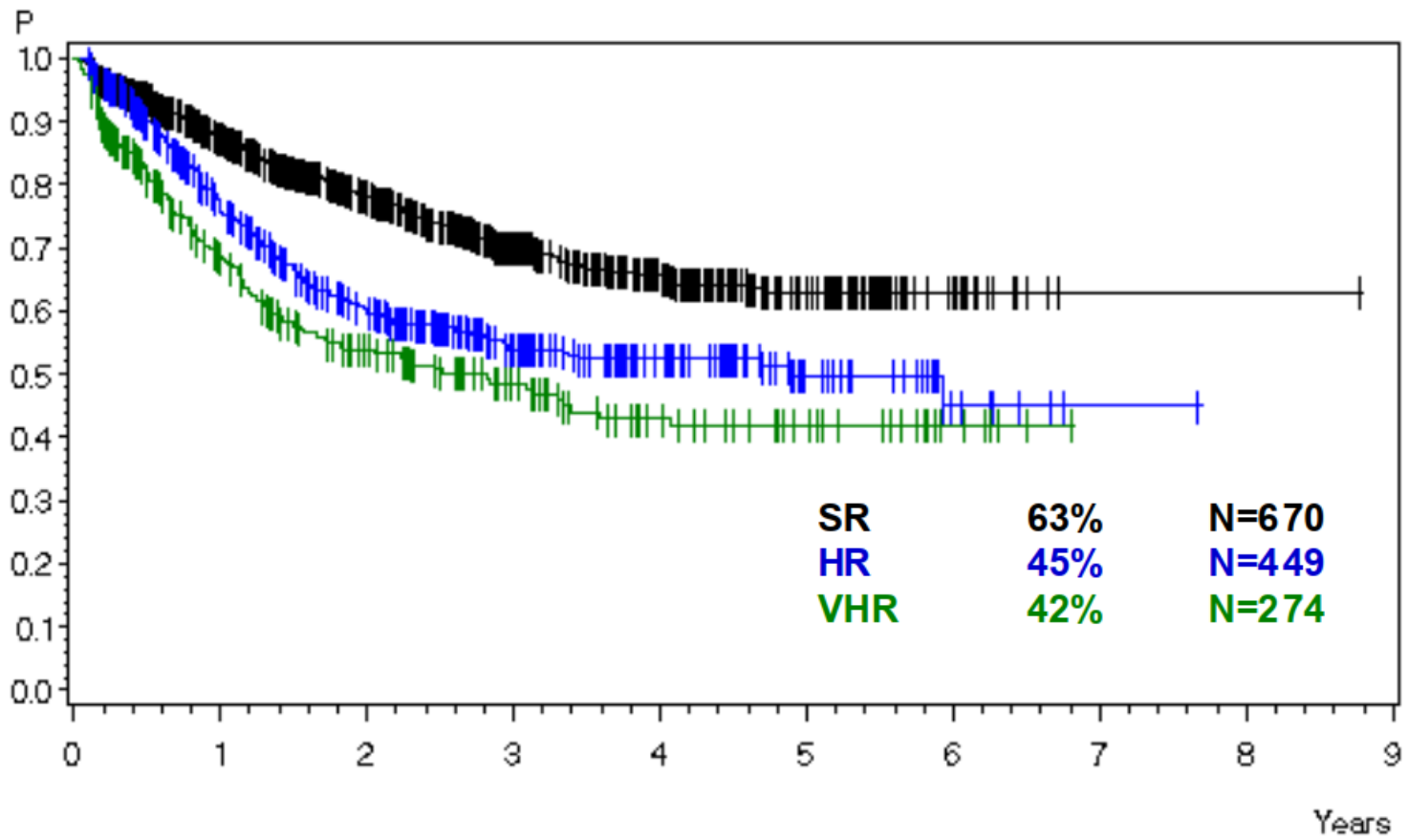




Ph+ ALL



Gesamtüberleben GMALL 07/2003 nach Risikogruppe, Pat. <55 J.



Therapieoptionen

- Niedrig-dosierte Chemotherapie
- Tyrosinkinase-Inhibitoren (TKI)
 - Imatinib
 - Dasatinib
 - Ponatinib
 - Olverembatinib
- Blinatumomab
- Inotuzumab Ozogamicin
- CAR-T-Zellen
- Allogene
Blutstammzelltransplantation



Ph+ ALL

Ponatinib/Blinatumomab vs. Imatinib/Chemotherapy

Sabina Chiaretti. 439 First results of the Phase III GIMEMA ALL2820 trial comparing ponatinib plus blinatumomab to imatinib and chemotherapy for newly diagnosed adult ph+ acute lymphoblastic leukemia patients.



First results of the Phase III GIMEMA ALL2820 trial comparing ponatinib plus blinatumomab to imatinib and chemotherapy for newly diagnosed adult Ph+ acute lymphoblastic leukemia patients

S. Chiaretti, M. Di Trani, C. Skert, L. Elia, G. Almici, I. Della Starza, D. Cardinali, V. Bellomarino, S. Soddu, M. Messina, M.R. Marino, M.S. De Propriis, E. Borlenghi, F. Di Raimondo, M. Ansuinelli, C. Alati, D.G. Mattei, V. Mancini, P. Chiusolo, B. Scappini, M.P. Martelli, P. Salutari, M. Cerrano, B. Serio, A. Cucca, M. Luppi, D. Vallisa, C. Pasciolla, C. Romani, M. Chiarucci, F. Mosna, M. Bonifacio, N.S. Fracchiolla, M. Bocchia, S. Imbergamo, C. Califano, G.R. Nunziata, M. Annunziata, A. Mulé, P. Zappasodi, F. Giglio, D. Pietrasanta, M. Della Porta, M. Musso, M. Lunghi, F. Zaja, E. Todisco, C.M. Basilico, A. Piciocchi, P. Fazi, A. Rambaldi, R. Foà



SAPIENZA
UNIVERSITÀ DI ROMA

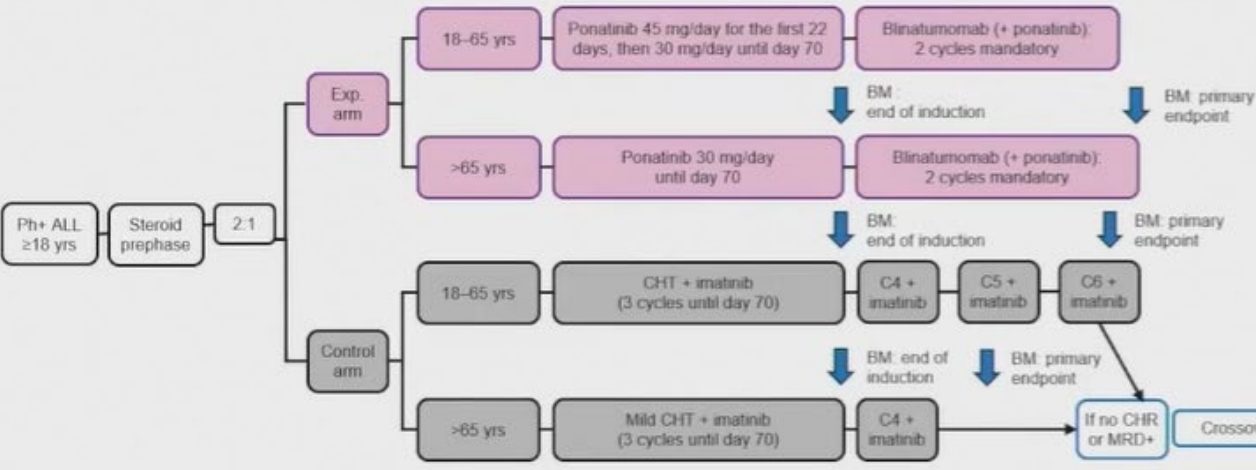


fondazione GIMEMA ^{onlus}
per la promozione e lo sviluppo della ricerca scientifica
sulle malattie ematologiche. FRANCO MANDELLI

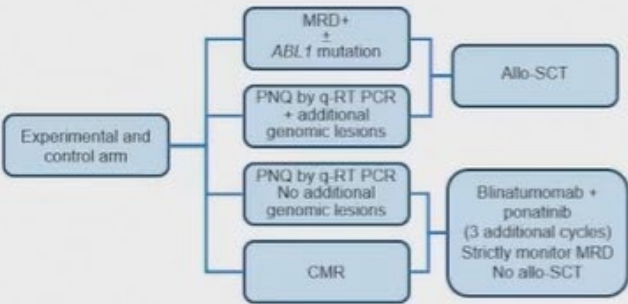


GIMEMA ALL2820 Phase III Trial

Frontline treatment of adult Ph+ ALL (≥18 years, no upper age limit) with ponatinib plus steroids followed by blinatumomab compared to chemotherapy with imatinib



- Protocol closed to enrolment in January 2025.
- Last patient reached primary endpoint in June 2025.



- CNS prophylaxis strengthened: 15 triple medicated lumbar punctures 18 if CNS+ at diagnosis.

Sabina Chiaretti. 439 First results of the Phase III GIMEMA ALL2820 trial comparing ponatinib plus blinatumomab to imatinib and chemotherapy for newly diagnosed adult ph+ acute lymphoblastic leukemia patients.



