Hot Topics in the Management of Acute Lymphoblastic Leukemia

w/ ASH 2021 Updates

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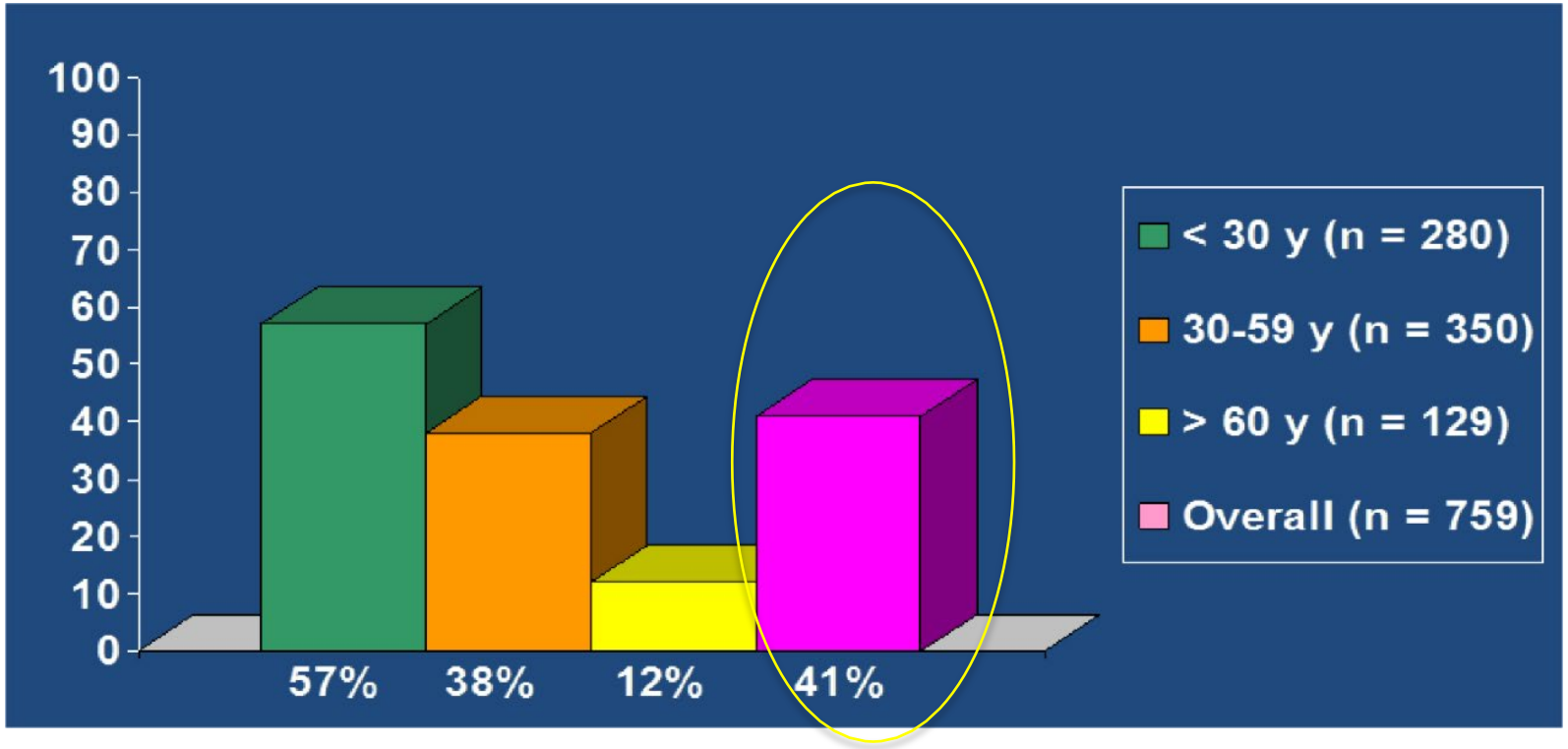
Historical Perspective- Adult Survival CALGB 1988-2006



Historical “One Size” fits all ages approach

Multi-agent chemotherapy +/- Cranial Irradiation + Maintenance (Predates TKI era)

Courtesy Ben Sanford, Richard Larson

The Modern Frontline ALL Approach is Tailored to the Specific Patient Population

Younger Adults	Older Adults (Ph-negative)	Adults (Ph-positive)
Pediatric Inspired Regimens	Adult Chemotherapeutics	Incorporation of TKI

ASH 2021 Updates

MRD-Adaptation

First Results of the Risk-Adapted, MRD-Stratified GMALL Trial 08/2013 in 705 Adults with Newly Diagnosed Acute Lymphoblastic Leukemia/Lymphoma (ALL/LBL)

Nicola Goekbuget, Matthias Stelljes, Andreas Viardot, Kathrin Nachtkamp, Björn Steffen, Nael Alakel, Max Topp, Boris Böll, Christoph Faul, Karsten Spiekermann, Knut Wendelin, Maher Hanoun, Ralph Wäsch, Joachim Beck, Sonja Martin, Vladan Vucinic, Claudia D. Baldus, Monika Brüggemann, Thomas Burmeister, Heike Pfeifer, Stefan Schwartz, Lena Baumann, Diana Tichy, Hubert Serve and Walter Fiedler

Lower Intensity CC + targeted

Fractionated Inotuzumab Ozogamicin Combined with Low-Intensity Chemotherapy Provides Very Good Outcome in Older Patients with Newly Diagnosed CD22+ Philadelphia Chromosome-Negative B-Cell Precursor Acute Lymphoblastic Leukemia: First Results from the EWALL-INO Study

A phase 2 prospective multicentric study (France, Czech Republic, Finland) ClinicalTrials.gov under the NCT number: NCT03249870.

Chevallier P, Leguay T, Kim R, Delord M, Doubek M, Huguet F, Cabannes A, Wartiovaara Kauto U, Saillard C, Raffoux E, Cluzeau T, Lepretre S, Thomas X, Berceanu A, Boissel N, Gardin C, Clappier E, Dombret H and Rousselot P.

Abstract 511

Reduced chemo vs Chemo-free approach?

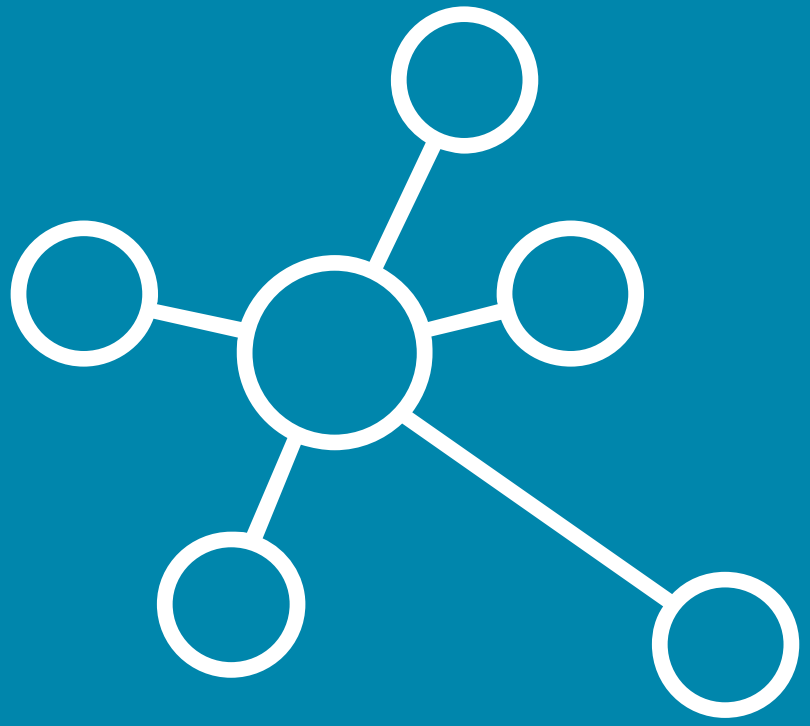
The omission of HD-ARAC during the consolidation schedules of Ph+ ALL patients treated with nilotinib and chemotherapy resulted in an increased risk of relapse despite non-inferior levels of BCR-ABL1 MRD response. First results of the randomized GRAAPH-2014 Study

A phase 3 prospective multicentric study (France, Switzerland, Belgium) from the GRAALL

Philippe Rousselot§, Yves Chalandon§ , Sylvie Chevret, Jean-Michel Cayuela, Francoise Huguet, Patrice Chevallier, Carlos Graux, Anne Thiebaut-Bertrand, Sylvain Chantepie, Xavier Thomas, Laure Vincent, Celine Berthon, Norbert Vey, Emmanuel Raffoux, Martine Escoffre-Barbe, Isabelle Plantier, Jean Pierre Marolleau, Pascal Turlure, Florence Pasquier, Amine Belhabri, Gabrielle Roth Guepin, Olivier Spertini, Veronique Lheritier, Emmanuelle Clappier, Nicolas Boissel and Hervé Dombret.

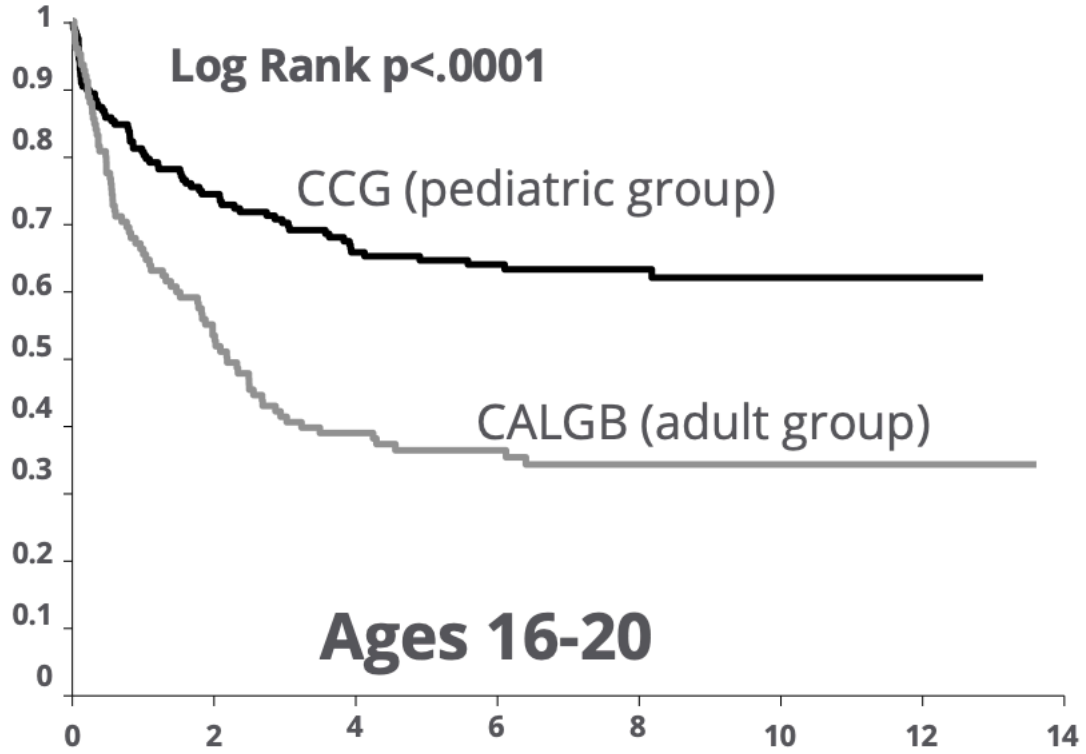
§ contributed equally.

