Leucemia Linfoblastica T

Trattamento: stato dell'arte

Valentino Conter

Emato-Oncologia Pediatrica- Monza

Bologna, 3 Ottobre 2023

XLVIII CONGRESSO NAZIONALE AIEOP

Bologna
2-4 Ottobre 2023

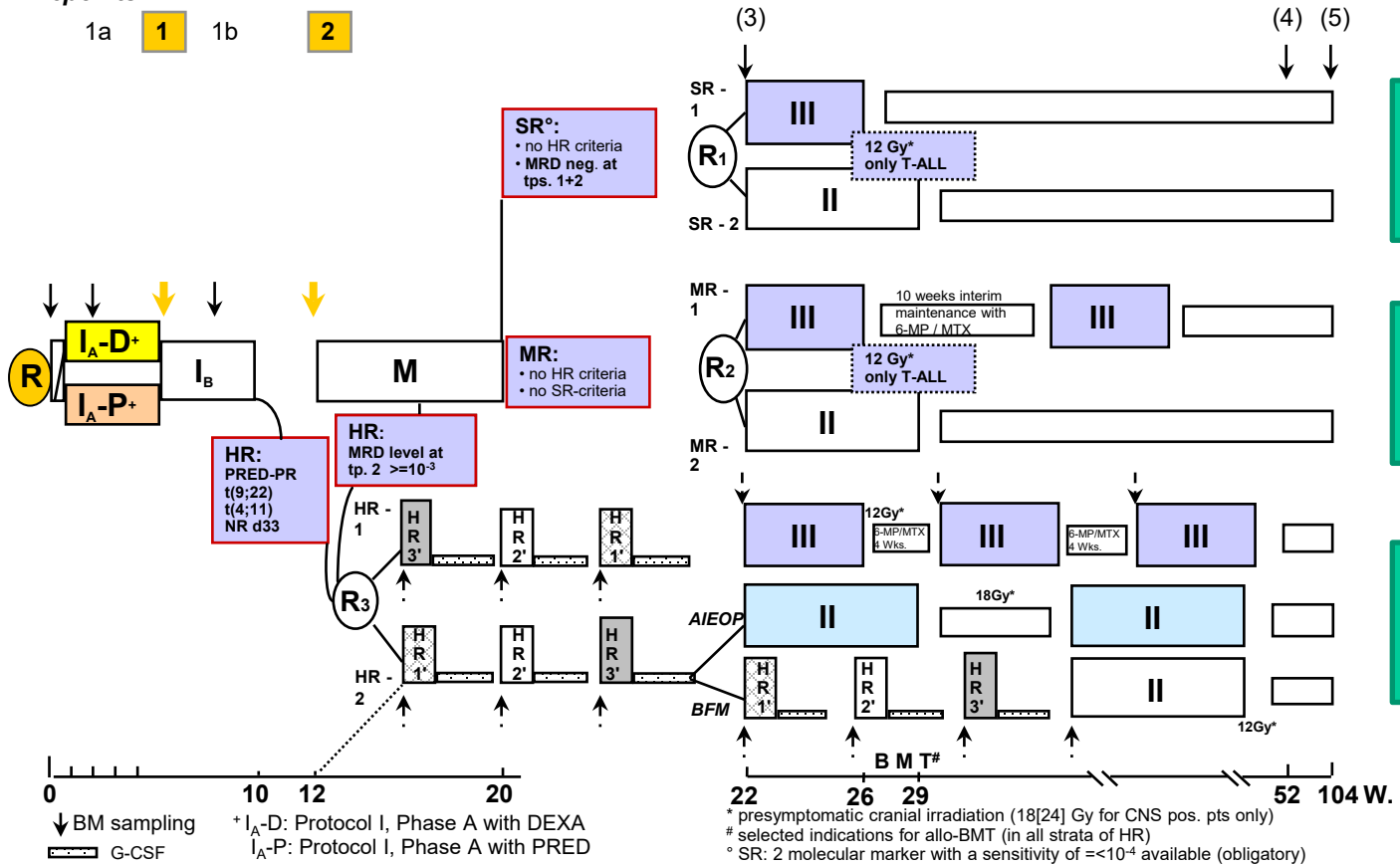
Il sottoscritto Valentino Conter

ai sensi dell'art. 3.3 sul Conflitto di Interessi, pag. 17 del Reg. Applicativo dell'Accordo Stato-Regione del 5 novembre 2009,

dichiara

che negli ultimi due anni NON ha avuto rapporti diretti di finanziamento con soggetti portatori di interessi commerciali in campo sanitario

AIEOP - BFM ALL 2000: Study questions in all risk groups



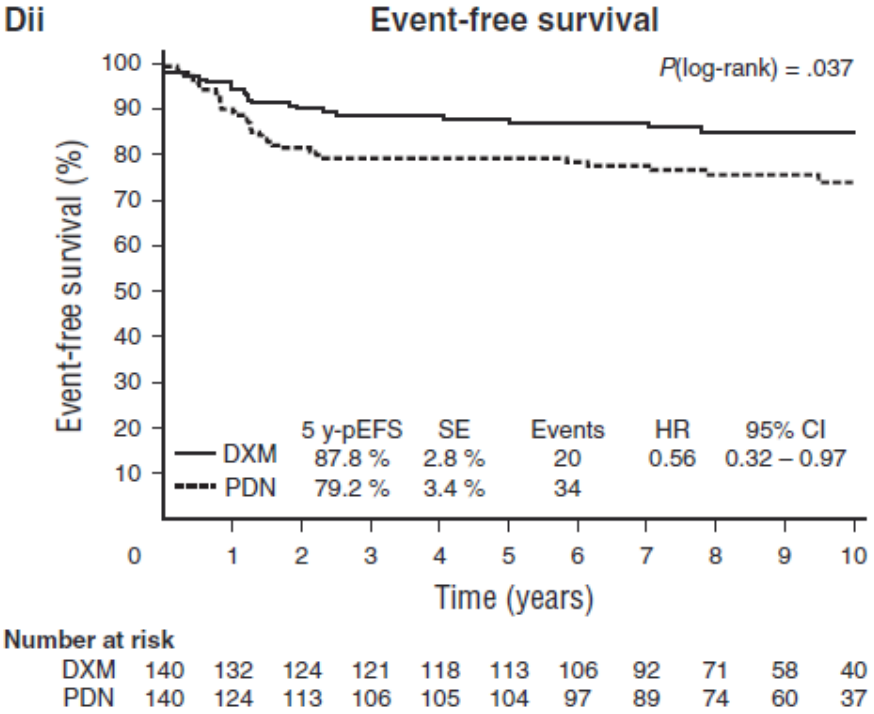
> Ricadute in SR-1 Schrappe et al, JCO 2018

