



9th EDITION

Highlights from EHA

9th Edition, Firenze 2016

ALL: HOT ISSUES



8th Edition, Firenze 2015 ALL: HOT ISSUES



Highlights from EHA

9th Edition, Firenze 2016

ALL: HOT ISSUES

- Ritenete i risultati dello studio Inno-Vate convincenti per la rapida introduzione di Inotuzumab-Ozogamicin nella pratica clinica ?
- Qual è il timing ideale dell'impiego di Blinatumomab nella ALL ?
- Quale età e quali comorbidità vanno considerate nell'approccio "pediatric-like" nella ALL ?

Highlights from EHA

7th Edition, Firenze 2014

ALL: HOT ISSUES

HOT ISSUES

- Should Ph-like ALL considered as a separate entity in the clinics?
- Should IKZ1 mutations be considered in the prognostic stratification of ALL ?

- Inglobato nella strategia terapeutica front-line delle LA Ph+
- Precoce impiego se persistenza/ricomparsa di MRD
- Utilizzo precoce alla recidiva
- Bridge to transplant per i pazienti eligibili x ABMT

- Has IGH@19 a role in the treatment of Ph+ ALL ?



Highlights from EHA

8th Edition, Firenze 2015

ALL: HOT ISSUES

- Is it the time for a new integrated/prognostic classification (MOL/GEN BASED) in ALL (either for children and adults?)
- Which patients should receive CART therapy?
- Which is the role of new monoclonal antibodies (Blinotumumab, Inotuzumab-GO) in the treatment of ALL?



LAL: Report del gruppo di lavoro

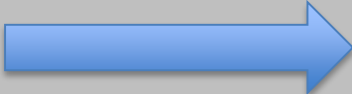
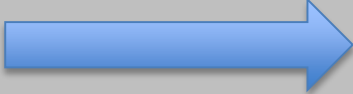
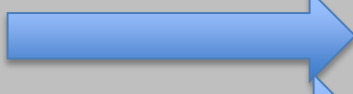
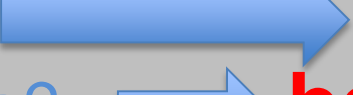
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Highlights from EHA

8th Edition, Firenze 2015

ALL: HOT ISSUES

- Is it the time for a new integrated/prognostic classification (MOL/GEN BASED) in ALL (either for children and adults?)
 - in tutti i pazienti?  **sì**
 - in che contesto (a casa propria o nel contesto di una rete)?  **sì**
 - quali indagini?  **rete, centralizzazione!**
 - hanno una ricaduta clinica?  **tutte!**
 - cosa facciamo a casa nostra?  **sì (bcr/abl)**
 -  **bcr/abl-Flow**

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Highlights from EHA

8th Edition, Firenze 2015

ALL: HOT ISSUES

Which patients should receive CART therapy?

Nessuno del gruppo ha esperienza (né altri in Italia)

- *consolidamento nell'alto rischio al posto del TMO?*
- *gli MRD+?*
- *R/R?*
- *nei R/R dopo Blinatumumab?*

Highlights from EHA

8th Edition, Firenze 2015

ALL: HOT ISSUES

Which is the role of new monoclonal antibodies (Blinatumumab, Inotuzumab-GO) in the treatment of ALL?

Blinatumumab e Inotuzumab-GO?	BLINA (per ora)
prima linea?	no (per ora)
in che contesto?	
- MRD+?	sì
- ricaduti?	sì
- sia per Ph- che per Ph+	si



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Highlights from EHA

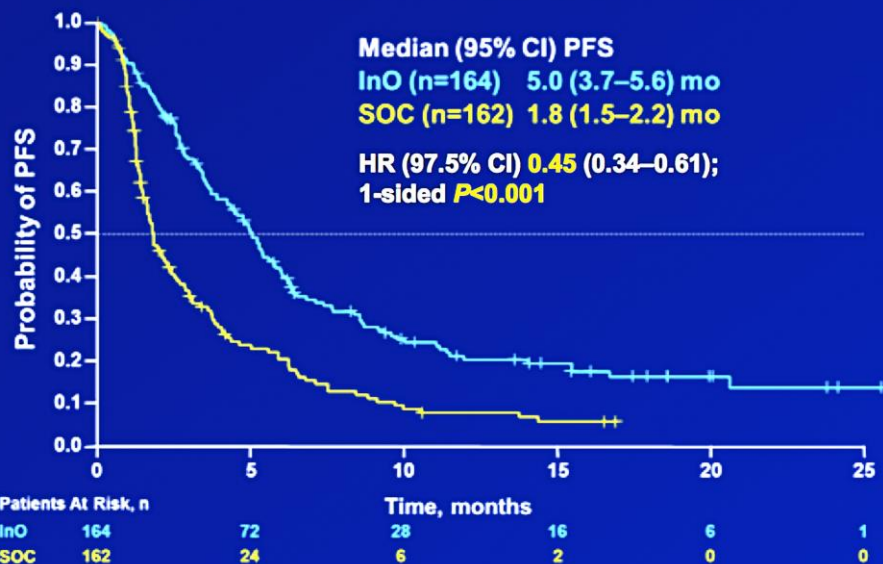
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ALL: HOT ISSUES