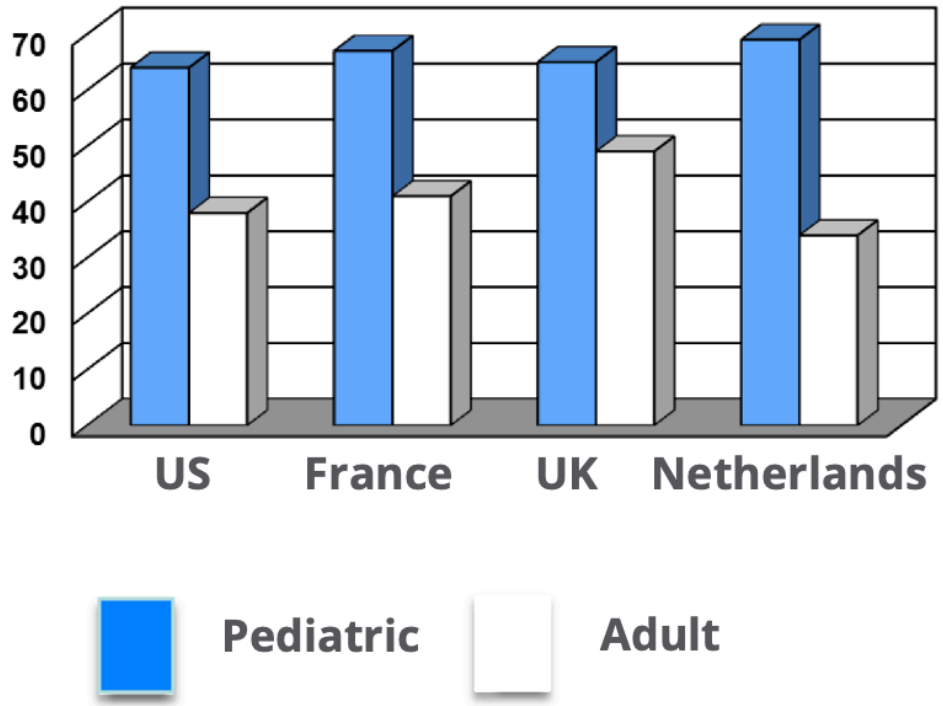
Abstract 512



ALL Treatment: Younger Adults

Survival Difference in AYA ALL: Historical difference between Peds vs Adult Tx?





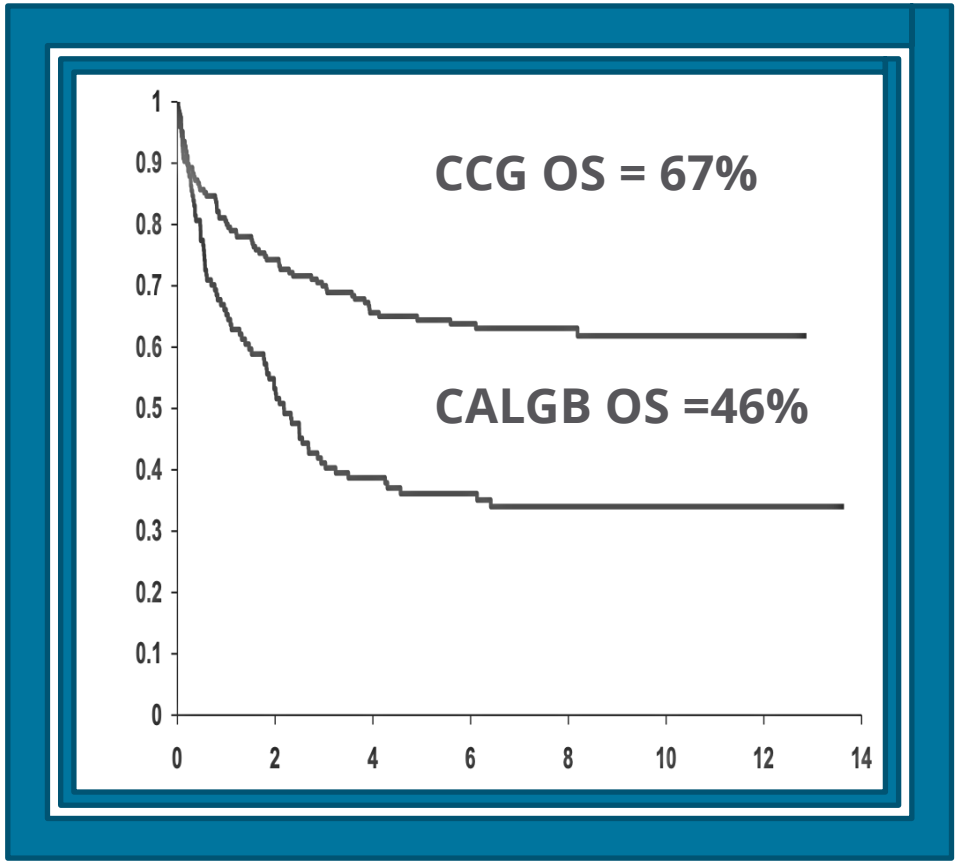
Survival of Adolescents/Young Adults (AYA)
Ages 16-20 years

Stock et al, Blood 112:1646, 2008

Young Adults: Treatment Standard has Changed

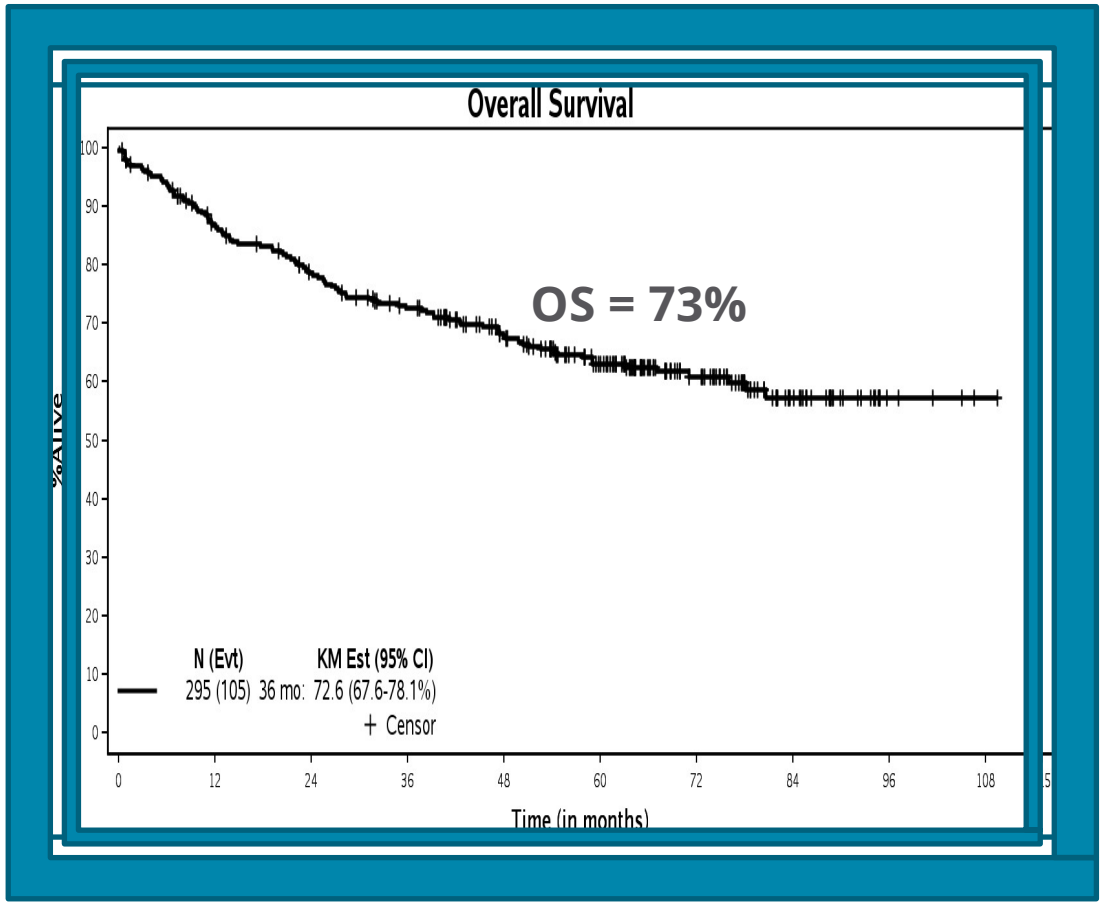
2000: Historical CALGB vs CCG

Age: 16-21 years



2019: CALGB 10403

Age: 16-21 years



Blood, 2008: 112, 1646-54 ; Blood, 2019: 133, 1548-1559

GMALL Trial 08/2013

First Results of the Risk-Adapted, MRD-Stratified GMALL Trial 08/2013 in 705 Adults with Newly Diagnosed Acute Lymphoblastic Leukemia/Lymphoma (ALL/LBL)

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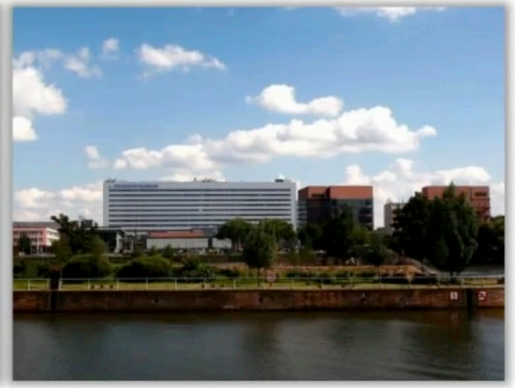


Adapted from Goekbuget et al, ASH 2021

GMALL Trial 08/2013

Planned patient number: 950
Planned recruitment: 5.5 years

Key Inclusion Criteria

1. **Newly diagnosed ALL or LBL**
2. **Age ≥ 18-55 years**
3. **Cytostatic pre-treatment with the exeption** of prephase, single application a cytostatic drug, steroids <= 7 days or up to 3 days hydroxyurea
4. **Severe uncontrolled complications of ALL or secondary diseases**