No differenza Locatelli et al, Blood 2017

No differenza Attarbaschi et al, Leukemia 2020

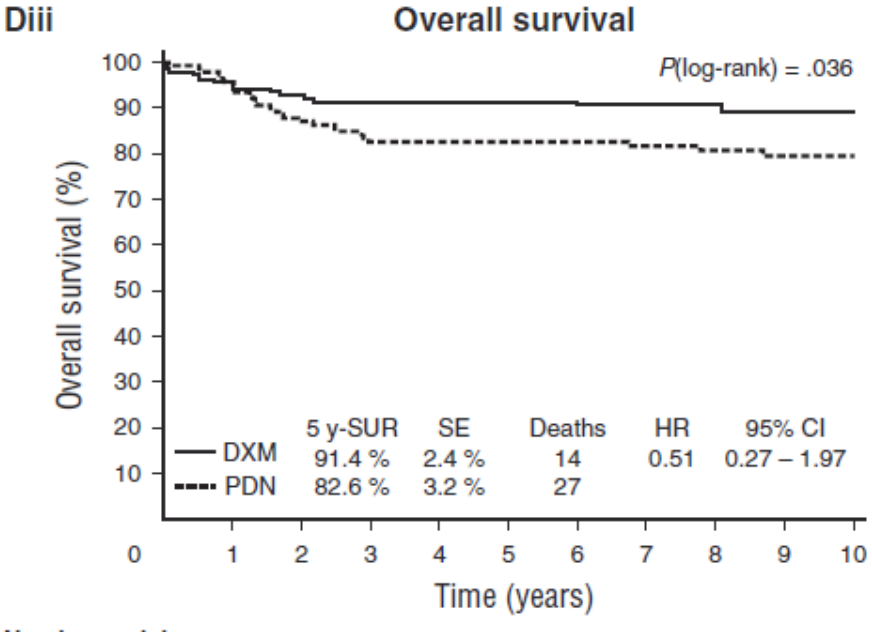
*AIEOP: RTC in T-ALL non-HR only for WBC count ≥ 100x10E9/L (Conter V et al, JCO 1997)