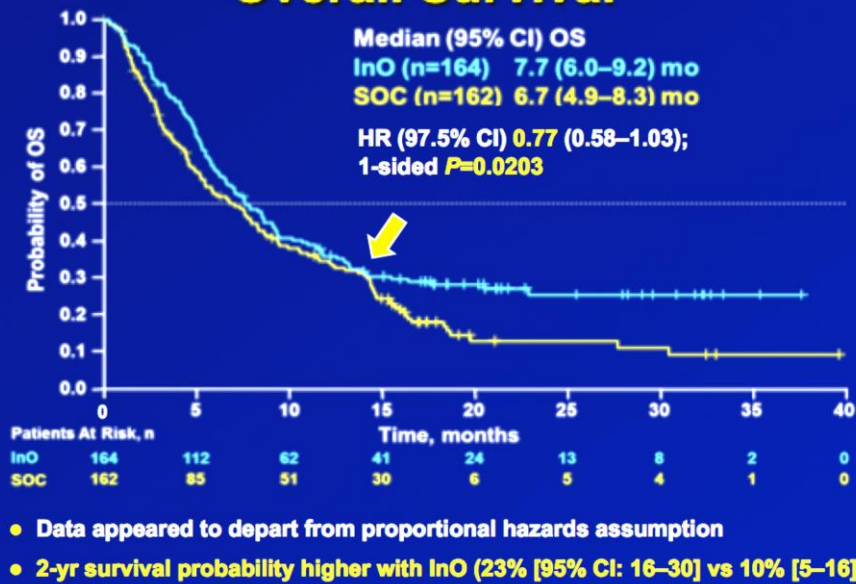
Ritenete i risultati dello studio Inno-Vate convincenti per la rapida introduzione di Inotuzumab-Ozogamicin nella pratica clinica ?

Overall Survival in Relapsed/Refractory B-Cell Acute Lymphoblastic Leukemia Patients Receiving Inotuzumab Ozogamicin vs Standard Care in the Phase 3 INO-VATE Study (EHA 2016: LB2233)

Progression-Free Survival



Overall Survival



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ALL: HOT ISSUES

Ritenete i risultati dello studio Inno-Vate convincenti per la rapida introduzione di Inotuzumab-Ozogamicin nella pratica clinica ?

- 1 • Quanti ne hanno avuto esperienza? **2 centri x 3 pazienti pazienti**
 - Dati convincenti? **SI/NO 2/1**
 - No dati nel setting MRD+
 - La poca differenza tra curve INO e SOC legata a diversi fattori?
 - espressione CD22?
 - caratteristiche biologiche
 - mancanza curve censurate x ALLO

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ALL: HOT ISSUES

Ritenete i risultati dello studio Inno-Vate convincenti per la rapida introduzione di Inotuzumab-Ozogamicin nella pratica clinica ?

- 2** • Risorsa nei pazienti in fase avanzata
- Ruolo nei R/R dopo precedenti trattamenti, anche dopo ALLO, dopo fallimento BLINA
- Sostenibilità