GIMEMA ALL2820. Hematologic responses

End of induction (d +70)	Experimental arm (n=158)	Control arm (n=78)	p
CHR	149 (94.3%)	62 (79.4%)	0.004
Deaths	4 (2.5%)	8 (10.2%)	
Refractory	-	1 (1.3%)	
Off-treatment	5 (2.8%)	7 (8.9%)	

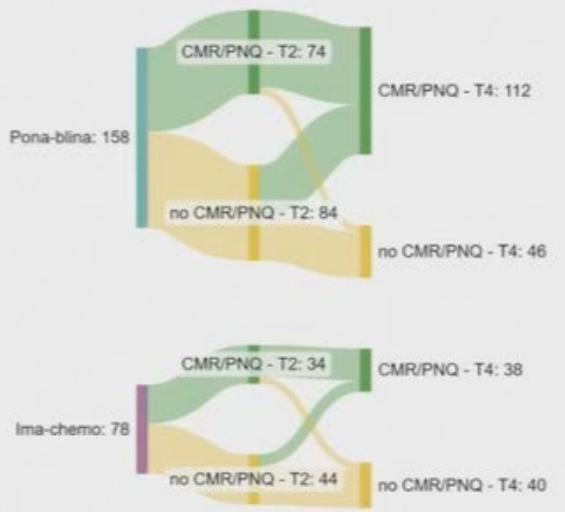
Sabina Chiaretti. 439 First results of the Phase III GIMEMA ALL2820 trial comparing ponatinib plus blinatumomab to imatinib and chemotherapy for newly diagnosed adult ph+ acute lymphoblastic leukemia patients.



GIMEMA ALL2820. Molecular responses by ITT

Experimental arm (n=158)	No molecular responses (%)	CMR	PNQ	Overall molecular responses (%)
End of induction	84 (53.2)	48 (30.4)	26 (16.5)	74 (46.8)
After 2 blina cycles	46 (29.1)	82 (51.9)	30 (19)	112 (70.9)
Control arm (n=78)				
End of induction	44 (56.4)	28 (35.9)	6 (7.7)	34 (43.6)
After 4/6 CHT cycles*	40 (51.3)	29 (37.2)	9 (11.5)	38 (48.7)

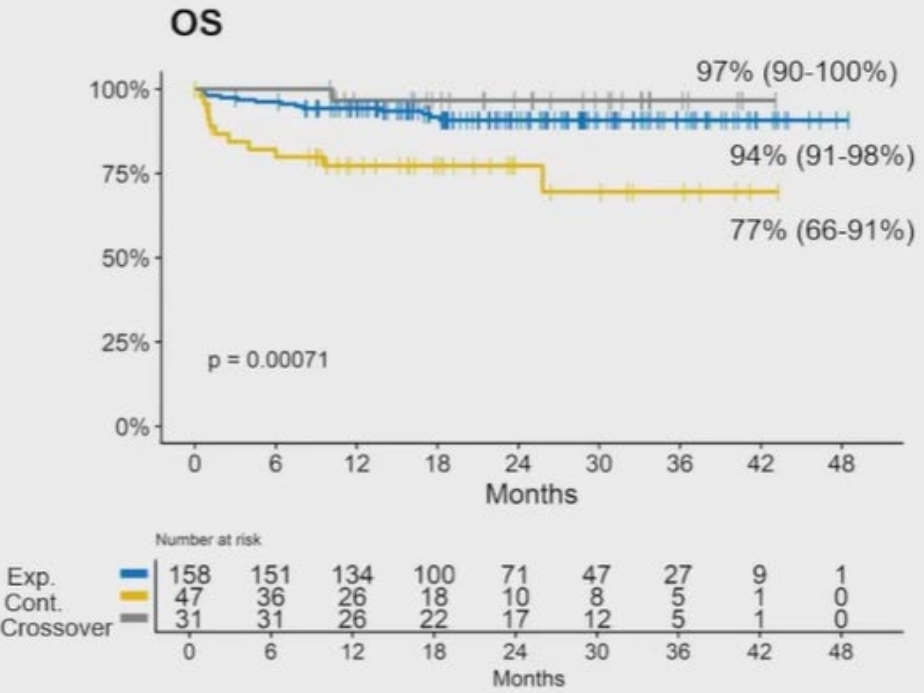
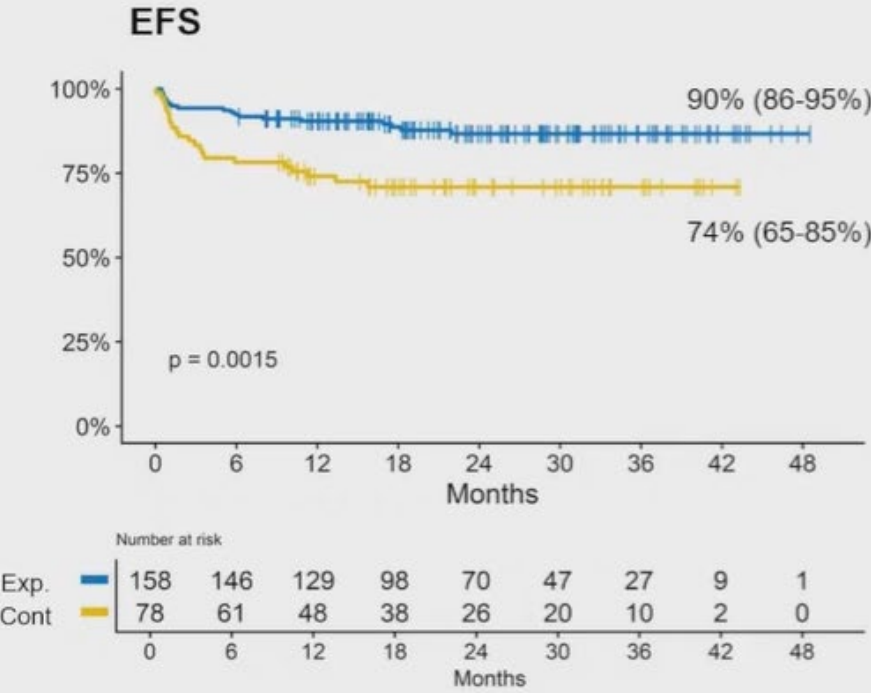
*Depending on age



Sabina Chiaretti. 439 First results of the Phase III GIMEMA ALL2820 trial comparing ponatinib plus blinatumomab to imatinib and chemotherapy for newly diagnosed adult ph+ acute lymphoblastic leukemia patients.



GIMEMA ALL2820. EFS and OS



Median follow-up: 23.4 months (0.1- 48.5)

Sabina Chiaretti. 439 First results of the Phase III GIMEMA ALL2820 trial comparing ponatinib plus blinatumomab to imatinib and chemotherapy for newly diagnosed adult ph+ acute lymphoblastic leukemia patients.



Ph+ ALL

Ponatinib oder Imatinib

Yosr Hicheri. 440 Randomized comparison of ponatinib versus imatinib in combination with chemotherapy in patients 55 years of age and older with newly diagnosed ph+ ALL: Molecular response and initial outcome analysis of the EWALL PH03 Study.