AIEOP-BFM ALL 2000 T-ALL PGR



Moericke Blood 2016

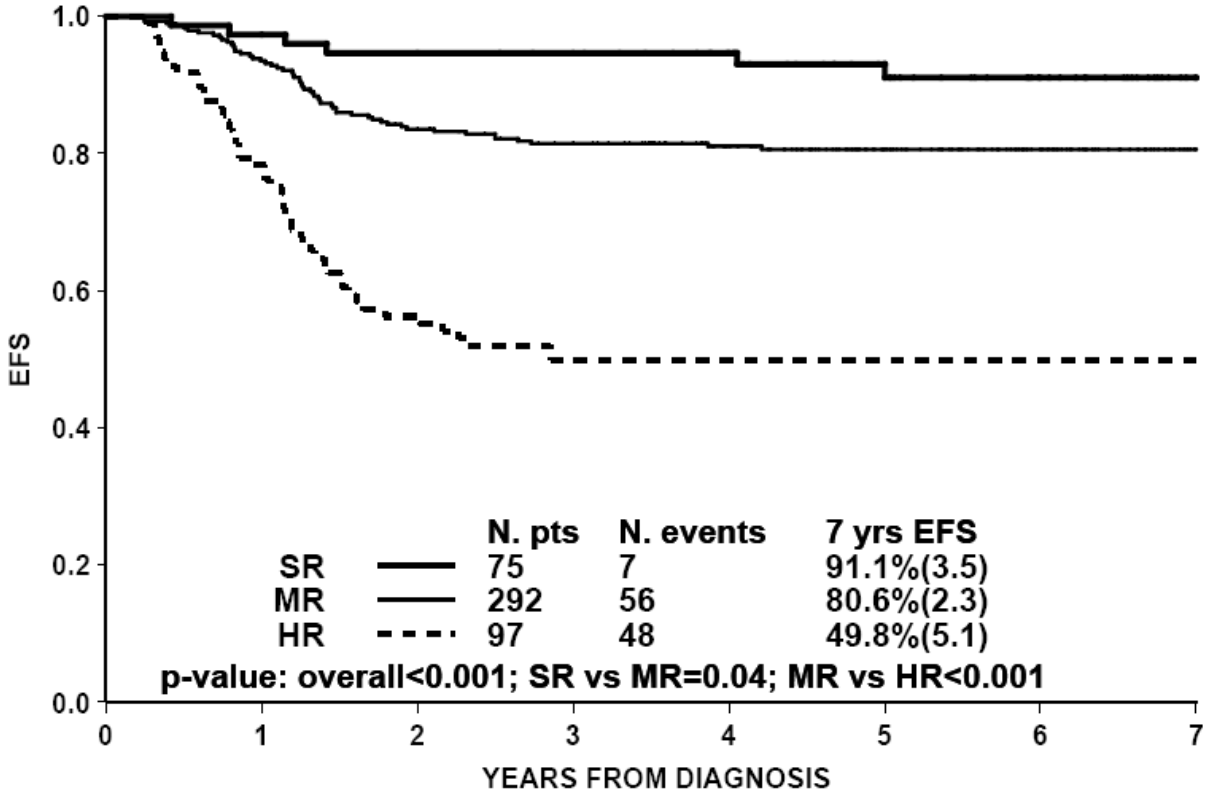
AIEOP-BFM ALL 2000 T-ALL PGR



Moericke Blood 2016

Combined timepoints for MRD assessment
pEFS in MRD risk groups of T-ALL

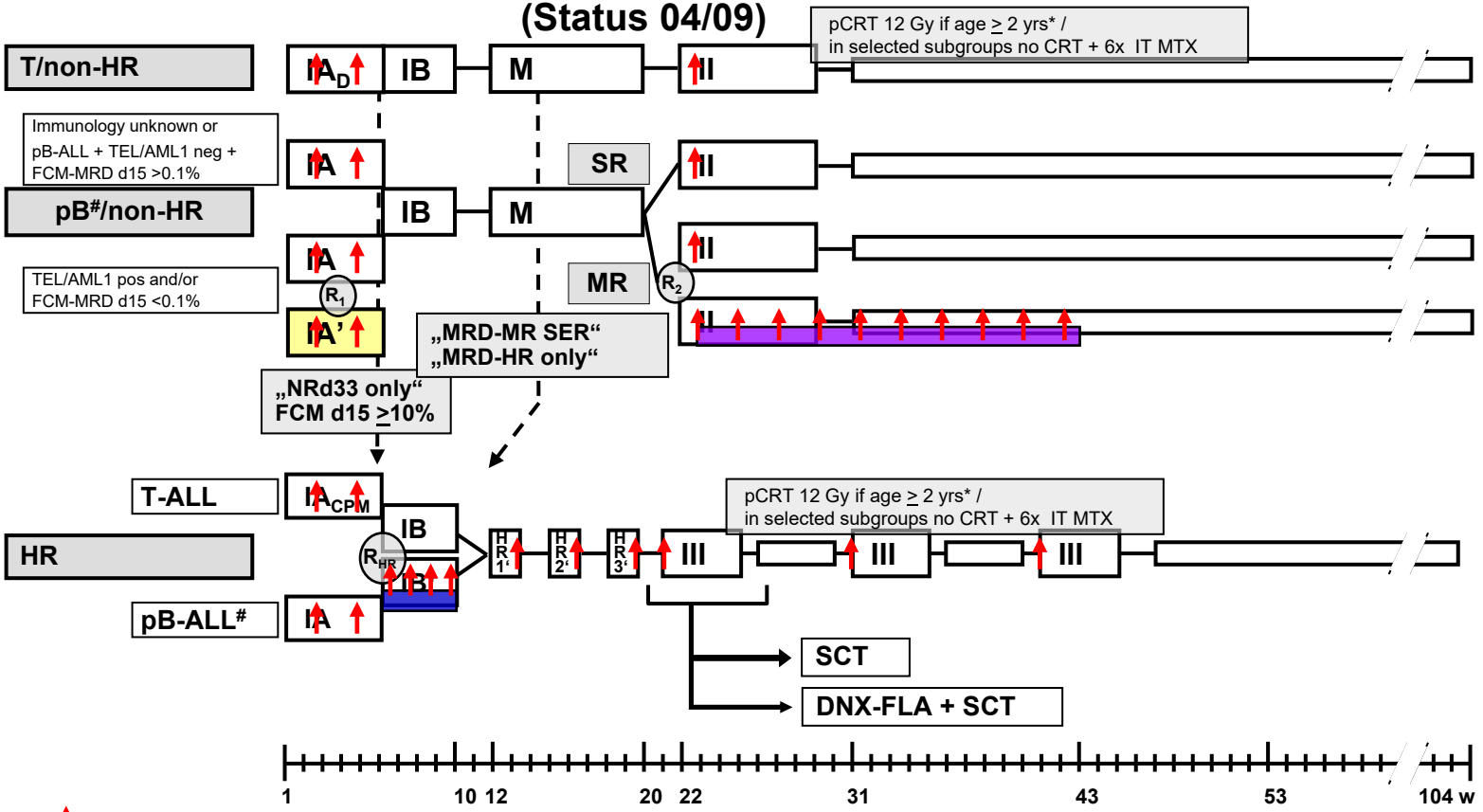
AIEOP-BFM ALL 2000



Schrappe M et al BLOOD (2011) 118: 2077-2084

AIEOP-BFM ALL 2009

(Status 04/09)



PEG L-asparaginase (2500 IU/m²)

IA Prot. IA with 4 DNR doses (day 8, 15, 22 and 29)

IA' Prot. IA with 2 DNR doses (day 8 and 15)

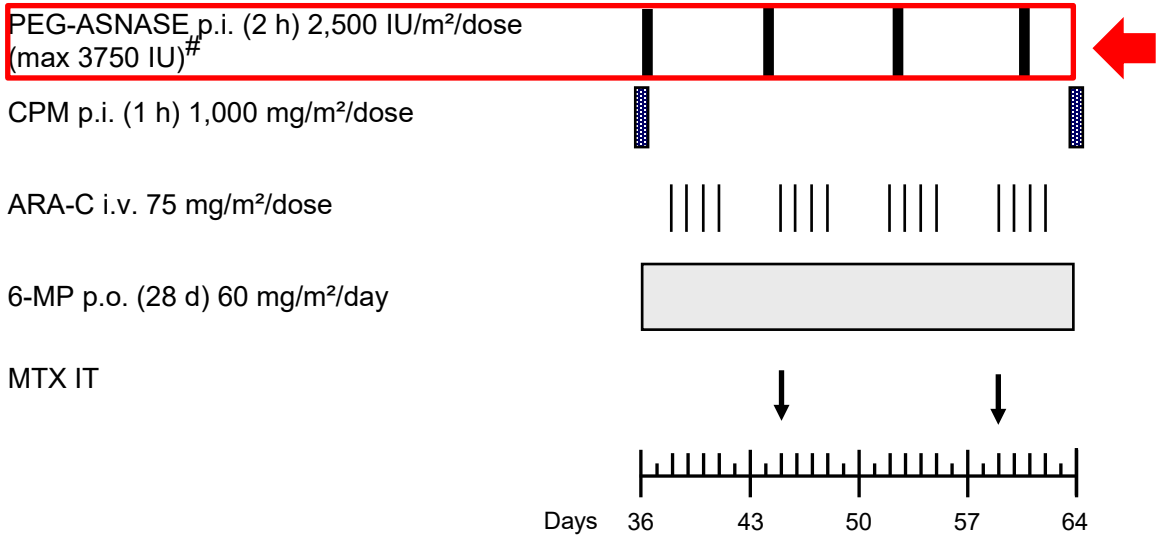
PEG-ASP 2500 IU/m² every 2 weeks, over 20 weeks in total