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Highlights from EHA

9th Edition, Firenze 2016

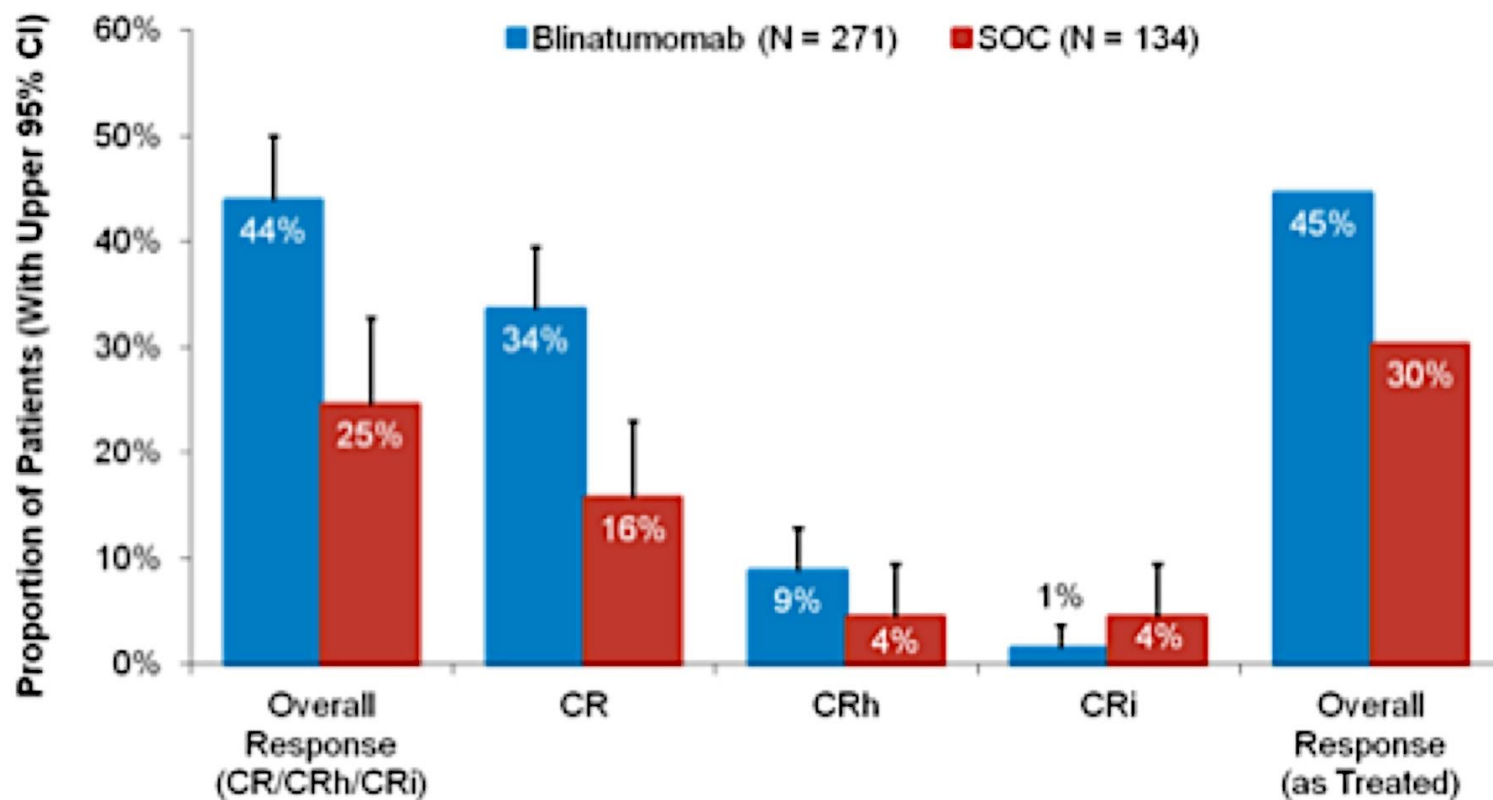
ALL: HOT ISSUES

Qual è il timing ideale dell'impiego di Blinatumomab nella ALL ?