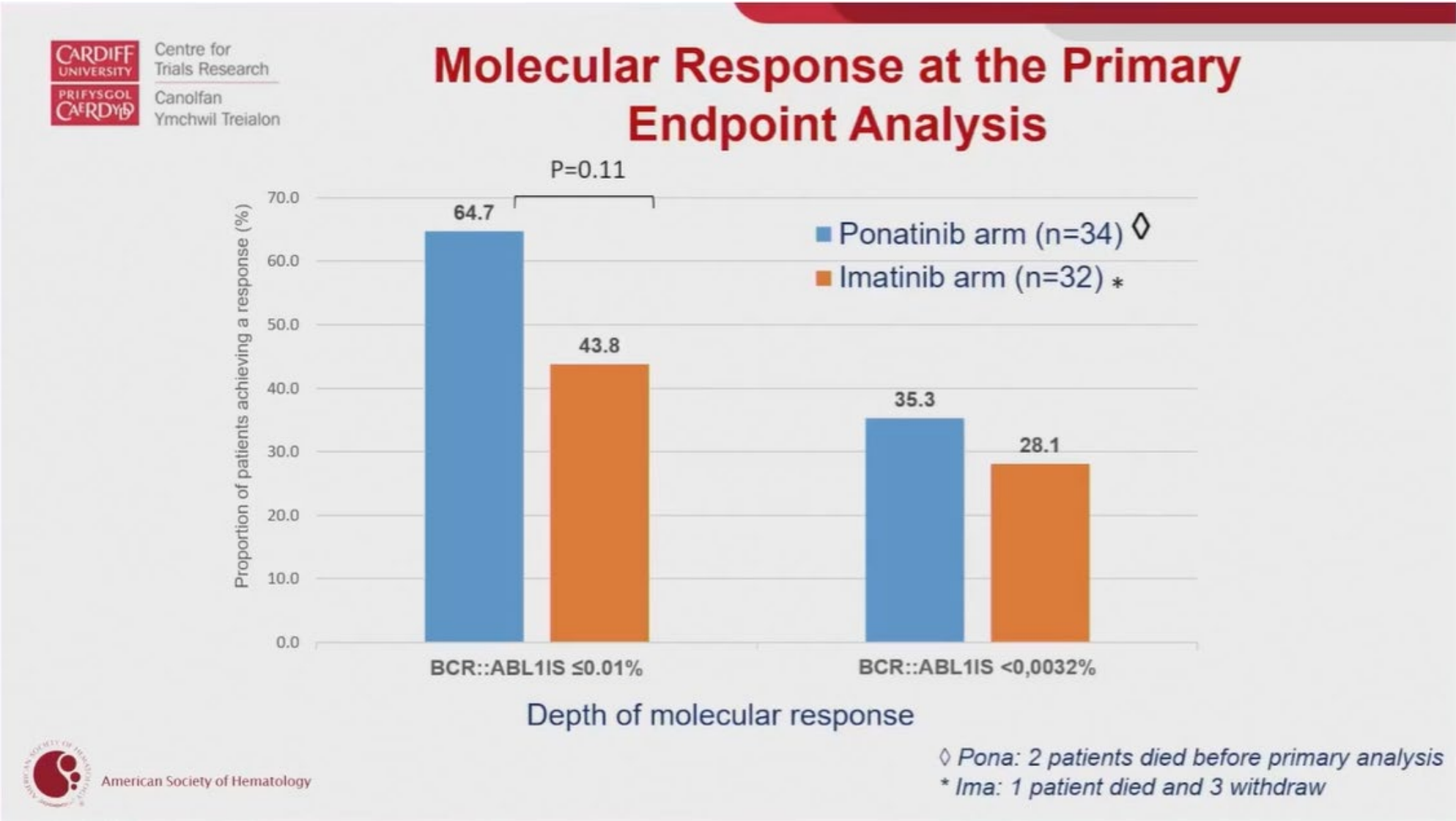


ABSTRACT #440

Randomised Comparison of Ponatinib Versus Imatinib in Combination with Chemotherapy in Patients 55 Years of Age and Older with Newly Diagnosed Ph+ ALL: Molecular Response and Initial Outcome Analysis of the EWALL PH03 Study

Oliver G. Ottmann, Tongtong Shi, Kimmo Porkka, Anna Lübking, Emmanuell Clappier, Yosr Hicheri, Thibault Leguay, Emilie Lemaste, Sarah Burns, Charlotte Letterme, Catharine Porter, Mia Sydenham, Ian Thomas, Jean-Michel Cayuela, Philippe Rouselot





Yosr Hicheri. 440 Randomized comparison of ponatinib versus imatinib in combination with chemotherapy in patients 55 years of age and older with newly diagnosed ph+ ALL: Molecular response and initial outcome analysis of the EWALL PH03 Study.





Tolerance / Main AEs

Grade	Ponatinib Arm n=36 (%)		Imatinib Arm n=36 (%)	
	3	4	3	4
Cardiovascular AEs	1 (2.8)	(0)	0 (0)	0 (0)
▪ Ischemic heart disease	1 (2.8)	(0)	0 (0)	0 (0)
Hypertension	4 (11.1)	(0)	1 (2.8)	(0)
Arterial ischemia, arterial or other thromboembolic event	2 (5.6)	(0)	2 (5.6)	0 (0)
▪ Thrombotic event	1 (2.8)	(0)	1 (2.8)	0 (0)
▪ Pulmonary embolism	1 (2.8)	(0)	1 (2.8)	0 (0)
Pancreatitis	2 (5.6)	1 (2,8)	0 (0)	0 (0)
Grade 5 AE	1 Cardiorespiratory arrest		1 Hemorrhagic stroke	



Yosr Hicheri. 440 Randomized comparison of ponatinib versus imatinib in combination with chemotherapy in patients 55 years of age and older with newly diagnosed ph+ ALL: Molecular response and initial outcome analysis of the EWALL PH03 Study.



Ph+ ALL

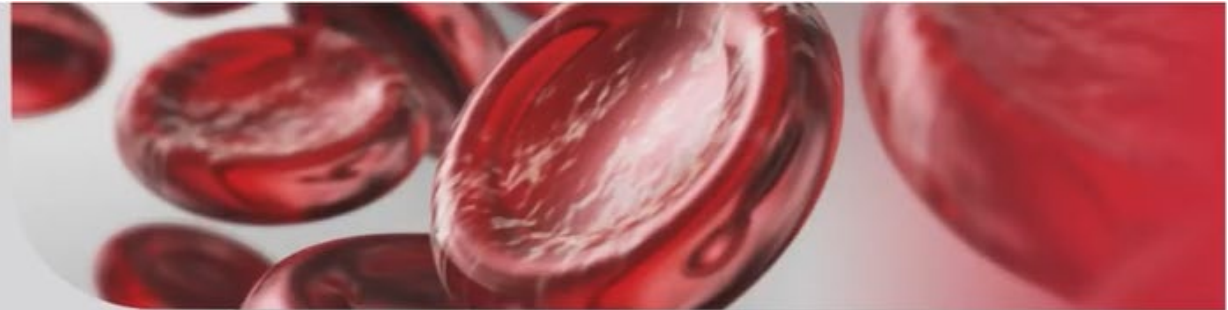
TKI und Inotuzumab ozogamicin-based

Anand Patel. 441 Primary efficacy analysis of phase II study investigating tyrosine kinase inhibitor (TKI) and inotuzumab ozogamicin-based therapy for newly diagnosed Philadelphia-chromosome positive acute lymphoblastic leukemia (Ph+ ALL).





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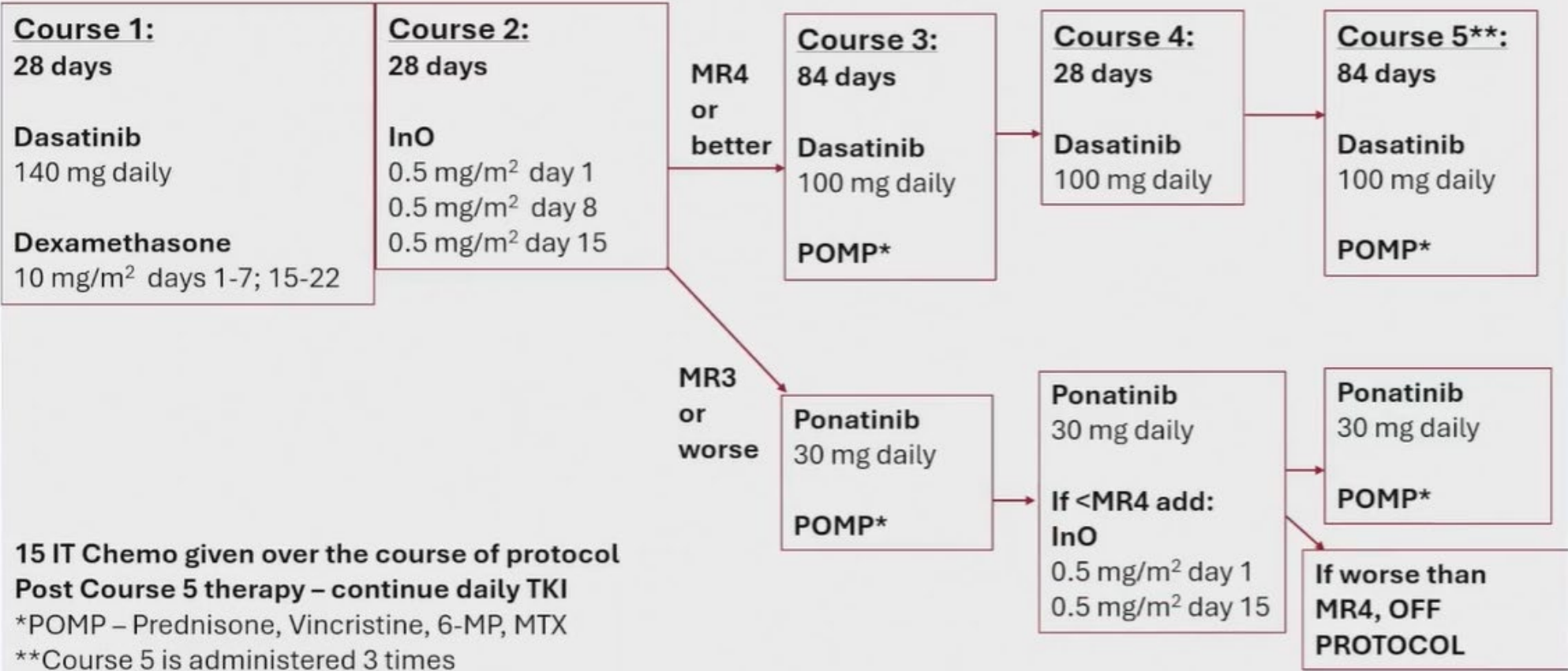


Primary efficacy analysis of phase II study investigating tyrosine kinase inhibitor (TKI) and inotuzumab ozogamicin-based therapy for newly diagnosed Philadelphia-chromosome positive acute lymphoblastic leukemia (Ph+ ALL)