PEG-ASP 4 x 2500 IU/m² over 4 weeks

or immunophenotype unknown

* in patients with CNS disease (CNS 3) tCRT with 12 Gy/18 Gy (dose age-adapted))

Protocol IB / IB-PEG



STUDY ENDPOINTS
- Primary: rate of MRD highly positive patients (MRD ≥5x10-4) at TP2 (EOC)
- Secondary: EFS

only in HR patients randomized (R_{HR}) to the experimental arm

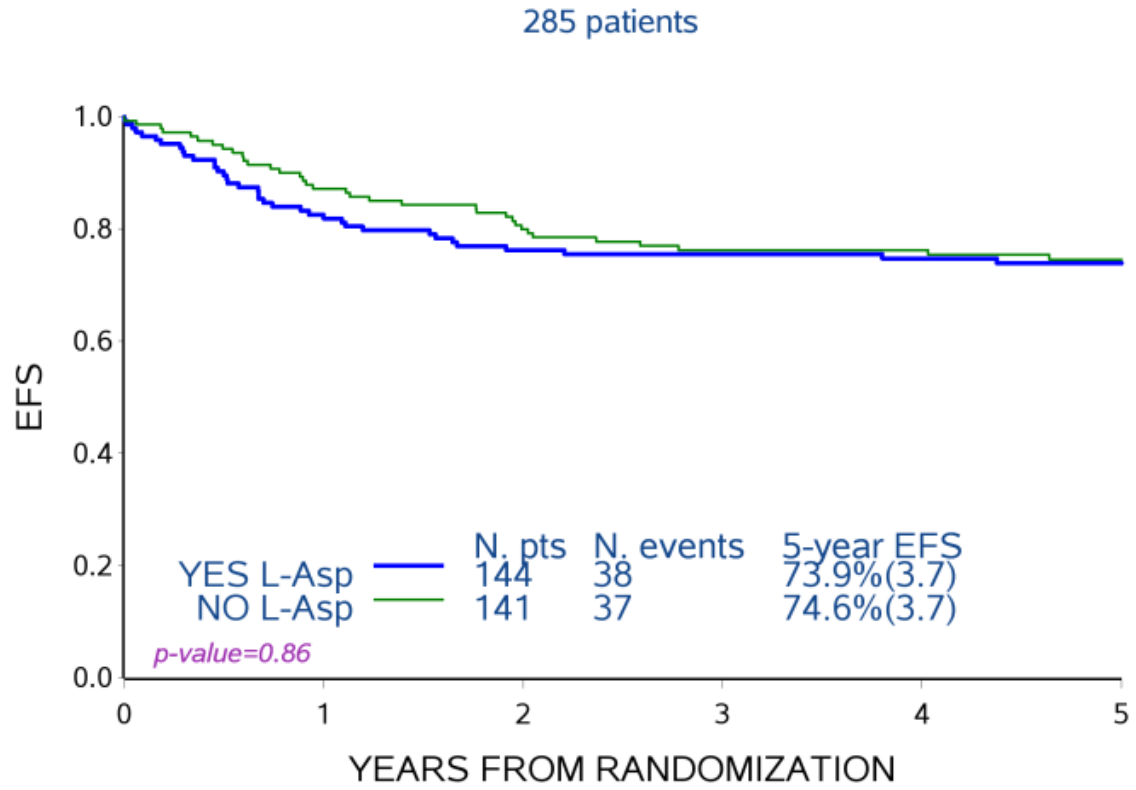
AIEOP-BFM ALL 2009 PROTOCOL: HR Primary endpoint: PCR-MRD at EOC

By immunophenotype

	Bcp ALL				T ALL			
	YES PEG-ASNASE		NO PEG-ASNASE		YES PEG-ASNASE		NO PEG-ASNASE	
	N	%	N	%	N	%	N	%
NUMBER OF PATIENTS	241		246		124		116	
Negative or POS NQ	186	*78.2*	186	*75.6*	79	*73.7*	72	*62.0*
POS <5x10^{-4}	27	*11.3*	21	*8.5*	22	*17.7*	22	*19.0*
POS ≥5x10^{-4}	28	*11.6*	39	*15.9*	23	*18.6*	22	*19.0*
p-value	*0.17*				*0.93*			

Conter V. et al, JCO, in Press

AIEOP-BFM ALL 2009 PROTOCOL: HR EFS – by ITT in T ALL



Early T-cell precursor acute lymphoblastic leukaemia in children treated in AIEOP centres with AIEOP-BFM protocols: a retrospective analysis

Valentino Conter, Maria Grazia Valsecchi, Barbara Buldini, Rosanna Parasole, Franco Locatelli, Antonella Colombini, Carmelo Rizzari, Maria Caterina Putti, Elena Barisone, Luca Lo Nigro, Nicola Santoro, Ottavio Ziino, Andrea Pession, Anna Maria Testi, Concetta Micalizzi, Fiorina Casale, Paolo Pierani, Simone Cesaro, Monica Cellini, Daniela Silvestri, Giovanni Cazzaniga, Andrea Biondi, Giuseppe Basso**