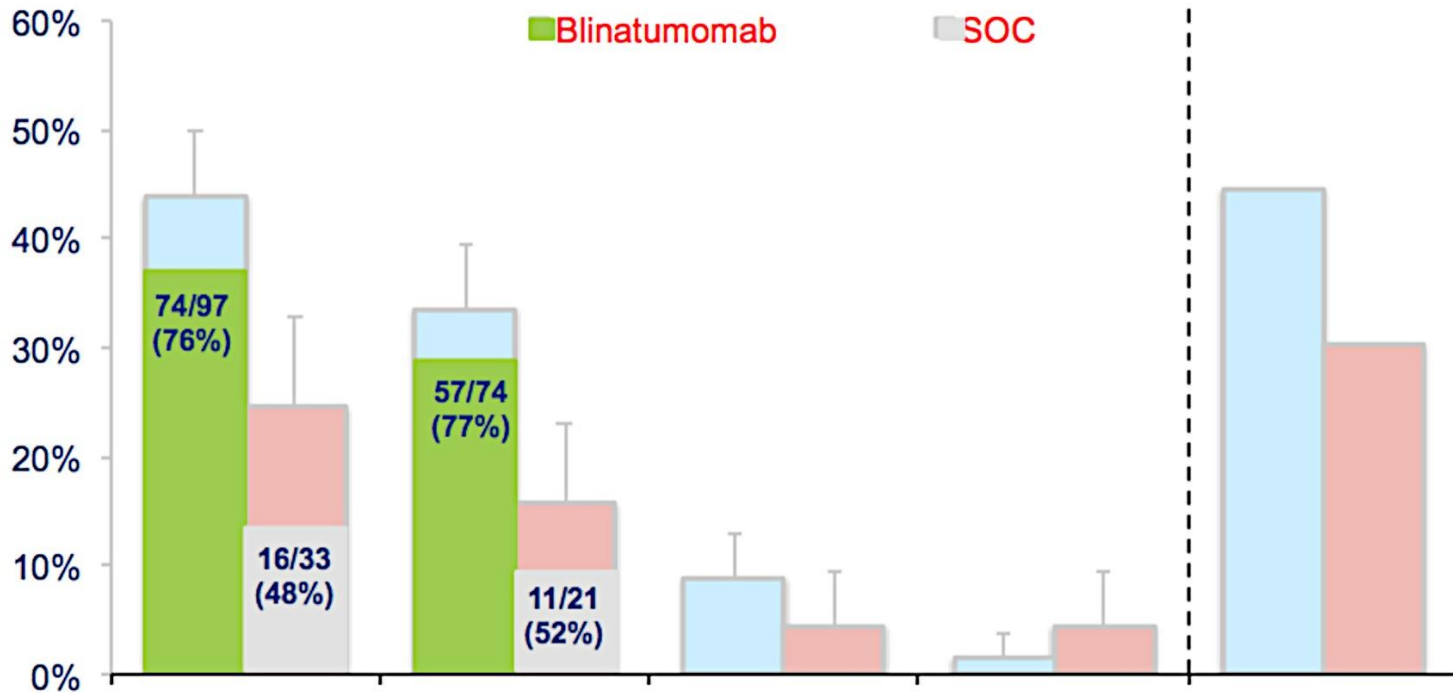
TOWER study: design

- **Phase 3, randomized, open-label study to evaluate the effect of blinatumomab on overall survival (OS) compared with SOC (FLAG± anthracycline; HD-ARA-C, HD-MTX) in adult patients with Ph- r/r BCP-ALL.**
- **Randomization 2:1**
- **Blinatumomab given at escalating dose of 9 µg/d in week 1 of cycle 1, then 28 µg/d for 4 weeks) as CIVI with 2 weeks wash-out.**
- **Primary endpoint: OS**
- **Secondary endpoints: Complete remission (CR) and combined CR or CR with partial or incomplete hematologic recovery (CR/CRh/CRi)**

TOWER study: results (I)



