Retrospective Chart Review of Hospitalisations During Chemotherapy for Adult Patients With Ph-Negative B-Precursor Relapsed or Refractory (R/R) Acute Lymphoblastic Leukaemia (All) in Italy

L Pagano[1], M Oberti[2], B Esposito[3], J Reitan[4], A Barlev[5], B Barber[5], F Ferrara[6]

[1]Università Cattolica del Sacro Cuore, Rome, Italy; [2]Spedali Civili, Brescia, Italy; [3]Amgen Health Economics, Italy; [4]RJM Group, Crown Point, IN, USA; [5]Amgen Global Health Economics, Thousand Oaks, CA, USA; [6]Cardarelli Hospital, Napoli, Italy

BACKGROUND

- Adults with Philadelphia chromosome-negative (Ph-) relapsed or refractory (R/R) B-precursor acute lymphoblastic leukemia (ALL) have an extremely poor prognosis.
- The incidence of adult R/R Ph (-) B-precursor ALL is 0.2 per 100,000 person-years, corresponding to 120 to 135 new patients per year in Italy [Katz 2015].
- There is no standard of care regimen for these patients. A variety of salvage chemotherapy regimens have been reported in Italian studies [Camera 2004, Specchia 2005, De Astis 2014], but long-term survival rates remain low and are predominantly dependent on receipt of a hematopoietic stem cell transplant (HSCT).
- Severe toxicity is nearly universal among patients treated with current salvage chemotherapies [Hummel et al, 2015], and treatment-related mortality ranges from 11% to 23% [Kantarjian et al, 2010; O'Brien et al, 2008]. Most patients require extensive inpatient management, but information is lacking on the length of time patients spend in hospital and the associated costs.

OBJECTIVE

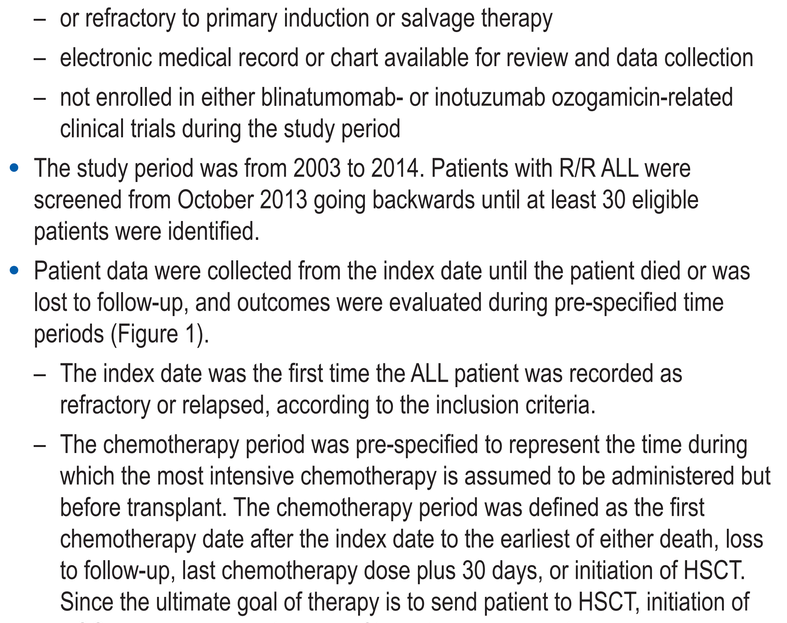
- To quantify hospitalisations and reimbursements among adults with Ph- R/R B-precursor ALL treated with current salvage chemotherapies in Italy.

METHODS

Study design and patient selection

- Retrospective chart review of adults with Ph- R/R B-precursor ALL treated in Italian hospitals.
- 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-precursor ALL
  - relapsed with first remission lasting less than 12 months
  - relapsed after first salvage therapy
  - relapsed any time after haematopoietic stem cell transplant HSCT
  - or 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
- The study period was from 2003 to 2014. Patients with R/R ALL were screened from October 2013 going backwards until at least 30 eligible patients were identified.
- Patient data were collected from the index date until the patient died or was lost to follow-up, and outcomes were evaluated during pre-specified time periods (Figure 1).
  - The index date was the first time the ALL patient was recorded as refractory or relapsed, according to the inclusion criteria.
  - The chemotherapy period was pre-specified to represent the time during which the most intensive chemotherapy is assumed to be administered but before transplant. The chemotherapy period was defined as the first chemotherapy date after the index date to the earliest of either death, loss to follow-up, last chemotherapy dose plus 30 days, or initiation of HSCT. Since the ultimate goal of therapy is to send patient to HSCT, initiation of HSCT was chosen as the end of the intensive chemotherapy period.
  - For patients who received HSCT after the index date, the HSCT period was defined as the time from starting HSCT to the earliest of death, loss to follow-up, or relapse of ALL.

Figure 1. Study Schema



METHODS (Continued)

Outcomes of interest

- The primary outcome is the proportion of time spent in the hospital during the chemotherapy period.
- Secondary outcomes include the number and types of hospital admissions, length of hospital stay(s), reasons for hospitalisation, and reimbursement of hospitalisations

Statistical analysis

- The proportion of time spent in the hospital during the chemotherapy period was calculated as the number of days in hospital divided by the total number of days during the chemotherapy period.
- Other outcomes related to the number of hospital admissions and length of hospital stay were calculated for the chemotherapy period. The same analyses were calculated from the index date until death or loss to follow-up, including and excluding the HSCT Period.
- Reimbursements were derived from the most recent national update of the Italian Diagnosis-Related Group (DRG) tariffs issued in 2014 (Conferenza Permanente per i Rapporti tra lo Stato le Regioni e le Province Autonome di Trento e Bolzano, 2014). Inpatient stays and outpatient visits were assigned DRG reimbursements from 3 medical DRG codes all pertaining to the MDC 17 (Myeloproliferative disorders or poorly differentiated neoplasms):
  - DRG 473 - Acute leukaemia without major surgical procedures, patient aged > 17 years.
  - DRG 481 - Allogeneic bone marrow transplant.DRG 492 - Chemotherapy following secondary diagnosis of acute leukaemia or high dose chemotherapy.