Anand A. Patel, Adam S. DuVall, Caner Saygin, Howard Weiner, Emily Dworkin, Afsheen Noorani, Jamie Mathews, Angela Lager, Sandeep Gurbuxani, Peng Wang, Rafael Madero-Marroquin, Austin Wesevich, Gregory W. Roloff, Mariam T. Nawas, Michael W. Drazer, Satyajit Kosuri, Michael Thirman, Richard A. Larson, Olatoyosi Odenike, Theodore Karrison, Wendy Stock



Revised Treatment Schema (2) : InO + TKI

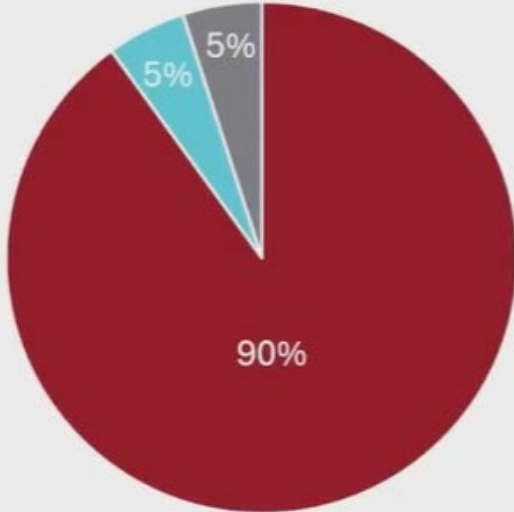


15 IT Chemo given over the course of protocol
 Post Course 5 therapy – continue daily TKI
 *POMP – Prednisone, Vincristine, 6-MP, MTX
 **Course 5 is administered 3 times



Efficacy by RT-PCR – Full Cohort (N=21)

Best Response by End of Course 3



Patient Characteristics of < MR4 (n=2)
-both p190
-none with WBC ≥ 70K
-none *IKZF1*^{plus}

■ MR4 ■ MR3 ■ CR

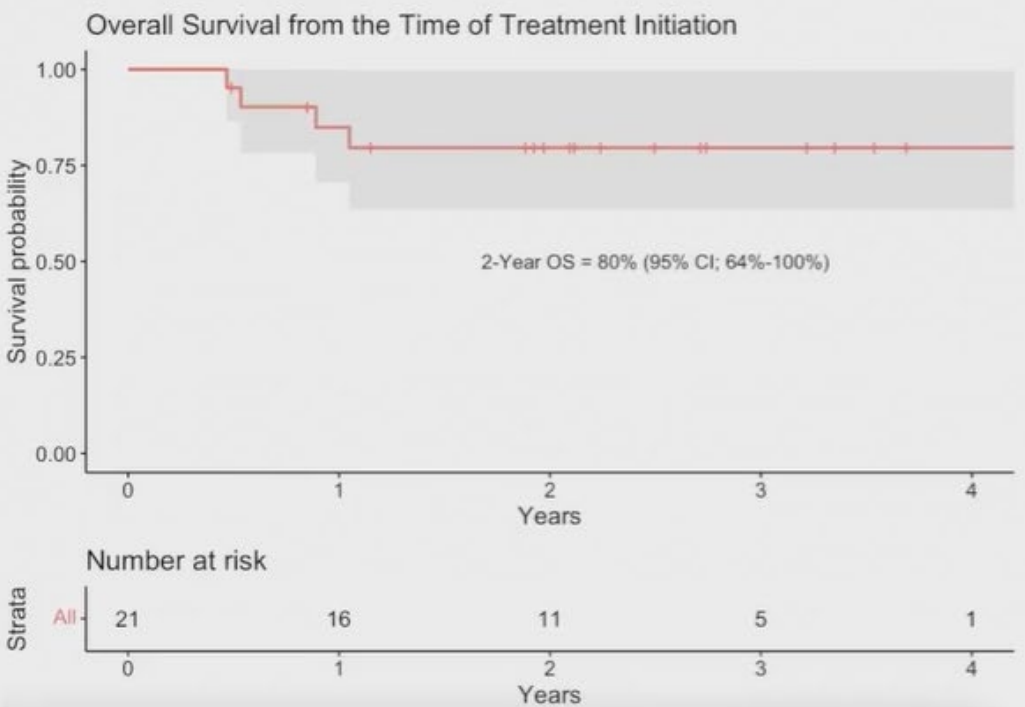
CR = <5% blasts on bone marrow biopsy with ANC >1000 and Plt > 100
MR3 = ≤0.1% by *BCR::ABL1* PCR and meeting CR criteria
MR4 = ≤0.01% by *BCR::ABL1* PCR and meeting CR criteria



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Survival and Patient Disposition



Total Cohort (21 patients)

- Median follow-up 2.1 years
- **0 patients received allogeneic transplant**
- **0 CNS relapses**
- 1 post-protocol systemic relapse
 - Features at diagnosis: p190, WBC≥70K, *IKZF1*m
 - Features at relapse: *IKZF1*m, *ABL1* T315I
- 4 deaths (3 off-protocol, 1 on protocol)
 - 2 due to sepsis
 - 1 due to GI bleed
 - On-protocol death during Course 5 (respiratory failure due to pneumonia and COPD)



Ph+ ALL

CAR-T-Zellen in CR1

Runxia Gu. 442 Single CAR-t infusion during front-line consolidation induces deep and sustained remission in newly diagnosed adult ph+b- ALL: A prospective phase 2 study.





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**Single CAR-T infusion during front-line consolidation induces deep
and sustained remission in newly diagnosed adult Ph⁺B- ALL:
A prospective phase 2 study**

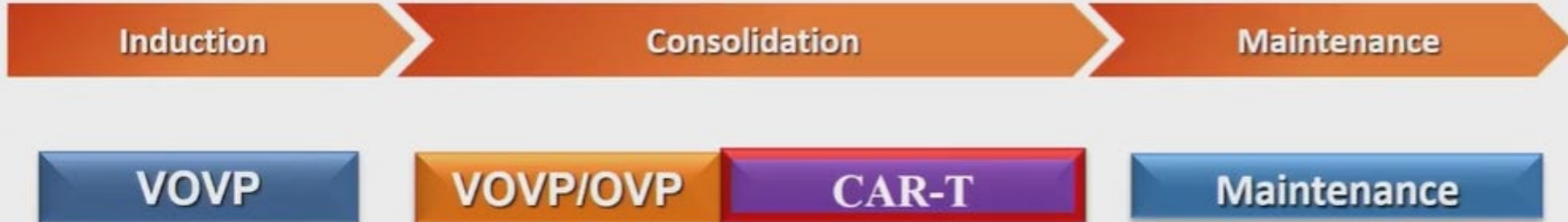
Runxia Gu, Shaowei Qiu, Xiaoyuan Gong, Shuning Wei, Guangji Zhang, Benfa Gong, Qiuyun Fang, Shouyun Li, Kaiqi Liu, Lin Dong, Ying Wang, Chunlin Zhou, Chengcai Guo, Bing Cheng Liu, Yingchang Mi, Hui Wei, Ying Wang, Jianxiang Wang

State Key Laboratory of Experimental Hematology, National Clinical Research Center for Blood Diseases, Institute of Hematology and Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, China



Treatment Schema

Institute of Hematology & Blood Diseases Hospital
Chinese Academy of Medical Sciences
Peking Union Medical College



Venetoclax 100 mg D1, 200mg D2, 400mg D3-28			
Olverembatinib 40 mg QOD D1-28			
VCR		VCR	VCR
Prednisone 60 mg/m ² D1-14; 40 mg/m ² D15-28			

CAR-T Infusion :
A single infusion of murine-derived 2nd CD19-directed CAR T-cells (with a 4-1BB co-stimulatory domain, dose : 1-2 × 10⁶ cells/Kg) during first CR

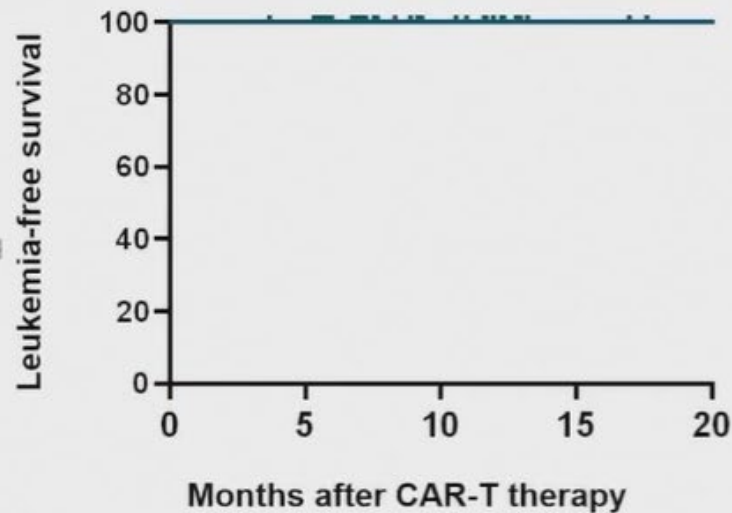
Maintenance therapy:
olverembatinib at a dose of 30 mg on alternate days, in combination with the MM regimen on a monthly basis, alternating with the VPV regimen

Prophylactic triple intrathecal injections were performed 11 times to patients who maintained a consistent CR



Survival rate

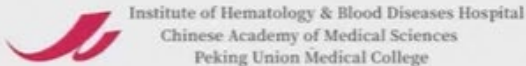
- After a median follow-up of 10.9 months, the 1-year estimate LFS rate was 100%



- No patients experienced bone marrow or extramedullary relapse
- Three patients underwent hematopoietic stem cell transplantation during CR1 by personal choice



Adverse Events during CAR-T therapy



- No severe CRS (grade ≥ 2) was observed within 3 months after CAR-T infusion
- No ICANS was observed

AEs	Grade 1	\geq Grade 2
CRS, % (n)	74.3% (26/35)	0% (0/35)
NT (ICANS), % (n)	0% (0/35)	0% (0/35)



Ph+ ALL

BCR::ABL oder IG/TR

Nicolas J Short. 551 A comprehensive analysis of PCR for BCR::ABL1 and next-generation sequencing (NGS)-based measurable residual disease (MRD) with Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL): Prevalence, association with transcript type, and clinical outcomes.