Primary Endpoint

Event-free survival compared to GMAL Trial 07/2003

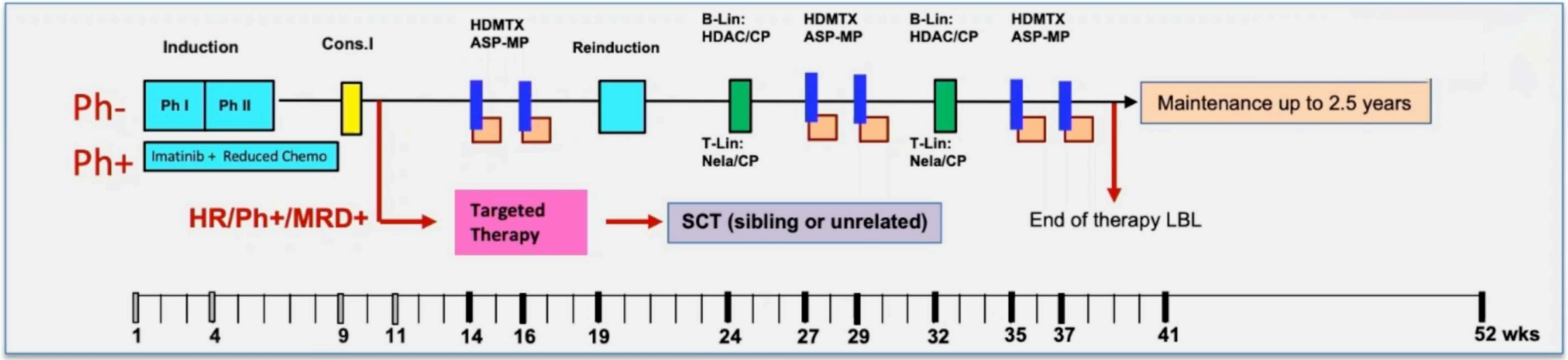
NCT02881086

Key Features

1. **Targeted therapy in molecular failure and molecular relapse**
2. **Risk adapted SCT indication**
3. **Reduction of SCT frequency in HR (Randomization II)**
4. **Optimized standard therapy**
   - **PEG-ASP intensification**
   - **Rituximab intensification**
   - **Optimized maintenance therapy**
   - **Increased time and dose intensity**
   - **New standard induction for Ph+ ALL**
5. **Nelarabine in 1st line for T-ALL**
6. **Reduction of local therapies (Randomization I)**
7. **Treatment optimization in LBL**

Adapted from Goekbuget et al, ASH 2021

GMALL Trial 08/2013



- BFM-based ‚pediatric' regimen
- Dexa during induction/consolidation I
- 9 x PEG-asparaginase (2000 - 1000 – 500 U/m²)
- 7x HDMTX (1.5 g/m²)
- Reinduction
- Risk-adapted SCT indication

Risk stratifikation: HR: >= 1 risk factor
- pro-B-ALL and / or KMT2A
- early / mature T
- B-precursor: WBC > 30.000
- No CR after induction I

+ Molecular Failure after Consolidation I

Targeted Consolidation II

SR/HR patients with molecular failure receive targeted consolidation II followed by SCT

B-precursor: **Blinatumomab**

T-ALL: **Nelarabin**

PH+ patients with molecular failure (>10-3) receive alternative TKI followed by SCT

(Amendment I)

Adapted from Goekbuget et al, ASH 2021

GMALL Trial 08/2013: Response after Consolidation I

Hematologic Response

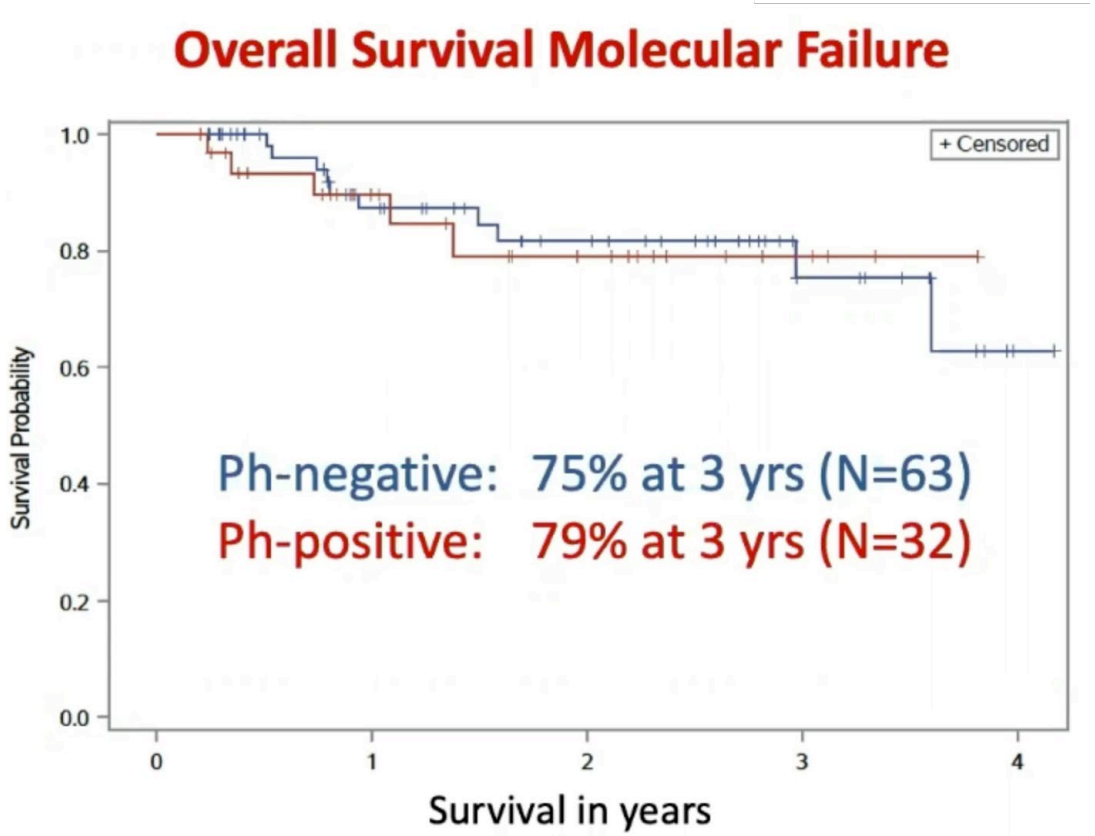
	Total	B-ALL Ph-	B-ALL PH+	T-ALL	B/T SR	B/T HR
N Evaluable	599	326	122	151	261	217
Hematologic CR	**93%**	**94%**	**95%**	**89%**	**96%**	**88%**
Early death	4%	5%	3%	5%	3%	7%
Failure/PR	3%	1%	2%	7%	1%	4%

Molecular Response

N Evaluable	542	306	116	120	248	178
Molecular CR	61%	65%	41%	67%	74%	54%
Molecular Failure	19%	18%	28%	11%	10%	25%
MRD Low Pos	14%	11%	17%	20%	12%	16%
Molecular NE	6%	6%	13%	3%	4%	5%
Molecular Response	**75%**	**76%**	**58%**	**87%**	**86%**	**70%**