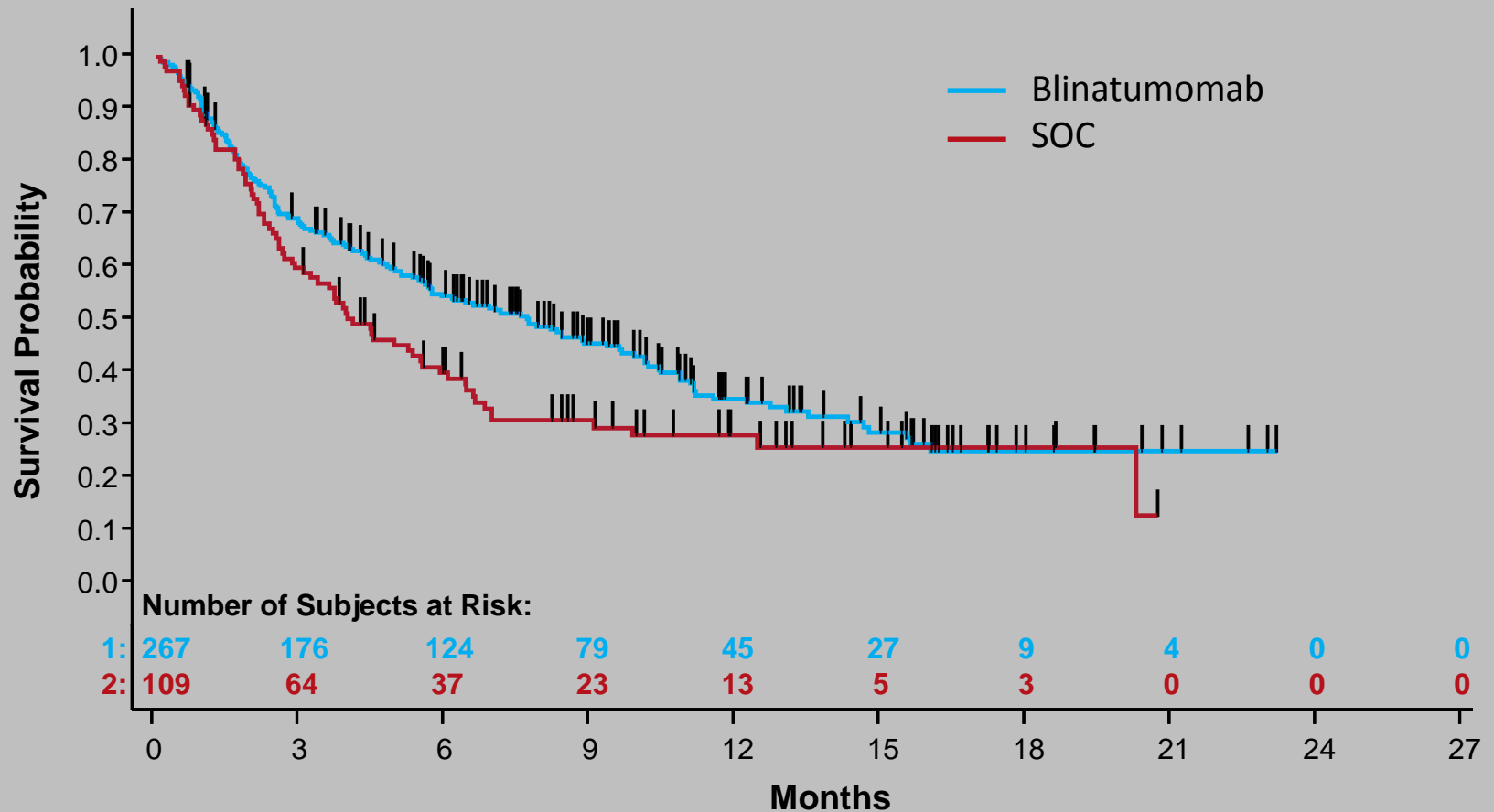
Molecular Remission Among Responders



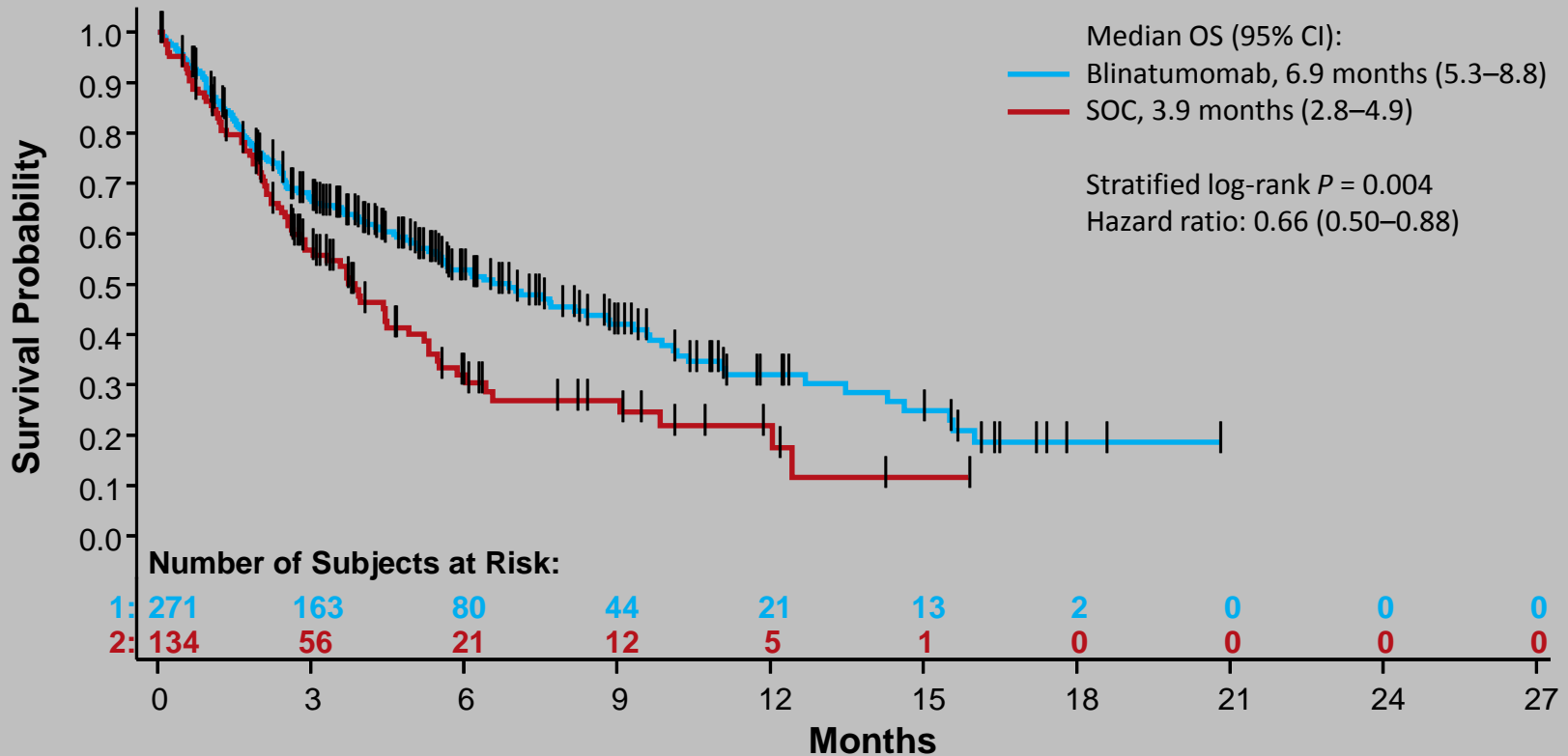
Molecular remission was defined as $< 10^{-4}$ blasts in the first 12 weeks

CR = complete remission; CRh = complete remission with partial hematologic recovery;
 CRi = complete remission with incomplete hematologic recovery; SOC = standard of care.

