Healthcare Burden and Economic Cost of Hospitalisation During Chemotherapy for Adult Patients With Ph-Negative B-Precursor Relapsed or Refractory Acute Lymphoblastic Leukaemia in France: A Retrospective Chart Review

H Dombret[1], X Thomas[2], P Chevallier[3], E Nivot[4], J Reitan[5], B Barber[6], A Barlev[6], M Mohty[7,8,9]

[1]Hôpital Saint-Louis, Paris, University Paris Diderot, France; [2]Hôpital Lyon-Sud, Lyon, France; [3]CHU de Nantes, Nantes, France; [4]Amgen Health Economics, Paris, France; [5]RJM Group, Crown Point, IN, USA; [6]Amgen Global Health Economics, Thousand Oaks, CA, USA; [7]Hôpital Saint-Antoine, Paris, France; [8]Université Pierre & Marie Curie, Paris, France; [9]INSERM U938, Paris, France

BACKGROUND

- Adults with Philadelphia chromosome-negative (Ph-) relapsed or refractory (R/R) B-precursor acute lymphoblastic leukemia (ALL) have an extremely poor prognosis.
- There is no standard of care regimen for these patients. French studies report use of a variety of regimens but outcomes remain poor, especially in those with short response duration and/or those unable to receive allogeneic hematopoietic stem cell transplant (HSCT) [Tavernier 2007, Desjonqueres 2014].
- The incidence of adult R/R Ph (-) B-precursor ALL Ph (-) B-precursor ALL is 0.2 per 100,000 person-years, corresponding to 120 to 130 new patients per year in France [Katz 2015].
- 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]. Therefore most patients require extensive inpatient management, which contributes to high healthcare costs.

OBJECTIVE

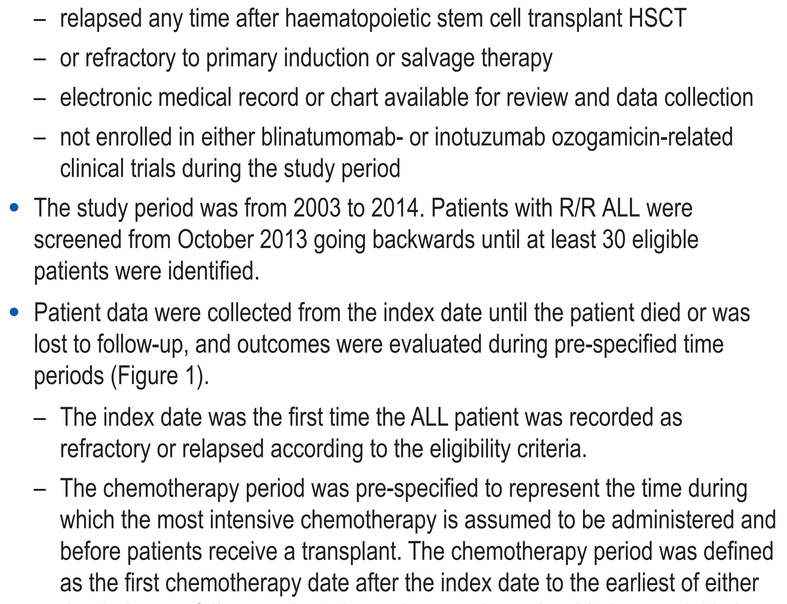
- To quantify hospitalisations and costs among adults with Ph- R/R B-precursor ALL treated with current salvage chemotherapies in France.

METHODS

Study design and patient selection

- Retrospective chart review of adults with Ph- R/R B-precursor ALL treated in French 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 eligibility criteria.
  - The chemotherapy period was pre-specified to represent the time during which the most intensive chemotherapy is assumed to be administered and before patients receive a 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.
  - 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



Outcomes of interest

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

METHODS (Continued)

Statistical analysis

- The proportion of time spent in the hospital during the chemotherapy period was calculated as the number of days in the 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.
- Calculation of reimbursement per hospitalisation:
  - A retrospective analysis of the PMSI (Programme de Médicalisation des Systèmes d'Information) database was conducted to determine the reimbursement of hospital stays for adult ALL during 2013. Reimbursement amounts increase as the severity level of the hospitalisation increases (levels range from 1 – 4)
  - The relative proportion of hospital stays for ALL in 2013 was multiplied by the respective mean amount reimbursed in 2013 for each severity of hospital stay. The weighted values for each severity level were added together and used as the estimated reimbursement per hospitalization.