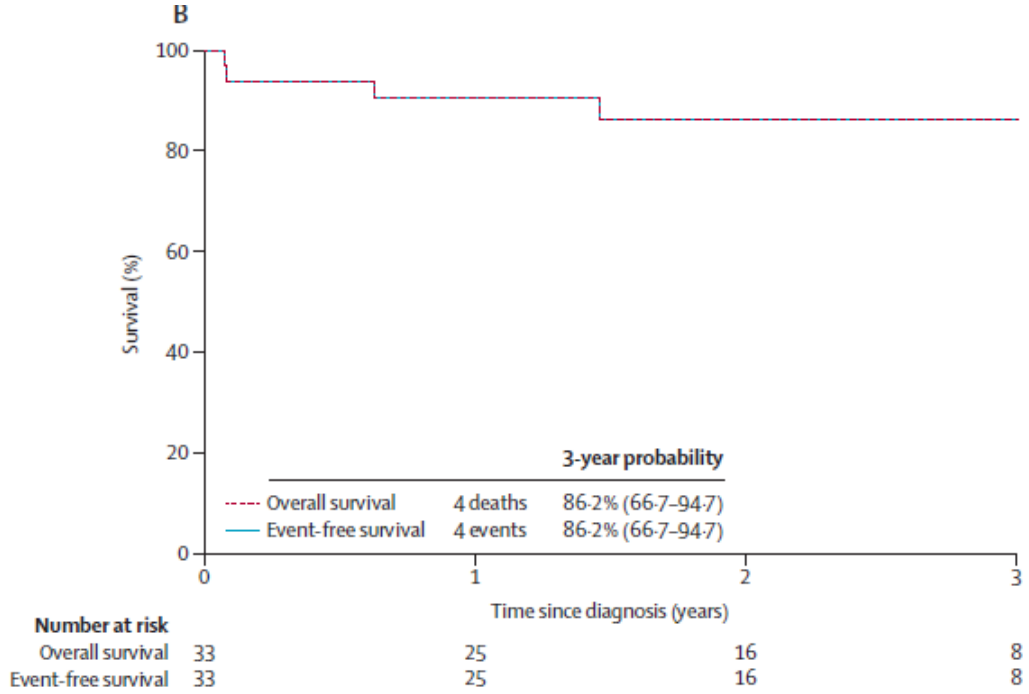
Summary

Interpretation **Early T-cell precursor acute lymphoblastic leukaemia is characterised by poor early response to conventional induction treatment. Consolidation phase IB, based on cyclophosphamide, 6-mercaptopurine, and ara-C at conventional (non-high) doses is eff ective in reducing minimal residual disease. Although the number of patients and observational time are limited, patients with early T-cell precursor acute lymphoblastic leukaemia treated with current BFM stratifi cation and treatment strategy have a favourable outcome compared with earlier reports. The role of innovative therapies and haemopoietic stem cell therapy in early T-cell precursor acute lymphoblastic leukaemia needs to be assessed.**

Lancet Haematology, January 2016

AIEOP ALL 2009

EFS and SURVIVAL: ETP ALL



COG AALL 0434 T-ALL

- 1848 pts; 5-y EFS 84%(1.3), OS 89% (1.1) Winter et al, JCO 2018

- No benefit from HDMTX

- Patients treated with the best-performing arm, C-MTX plus nelarabine, had a 5-year **DFS** of 91%

- Patients who received nelarabine had significantly fewer isolated and combined CNS relapses compared with patients who did not receive nelarabine (1.3% ± 0.63% v 6.9% ± 1.4%, respectively; P = .0001)

Dunsmore et al, JCO 2020

ETP (n=145; 11.5%)

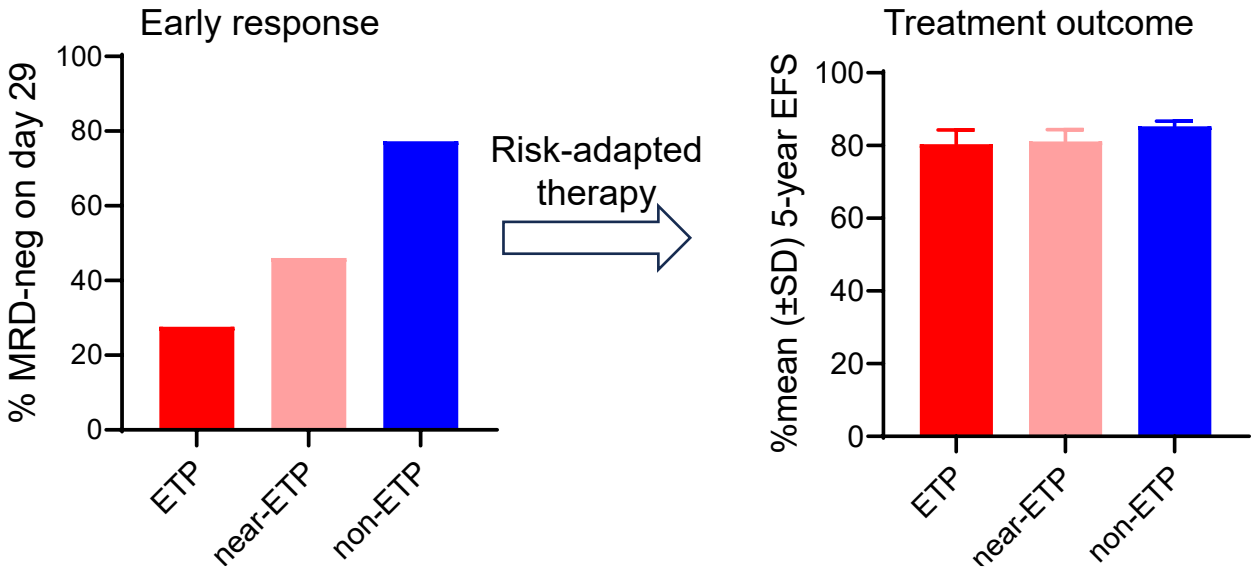
- Negative CD1a & CD8
  and
- Positive myeloid/stem cell markers (e.g., CD13, CD33, CD34, CD117, HLA-DR)
  and
- CD5: <75% positive leukemic cells or median intensity lower than that of mature T cells by at least 1 log

near-ETP (n=209; 16.7%)