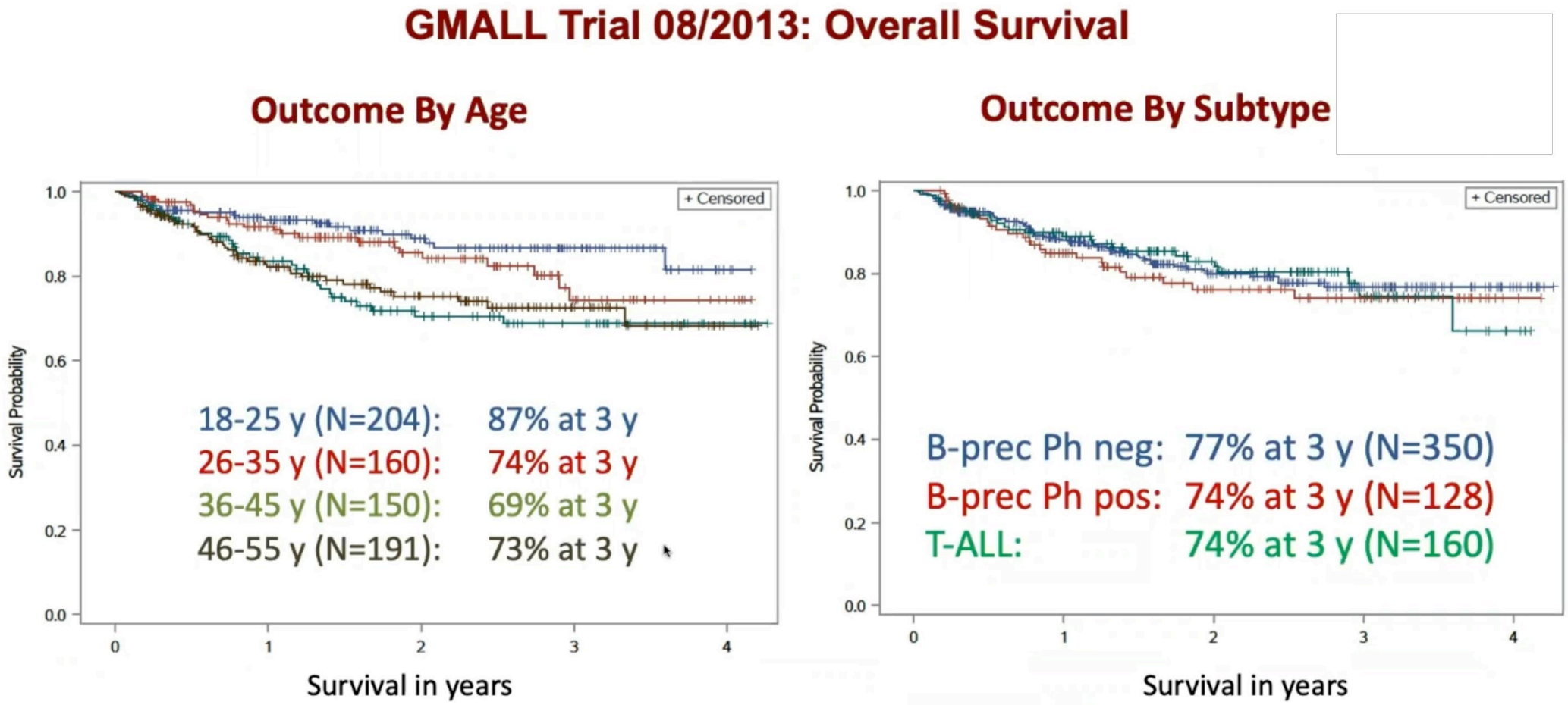
Adapted from Goekbuget et al, ASH 2021

GMALL Trial 08/2013: Targeted Consolidation II



Adapted from Goekbuget et al, ASH 2021

GMALL Trial 08/2013: Overall Survival

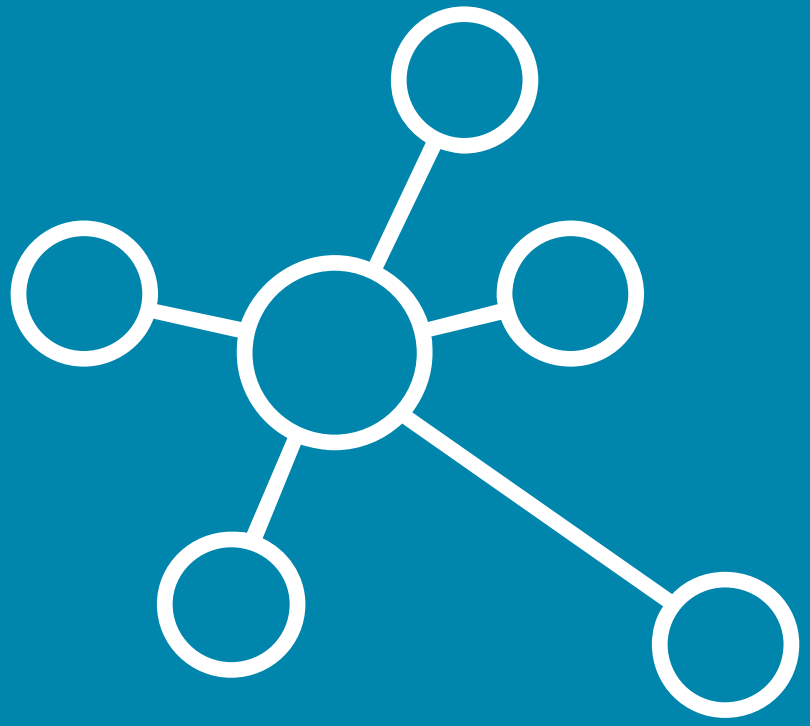


Adapted from Goekbuget et al, ASH 2021

GMALL Trial 08/2013: Conclusions

- Promising preliminary results in a large unselected patient cohort
- Pediatric-based regimen feasible and effective also in older adults up to 55years
- Intensive / individualized ASP therapy was feasible in a large multicenter setting
- MRD-based targeted treatment was realized in a high proportion of patients
- OS of MolFail pts promising with the combination of targeted therapy and SCT

Adapted from Goekbuget et al, ASH 2021



ALL Treatment: Ph-negative Older Adults

Poorer Chemotherapy Outcomes in Older Adults

	Age (Years)	N	CR (%)	Early Mortality (%)	OS (%)	Death in CR (%), *Among those achieving CR*
CALGB 9111	≥ 60	41	77	17	17% 3-yr	-
ECOG 2993	55-65	100	73	18	21% 5-yr	23
Hyper CVAD	≥ 60	122	84	10	20% 5-yr	34
DFCI Regimen*	51-75	30	67	13	52% 2-yr	-
GMALL*	55-85	268	76	14	23% 5-yr	6
PETHEMA ALLOLD07* (EWALL backbone)	>55	54	74	14	30% 2-yr	-

*Prospective trials for older adults.

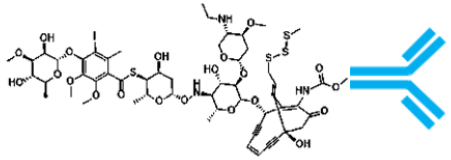
Larson et al. Blood 1998; 92: 1556-64; Sive et al. Br J Haematol 2012; 157:463-71; O'Brien et al. Cancer 2008; 113: 2097-101;
Fathi et al. Cancer 2016;122:2379-88; Gokbuget et al. Blood 2012;120:Abstract 1493; Ribera et al. Leuk Res 2016;41:12-20

Moving the Newer Agents Forward

Blinatumomab

- **CD19 - CD3 BiTE[1]**
- **CR:** 34%
- **ORR:** 44%
- **MRD-neg:** 76% of ORR
- **SCT:** 24%
- **Median OS:** 7.7 mos

Inotuzumab ozogamicin



- **CD22 Ab drug conjugate[2]**
- **CR:** 36%
- **ORR:** 81%
- **MRD-neg:** 78% of ORR
- **SCT:** 41%
- **Median OS:** 7.7 mos

1: Kantarjian et al, N Engl J Med 2017; 376:836-847 2: Kantarjian et al, N Engl J Med 2016; 375:740-53

Novel Approaches to Ph-ALL in Older Adults

N=70

MDACC

Reference	Regimen	Phase	N	Line	Age, y	Regimen-related deaths	Response	Survival
Kantarjian et al (2018)[22] Short et al (2020)[23] *NCT01371630*	IO + mini-hyper-CVD (Blina consolidation)	2	70	First	≥60	0% early mortality 34% mortality in remission	98% ORR 88% CR (96% MRD negative)	Continuous CR 3 years: 79% Median CCR NR OS 3 years: 56%
Stelljes et al (2020)[24] GMALL (INITIAL-1) *NCT03460522*	IO induction CC consolidation	2	36	First	≥56	0% early mortality	100% CR/CRi (78% MRD negative)	EFS 1 year: 87% (95% CI, 70–100) OS 1 year: 87% (95% CI, 70–100)
Jain et al (2019)[25] DFCI/MDACC IST *NCT03319901*	Venetoclax + mini-hyper-CVD	1b/2	19	R/R (8) First (11)	All ages ≥60	0% early mortality	91% CR (100% MRD negative)	—
Advani et al (2018)[26] SWOG 1318 *NCT02143414*	Blina induction Blina consolidation	2	29	First	≥65	0%	66% CR/CRi (92% MRD negative)	DFS 1 year: 56% (95% CI, 58–90) OS 1 year: 65% (95% CI, 43–80)
Alliance 041703 *NCT03739814*	IO induction Blina consolidation	2	—	R/R First	All ages ≥60	Results pending	Results pending	Results pending

*Results at most recent publication.

Blina, blinatumomab; CCR, continuous complete remission; CRi, complete remission with incomplete count recovery; NR, not reached.

Luskin, M. Hematology 2021.

Inotuzumab + Low-Intensity Chemo: MDACC

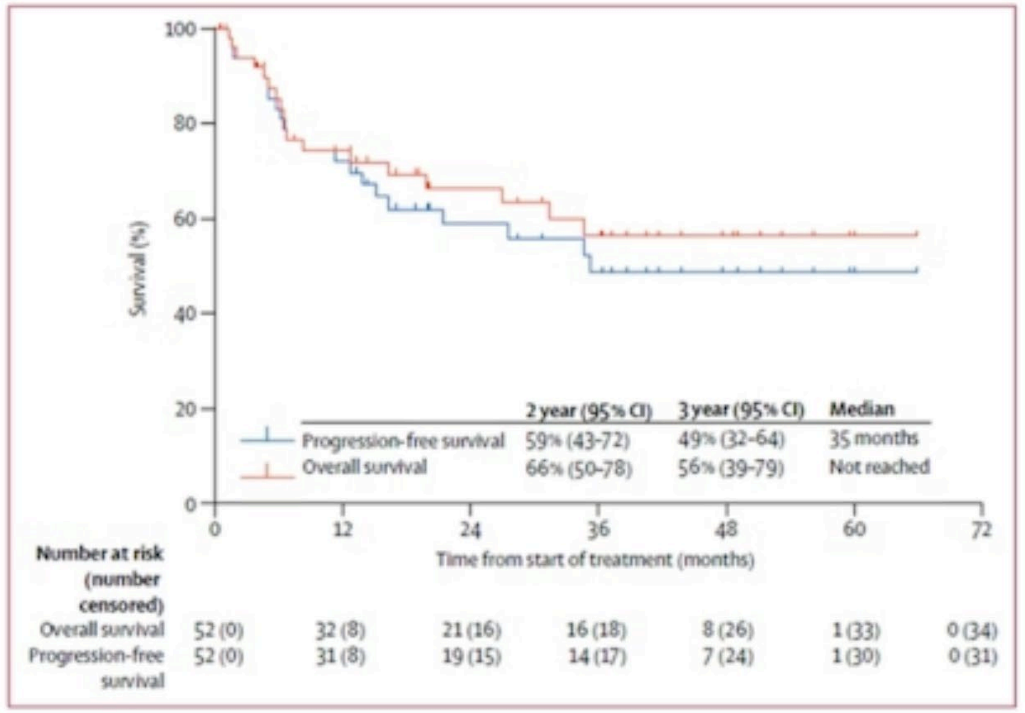
Inotuzumab ozogamicin in combination with low-intensity chemotherapy for older patients with Philadelphia chromosome-negative acute lymphoblastic leukaemia: a single-arm, phase 2 study

Hagop Kantarjian, Farhad Ravandi, Nicholas J Short, Xuelin Huang, Nitin Jain, Koji Sasaki, Naval Daver, Naveen Pemmaraju, Joseph D Khoury, Jeffrey Jorgensen, Yesid Alvarado, Marina Konopleva, Guillermo Garcia-Manero, Tapan Kadia, Musa Yilmaz, Gautam Borthakur, Jan Burger, Steven Kornblau, William Wierda, Courtney DiNardo, Alessandra Ferrajoli, Jovitta Jacob, Rebecca Garris, Susan O'Brien, Elias Jabbour

Lancet Oncol 2018; 19: 240-48

Mini-Hyper-CVD
+INO 1.3 mg/m² cycle 1
+INO 1 mg/m² >cycle 1

No anthracyclin
Rituximab if CD20+



Novel Approaches to Ph-ALL in Older Adults

N=90

ASH 2021

Reference	Regimen	Phase	N	Line	Age, y	Regimen-related deaths	Response	Survival
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EWALL-INO *NCT03249870*	IO + mild-intensity chemotherapy CC consolidation	2	—	First	≥55	—	—	—
Stelljes et al (2020)[24] GMALL (INITIAL-1) *NCT03460522*	IO induction CC consolidation	2	36	First	≥56	0% early mortality	100% CR/CRi (78% MRD negative)	EFS 1 year: 87% (95% CI, 70–100) OS 1 year: 87% (95% CI, 70–100)
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Luskin, M. Hematology 2021.

Inotuzumab + Low-Intensity Chemo: EWALL-INO Study

Fractionated Inotuzumab Ozogamicin Combined with Low-Intensity Chemotherapy Provides Very Good Outcome in Older Patients with Newly Diagnosed CD22+ Philadelphia Chromosome-Negative B-Cell Precursor Acute Lymphoblastic Leukemia: First Results from the EWALL-INO Study

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Chevallier P, Leguay T, Kim R, Delord M, Doubek M, Huguet F, Cabannes A, Wartiovaara Kauto U, Saillard C, Raffoux E, Cluzeau T, Lepretre S, Thomas X, Berceanu A, Boissel N, Gardin C, Clappier E, Dombret H and Rousselot P.

