Hospitalisations Among Adult Patients With Ph-Negative B-Precursor Relapsed or Refractory (R/R) Acute Lymphoblastic Leukaemia (All) Receiving Chemotherapy in Germany: A Retrospective Chart Review

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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 160 to 175 new patients per year in Germany [Katz 2015].
- There is no consensus on the standard of care chemotherapy regimen for adult patients with Ph-negative B-precursor R/R ALL.
- Among the salvage chemotherapies used in Ph-negative B-precursor R/R ALL patients, severe toxicity is nearly universal [Hummel et al, 2015], with treatment-related mortality ranging from 11% to 23% [Kantarjian et al, 2010; O'Brien et al, 2008].
- Chemotherapy administrations, monitoring and toxicities requires extensive inpatient management, but information is lacking on the length of time patients spend in the hospital.

OBJECTIVE

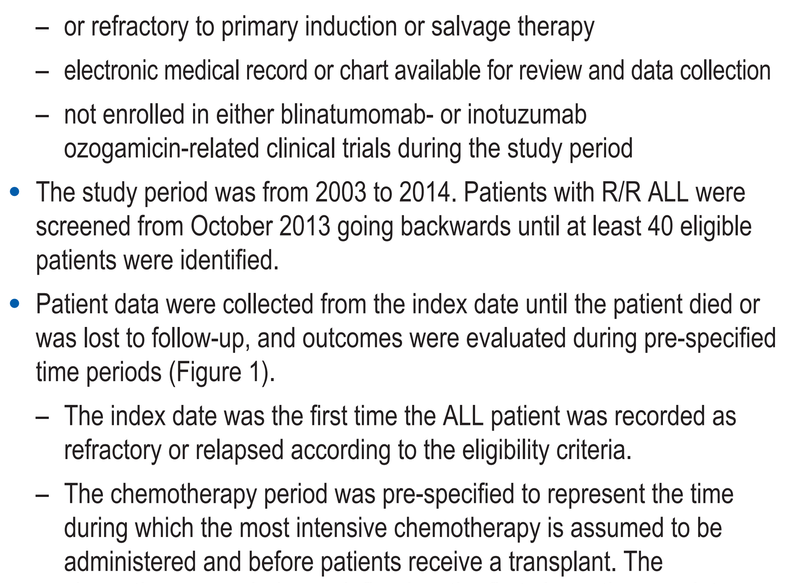
- To quantify hospitalisations and costs among adults with Ph- R/R B-precursor ALL treated with current salvage chemotherapies in Germany.

METHODS

Study design and patient selection

- Retrospective chart review of adults with Ph- R/R B-precursor ALL treated in German 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 40 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



METHODS (Continued)

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 cost of hospitalisations.

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 was conducted at one study site where data needed were available, to determine the reimbursement amount of hospital stays for adult ALL during 2013 – the most recent year from which full reimbursement data were available.
  - Patients with reimbursement data were categorized into six categories based on the DRG codes and severity level.
    - No comorbidit
    - Chemotherapy
    - Transfusion
    - Fevery
    - Infection
    - Sepsis
  - The weighted average of hospital reimbursement from six categories of hospitalization was calculated.

RESULTS

Study population

- Forty patients from 3 sites met the eligibility criteria and were included in the analyses.

Table 1. Patient Characteristics and Treatment Received During Salvage

	N = 40
Age (range) at index date, years	
Mean (SD)	41 (15)
Male, n (%)	16 (40)
Disease status at index date, n (%)	
Relapsed with first remission ≤ 12 months	17 (43)
Relapsed after HSCT	14 (35)
Refractory to primary induction or salvage therapy	9 (23)
Status at the end of follow-up, n (%)	
Dead	30 (75)
Alive	10 (25)
Treatment received during salvage, n (%)	
Chemotherapy	39 (98)
HSCT	24 (60)

Hospitalisations and costs during the chemotherapy period

- Primary Outcome: During the chemotherapy period patients spent 63% (95% CI: 52%–73%) of their time in the hospital.

- The mean (SD) number of inpatient hospitalisations per patient was 1.5 (1.2), with a mean (SD) length of stay of 25 (24) days per hospitalization (Table 2).
- The calculated total hospitalisation cost per patient during the chemotherapy period was €45,451 (Table 3).

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

- Excluding the HSCT period, there was a mean (SD) of 2.6 (4.7) inpatient hospitalisations per patient and the mean (SD) length of stay was 21 (25) days (Table 2). The calculated total hospitalisation cost per patient excluding the HSCT period was €65,322 (Table 3).
- Hospitalisations and costs were evaluated during the HSCT period for the 24 patients who received a transplant after the index date. There was a mean (SD) of 1.4 (2.2) inpatient hospitalisations with a mean (SD) length of stay of 38 (33) days. The calculated total cost per patient in the HSCT Period was €94,774.

RESULTS (Continued)

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

	Chemotherapy period N = 39 patients	Index date to death excluding the HSCT period N = 40 patients	HSCT period only N = 24 patients
Hospital admissions data			
Mean length of stay in days per hospitalisation (SD)	25 (24)	21 (25)	38 (33)
Patient data			
Mean (SD) number of hospital admissions per patient			
Inpatient	1.5 (1.2)	2.6 (4.7)	1.4 (2.2)
Day hospital stay	0.2 (0.5)	0.2 (0.5)	0.0 (0.0)
Outpatient visit	0.0 (0.2)	0.1 (0.5)	0.0 (0.0)

Inpatient = overnight stay in the hospital; day hospital stay = hospital visit that does not include an overnight stay; outpatient visit = visit to outpatient clinic.

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

	Chemotherapy period N = 39 patients	Index date to death excluding the HSCT period N = 40 patients	HSCT period only N = 24 patients
Mean (SD) reimbursement per hospital admission (2013€)			
Inpatient	30,301 (15,726)	25,124 (17,116)	67,696 (43,379)
Day hospital stay	1,267 (0)	1,267 (0)	-
Outpatient visit	1,267 (0)	1,267 (0)	-
Total reimbursement per patient, Euros*	45,451	65,322	94,774

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

DISCUSSION

- Given the rarity of the disease population (incidence rate of 0.2 per 100,000 person-years), this study captures a significant proportion of the Ph-negative B-precursor R/R ALL patient population in Germany.
- A relatively large proportion (60%) of patients received HSCT after salvage chemotherapy.
- We used reimbursement amount as a measurement of the financial burden of disease. Reimbursement data were captured from only one study site; however, we can assume the DRG-based reimbursement amounts are representative for the other sites.

CONCLUSIONS

- In Germany, adults with R/R Ph (-) B-precursor ALL have repeated and prolonged hospitalisations during chemotherapy treatment. Over 60% of the chemotherapy period is spent in hospital, and hospitalisation is associated with heavy financial burden.
- This study highlights the hospital and economc burden of treating relapse Ph- B-cell precursor R/R ALL using current salvage chemotherapies.

ACKNOWLEDGEMENTS

- This study was sponsored by Amgen. The cost analysis was provided by Florian Kron and Anna Kostenko, employees of Universitätsklinikum Köln, who received funding from Amgen. Medical writing assistance was provided by James O'Kelly, an employee of Amgen.

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