Time and Cost of Hospitalisation for Salvage Therapy Among Adults With Philadelphia (Ph)-Negative B-Cell Relapsed/Refractory (R/R) Acute Lymphoblastic Leukaemia (ALL) in Spain

PCN98

B Boluda,[1] R Rodríguez-Veiga,[1] D Martínez-Cuadrón,[1] I Lorenzo,[1] G Sanz,[1] J Sanz,[1] A Regadera,[1] A Sempere,[1] L Senent,[1] J Cervera,[1] J Reitan,[2] S Gea,[3] M Sanz,[1] P Montesinos[1]

[1]Hematology Department, Hospital Universitario La Fe Valencia, Spain; [2]RJM Group, Crown Point, IN, USA; [3]Amgen Health Economics, Barcelona, Spain

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.[1]
- The median age in this setting is around 34–39 years old.[2,3]
- Adult patients with Ph-negative B-precursor R/R ALL have extremely poor outcomes (3-year survival rates ranging from 4% to 11%), depending on important prognostic factors such as age, number of prior therapies and duration of first remission.[2]
- In Spain, the most commonly-used salvage therapy for R/R ALL is FLAG-IDA, which results in a high myelotoxicity, leading to an elevated risk of treatment-related mortality.[4-6]
- 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

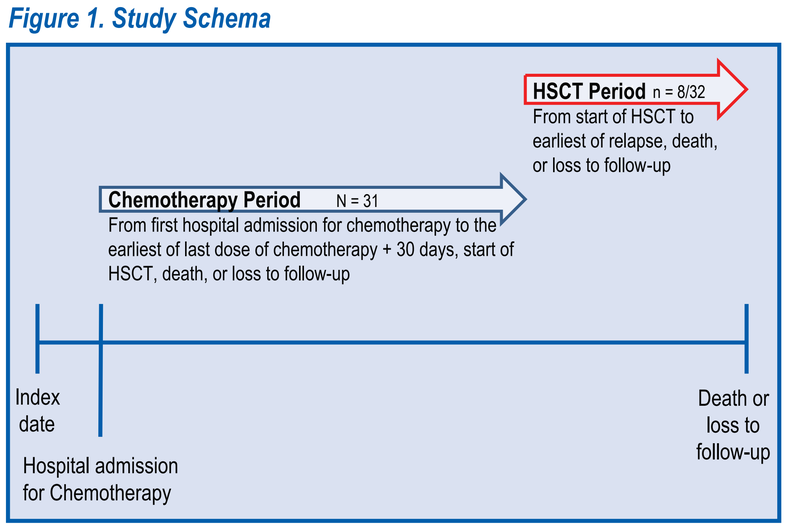
Patients

- 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 salvage 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 blinatumomab- or inotuzumab ozogamicin-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 earliest 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).

Figure 1. Study Schema



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 (€60,599) plus €692 per day beyond 40 days.[7]
- If HSCT was not performed and chemotherapy was received the following DRG code was assigned.[8] 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 576 (€27,274) 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 (€12,444) if the overnight stay includes or is due to consolidation or intensification using intensive chemotherapy.
  - ✓ DRG 577 (€12,444) if the overnight stay is not related to intensive chemotherapy administration but associated with a major complication (eg, sepsis, pneumonia, parenteral nutrition or respiratory failure).
  - ✓ DRG 876 (€4,475) 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 within 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 (n = 16, 50%) had first remission duration ≤ 12 months, 11 (34%) relapsed after HSCT, 4 (13%) were refractory to salvage chemotherapy and 1 (3%) relapsed after first salvage (Table 1).

Table 1. Patient Characteristics and Treatment Received During Salvage

	N = 32
Age at index date, years	
Median (range)	41 (30–58)
Mean (SD)	49 (18)
Female, n (%)	21 (66)
Disease stage, n (%)	
Relapsed with first remission ≤ 12 months	16 (50)
Relapsed after first salvage (with first remission > 12 months)	1 (3)
Relapsed any time after HSCT	11 (34)
Refractory to primary induction or salvage therapy	4 (13)
Status at the end of follow-up, n (%)	
Dead	28 (88)
Alive (lost to follow-up)	4 (13)
Treatment received during salvage, n (%)	
Chemotherapy	31 (97)
Stem cell transplantation	8 (25)

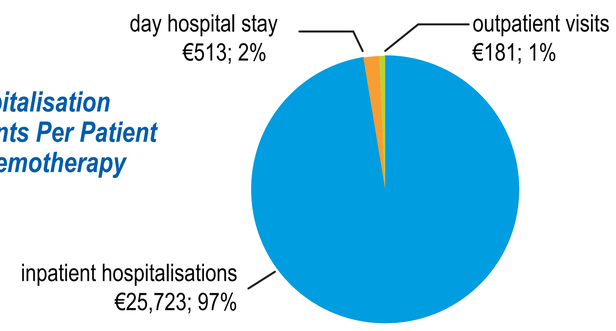
Outcomes during the chemotherapy period

- 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 the hospital.
- Mean reimbursement was €26,417 in total per patient.

