



OUTCOME OF RELAPSED OR REFRACTORY ACUTE B-LYMPHOBLASTIC LEUKEMIA PATIENTS WITH EXTRAMEDULLARY DISEASE RECEIVING INOTUZUMAB OZOGAMICIN



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Abstract

Extramedullary involvement of B-cell acute lymphoblastic leukemia (EM-ALL) is a rare occurrence, characterized by dismal outcome and the lack of a defined and shared therapeutic approach. Inotuzumab ozogamicin (InO) is a humanized anti-CD22 monoclonal antibody conjugated to calicheamicin. It was developed as a targeted therapy for B-cell malignancies (1).

The aim of this work is to evaluate outcome after InO treatment in a series of relapsed/refractory (r/r) EM-ALL patients (pts). This is a retrospective analysis on 17 CD22+ pts, treated in outpatient setting or during hospitalization, based on clinical conditions, between 2015 and 2020 within a compassionate use program (n=7) or in-label (n=10).

Objective

To evaluate outcome after Inotuzumab Ozogamicin (InO) treatment in a series of relapsed/refractory (r/r) EM-ALL patients (pts). Main Outcome Measures: Response rates (complete response, CR, or partial response, PR) after InO, and overall survival (OS).

Materials & Methods

•Inclusion:	n=17 adults with r/r ALL and EM
•CD22 positivity:	disease* confirmed in all 17 patients
•Treatment:	<u>InO between 2015 and 2020</u> N
•Compassionate use program:	7
•In-label after EMA approval:	10
Applied InO cycles	N
	≤ 2 11
	3-4 4
	5-6 2

EM response assessment: by PET-CT

*Three patients were previously treated with TKI for CML and progressed to blast crisis of B-lymphoid lineage

Results

Localization of EM disease:

	Number
Lymph nodes^	9
Bones	4
Kidney	1
Peripheral nerves	1
Pancreas and bone	1
Ovary	1

^including gastric and skin; bone and skin; lung, bone and skin; hepatic and bone; hepatic, n=1 in each of these combinations)

Patient characteristics at the time-point of r/r EM-ALL:

	Number n=17	%
Female gender	11	65
	Value	Range
Median age (years)	31	19-68
Median WBC (x10 ⁹ /l)	4.9	0.7-10.3
Platelets (x10 ⁹ /l)	94.5	11-515
Hemoglobin (g/dl)	11.4	7-14.4
Median BM blasts	60	0-100

- ECOG PS: ≤ 2 in all patients
- Cytogenetics: normal: n=1, complex: n=2, t(9;22): n=2 (available in n=5)

Response after the first InO cycle (n=17)*

	Number	%
Early death**:	1	6
CR:	7	41
PR:	7	41
Stable disease:	1	6
No assessment after 1 st cycle:	1	6

*remission assessed by PET-CT & bone marrow assessment

** death at day 11 of InO due to cerebral hemorrhage

Response after two InO cycles (n=16)***

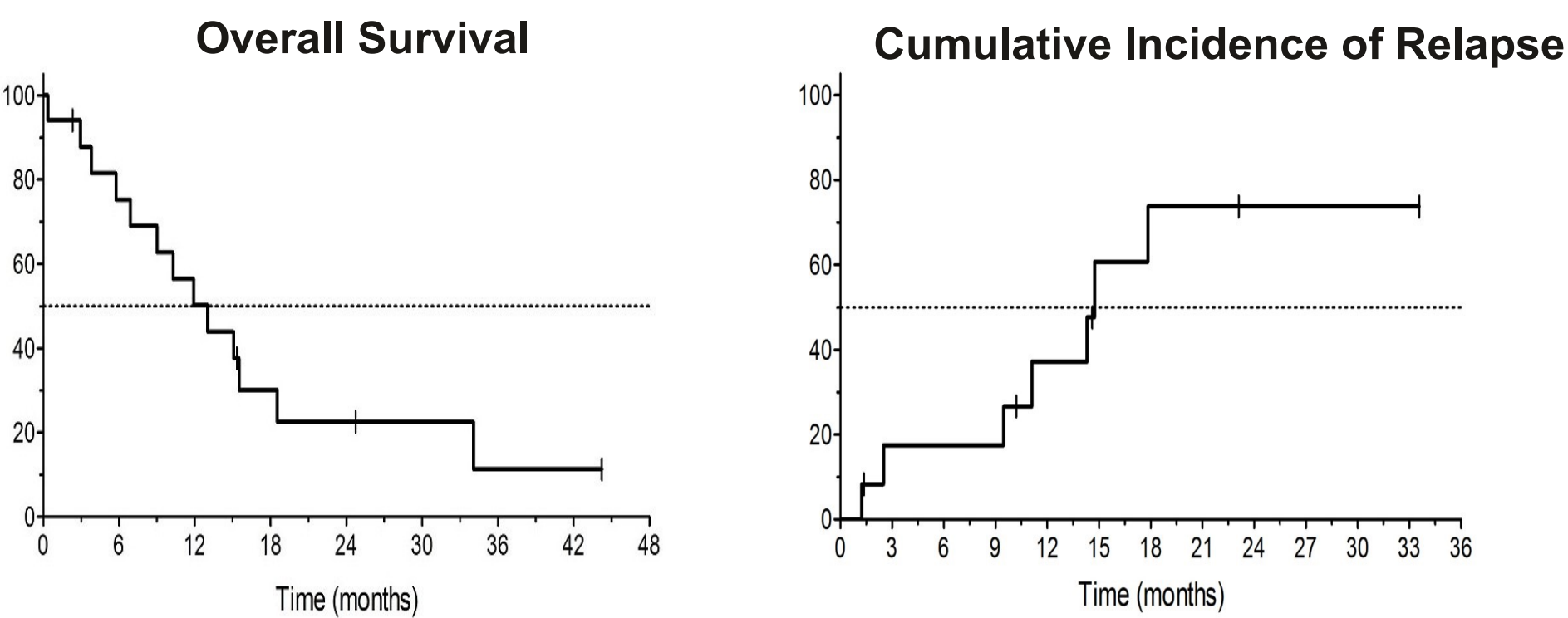
CR rate:	9	56
PR rate:	6	38

*** the patient with SD did not receive further InO treatment (6%)

Survival

Time	OS rate (%)	95%-CI
1-year	50	25-71
2-years	23	6-46

- Median follow-up: 12.1 months (range, 0.4-44.9 months)
- Median overall survival (OS): 11.9 months (95%-CI, 8-20 months)



•Age >60 years had no impact on OS (p=0.48, univariable analysis)

•Allo-SCT after InO treatment:	7
•Disease status prior to allo-SCT :	
CR	3
PR	3
progressive disease	1
•Applied InO cycles prior to allo-SCT: ≤2 cycles	4
≥4 cycles	3
•Relapse/progressive disease:	7
•Molecular relapse*:	1
•Death in remission:	4
•Ongoing CR#	4

*successfully treated with InO again

#including the patient with prior molecular relapse and InO re-exposure

•No occurrence of veno-occlusive disease / sinusoidal obstruction syndrome was reported

Summary

This outcome analysis demonstrates that treatment with InO is an effective and promising approach including successful bridge-to- transplant in this rare subgroup of patients with r/r EM-ALL and abysmal prognosis.

References

1. Kantarjian H et al, Inotuzumab Ozogamicin versus Standard Therapy for Acute Lymphoblastic Leukemia, *New England Journal of Medicine* 2016