RESULTS

Study population

- Thirty patients from 4 sites met the eligibility criteria and were included in the analyses.

Table 1. Patient Characteristics and Treatment Received During Salvage

	N = 30
Age (range) at index date, years	
Mean (SD)	46 (18)
Male, n (%)	17 (59)
Disease status at index date, n (%)	
Relapsed with first remission ≤ 12 months	17 (57)
Relapsed after HSCT	5 (17)
Refractory to primary induction or salvage therapy	8 (27)
Status at the end of follow-up, n (%)	
Dead	27 (90)
Alive (lost to follow-up)	3 (10)
Treatment received during salvage	
Chemotherapy	26 (87)
HSCT	8 (27)

Hospitalisations and costs during the chemotherapy period

- Primary endpoint: During the chemotherapy period patients spent 58% (95% CI: 47%–70%) of their time in the hospital.
- The mean (SD) number of inpatient hospitalisations per patient was 1.9 (1.4), with a mean (SD) length of stay of 20 days (15) per hospitalisation (Table 2).
- The calculated total hospitalisation cost per patient during the chemotherapy period was €47,779 (Table 3).

Total hospitalisations and costs from R/R ALL diagnosis to death

- Most patients were hospitalised for more than one reason during each inpatient admission. The most common reasons were chemotherapy administration (68%) and transfusion (43%) (Figure 2).
- Excluding hospital visits for HSCT, there was a mean (SD) of 2.3 (1.5) inpatient hospitalisations per patient and the mean (SD) length of stay was 18 (18) days (Table 2). The calculated total hospitalisation cost per patient excluding the HSCT period was €59,563 (Table 3).
- Hospitalisations and costs were evaluated during the HSCT period for the 8 patients who received a transplant after the index date. There was a mean (SD) of 1.3 (0.7) inpatient hospitalisations per patient with a mean (SD) length of stay of 40 (25) days. The calculated total cost per patient in the HSCT Period was €99,901.

RESULTS (Continued)

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

	Chemotherapy period N = 26 patients	Index date to death excluding the HSCT period N = 30 patients	HSCT period only N = 8 patients
Hospital admissions data			
Mean length of stay in days per hospitalisation (SD)	20 (15)	18 (16)	40 (25)
Patient data			
Mean (SD) number of hospital admissions per patient			
Inpatient	1.9 (1.4)	2.3 (1.5)	1.3 (0.7)
Day hospital stay	2.7 (5.2)	4.2 (6.7)	4.3 (8.0)
Outpatient visit	1.3 (2.7)	3.5 (6.6)	0 (0)

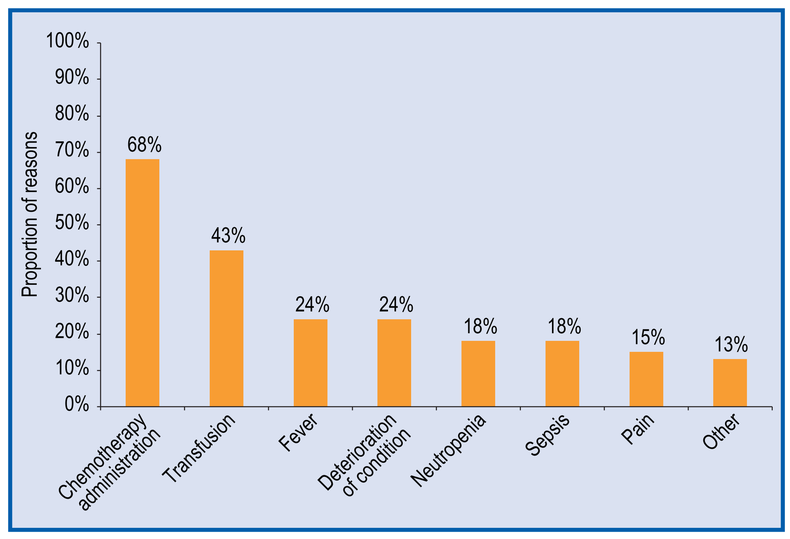
Table 3. Relapsed/Refractory Ph- B-cell Precursor ALL Hospitalization Reimbursement

	Chemotherapy period N = 26 patients	Index date to death excluding the HSCT period N = 30 patients	HSCT period only N = 8 patients
Mean (SD) reimbursement per hospital admission (€)			
Inpatient	23,568 (3,454)	23,386 (3,427)	74,366 (37,858)
Day hospital stay	750 (0)	750 (0)	750 (0)
Outpatient visit	750 (0)	750 (0)	-
Total reimbursement per patient (€)*	47,779	59,563	99,901

*calculated by multiplying the cost per admission by mean number of admissions per patient for each type of hospitalisation.

Figure 2. Reasons for Hospital Admission After the Index Date.

- Reasons with a frequency of ≥ 10% are presented. More than one reason is possible for each admission.



CONCLUSIONS

- In Italy, adults with R/R Ph (-) B-precursor ALL have repeated and prolonged hospitalizations during salvage chemotherapy. Over half of the chemotherapy period is spent in hospital, and this time is associated with extremely high costs.
- This study highlights the hospital and economic burden of treating Ph-negative B-cell precursor R/R ALL using salvage chemotherapies.

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