Market access and its impact on decision making in Spain. An example in acute myeloid leukemia.

Authors: Sánchez, N., Asoanano, M., Dorja, J.

Economía de la Salud

Introduction

- Different stakeholders are involved in the assessment of new drugs in Spain. These are specific entities at the regional, hospital level. At the national level, the Spanish Agency for Medicines and Health Products (AEMPS) performs the therapeutic positioning reports for new drugs.
- These evaluations include parameters such as efficiency, safety, benefit/risk ratio, drug cost, and its place in the treatment algorithm.
- Drug assessments are aimed to analyze and assess the added therapeutic value of new drugs according to scientific evidence and provide recommendations to professionals for the respective use of new drugs.
- In this analysis, a drug review was conducted to determine the current point of the management of acute myeloid leukemia (AML) and the benefit of new therapeutic interventions in elderly patients.

Materials and Methods

- A database has provided an overview of the evaluation of new medicines in Spain. This database summarizes the outcome measures in terms of efficacy, adverse events, and economic parameters of these drugs in order to determine their therapeutic positioning given a clinical indication.
- This database also includes recommendations on the use of these drugs and evaluates the current treatment algorithms according to clinical guidelines and protocols.
- In the example of drug review performed for AML, one clinical guideline was reviewed in order to determine the pharmacological treatment of AML and the current treatment algorithms of disease.
- To draw conclusions on the use of drugs for AML, all drug assessments and therapeutic positioning reports published in Spain were identified. These correspond to 1 therapeutic positioning report from the AEMPS and 8 reviews at the regional and hospital level (Table 1).

Table 1. List of drug assessment reports on AML

<table>
<thead>
<tr>
<th>Name of the drug</th>
<th>Active substance</th>
<th>Pharmaceutical laboratory</th>
<th>Authorization date</th>
<th>Drug assessment reports</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donorcyte PMK</td>
<td>- powder concentrate for solution for infusion</td>
<td>Donorcyte</td>
<td>15/10/2012</td>
<td></td>
</tr>
<tr>
<td>Vidaza 90 mg</td>
<td>- reg. inject. concentrate for solution for infusion</td>
<td>Vidaza</td>
<td>09/06/2010</td>
<td></td>
</tr>
</tbody>
</table>

Results

- Given the high progression rate of disease in AML, therapeutic intervention is urgent in those patients normally requiring hospitalization.
- The different therapeutic alternatives are assessed individually for each patient considering age, general state of health and prognostic factors (Figure 1).
- Conventional treatment can consist of intensive chemotherapy or a less aggressive treatment for those in poor health who cannot tolerate intensive treatment, which are both supportive therapy or cytoreductive at low doses.
- Azacitidine and decitabine are new drugs that provide a low response in remission of disease, their significant improvement in hematologic response and their reduced toxicity contribute to better results in survival and quality of life.

Figure 1. Pharmacological treatments for AML according to clinical guidelines

- The feasible evaluations of drugs used in AML correspond to the hypomethylating agents: azacitidine and decitabine (Table 2).
- The hematoepoietic cytokines evaluate the efficacy of both azacitidine and decitabine in the median overall survival (OS).
- Other secondary outcomes evaluated include:
  - Progression-free survival (PFS)
  - Arrival survival-Specialists
  - Event-free survival (EFS)
  - Relapse-free survival (RFS)
  - Complete remission (CR) and CR with incomplete platelet recovery
  - Complete cytogenetic remission
  - Duration of response in patients with CR
  - Relapse post CR

- One clinical trial has evaluated decitabine vs supportive therapy in patients with AML >65 years non-candidates for standard induction chemotherapy.
- One clinical trial has evaluated azacitidine in elderly patients with newly diagnosed AML with >30% blast cells.

Table 2. Review of drugs evaluated in AML

<table>
<thead>
<tr>
<th>Drug name</th>
<th>Therapeutic positioning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donorcyte PMK</td>
<td>- Decitabine has demonstrated a significant but modest improvement in terms of OS only in a second study compared to supportive therapy/Chlorambucil.</td>
</tr>
<tr>
<td>Vidaza 90 mg</td>
<td>- Adult patients &gt;60 years not considered candidates for standard induction chemotherapy are resistant to chemotherapy.</td>
</tr>
<tr>
<td>Donorcyte PMK</td>
<td>- Adult patients with newly diagnosed de novo or secondary acute myeloid leukemia (AML) who have not received previous treatment with azacitidine and the type of AML.</td>
</tr>
<tr>
<td>Vidaza 90 mg</td>
<td>- Azacitidine has demonstrated significant differences versus a combination of conventional therapies (best supportive therapy, chemotherapy...) in a sensitivity analysis for the variable median OS.</td>
</tr>
<tr>
<td>Donorcyte PMK</td>
<td>- Azacitidine has demonstrated significant differences versus a combination of conventional therapies (best supportive therapy, chemotherapy...) in a sensitivity analysis for the variable median OS.</td>
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</tr>
<tr>
<td>Donorcyte PMK</td>
<td>- The evaluation of the hypomethylating agents, decitabine and azacitidine, has demonstrated the efficacy of these Therapies in treatment of AML.</td>
</tr>
<tr>
<td>Vidaza 90 mg</td>
<td>- Given the progression of disease and the low expectation of life for these patients, the efficacy outcomes of decitabine can be considered clinically significant.</td>
</tr>
<tr>
<td>Donorcyte PMK</td>
<td>- Regarding safety issues, decitabine has a similar safety profile than azacitidine related with myelosuppression.</td>
</tr>
<tr>
<td>Vidaza 90 mg</td>
<td>- Regarding economic issues, the cost of decitabine is superior to azacitidine.</td>
</tr>
</tbody>
</table>

Conclusions

- This database on drug reviews has demonstrated to be a robust tool to assess the efficacy and safety measures of new drugs, including recommendations on crucial aspects for future drug assessments that can optimize the market access of a new drug.

Recommendations for future drug assessments

- It would be recommended to develop more studies based on a direct comparison of decitabine vs azacitidine, which is a condition that would be considered as an option for chemotherapy of low intensity. It would allow a better positioning of the two available hypomethylating agents.
- In contrast with other studies that have evaluated the administration of decitabine during 10 days, it is estimated that this regimen provides better response and survival versus the 5 days administration according to its biological profile. It would be encouraged to corroborate this evidence, since a better regimen of administration could reduce the number of visits to hospital.
- Finally, it would be necessary to develop more studies to define the best therapy for patients with AML, in order to define chemotherapy or HSCT.

References