**A comprehensive analysis of PCR for
BCR::ABL1 and NGS-based MRD in Ph+ ALL:
prevalence, association with transcript type,
and clinical outcomes**

**M Maroun, H Kantarjian, N Jain, O Karrar, F Haddad, G Tang, S Loghavi, K Patel,
W Macaron, P Kebriaei, I Khouri, J Matthews, R Garris, F Ravandi, E Jabbour,
NJ Short**

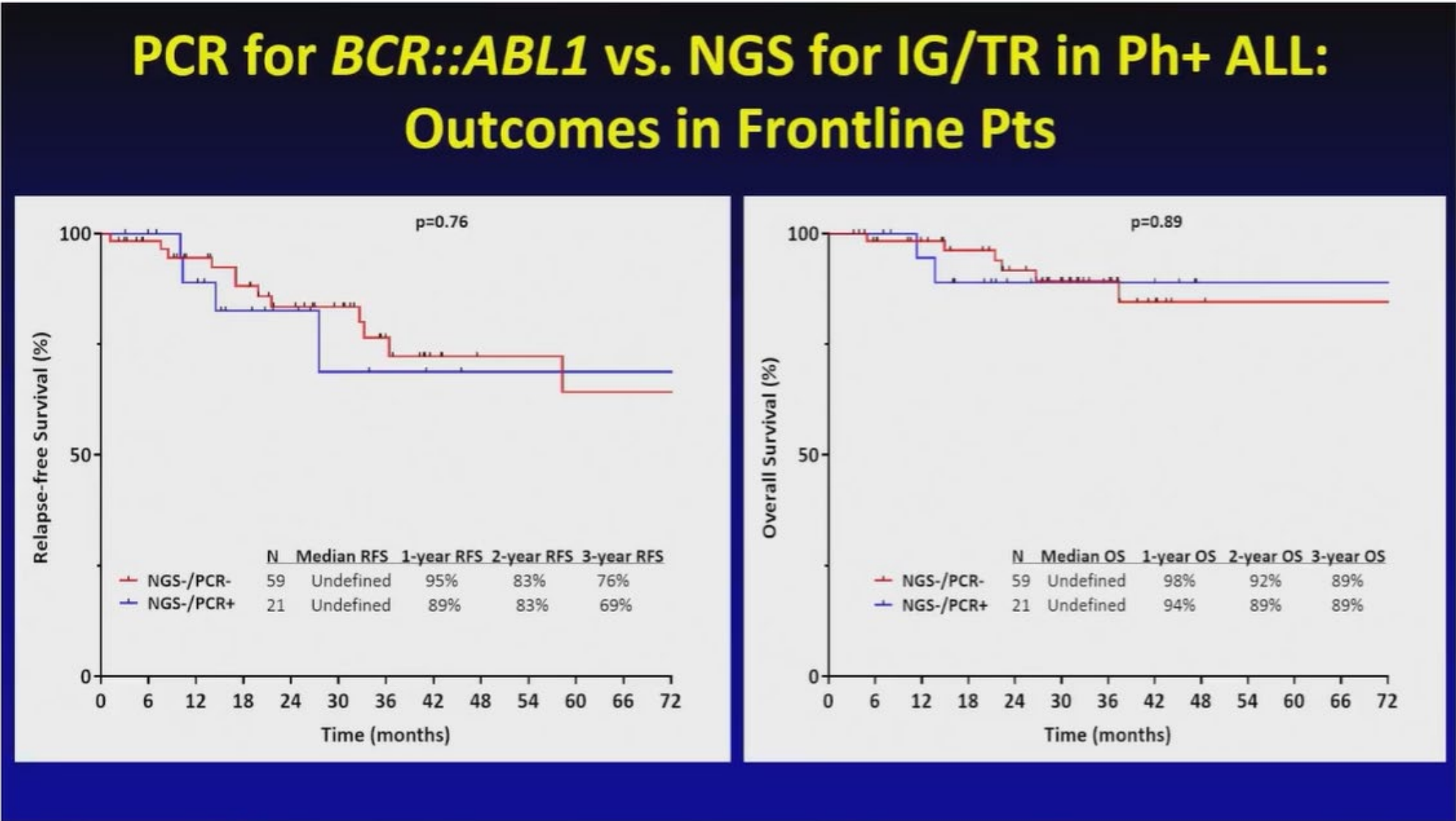
Department of Leukemia

The University of Texas MD Anderson Cancer Center, Houston, TX

Nicolas J

disease (MRD) with Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL): Prevalence, association with transcript type, and clinical outcomes.

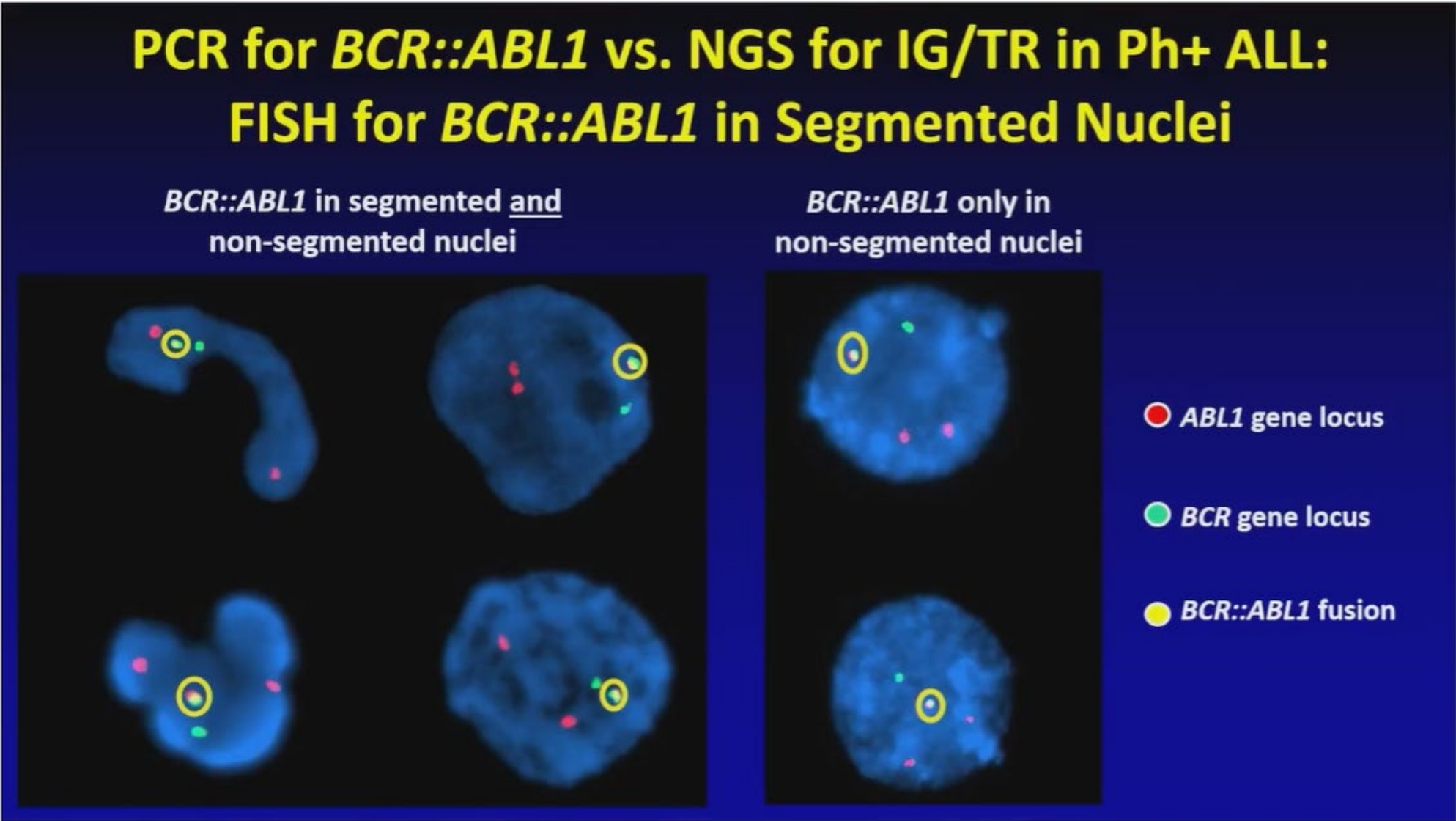




Nicolas J

disease (MRD) with Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL): Prevalence, association with transcript type, and clinical outcomes.





