Background

Acute promyelocytic leukemia (APL) is a distinct subtype of acute myeloid leukemia (AML) –

- Previously considered the most fatal leukemia in adults, the use of all-trans retinoic acid (ATRA), anthracyclines, and arsenic trioxide (ATO) revolutionized treatment and transformed APL into the most highly curable acute leukemia.

- The average age at diagnosis is 40 years (vs. 65 years for AML).

- 80% of people with APL are between 15 and 55 years of age.

- Current 1st-line treatment in Italy –
  - Induction/consolidation: ATRA plus anthracycline-based chemotherapy. Maintenance: ATO and low-dose chemotherapy
  - Can lead to a cure in more than 90% of patients

- Associated with significant toxicity

- ATO:
  - Less toxic and highly effective
  - Currently licensed for the treatment of patients with APL who are refractory to or have relapsed from previous treatment with retinoic acid and anthracycline chemotherapy

- Clinical studies and guidelines indicate that ATO is a possible 1st-line alternative option for APL.

Objective

To estimate the cost of treatment from using ATO in a 1st-line APL patient from the perspective of Italian national health system

Methods

Target Population

- APL patients with newly diagnosed, low risk (based on a white blood cell count of <10,000 APL)

Comparators

- ATRA combined with idarubicin (AIDA) regimen – the only treatment regimen currently approved in Italy for 1st-line APL

Time Horizon

- A three-year time horizon was utilized to encompass a full treatment cycle with either regimen, as well as align

- Analyses were also conducted for both one- and two-year time horizon models

Model Structure

- A three-state Markov (“state-transition”) model was developed depicting the natural history and outcomes of APL.

- All patients begin in the “stable disease” health state and stay in this state while receiving their initial therapy until they experience a disease event or die

- Patients who enter the disease event state discontinue their assigned treatment and begin 2nd-line chemotherapy in the next cycle

- Patients can move to death from either the stable disease or disease event states

- Efficacy data, including the definition of disease events, event-free survival, overall survival, and the probability of adverse events (AEs) were defined by the Lo-Coco (2013) multinational Phase III clinical trial

- A one-month cycle length was chosen as this closely approximated the length of chemotherapy phases from the clinical trial

- The schedule of pharmacy cost, direct medical costs, and AE costs, probabilities of disease events were derived from Lo-Coco (2013)

- Probabilities of death and disease event transition were estimated from previous studies in Italy.

- AIDA consolidation costs were lower in ATO patients

Sensitivity Analysis

- A one-way sensitivity analysis was performed to identify parameters with the highest impact on treatment cost

- The results were collected for a single hypothetical patient beginning the model in Year 1: efficacy parameters were calibrated using Microsoft Excel® from EFS and OS curves in Lo-Coco (2013)

- The figures 2 and 3 display the monthly survival data from the trial alongside the calculated survival curves

- The relative distributions of cost components are shown in Figure 5

- Costs were varied by +/- 25% of the base case value

- The base case Year 2 treatment arm difference (€22,800) is marked with the vertical line in the center of the figure

- For AIDA, the increase from year 1 to year 2, followed by a 2% increase from year 2 to year 3

- Monitoring cost, AIDA Induction (€10,122-€6,073)

- Monitoring cost, AIDA CONSOLIDATION (€10,122-€6,073)

- Monitoring cost, AIDA Maintenance (€10,122-€6,073)

- AIDA CONSOLIDATION costs differed by cycle; the value presented is the average

- AIDA and ATO costs are shown in the table below in the following categories: regimen costs, medical costs, AE probability, AE costs, efficacy (i.e., transition probabilities)

- The relative distributions of cost components are shown in Figure 5

Sensitivity Analysis

- A total of 64 parameters were included in the deterministic sensitivity analysis (DSA) in the following categories: regimen costs, medical costs, AE probability, AE costs, efficacy, (i.e., transition probabilities)

- Further research is needed to determine the cost-effectiveness of ATO in the 1st-line setting, especially in light of new studies supporting better clinical and quality of life outcomes for APL patients when the treatment regimen does not contain conventional cytotoxic chemotherapy

Conclusions

- ATRA pharmacodynamics were higher for ATO than AIDA; non-pharmacodynamics costs in all categories (including direct medical, ATO, and disease events) were lower for ATO patients over time

- Due to lower risks of both disease events and AEs

- Due to shorter treatment duration (8 months versus 28 months for AIDA in Year 3 for ATO patients)

- Within the non-pharmacodynamic medical care component, induction and consolidation costs were lower in ATO patients

- There were no maintenance costs (pharmacy or medical) in ATO patients

- Further research is needed to determine the cost-effectiveness of ATO in the 1st-line setting, especially in light of new studies supporting better clinical and quality of life outcomes for APL patients when the treatment regimen does not contain conventional cytotoxic chemotherapy

Reference