- Negative CD1a & CD8
  and
- Positive myeloid/stem cell markers (e.g., CD13, CD33, CD34, CD117, HLA-DR)
  and
- **CD5 expression higher than ETP**

non-ETP (n=902; 71.8%)

- Does not express the ETP or near-ETP phenotype



Wood BL et al; Editorial Coustan-Smith E. and Conter V; Blood, in press

Risultati 1231

Bortezomib: N. Patients 615 ALL; (LL: 209)

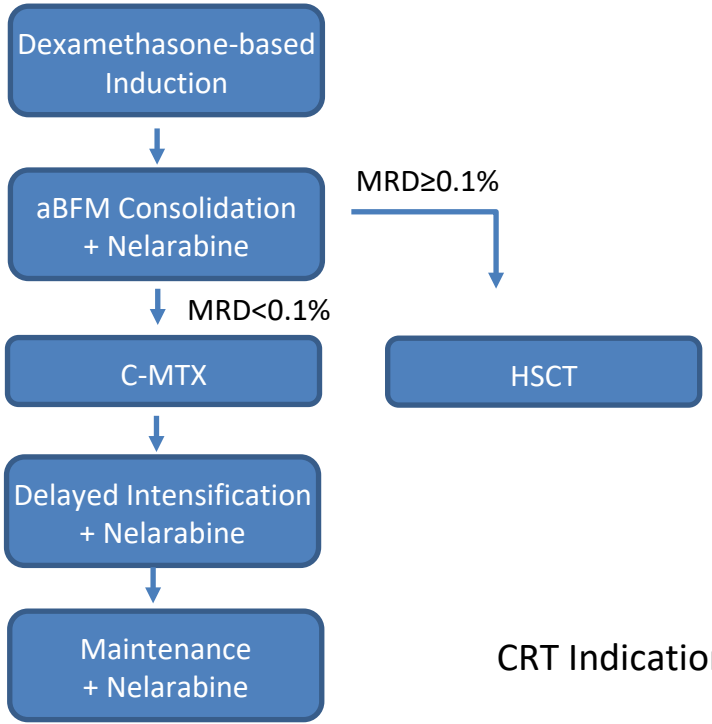
4-y EFS 82% (1.7)

5-y OS 88% (1.5)

Bortezomib: No difference in ALL; (LL: 10% higher EFS and OS)

Teachey DT et al, JCO 2022

GOG Current Approach: *De Novo* T-ALL



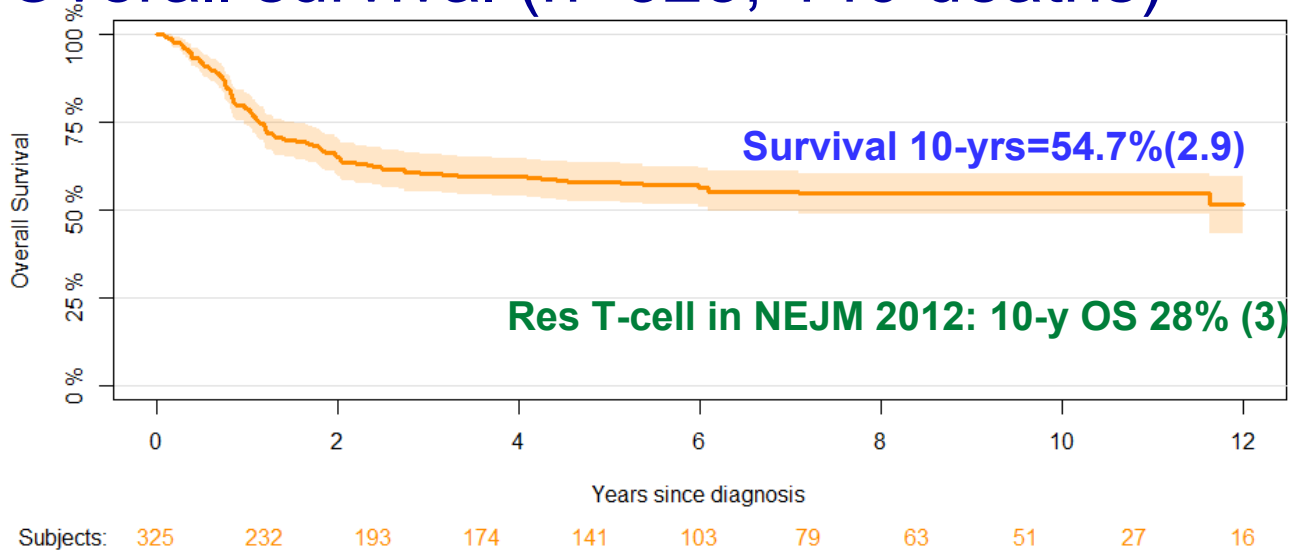
CRT Indication: CNS3

T-ALL Resistant to Induction therapy

- **Diagnosis from Jan 2000 to Dec 2017**
- **Age < 21 years**
- **Any patient with T-ALL who was resistant (≥5% blasts by morphology) after induction therapy (at approx. 1 month from dx)**