Abstract 511

Adapted from Cevallier et al, ASH 2021

Inotuzumab + Low-Intensity Chemo: EWALL-INO Study

Inclusion criteria

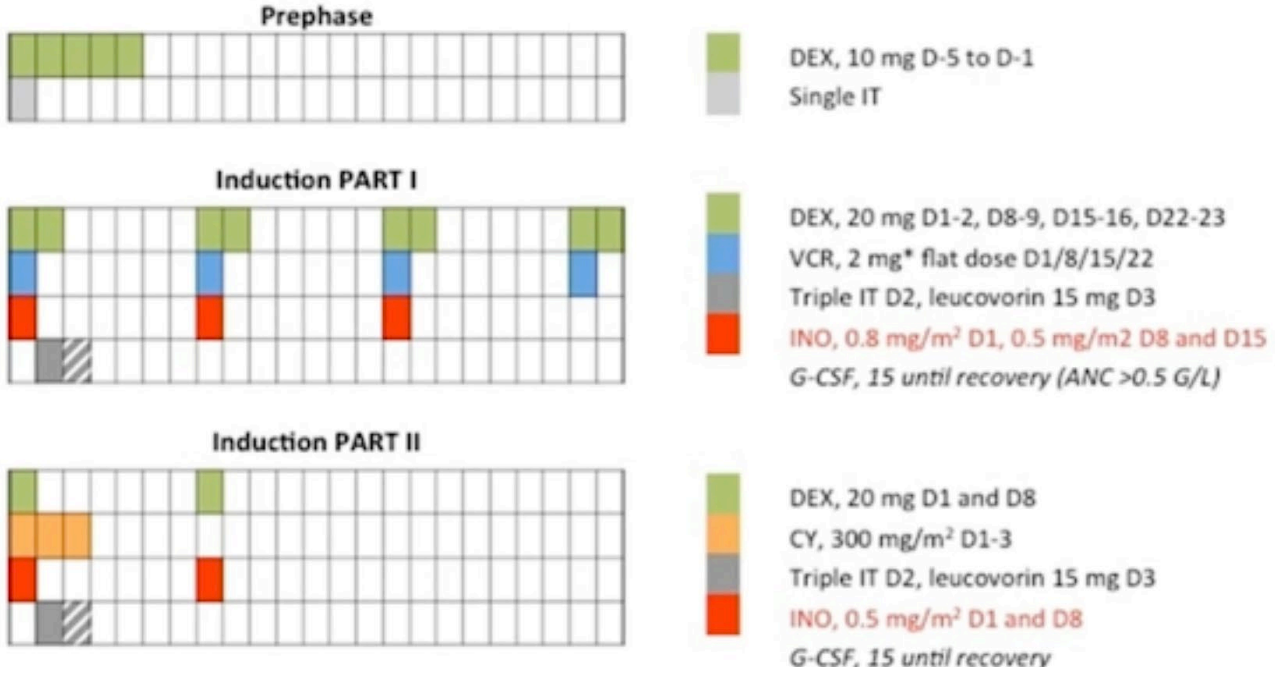
- Age ≥ 55 yo
- BCP ALL CD22+ (≥20% of CD22 positive blast cells)
- Philadelphia chromosome negative
- No central nervous system involvement
- Not previously treated
- ECOG status ≤ 2
- AST and ALT ≤ 2.5 N, Bilirubin ≤ 1.5 N, Creatinine ≤ 1.5 N
- Informed consent

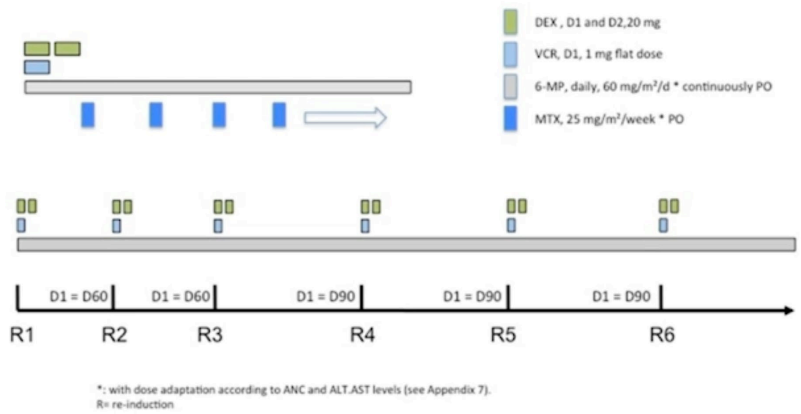
- **Primary endpoint**
  - 1-year OS observed in patients having received at least one day of INO

- **Secondary endpoints**
  - CR, death during induction, molecular response, leukemia free survival, relapse, impact of Ig-TCR MRD and other factors related to the patient and disease such as oncogenetics.

Adapted from Cevallier et al, ASH 2021

Backbone: 2 Inductions and 5 Doses of INO
Maintenance: POMP for 18 Months





No anthracyclin

No Ara-C

No Rituximab

Adapted from Cevallier et al, ASH 2021

EWALL-INO: Demographics (n=90)

Patients	
Gender: male/female	39 (43%)/51 (57%)
Median age: years (range)	69 (55-84)
Median WBC: Giga/L (range)	4.6 (0.5-601)
Median % of CD22+ expression (IQR)	86,5% (60.7-97)
Oncogenetics Low hypodiploidy/near triploidy Ph-like KMT2A rearrangement Others (including patients not evaluable)	 25 (28%) 10 (11%) 9 (10%) 46 (51%) (including 5 hyperdiploidy, 3 BCL2/MYC, 3 PAX5alt, 2 PAX5 P80R, 2 ZNF384, 1 iAMP21)
Median follow-up for alive patients: years (range)	1.18 (0.3-3.5)

Adapted from Cevallier et al, ASH 2021

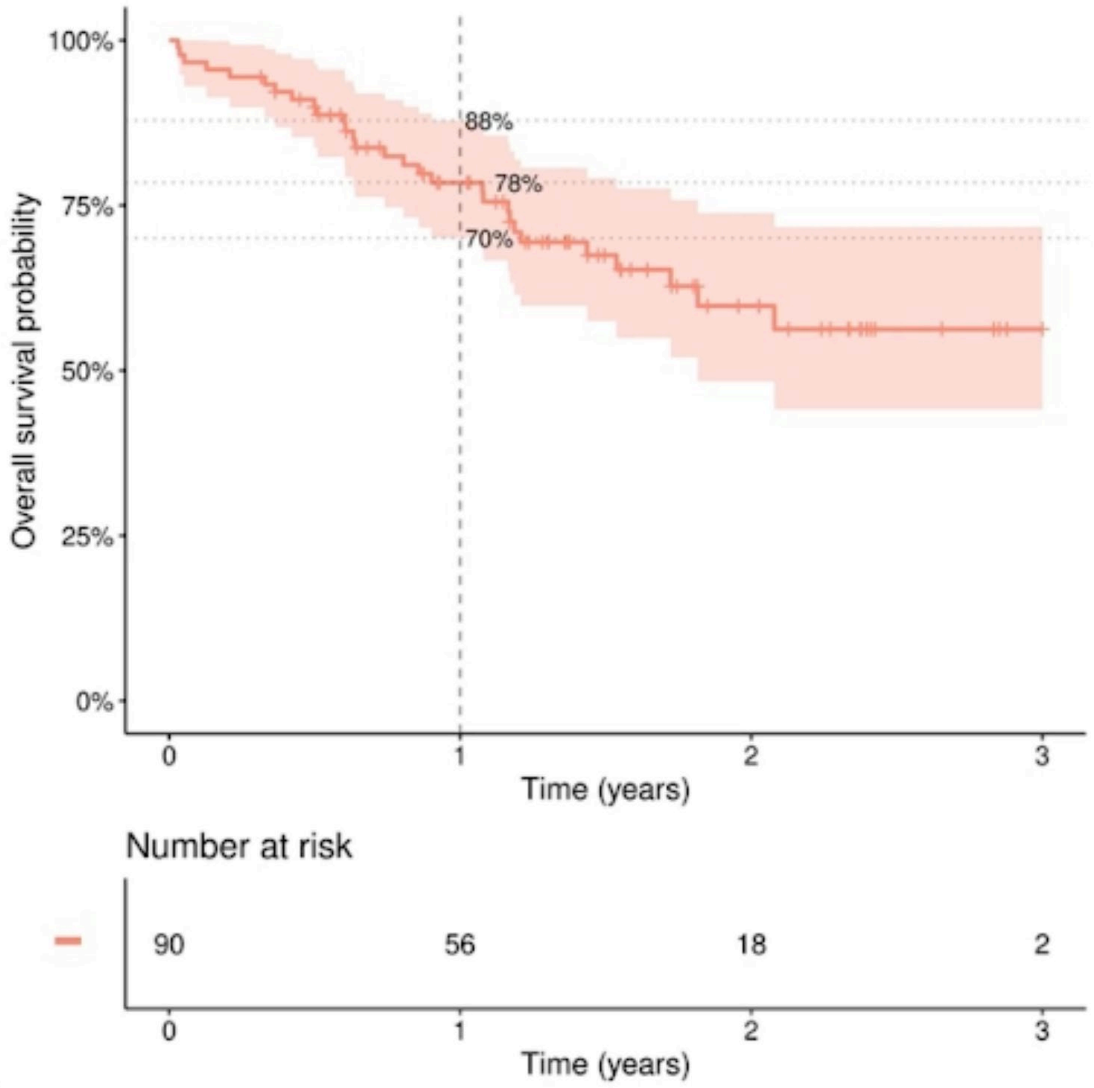
EWALL-INO: Efficacy

	CR rate	CR/CRp
After Ind 1	86.7% (n=78/90)	72/6
After Ind 2	88.8% (n=80/90)	72/8

Ig-TcR MRD post-ind 2 <10-4	N=80 RC/RCp 67 evaluable patients
Negative	49 (73%)
Positive	18 (27%)
Missing	13