Table 2. Relapsed/Refractory Ph- B-cell Precursor ALL Hospitalizations

	Inpatient hospitalisations	Day hospital stay	Outpatient visits
Per hospitalisation			
Number of hospitalisations	42	23	52
Mean (SD) length of stay – days	26 (18)	1 (0)	1 (0)
Mean (SD) reimbursement (€)	18,986 (9,272)	691 (0)	108 (0)
Per patient			
Number of patients	31	31	31
Mean (SD) number of stays	1.4 (1.0)	0.7 (1.9)	1.7 (3.0)
Mean (SD) length of stay – days	36 (29)		-
Mean (SD) reimbursement (€)	25,723 (16,957)	513 (1,324)	181 (329)

Figure 2. Hospitalisation Reimbursements Per Patient During the Chemotherapy Period



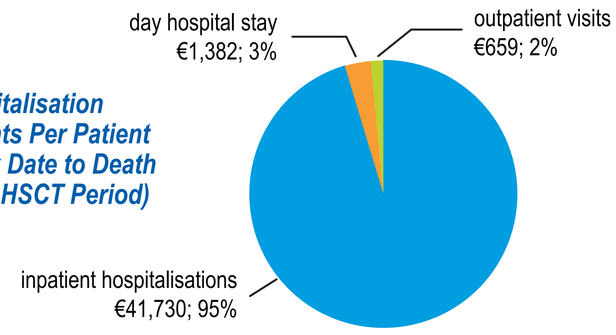
Outcomes from the index date to death (excluding HSCT)

- 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 3).
- Mean reimbursement was €43,753 in total per patient.

Table 3. Outcomes During the Period From Index Date to Death (Excluding HSCT)

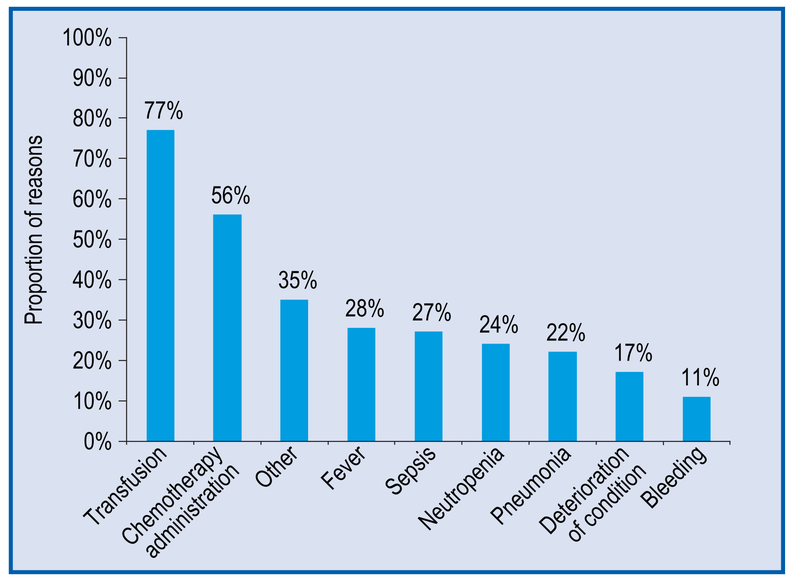
	Inpatient hospitalisations	Day hospital stay	Outpatient visits
Per hospitalisation			
Number of hospitalisations	80	63	196
Mean (SD) length of stay – days	24 (19)	1 (0)	1 (0)
Mean (SD) reimbursement (€)	16,692 (9 473)	691 (0)	108 (0)
Per patient			
Number of patients	2	32	32
Mean (SD) number of stays	2.5 (1.6)	2.0 (3.1)	6.1 (7.5)
Mean (SD) length of stay – days	59 (37)	-	-
Mean (SD) reimbursement (€)	41,730 (21 282)	1,361 (2 133)	662 (815)

Figure 3. Hospitalisation Reimbursements Per Patient From the Index Date to Death (Excluding the HSCT Period)



- The most common reasons for hospitalisation were: transfusion; to receive chemotherapy; fever, neutropenia, and sepsis (Figure 4).

Figure 4. Reasons for Hospitalisation After the Index Date (Reasons With a frequency of ≥ 10%)



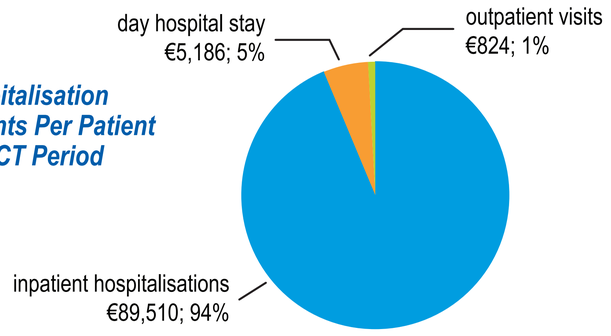
Outcomes related to transplant

- 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 (€39 782 vs €18,986) for transplant than chemotherapy. AlloHSCT was associated with mean total reimbursement of €95,519 per patient, with almost all reimbursements attributable to inpatient stays (Figure 5).

Table 4. Outcomes During the HSCT Period

	Inpatient hospitalisations	Day hospital stay	Outpatient visits
Per hospitalisation			
Number of hospitalisations	18	60	61
Mean (SD) length of stay – days	33 (30)	1 (0)	1 (0)
Mean (SD) reimbursement (€)	39,782 (34,228)	691 (0)	108 (0)
Per patient			
Number of patients	8	8	8
Mean (SD) number of stays	2.3 (1.4)	7.5 (11.1)	7.6 (7.2)
Mean (SD) length of stay – days	73 (34)	-	-
Mean (SD) reimbursement (€)	89,510 (21,379)	5,186 (7,646)	824 (781)

Figure 5. Hospitalisation Reimbursements Per Patient During the HSCT Period



LIMITATIONS

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

CONCLUSIONS

- Salvage chemotherapy for adult patients with Ph-negative B-cell R/R ALL is associated with extensive hospitalisation and high economic cost in Spain.

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DISCLOSURES

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