Nicolas J

disease (MRD) with Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL): Prevalence, association with transcript type, and clinical outcomes.



B-ALL



City of Hope

Ibrahim Aldoss

Novartis - Research Funding; Takeda - Consultancy (Includes expert testimony); Syndax - Consultancy (Includes expert testimony); Ascentage - Consultancy (Includes expert testimony); Janssen - Consultancy (Includes expert testimony); JAZZ - Consultancy (Includes expert testimony); Pfizer - Consultancy (Includes expert testimony); KITE - Consultancy (Includes expert testimony); AbbVie - Research Funding; JAZZ - Research Funding; Servier - Consultancy (Includes expert testimony); Adaptive - Consultancy (Includes expert testimony)

Ibrahim Aldoss, Xiuli Wang, Jianying Zhang, Min Guan, Ruby Espinosa, Mary C Clark, Vaibhav Agrawal, Andrew Artz, Nequine Sanani, Lior Goldberg, Cashmir Gephart, Stephanie Kasten, Dileshni Tilakawardane, Jamie R Wagner, Jinny Paul, Paul Koller, L Elizabeth Budde, Anthony S. Stein, Vinod Pullarkat, Amandeep Salhotra, Ahmed Aribi, Guido Marcucci and Stephen J. Forman

Division of Leukemia, Department of Hematology/HCT,
City of Hope, Duarte, CA

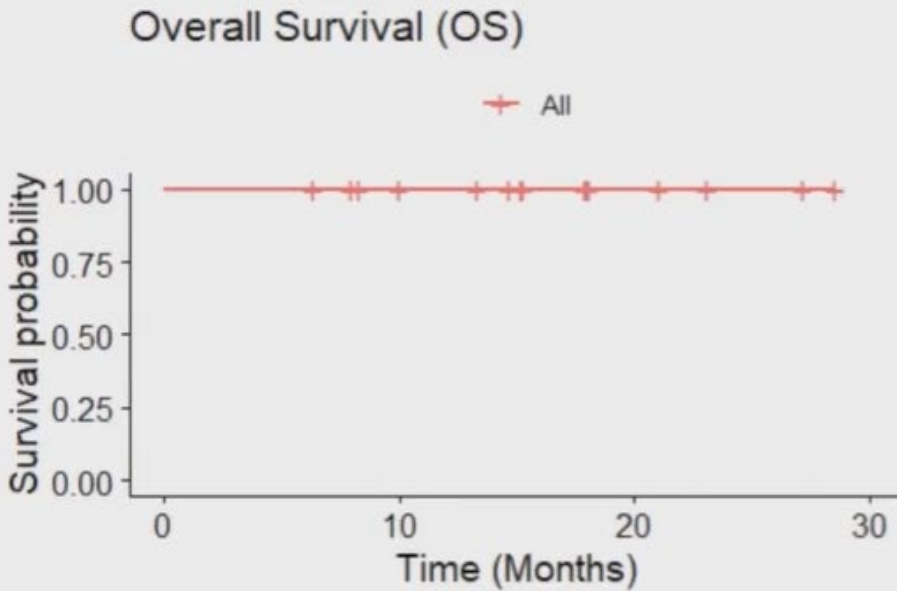
67th ASH® Annual Meeting

CD19-CAR T cell therapy as a definitive consolidation in older adults with B-ALL in CR1 is safe and induces durable MRD-remission.

Ibrahim Aldoss. 443 CD19-CAR T cell therapy as a definitive consolidation in older adults with b-ALL in CR1 is safe and induces durable MRD- remission.

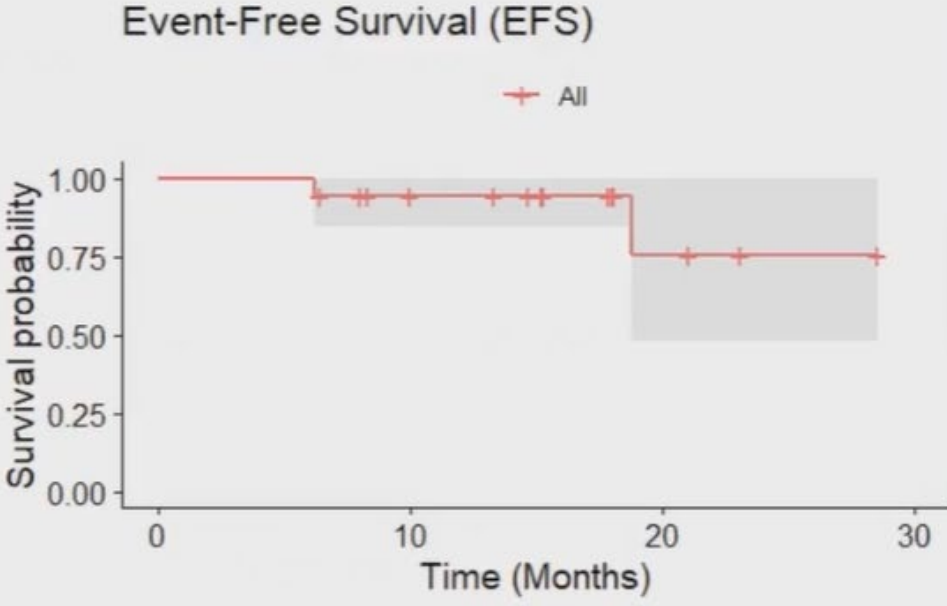


Survival outcomes



Number at risk

Time (Months)	All
0	18
5	15
10	12
15	6
20	2
25	0



Number at risk

Time (Months)	All
0	18
5	14
10	11
15	4
20	1
25	0



Ibrahim Aldoss. 443 CD19-CAR T cell therapy as a definitive consolidation in older adults with b-ALL in CR1 is safe and induces durable MRD- remission.



CAR T-Cell Therapy Demonstrates a Favorable Safety Profile in Older Adults in MRD- CR1

- No DLT was observed
- Grade 1 CRS= 13 (72%)
- **Grade ≥ 2 CRS= 0**
- **Any grade ICANS= 0**

R/R B-ALL study (same product/dose)

- **CRS grade ≥ 2 = 70%**
 - G3= 7%
- **Neurotoxicity (any grade) = 78%**
 - G ≥ 3 = 17%

- **Cytopenia**
 - Median time for ANC ≥ 1000 K/uL post CAR was 11 (6-86) days
 - Median time for platelet > 100 K/uL post CAR was 5 (0-461) days
- **No death on the study has been reported as the date of data cut off**

Aldoss I et al. Clin Cancer Res. 2023



Ibrahim Aldoss. 443 CD19-CAR T cell therapy as a definitive consolidation in older adults with b-ALL in CR1 is safe and induces durable MRD- remission.



B-ALL

Inotuzumab ozogamicin, dann Blinatumomab

Matthew Joseph Wieduwilt 444 Inotuzumab ozogamicin then blinatumomab for older adults with newly diagnosed, ph-negative, CD22-positive, B-cell acute lymphoblastic leukemia: Extended follow-up of alliance for clinical trials in oncology A041703 cohort 1 reveals durable remission and survival.



Inotuzumab ozogamicin then blinatumomab for older adults with newly diagnosed, Ph-negative, CD22-positive, B-cell acute lymphoblastic leukemia: Extended follow up of Alliance for Clinical Trials in Oncology A041703 cohort 1 reveals durable remission and survival

Matthew Wieduwilt , Jun Yin , Oudom Kour , Rebecca Teske, Wendy Stock, Carolin Escherich, Jun Yang, Zhenhua Li, Ken Byrd, Kimberley Doucette, James Mangan, Scott Hall, Alice Mims, Katarzyna Jamieson, Shira Dinner, Ali Bseiso, Georgia Giordano, Caner Saygin, Geoffrey Uy, Mark Litzow, Richard Stone