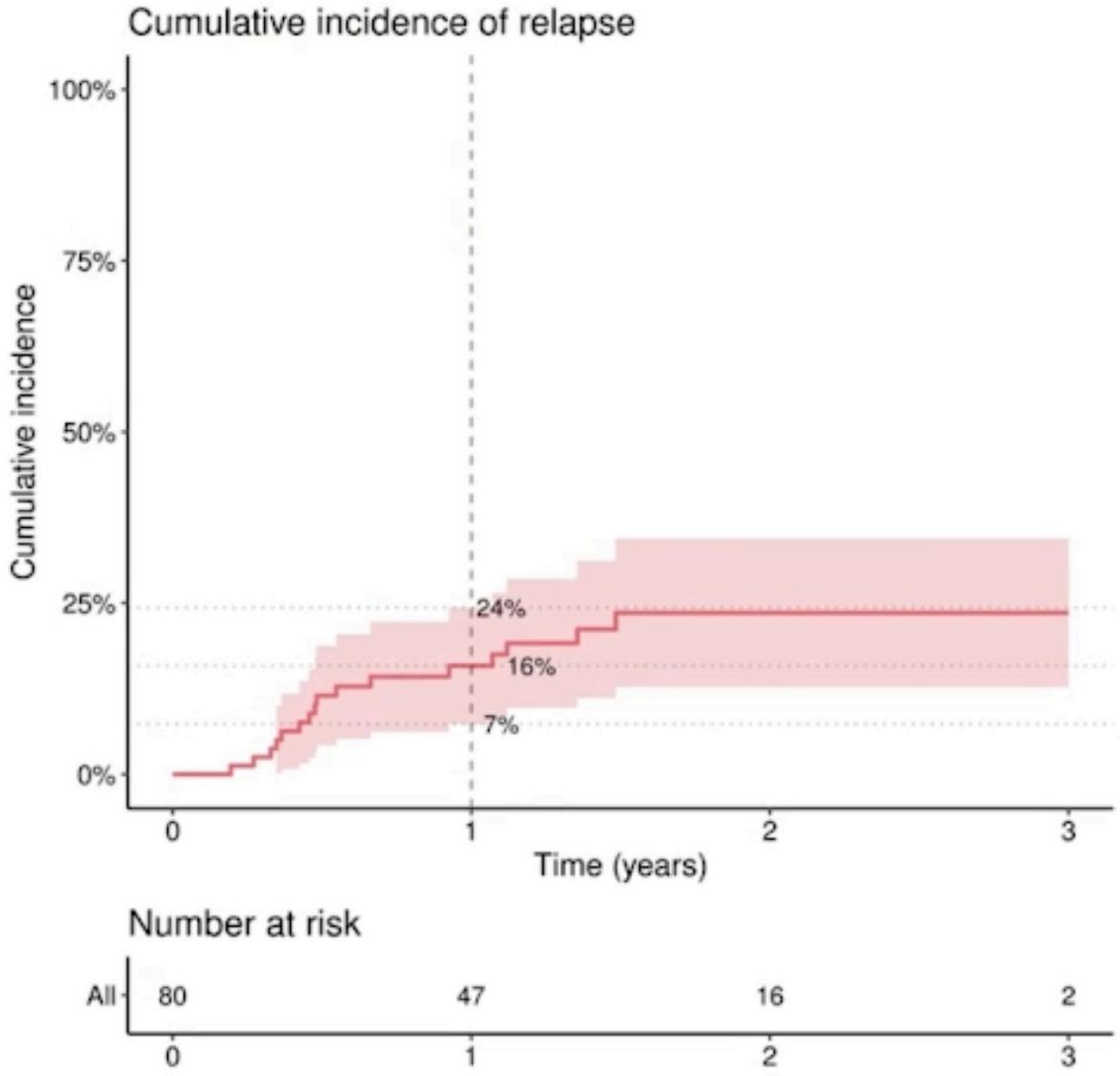
Adapted from Cevallier et al, ASH 2021

EWALL-INO: Survival – 78% @ 1 Year



Adapted from Cevallier et al, ASH 2021

EWALL-INO: Relapse Incidence 16% @ 1 Year



Adapted from Cevallier et al, ASH 2021

EWALL-INO: Conclusion

- Fractionated inotuzumab ozogamicin regimen at reduced dose (0.8/ - 0.5/ - 0.5/ - 0.5 / -0.5 mg/m²) combined with low-intensity chemotherapy is a very active and well tolerated frontline therapy for older patients with CD22+ Ph-neg BCP-ALL.

- Aged population (median age 69y)
- High CR rate : 88.8% after Ind 2
- Median survival not reached, 1 year OS : 78%
- Low SOS rate : 3 patients, 3.3%
- Few patients received Allo HSCT

- On going:
  - continuation of inclusions (130 patients expected)
  -Impact of prognostic factors including MRD

Adapted from Cevallier et al, ASH 2021

Treating PH- ALL in Older Adults

- Careful assessment of comorbidities and performance status.
- Formal geriatric assessment if able.
- Enroll in clinical trial of novel agent therapy, wherever possible.
- If treating with conventional chemotherapy, apply dose reductions as appropriate (particularly for asparaginase).
- Ensure CNS prophylaxis is administered per regimen.
- Monitor response per protocol and include MRD assessment (flow cytometry or molecular).
- Consider referring for allogeneic HSCT if fit and high-risk genetics or persistent MRD.

Luskin, M. Hematology 2021.

Treating PH- ALL in Older Adults: The Future

B-cell Ph-Negative Older Adult Approach (US)

<u>Randomized</u> phase 2
A042001 (Alliance/NCTN) planned
newly diagnosed older (50+)
Inotuzumab + mini-hyperCVD *vs* age-adjusted hyperCVAD

Establish a new "novel agent" standard of care

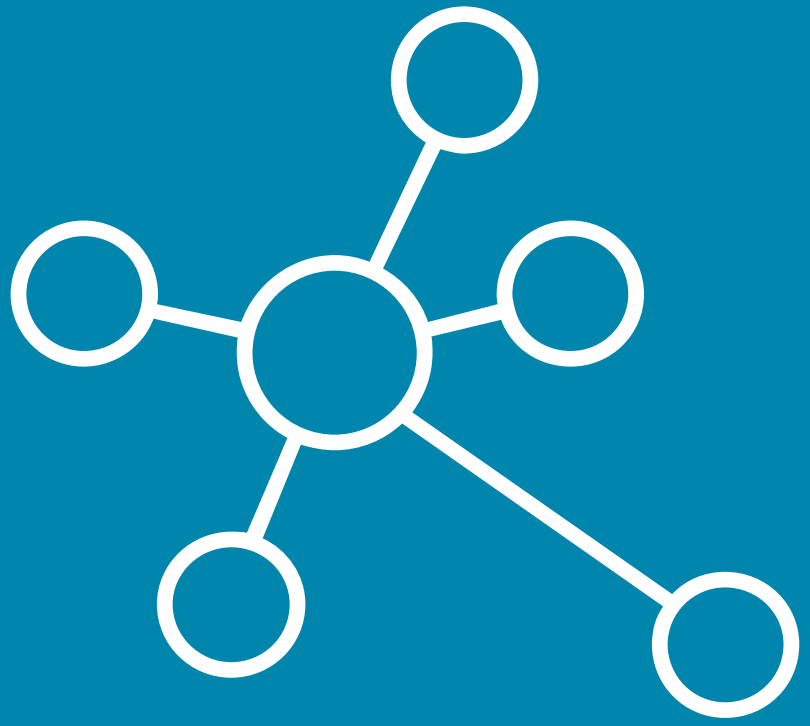
While

Single-arm phase 1 and phase 2s (Table 2)

Establish candidate competitors
Novel agent + dose-reduced conventional chemo
Chemotherapy free (1 or more novel agents)

<u>Randomized</u> phase 2 and 3 comparisons
A042001 (Alliance/NCTN) **winner**
Vs
Most promising candidate regimens

Luskin, M. Hematology 2021.



ALL Treatment: Ph+ Adults

Novel Approaches to Ph+ALL in Adults

The NEW ENGLAND JOURNAL of MEDICINE

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Dasatinib–Blinatumomab for Ph-Positive Acute Lymphoblastic Leukemia in Adults

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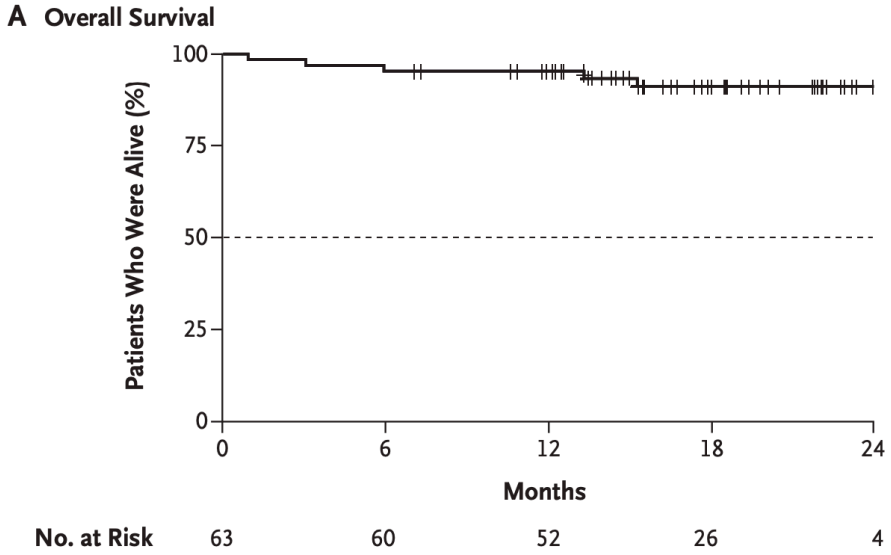
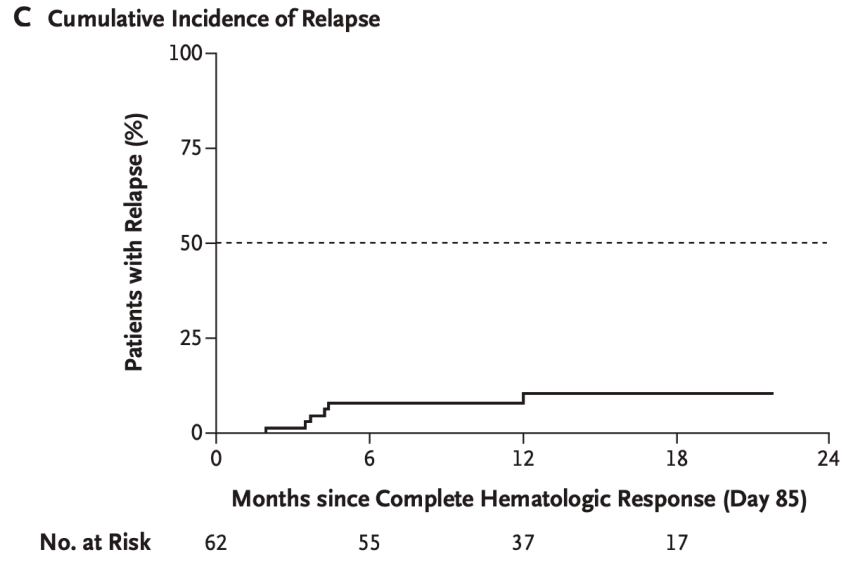




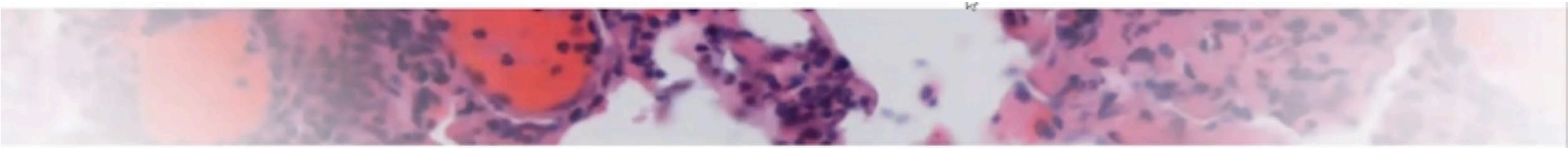
Foa, R et al NEJM 2020.

