**BACKGROUND**

- Ph-negative B-precursor relapsed/refractory acute lymphoblastic leukaemia (R/R ALL) in adults is a rare condition. The projected incidence in Spain is 80 to 85 patients per year.
- The median age in this setting is around 34–38 years old.
- Adult patients with Ph-negative B-precursor R/R ALL have extremely poor outcomes (3-year survival rates ranging from 4% to 10%), depending on important prognostic factors such as age, number of prior therapies and duration of first remission.
- In Spain, the most commonly-used salvage therapy for R/R ALL is FLAG-IDA, which results in a high mortality, leading to an elevated risk of treatment-related mortality.
- Management of the disease and treatment side-effects requires considerable effort, but the hospital and financial burden has not been documented extensively.
- The objective of this study was to quantify the time and reimbursement associated with hospitalisations for R/R ALL salvage chemotherapy in Spain.

**METHODS**

**Patients**

- **Eligibility criteria:**
  - 18 years of age or older
  - Hospitalised for management of at least one episode of R/R ALL
  - Diagnosis of Ph-negative B-cell precursor ALL with one of the following:
    - Relapsed with first remission lasting less than 12 months
    - Relapsed after first therapy
    - Relapsed any time after HSCT
    - Refractory to primary induction or salvage therapy
  - Electronic medical record or chart available for review and data collection
  - Not enrolled in either hematopoietic- or immunosuppression-related clinical trials during the study period

- **Study Design**
  - Retrospective chart review.
  - Study period: 1998 to 2014. Data were collected from the index date until death or loss to follow-up. The index date was defined as the first time the ALL patient was recorded as refractory or relapsed in the medical records.
  - The chemotherapy period was defined as the first chemotherapy date after the index date to the date of death, loss to follow-up, last chemotherapy dose plus 30 days, or initiation of allogeneic HSCT (alloHSCT). Only patients with a record of receiving a salvage chemotherapy regimen were included in the chemotherapy period.
  - For patients who received alloHSCT after the index date, the HSCT period was defined as the time from starting alloHSCT to the earliest of death, loss to follow-up, or relapse (Figure 1).

**Outcomes**

- The primary outcome was the percentage of time hospitalized during the chemotherapy period.
- Secondary outcomes included frequency, type, duration, reasons and reimbursement of hospitalisations.

**Calculation of hospital reimbursement**

- **Reimbursement** followed the algorithm for haematology hospitalisations in the centre.
  - If alloHSCT was performed: DRG (Diagnosis-related group) 803 (€680.59) plus €692 per day beyond day 100.
  - If HSCT was not performed and chemotherapy was received the following code DRG was assigned. Additional reimbursement for chemotherapy was not added for any patients, as it was considered to be included in the reimbursement of the assigned DRG.
  - **DRG 579 (827.24)** if the overnight stay includes or is due to induction using intensive chemotherapy administration (eg, FLAG-IDA or any other intensive induction schedules).
  - **DRG 577 (612.44)** if the overnight stay includes or is due to consolidation or intensification using intensive chemotherapy.
  - **DRG 577 (612.44)** if the overnight stay is not related to intensive chemotherapy administration but associated with a major complication (eg, sepsis, pneumonia, gastrointestinal or respiratory failure).
  - **DRG 579 (64.47)** if the overnight stay is not related to intensive chemotherapy administration or associated with a major complication (eg, administration of chemotherapy and discharge when the schedule is over or hospitalisation due to any non-major complication).
  - The National DRG list provides the amount reimbursed to the hospital and the average length of stay for each DRG code. Among some hospitalisations, the length of stay was longer than the mean observed in the DRG list, those cases were assumed to be associated with major complications and the DRG 577 was used.

**RESULTS**

**Patients**

- Thirty-two patients were eligible for the study and 31 patients received intensive salvage chemotherapy and were included in the chemotherapy period. One patient was hospitalised but did not receive salvage chemotherapy.
- **Patient characteristics:** The median age was 41 years and 34% were male.
- **Disease status at index date:** Half were ≤ 50% first remission duration ≤ 12 months, 11 (34%) relapsed after HSCT, 4 (13%) were relapsed after salvage chemotherapy (Table 1).

**Outcomes during the chemotherapy period**

- **The median duration of the chemotherapy period was 68 days (range: 34–72 days).**
- **During the chemotherapy period there were 42 inpatient hospitalisations with a mean duration of 26 days (Table 2).** Almost all reimbursements were attributable to inpatient stays (Figure 2).
- **Primary outcome:** patients spent a mean of 71% (95% CI: 61%–82%) of the chemotherapy period in hospital.
- **Mean reimbursement** was €28,417 in total per patient.

**Outcomes from the index date to death (excluding HSCT)**

- From the index date to death (excluding HSCT) there were 80 inpatient hospitalisations with a mean duration of 24 days per hospitalisation (Table 3). Almost all reimbursements were attributable to inpatient stays (Figure 5).
- **Mean reimbursement** was €43,753 in total per patient.

**Outcomes during the chemotherapy period**

<table>
<thead>
<tr>
<th>Table 1. Patient Characteristics and Treatment Received During Salvage</th>
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</thead>
<tbody>
<tr>
<td>Age at index date, years</td>
</tr>
<tr>
<td>Male, n (%)</td>
</tr>
<tr>
<td>Disease stage, n (%)</td>
</tr>
<tr>
<td>Relapsed with first remission ≤ 12 months</td>
</tr>
<tr>
<td>Relapsed after first salvage (with first remission &gt; 12 months)</td>
</tr>
<tr>
<td>Relapsed any time after HSCT</td>
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<tr>
<td>Refractory to primary induction or salvage therapy</td>
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<tr>
<td>Status at the time of follow-up, n (%)</td>
</tr>
<tr>
<td>Dead</td>
</tr>
<tr>
<td>Alive (not to follow-up)</td>
</tr>
<tr>
<td>Treatment received during salvage, n (%)</td>
</tr>
<tr>
<td>Chemotherapy</td>
</tr>
<tr>
<td>Stem cell transplantation</td>
</tr>
</tbody>
</table>

**Outcomes related to the transplant**

- Eight patients received an alloHSCT (Table 4). Mean length of hospital stay was longer (33 vs 24 days) and reimbursement per inpatient hospitalisation was higher (€38,762 vs €18,989) for transplant in chemotherapy-alloHSCT was associated with mean total reimbursement of €95,518 per patient, with almost all reimbursements attributable to inpatient stays (Figure 5).

**Table 4. Outcomes During the HSCT Period**

<table>
<thead>
<tr>
<th>Table 4. Outcomes During the HSCT Period</th>
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</thead>
<tbody>
<tr>
<td>Per hospitalisation</td>
</tr>
<tr>
<td>Mean (SD) length of stay – days</td>
</tr>
<tr>
<td>Mean (SD) reimbursement (€)</td>
</tr>
<tr>
<td>Per patient</td>
</tr>
<tr>
<td>Number of patients</td>
</tr>
<tr>
<td>Mean (SD) number of stays</td>
</tr>
<tr>
<td>Mean (SD) length of stay – days</td>
</tr>
<tr>
<td>Mean (SD) reimbursement (€)</td>
</tr>
</tbody>
</table>

**DISCLOSURES**

- The study was sponsored by Amgen. Medical writing support was provided by James O’Toole, an employee of Amgen.

**REFERENCES**


**LIMITATIONS**

- Single-centre study.
- Small numbers of patients, although this was expected given the rarity of the patient population.