DGI-038

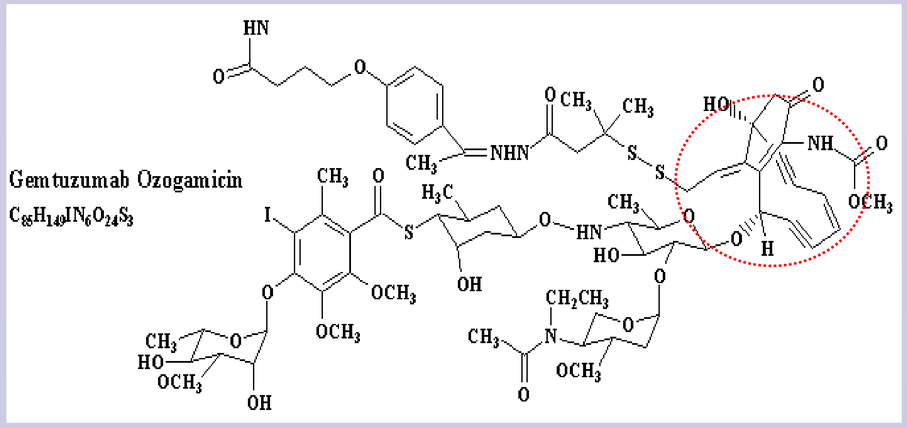
Gemtuzumab ozogamicin as salvage treatment in children with relapsed/refractory acute myeloid leukemia : a retrospective study

A.Giroud[1], K.Morand[1], G.Benoit[1], G.Leverger[2]

Pharmacy[1], Pediatric oncology/haematology[2], Armand Trousseau Hospital, Paris, France

Background

Gemtuzumab ozogamicin (GO) is a humanized anti-CD33 monoclonal antibody conjugated to calicheamicin.



- Several studies have shown its safety and efficacy in refractory/relapsed acute myeloid leukemia (AML).
- Nevertheless in july 2010 it was withdrawn from the US market further to a study failing to confirm clinical benefits
- It remains available in Europe only in the context of a Temporary Authorisation for Use, until the closure of the production site due to breaches in production practices in december 2011.

Purpose

Following this controversy, we conducted a retrospective study to evaluate its efficacy and safety in children with refractory/relapsed AML.

Materials and Methods

The study focused on 19 children treated after approval by the French agency of drug security, between october 2006 and october 2012.

Results

➢ Population caracteristics

- median age at initial diagnosis: 6.7 years (0.5-15.3)
- 11 boys and 8 girls.

➢ Types of leukemia

- 15 AML
- 2 acute biphenotypic leukemias
- 2 acute lymphoblastic leukemias

➢ Status of patients on GO onset

- Three were refractory to first line
- Two were in relapse refractory
- Ten were in first relapse
- Three in second relapse
- One in third relapse
- Seven had a previous Stem Cell Transplantation (SCT)

➢ High risk cytogenetic

- one partial monosomy 5
- two trisomy 8
- one monosomy 7
- one 11q23 rearrangement

Patients received:

- One dose of GO of 3 mg/m² with cytarabine (day 1 to 7);

OR

- 9 mg/m² fractionated dose (on days 1, 4, 7) in monotherapy or associated with cytarabine (day 1 to 7);

OR

- 4,5 mg/m² on day 6 associated with cytarabine, fludarabine and daunorubicin liposomal.

➢ Efficacy:

- Nine complete remissions (CR) were obtained (48%) in 32 days (24-60 days), leading to further curative treatment.
- The one year overall survival (OS) is 26,3% (95% CI: 9.6 – 46.8%). Five patients were alive at the cut-off date. In the others four responders CR was maintained for 6-9 months before relapse or death.
- Ten patients have not responded, they received palliative chemotherapy and died on average in 3.4 ± 1.4 months.
- The difference between responders (CR) and non responders is significant (P < 0.0001) (logrank test).