Novel Approaches to Ph+ALL in Adults

Reference	Regimen	Phase	N	Line	Age, y	Regimen-related deaths	Response	Survival
Rousselot et al (2016)[35] EWALL PH-01 *NCT028889777*	Dasatinib 140mg daily + low-intensity CC	2	71	First	≥55	4% (3/71) induction 12% (6/71) treatment-related mortality in CR	96% CR 65% 3-log reduction in *BCR-ABL*	27% (95% CI, 17–37) 5-year EFS 36% (95% CI, 25–47) 5-year OS 7 received HSCT 75% of relapses T315I
Ottmann et al (2018)[36] EWALL PH-02 *NCT028889777*	Nilotinib 400mg twice daily + low-intensity CC	2	79	First	≥55	1% (1/79) induction 11 died in CR (6 after HSCT)	94.4% CR	42% 4-year EFS 47% 4-year OS (61% transplanted, 39% nontransplanted) 24 received alloHSCT, 3 received autoHSCT
Vignetti et al (2007)[38] GIMEMA LAL0101-B	Imatinib 800mg daily + prednisone (induction protocol only)	2	29	First	>60	0% induction 2 died in CR	100% CR 1/27 CMR	48% (95% CI, 28–69) 1-year DFS 74% (95% CI, 54–94) 1-year OS
Foà et al (2011)[39] GIMEMA LAL1205	Dasatinib 70mg twice daily + prednisone (induction protocol only)	2	53	First	≥18 (22%> 60)	0% induction	100% CR 52.1% 3-log reduction in *BCR-ABL* by day 85	69% (95% 61–79) 20-month OS 51% (95% CI, 44–59) 20-month DFS
Martinelli et al (2017)[40] GIMEMA LAL1811 *NCT01641107*	Ponatinib 45mg daily + prednisone (induction protocol only)	2	42	First	>60 or unfit	0% induction 1 death in follow-up ponatinib	95.5% CR 45% CMR at 24 weeks	87.5% (95% CI, 76.5%-99.9%) 1-year OS
Luskin et al (2019)[42] DFCI IST *NCT03595917*	Dasatinib 140 + asciminib (dose escalation) (induction protocol only)	1	8	First	>50	0% induction	100% CR	Not reported
Foà et al (2020)[43] GIMEMA LAL2116 *NCT02744768*	Dasatinib 140 + prednisone Blinatumomab consolidation	2	63	First	≥18 (median 54)	1.6% induction (1 patient) No regimen related deaths in CR	95% CR	With median follow-up 18 months 95% (95% CI, 90–100) OS 88% (95% CI, 80–97) DFS
Wieduwilt et al (2018)[41] NCTN/Alliance 10701 *NCT01256398*	Dasatinib 140 + dexametha-sone induction CC consolidation Allo- vs autoHSCT	2	64	First	≥18 (median 60)	0% induction deaths	97% CR	43% 3-year DFS (55% allo, 43% auto, 46% chemo) 55% 3-year OS (63%≤60 years, 49%> 60 years) (75% allo, 71% auto, 55% chemo) Relapse 25% allo, 43% auto, 37% chemo

Luskin, M. Hematology 2021.

Ph+ ALL: GRAAPH-2014 – Nilotinib without HD-ARA-C



The omission of HD-ARAC during the consolidation schedules of Ph+ ALL patients treated with nilotinib and chemotherapy resulted in an increased risk of relapse despite non-inferior levels of BCR-ABL1 MRD response. First results of the randomized GRAAPH-2014 Study

A phase 3 prospective multicentric study (France, Switzerland, Belgium) from the GRAALL

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§ contributed equally.

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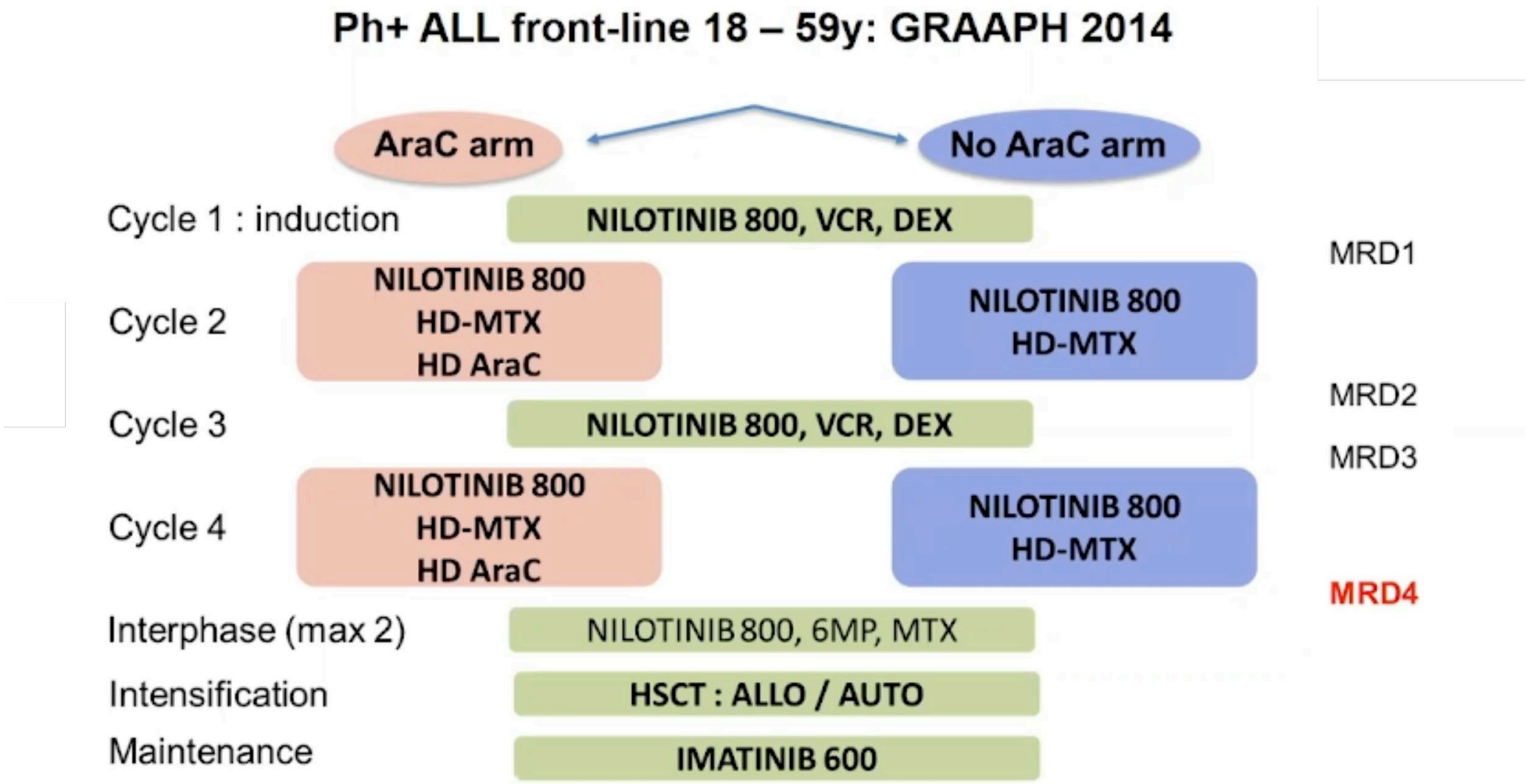
Adapted from Rousselot et al, ASH 2021

Ph+ ALL: GRAAPH-2014 – Nilotinib without HD-ARA-C



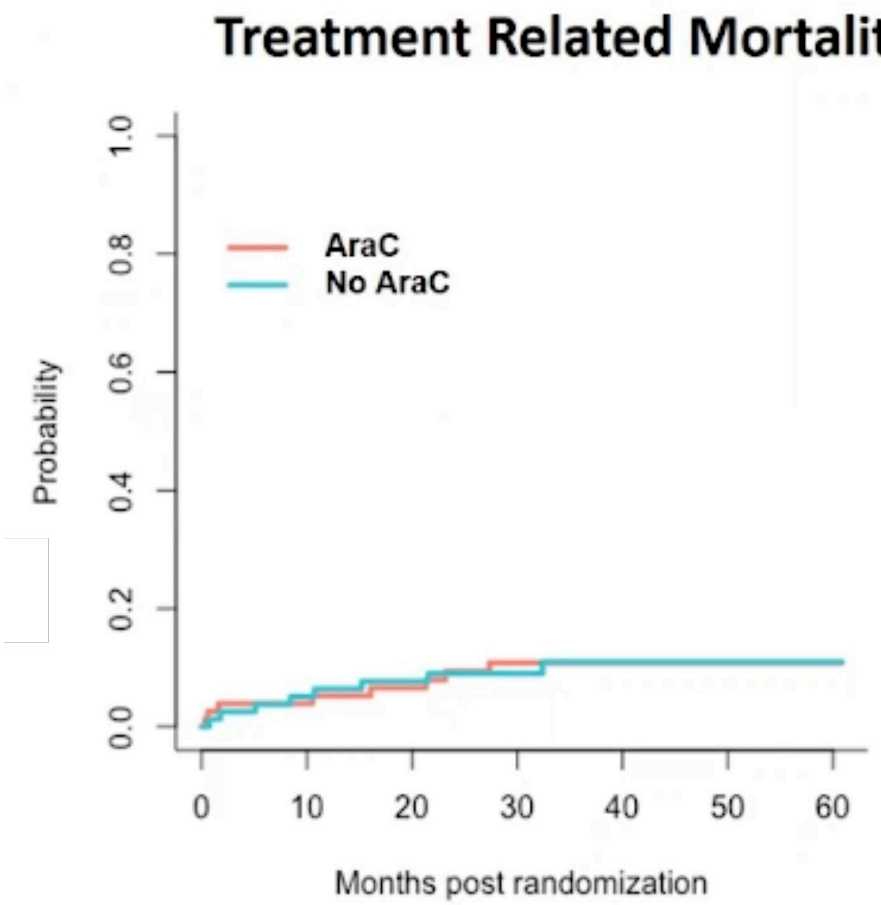
Adapted from Rousselot et al, ASH 2021

Ph+ ALL: GRAAPH-2014 – Nilotinib without HD-ARA-C

	Cytarabine 77 patients	No Cytarabine 79 patients
Age, median (IQR)	48 (39-54)	47 (39-53)
Male sex	49%	53%
ECOG 0-1 2-3	82% 18%	83% 17%
Medullary Blasts, median (IQR)	88% (71-94)	89% (82-93)
Transcript minor BCR Major BCR	70% 30%	71% 29%
IKZF1 deletion (153 pts evaluable)	91%	89%