RESULTS

Study population

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

Table 1. Patient Characteristics and Treatment Received During Salvage

	N = 33
Age (range) at index date, years	
Mean (SD)	49 (18)
Male, n (%)	20 (61)
Disease status at index date, n (%)	
Relapsed with first remission ≤ 12 months	17 (52)
Relapsed after first salvage	5 (15)
Relapsed after HSCT	7 (21)
Refractory to primary induction or salvage therapy	4 (12)
Status at the end of follow-up, n (%)	
Dead	29 (88)
Alive (lost to follow-up)	4 (12)
Treatment received during salvage, n (%)	
Chemotherapy	33 (100)
HSCT	7 (21)

Hospitalisations and costs during the chemotherapy period

- Primary Outcome: During the chemotherapy period, patients spent 46% (95% CI: 34%-57%) of their time in the hospital.
- The mean (SD) number of inpatient hospitalisations per patient was 2.2 (1.5), with a mean (SD) length of stay of 16.8 days (14.8) per hospitalization (Table 2).
- The calculated total hospitalisation cost per patient during the chemotherapy period was €68,344 (Table 3).
- Most patients were hospitalised for more than one reason during each admission. The most common reason was to administer chemotherapy and manage toxicities, cited in 76% of hospital admissions (Figure 2).

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

- Excluding hospital visits for HSCT, there was a mean (SD) of 3.7 (3.1) inpatient hospitalisations per patient and the mean (SD) length of stay was 13.7 (13.5) days (Table 2). The calculated total hospitalisation cost per patient excluding the HSCT period was €108,873 (Table 3).
- Hospitalisations and costs were evaluated during the HSCT period for the 7 patients who received a transplant after the index date. There was a mean (SD) of 2.6 (2.2) inpatient hospitalisations with a mean (SD) length of stay of 33.9 (38.0) days. The calculated total cost per patient in the HSCT Period was €118,672.

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RESULTS (Continued)

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

	Chemotherapy period N = 33 patients	Index date to death excluding the HSCT period N = 33 patients	HSCT period only N = 7 patients
Hospital admissions data			
Mean length of stay in days days per hospitalisation (SD)	16.8 (14.8)	13.7 (13.5)	33.9 (38.0)
Patient data			
Mean (SD) number of hospital admissions per patient			
Inpatient	2.2 (1.5)	3.7 (3.1)	2.6 (2.2)
Day hospital stay	2.1 (3.3)	4.3 (6.3)	2.9 (6.3)
Outpatient visit	0.2 (0.5))	0.7 (1.8)	11.3 (24.3)

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

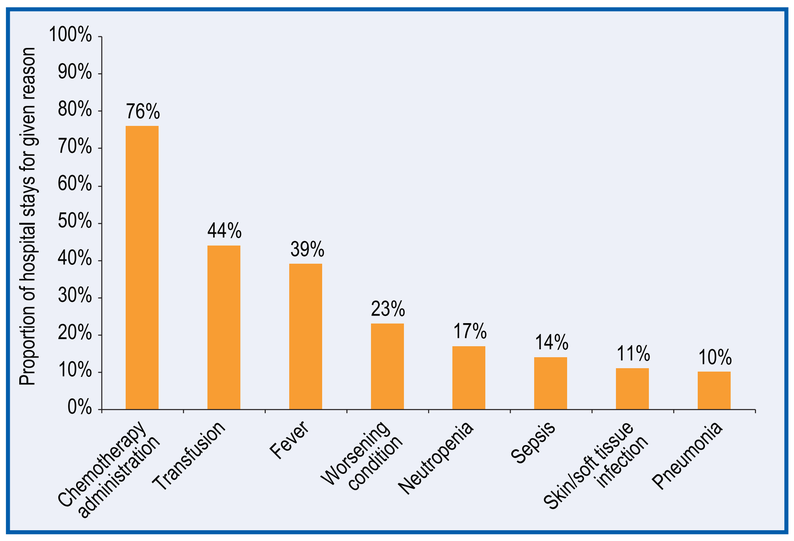
	Chemotherapy period N = 33 patients	Index date to death excluding the HSCT period N = 33 patients	HSCT period only N = 7 patients
Mean (SD) reimbursement per hospital admission (€)*			
Inpatient	31,067 (4,850)	28,832 (8,867)	43,672 (33,241)
Day hospital stay	674 (0)	674 (0)	674 (0)
Outpatient visit	394 (0)	394 (0)	394 (0)
Total reimbursement (€) per patient**	68,344	108,873	118,672

*based on a weighted average of hospitalisation costs for ALL from the 2013 French PMSI database

**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 During the Chemotherapy Period

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



LIMITATIONS

- The sample size was small, although this was expected given the rarity of the patient population.
- The median patient age was older than seen in other observational studies in patients with R/R ALL [Fielding 2007, Tavernier 2007, O'Brien 2008, Oriol 2010], which may be due to the small sample size or may reflect the particular patients referred to the sites used in this study.
- The number of outpatient visits may be underestimated if patients are seeing physicians outside of the hospital setting; however, the inpatient hospitalisations will account for the large majority of costs.

CONCLUSIONS

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

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