Overall Survival (as Treated)



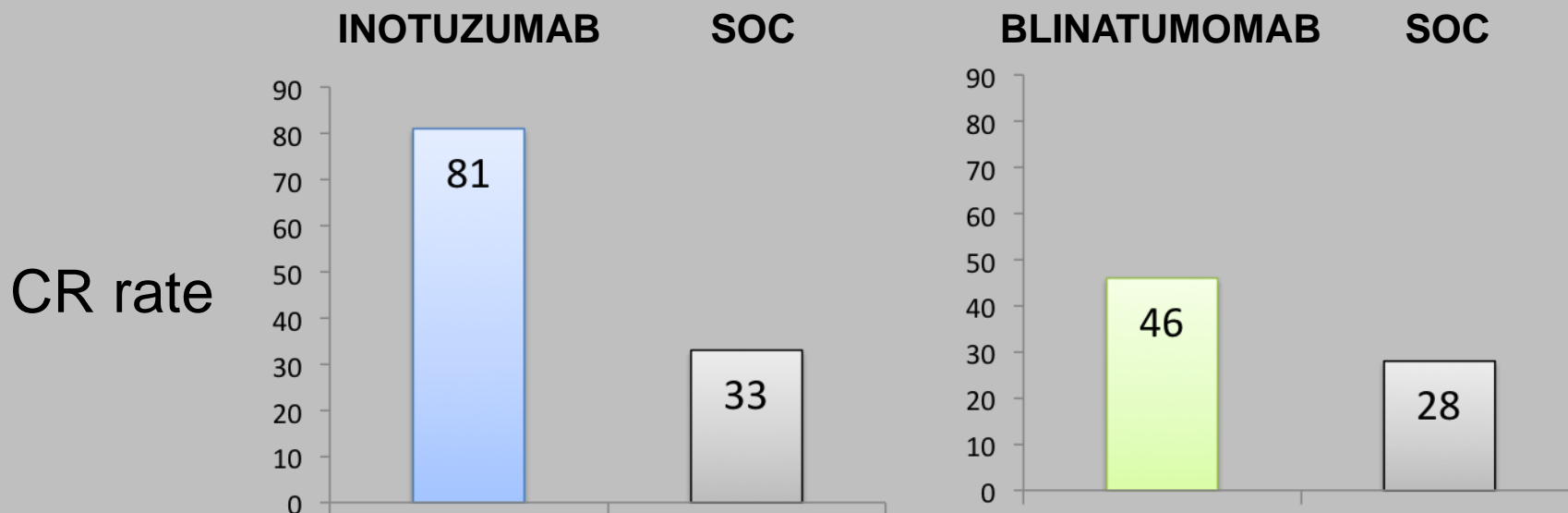
Overall Survival (OS) Censoring for alloHSC T



	Blinatumomab (N = 271)	SOC (N = 134)
alloHSC T post-baseline – n (%) (95% CI)	65 (24%) (19%–30%)	32 (24%) (17%–32%)

alloHSC T = allogeneic hematopoietic stem cell transplantation; CI = confidence interval; SOC = standard of care.

Two big randomized trial for R/R BCP-ALL reported at EHA 2016



but...

OS (months)