Adapted from Rousselot et al, ASH 2021

GRAAPH-2014 Ph+ ALL: No Difference in CR Rate, TRM



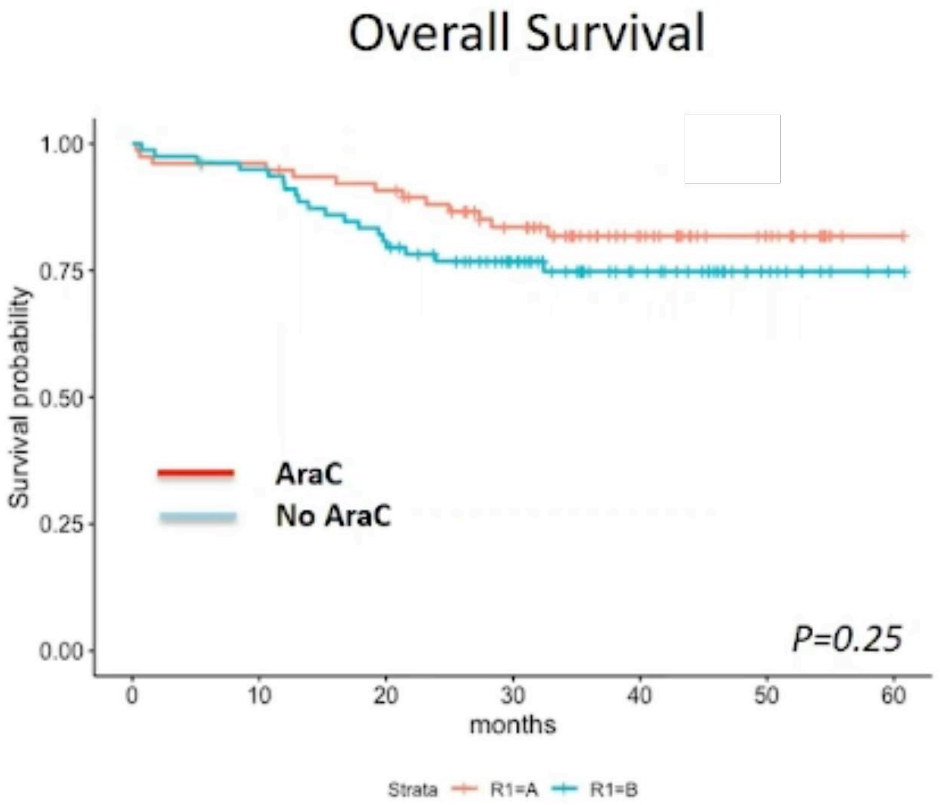
	Cytarabine 77 patients	No Cytarabine 79 patients	
CR rate after induction	94.2% (n=147)		
	93.5% (n=72)	94.9% (n=75)	*p=0,74*

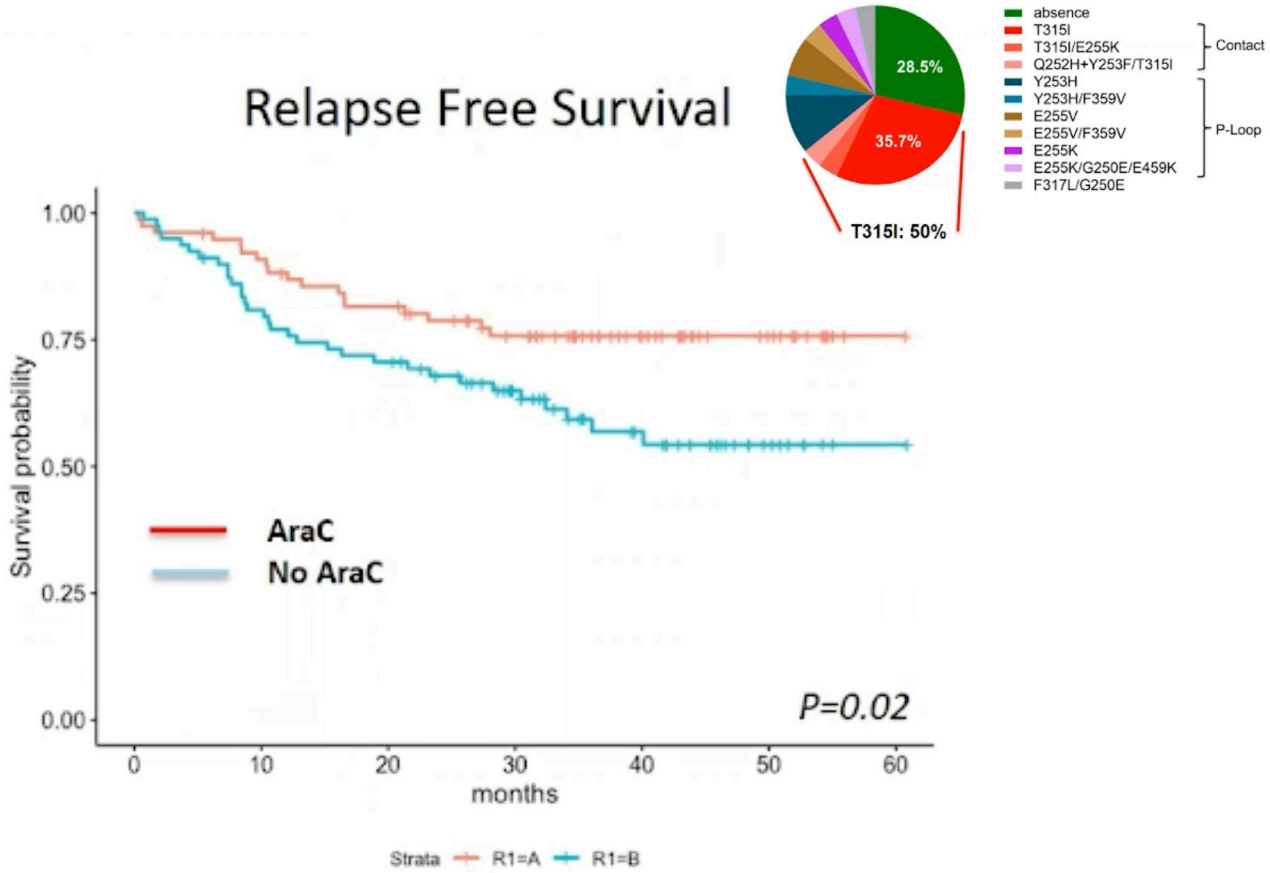
88% of the patients received the 4 planned cycles (n=137)

	Cytarabine 77 patients	No Cytarabine 79 patients
Main endpoint **MMolR at cycle 4**	**71.4%** (n=55)	**77.2%** (n=61)
Risk difference, 90%CI	+5.8% (-17.4 to 5.8)	

Adapted from Rousselot et al, ASH 2021

GRAAPH-2014 Ph+ ALL: Increase in Relapse without AraC





Adapted from Rousselot et al, ASH 2021

GRAAPH-2014 Ph+ ALL: Conclusions

- Nilotinib and chemotherapy is a safe regimen for Ph+ ALL in young adults
- The 3 years outcome looks promising (**78.2% OS and 66.5% RFS**)
- The responses rates were comparable between the two arms
  - Trend for a slower kinetic of BCR-ABL1 MRD when HD-AraC was omitted
- In the setting of combined "mild" chemotherapy and nilotinib, omitting HD-AraC was significantly associated with higher incidence of relapse.
  - A majority of relapses were associated with mutations (T315I : 50%)
- The negative impact of HD-AraC omission might be overcome by allogenic HSCT (contrary to autologous HSCT)
  - Our results suggest that not only BCR-ABL1 MRD but also an optimal combined therapy may determine the decision to proceed to allogenic HSCT. This hypothesis will be tested in the next GRAAPH 2022 study.

Adapted from Rousselot et al, ASH 2021

Novel Approaches to Ph+ALL in Adults / Older Adults: Ongoing Randomized Trials

Reference	Regimen	Phase	N	Line	Age, y	Regimen-related deaths	Response	Survival
NCTN/EA9181 *NCT04530565*	TKI + prednisone induction TKI + hyper-CVAD vs TKI + blinatumomab consolidation	3	—	First	≥18–75	Results pending	Results pending	Results pending
SWOG 1318 *NCT02143414*	Dasatinib + prednisone induction Dasatinib + blinatumomab consolidation	2	—	First	≥65	Results pending	Results pending	Results pending

*Results at most recent publication.

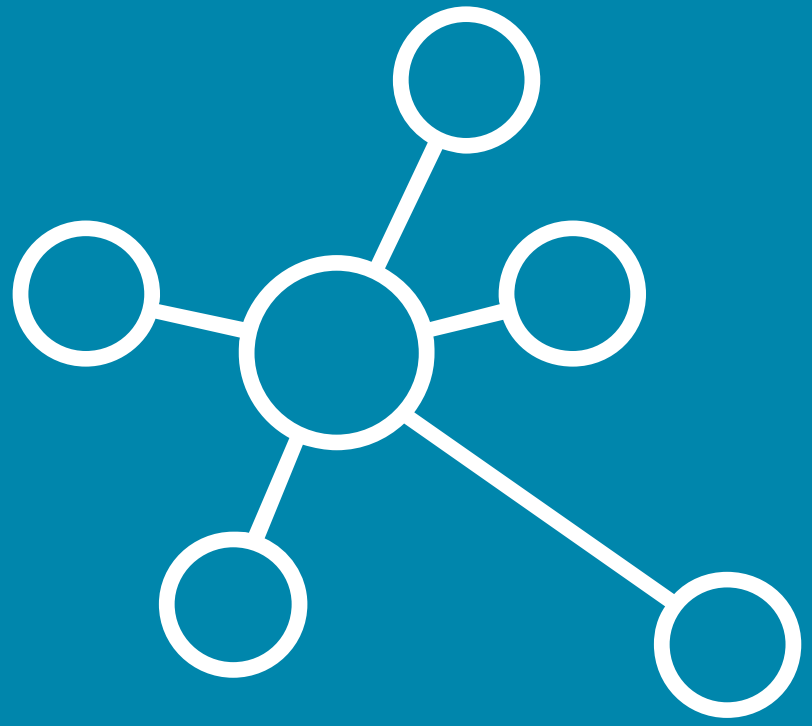
CMR, complete molecular response; DFS, disease-free survival; EFS, event-free survival.

Luskin, M. Hematology 2021.

Ph+ ALL Treatment in Older Adults

- Careful assessment of comorbidities and performance status.
- Formal geriatric assessment if able.
- Enroll in clinical trial of novel agent therapy, wherever possible.
- I prefer a chemotherapy-free TKI-based induction using imatinib or dasatinib, or follow published regimen (Table 3).
- Ensure CNS prophylaxis is administered per regimen.
- Monitor response per protocol and include MRD assessment (BCR-ABL transcript).
- Escalate treatment (later-generation TKI or additional novel agents) if inadequate response.
- Refer for consideration of allogeneic HSCT if fit.

Luskin, M. Hematology 2021.



Thank you for your attention!