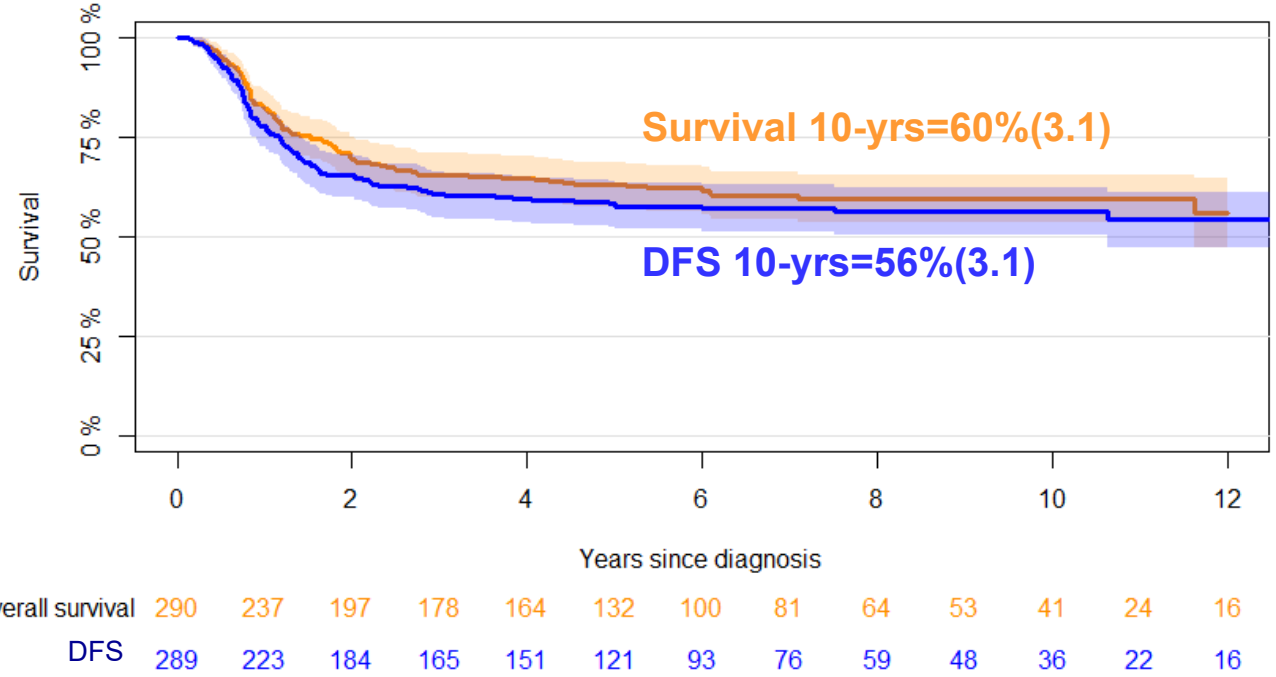
Outcome for Children and Young Adults With T-Cell ALL and Induction Failure in Contemporary Trials
Raetz E, Rebora P, Conter V et al JCO 2023

Overall survival (n=325, 140 deaths)

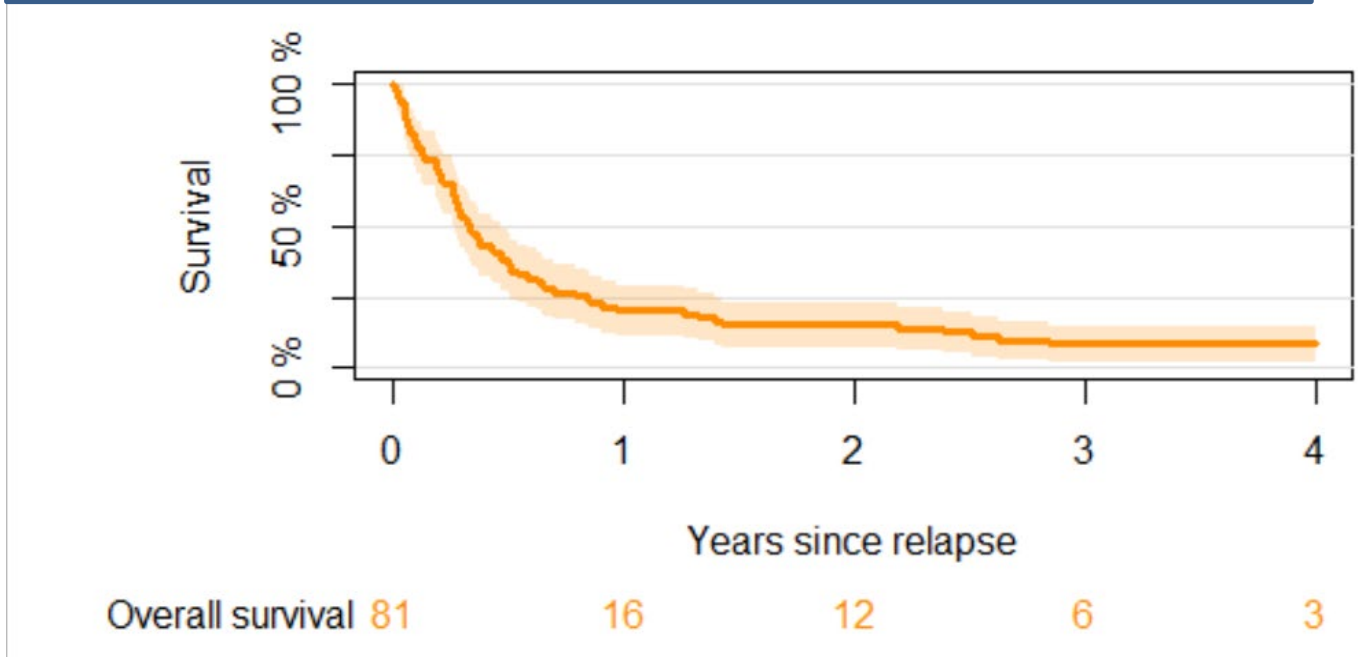


Median follow-up time 6.4 years (range 0.3 – 17.9 y).
70% of patients without events were followed for more than 5 y.