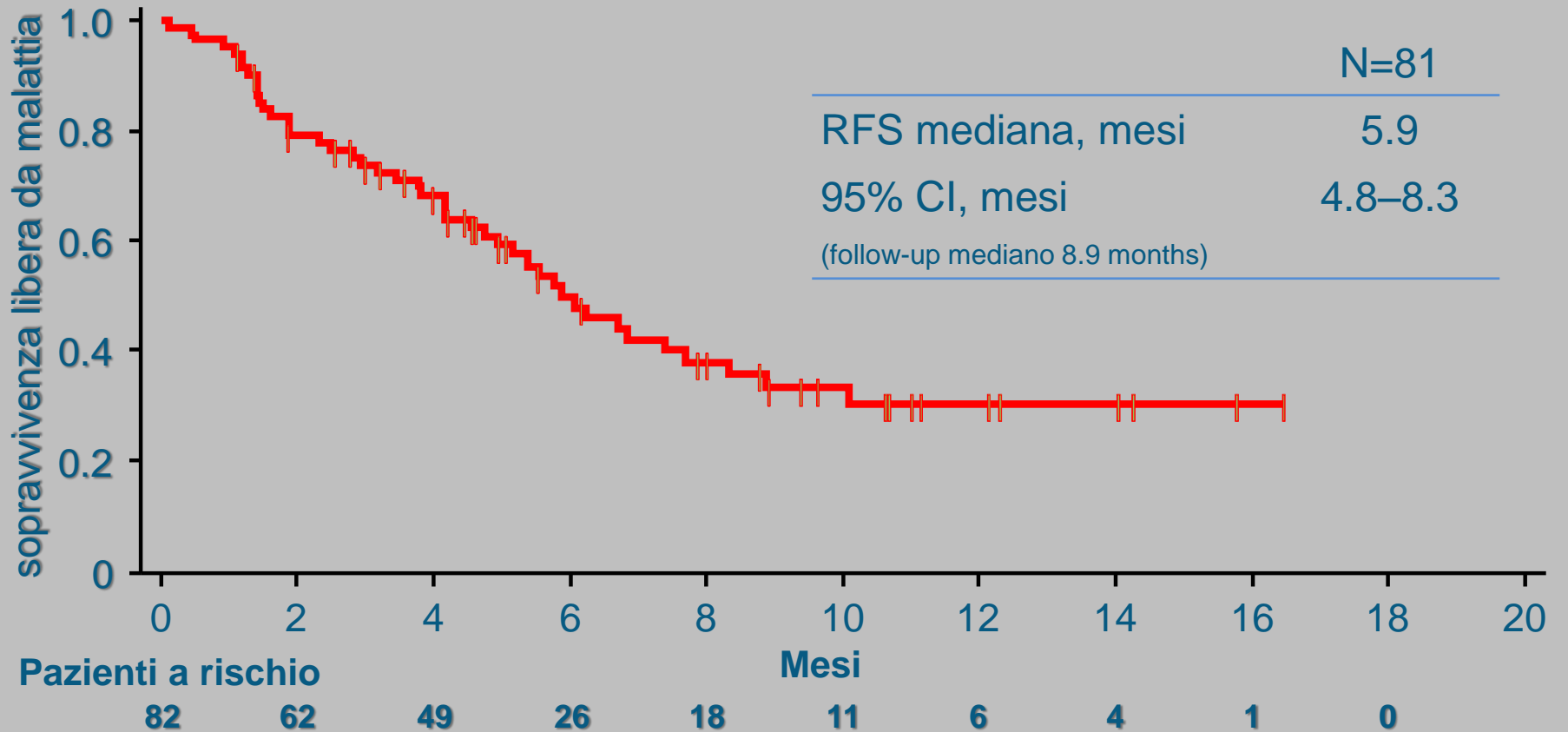
Treatment	OS (months)
INOTUZUMAB	7.7
SOC	6.7

Treatment	OS (months)
BLINATUMOMAB	7.8
SOC	4.0

SOC: Standard Of Care (chemotherapy)

Blinatumumab nella LAL-B

Studio multicentrico pilota MT103-211 in 81 pazienti R/R

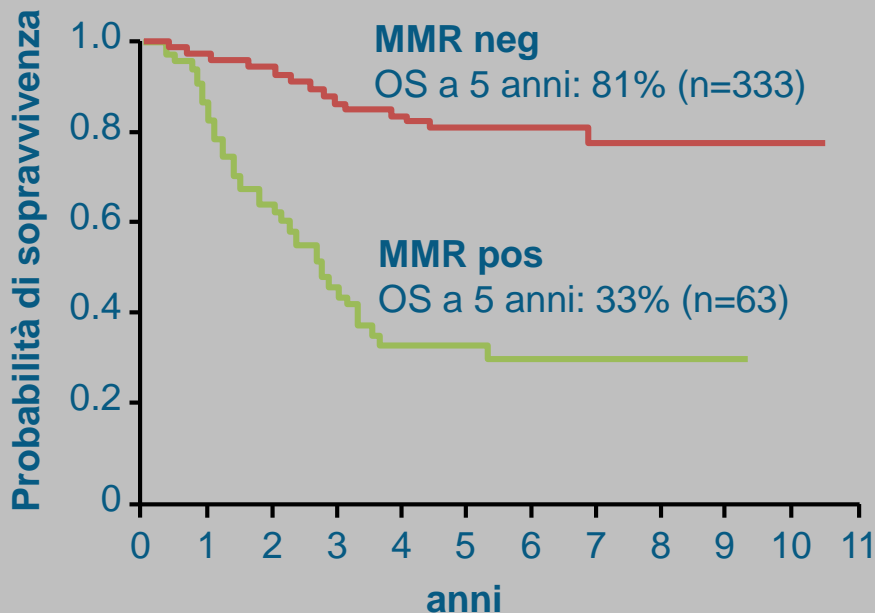


	N=81
RFS mediana, mesi	5.9
95% CI, mesi	4.8–8.3
(follow-up mediano 8.9 months)	