B-ALL

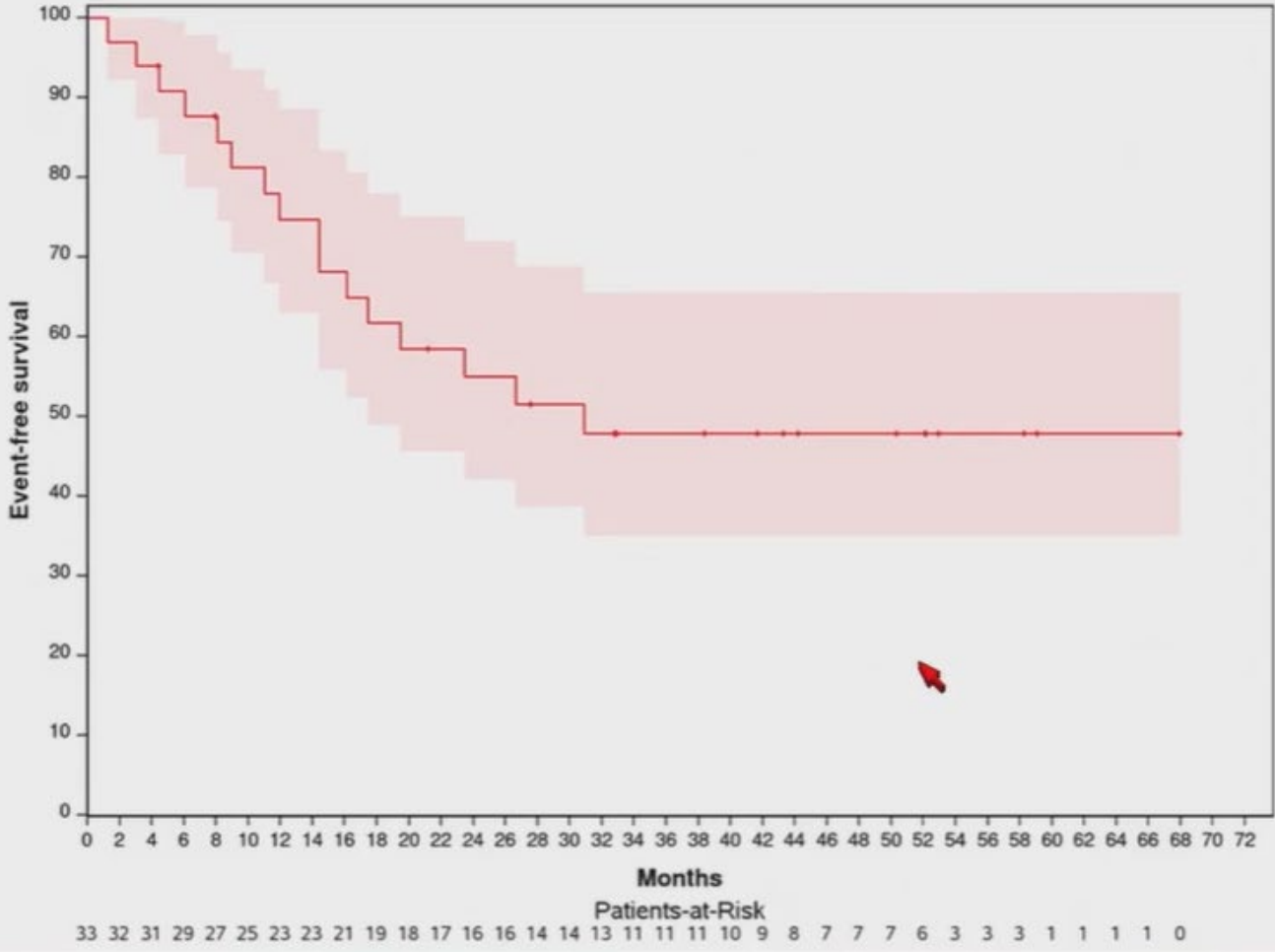
Inotuzumab ozogamicin, dann Blinatumomab

Event-free survival (refractory, morphologic relapse, death)

Median f/u (KM method):
45 months

3-yr EFS: 48%

Median EFS: 31 months

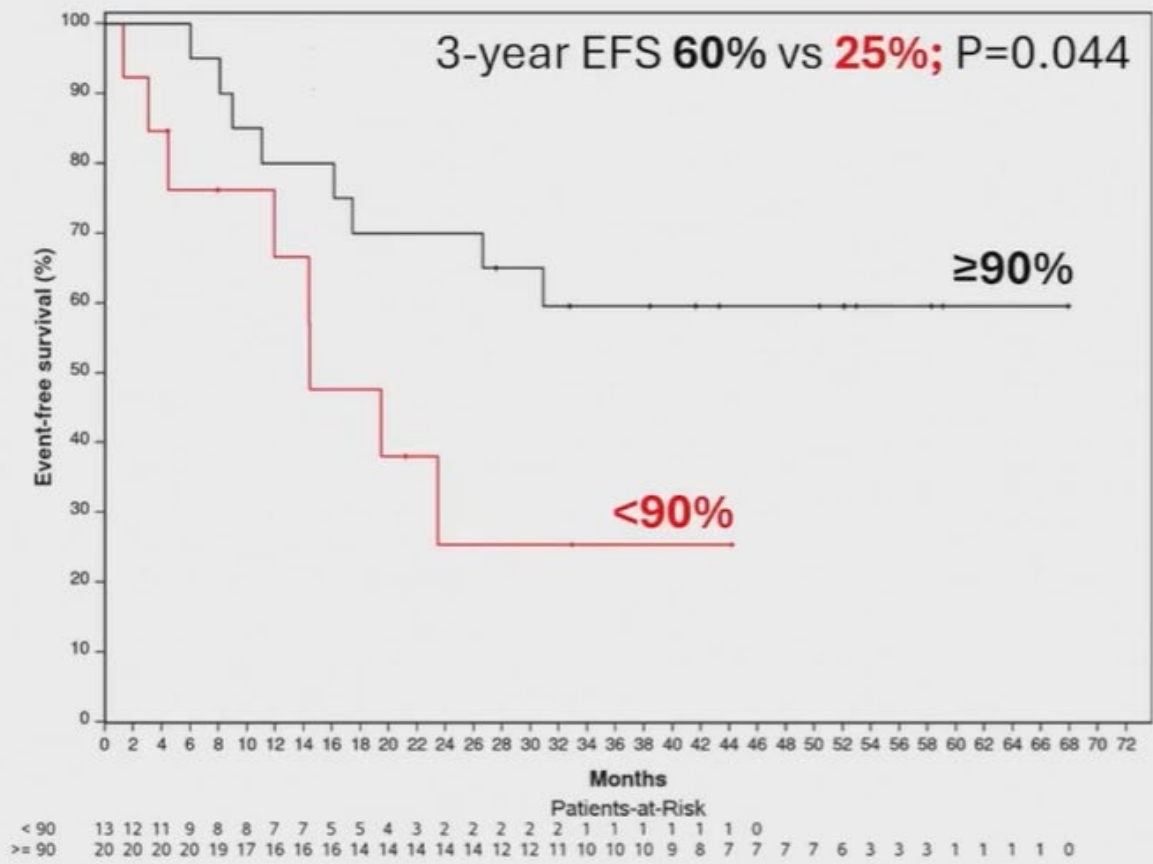


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B-ALL Inotuzumab ozogamicin, dann Blinatumomab

EFS by CD22 expression ($\geq 90\%$ vs $< 90\%$)

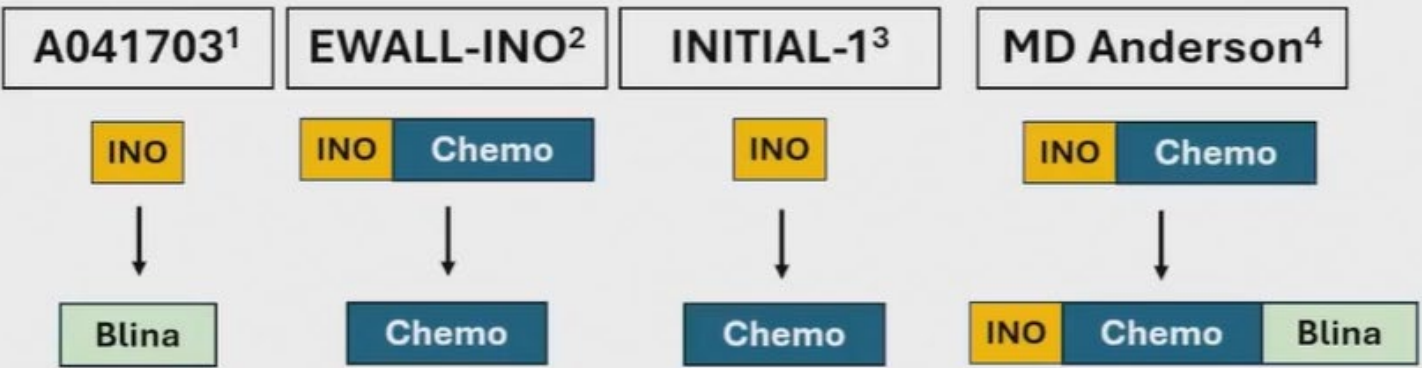


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B-ALL Inotuzumab ozogamicin, dann Blinatumomab

Inotuzumab ozogamicin Front-line Older Ph-negative B-cell ALL, 3 year



Age (Range)	71 (60-84)	68 (58-84)	64 (56-84)	68 (60-87)
EFS, 3 year	48%	40%	55%	47%
OS, 3 year	59%	48%	73%	55%
CI Relapse, 3 yr	38%	45%	27%	15%
CI NRM, 3 yr	9%	12%	17%	33%

1. Jabbour et al. *Lancet Haematology* 2023
2. Chevallier et al. *JCO* 2024

3. Stelljes et al. *JCO* 2024
4. Wieduwilt et al. *ASH* 2025

Matthew Joseph Wieduwilt 444 Inotuzumab ozogamicin then blinatumomab for older adults with newly diagnosed, ph-negative, CD22-positive, B-cell acute lymphoblastic leukemia: Extended follow-up of alliance for clinical trials in oncology A041703 cohort 1 reveals durable remission and survival.



r/r B-ALL



r/r B-ALL Blinatumomab oder Inotuzumab ozogamicin und SZT

Roberta S. Azevedo. 549 Predictors of survival with and without allogeneic stem cell transplantation after first salvage therapy with blinatumomab and/or inotuzumab ozogamicin for Relapsed/Refractory B-cell acute lymphoblastic leukemia.