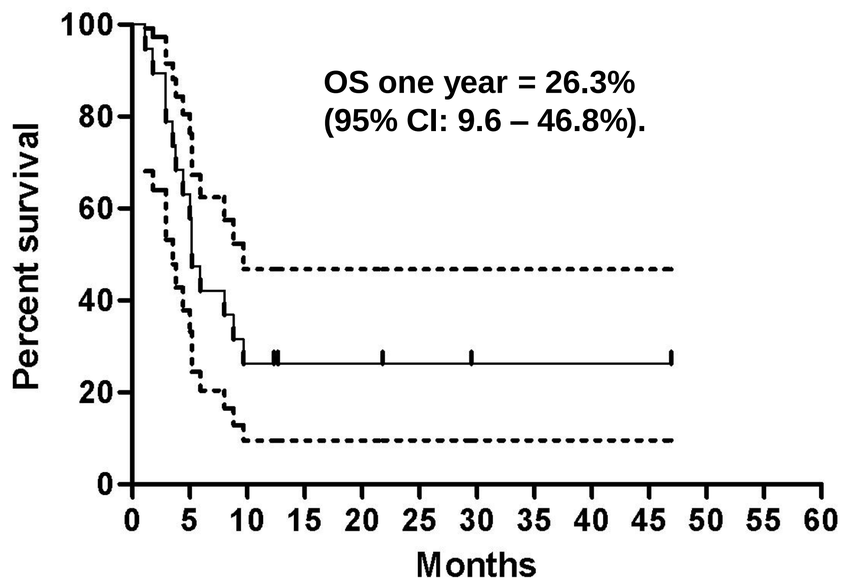


Fig 1: The Kaplan-Meier curve for one year OS

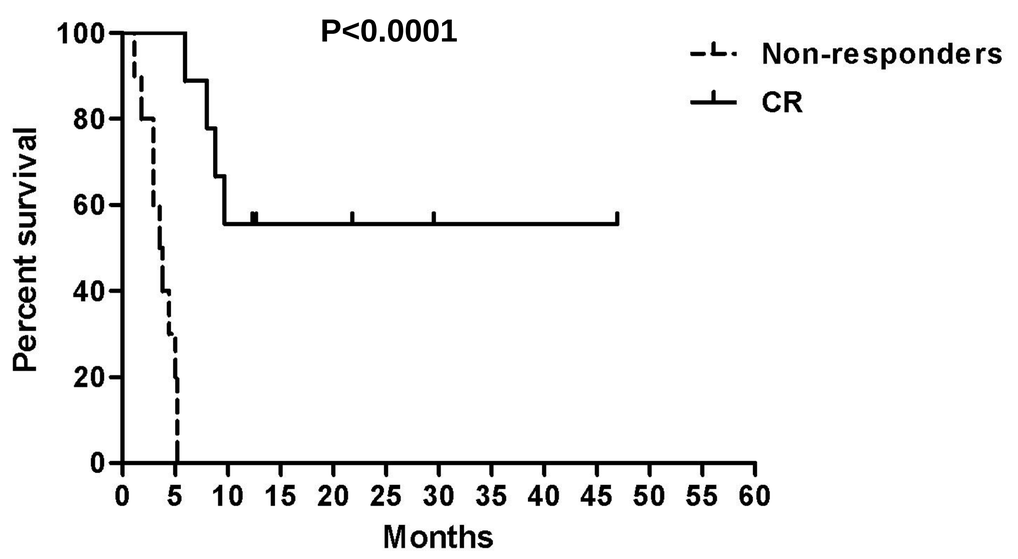


Fig 2: Logrank test between CR and non responders

➢ Toxicity

Table 1 Adverse events after GO

	No. cases (%)
Haematological toxicity	19 (100%)
Sepsis	2 (11%)
Hemorrhagic signs	2 (11%)
Febrile aplasia	3 (16%)
Digestive disorders	7 (37%)
Myalgias	3 (16%)
Hypertransamisaemia	2 (11%)
Sinusoidal obstructive syndrome	1 (5%)

Conclusion

Children with refractory/relapsed AML have a dismal outcome and there is a lack of effective treatments. GO is an antibody targeting leukemic blasts. In our study, GO was used as a single agent or in combination with chemotherapy.

We found that GO-containing treatments led to nearly 50% of CR and the grade 3-4 hematological toxicities were manageable. Even if the long term survival is still unsatisfactory, GO is clinically active in some patients and it should remain available in this indication.

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