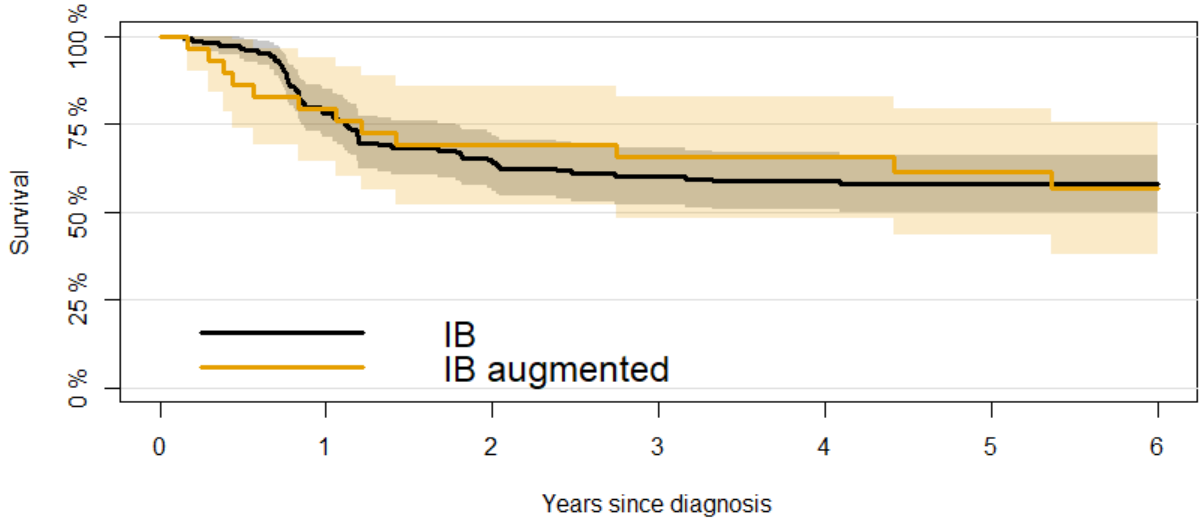
DFS and OS (from dx) (n=290 in CR post IND)



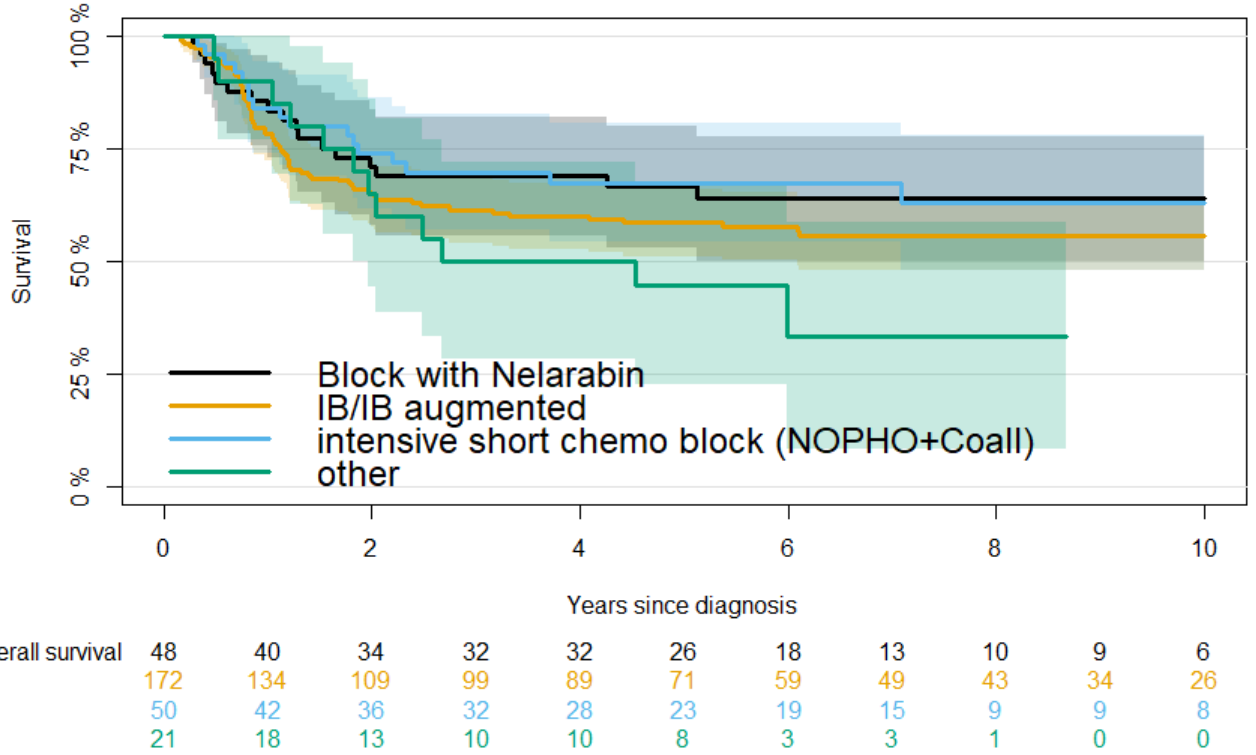
OS AFTER RELAPSE



1 patient with date of relapse missing


Survival
100 %
75 %
50 %
25 %
0 %
IB
IB augmented
0
1
2
3
4
5
6
Years since diagnosis
Overall survival
143
111
89
80
72
57
49
29
23
20
19
17
14
10

	GROUP(Group)															
	AIEOP	BFM-G	BFM-A	CoALL	COG	CPH	DFCI	DCOG	EORTC	INS	JPLSG	NOPHO	Ma-Spore	SJCRH	UK	Total
.	7	0	1	2	0	1	6	0	7	0	10	0	0	0	0	34
IB/IB augmented	39	63	11	0	0	0	0	11	12	14	0	0	3	4	15	172
Block with Nelarabin	1	0	0	0	41	0	6	0	0	0	0	0	0	0	0	48
intensive short chemo block (NOPHO+CoALL)	0	0	0	31	0	0	0	0	0	0	0	19	0	0	0	50
other	0	0	0	0	0	0	4	3	0	0	13	0	1	0	0	21



NEW AIEOP-BFM T-ALLPROTOCOL … WORK IN PROGRESS

UNMET NEEDS IN T-ALL ARE:

- REDUCTION OF TREATMENT INTENSITY IN HR

- PRIMARY RESISTANCE

- RELAPSE

I MIEI RINGRAZIAMENTI VANNO A TUTTI GLI OPERATORI IMPEGNATI NELL'ASSISTENZA AI BAMBINI E ADOLESCENTI NEI CENTRI AIEOP.

UN GRAZIE PARTICOLARE A COLORO CHE HANNO PIACERE DI CONDIVIDERE SCELTE DELICATE PER IL RATTAMENTO DELLA LLA IN PAZIENTI PARTICOLARMENTE COMPLESSI