r/r B-ALL Blinatumomab oder Inotuzumab ozogamicin und SZT

Predictors of Survival with and without Allo-SCT after First Salvage Therapy with Blinatumumab and/or Inotuzumab Ozogamicin for R/R B-cell ALL

Roberta S. Azevedo, Elias Jabbour, Nitin Jain, Fadi G. Haddad, Partow Kebriaei, Issa Khouri, Elizabeth Shpall, Richard Champlin, Jayastu Senapati, Eitan Kugler, Omer Karrar, Manuel Maroun, Rebecca Garris, Farhad Ravandi, Hagop Kantarjian, Nicholas J. Short

**Department of Leukemia
The University of Texas MD Anderson Cancer Center**

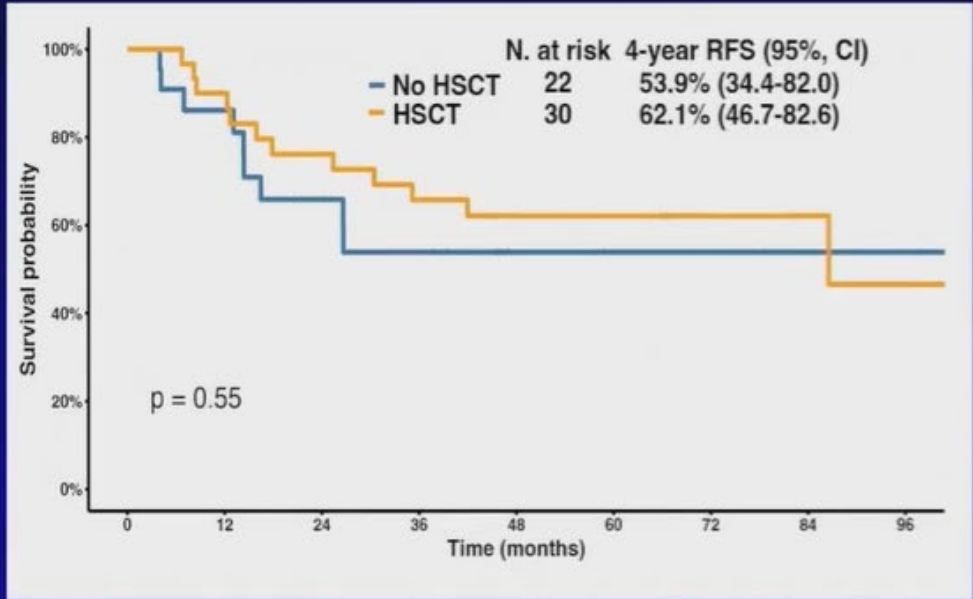
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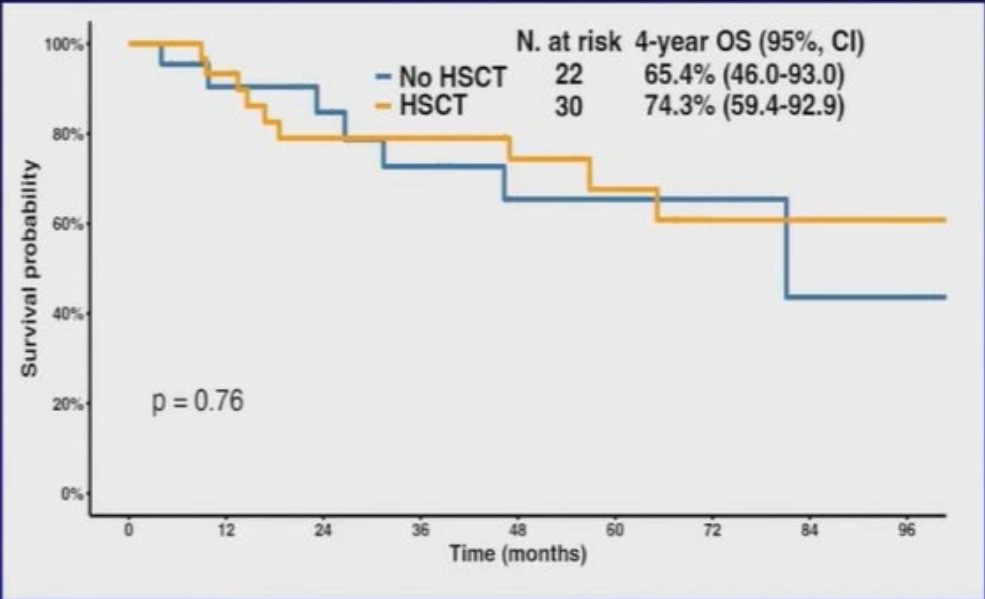
r/r B-ALL Blinatumomab oder Inotuzumab ozogamicin und SZT

Outcomes after First Salvage in R/R B-ALL: Survival of “Lower-risk” Patients Stratified by Allo-HSCT

Relapse-free Survival



Overall Survival



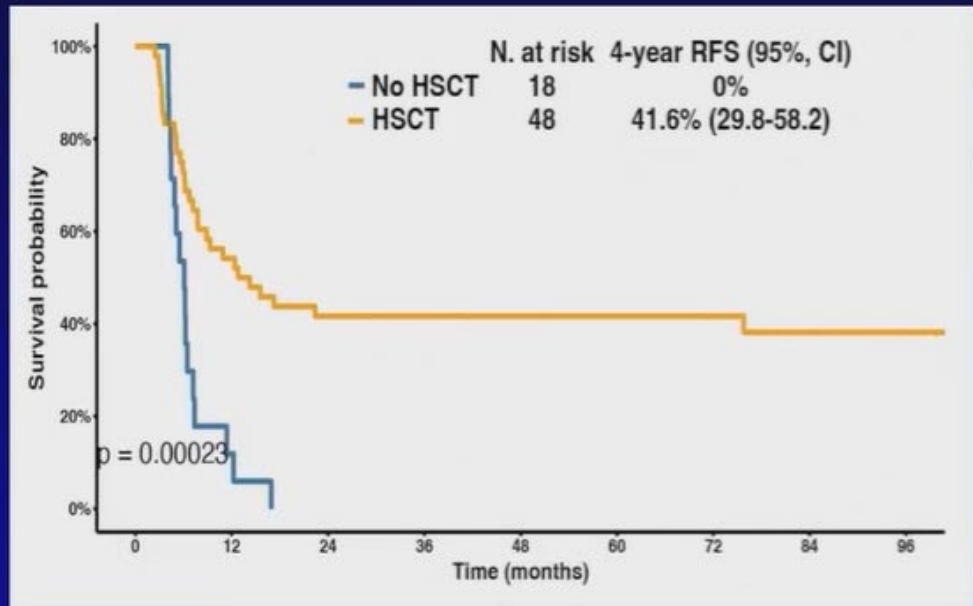
No benefit of allo-HSCT in pts with flow MRD negativity after cycle 1 and late relapse (i.e. CR1 \geq 12 months) or refractory disease



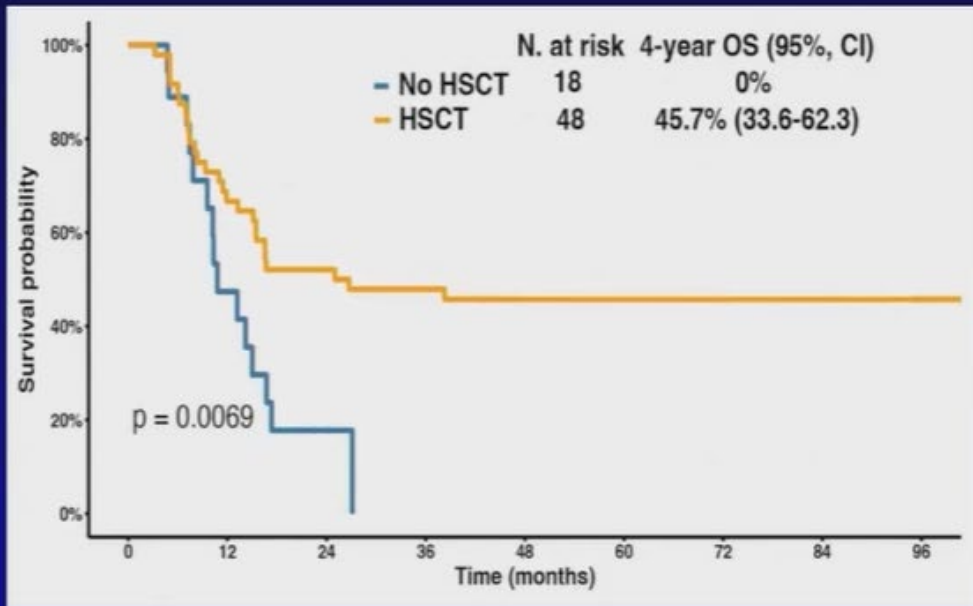
r/r B-ALL Blinatumomab oder Inotuzumab ozogamicin und SZT

Outcomes after First Salvage in R/R B-ALL: Survival of “Higher-risk” Patients Stratified by Allo-HSCT

Relapse-free Survival



Overall Survival



Allo-HSCT significantly improved outcomes in pts with flow MRD positivity after cycle 1 and/or early relapse (i.e. CR1 <12 months)



