based on local practice. For SOC chemotherapy, the combination most used in Spain (idarubicin and cytarabine) was assumed.
- Induction therapy: course 1, GO 3 mg/m²/day on D1, D4, D7 + SOC vs SOC; course 2, if necessary, GO should not be included. Consolidation therapy: courses 1 and 2, GO 3 mg/m²/day on D1 + SOC vs SOC.
- Model transitions were derived from patient-level outcomes from response rates, relapse-free survival and overall survival, adverse events (AEs) and hematopoietic stem-cell transplants (HSCT) from the modified intent-to-treat population of the ALFA-0701 trial³.
- QALYs were estimated by applying utility values, taken from the literature⁶⁻⁸ (Figure 1). Utility decrements⁵ associated with AEs were also considered.
- The Spanish National Health System perspective was used to estimate total costs (€, 2019 cost value year): drug-acquisition costs (ex-factory price⁹ with mandatory deduction¹⁰), HSCT cost, disease cost/health state, AE management costs and end-of-life costs. Unit costs derived from local cost databases¹¹.
- All parameters were validated and agreed by an expert panel of 5 hematologists.
- A 3% annual discount rate was applied for cost and health outcomes¹².
- Probabilistic sensitivity analyses (PSA) were performed.

Results

- In the base-case analysis, higher costs per patient (€183,141 vs €157,676) and greater QALYs (5,70 vs 4,62) were obtained with GO+SOC vs SOC. The incremental cost-utility ratio (ICUR) was €23,539/QALY gained for GO+SOC vs SOC (Table 2).

Table 2. Base case results

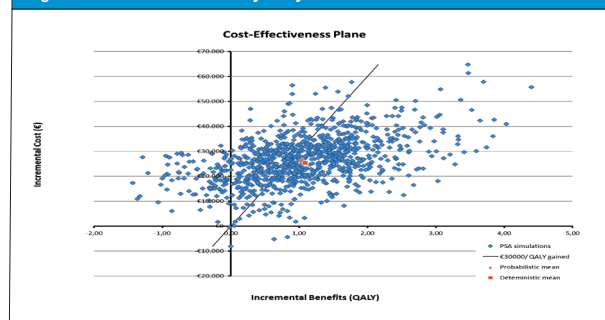
Accumulated results per patient	GO+SOC	SOC
LYG / QALYs	7.81 / 5.70	6.37 / 4.62
Total costs	€183,141	€157,676
Induction health state cost		
Induction course 1	€51,028	€29,578
Induction course 2	€4,467	€4,406
CR/CRp health state cost		
Consolidation course 1	€22,079	€16,444
Consolidation course 2	€19,136	€15,192
Off treatment	€21,240	€13,657
Relapse health state cost		
Salvage therapy	€6,016	€8,879
Non-curative therapy	€6,464	€12,530
BSC	€6,847	€10,137
Salvage therapy	€4,780	€4,767
Refractory health state cost		
Non-curative therapy	€5,640	€5,640
BSC	€4,474	€4,474
HSCT health state cost	€17,555	€22,873
CR/CRp with GVHD health state cost	6651	6848
AEs cost	€10,765	€8,251
ICER (€/LYG) / ICUR (€/QALY)	€17,734/LYG / €23,539/QALY	

AEs, adverse events; BSC, best supportive care; CR, complete remission; CRp, complete remission with incomplete platelet recovery; GO, Gemtuzumab ozogamicin; GVHD, graft versus host disease; HSCT, hematopoietic stem-cell transplant; ICER, incremental cost-effectiveness ratio; ICUR, incremental cost-utility ratio; QALY, Quality-adjusted life year; LYG, Life years gained; SOC, standard of care

Results

- The mean probabilistic ICUR resulting from the 1,000 MonteCarlo iterations of the PSA was €25,351/QALY gained (95%CI: €23,500 - €27,490) (Figure 2).

Figure 2. Probabilistic sensitivity analyses results



Limitations

- Data of the ALFA-0701 trial³ were used in the analysis assuming equivalence between SOC chemotherapy in the trial (daunorubicin + cytarabine) and the most common combination used in Spain (idarubicin + cytarabine).
- No possible comparison as no previous economic analyses for de novo AML were identified.

Conclusions

- In newly diagnosed patients with AML, the increased costs of adding GO to SOC were partially offset by improved clinical outcomes (relapse prevention and fewer HSCTs) compared with SOC alone.
- GO added to standard AML induction chemotherapy, idarubicin and cytarabine, can be considered a cost-effective option for AML patients; the ICUR obtained is below the most widely accepted willingness-to-pay threshold in Spain (€10,000-30,000/QALY)¹³.

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