Impatto della MRD nelle LAL dell'adulto

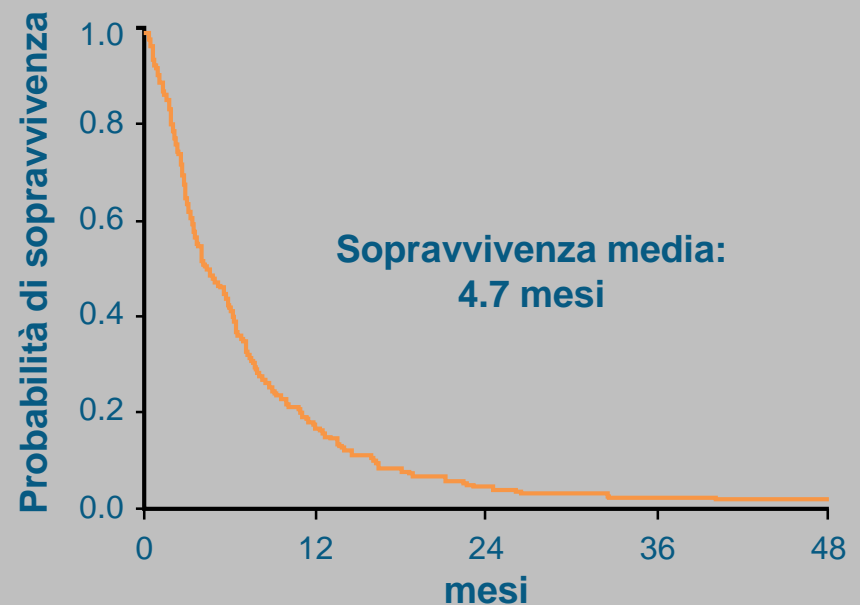
Pazienti con MMR

Studi GMALL ¹ OS in relazione alla MMR



Pazienti ricaduti/refrattari

OS nei refrattari o ricaduti precoci²



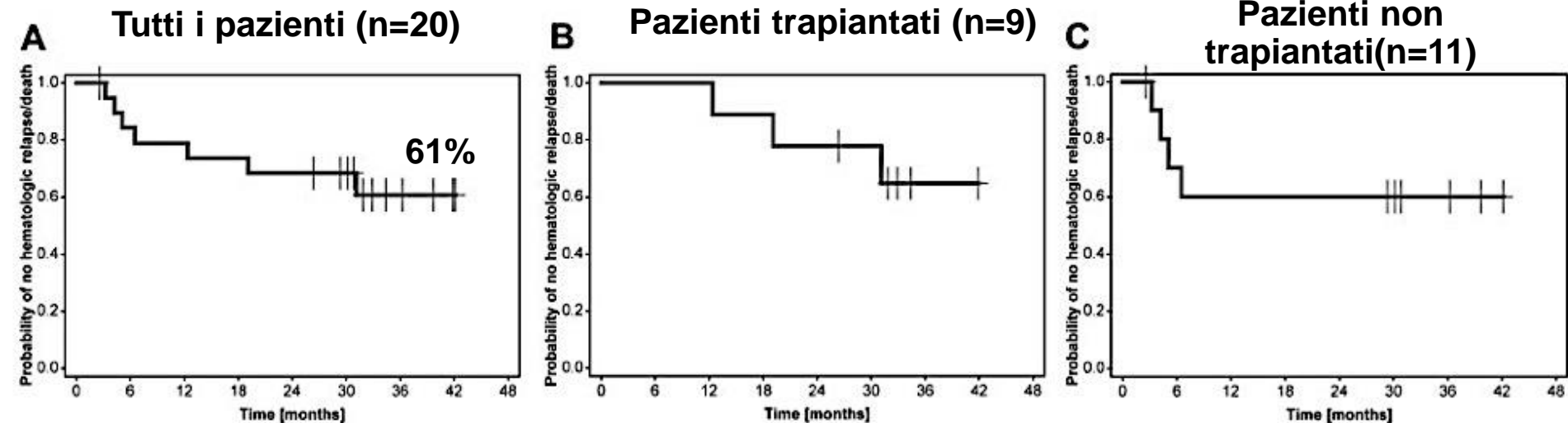
¹ Gokbuget et al. Blood 2012;120:1868-1876.

² Kantarjian et al. Cancer 2010;116:5568-5574.

Blinatumumab nella LAL-B MRD⁺

Studio tedesco pilota MT103-202: pazienti in RC ma MMR⁺

Negativizzazione della MMR dopo il 1° ciclo: 80%



ASH 2015 Abstract n° 680

Open-label, Multicenter, Confirmatory Phase 2 Study in MRD-positive B-precursor ALL

ClinicalTrials.gov identifier, NCT01207388

December 2010 – December 2013

46 Centers

11 Countries

This presentation includes the final data from the
preplanned 18-month follow-up analysis;
the primary results were presented at ASH 2014

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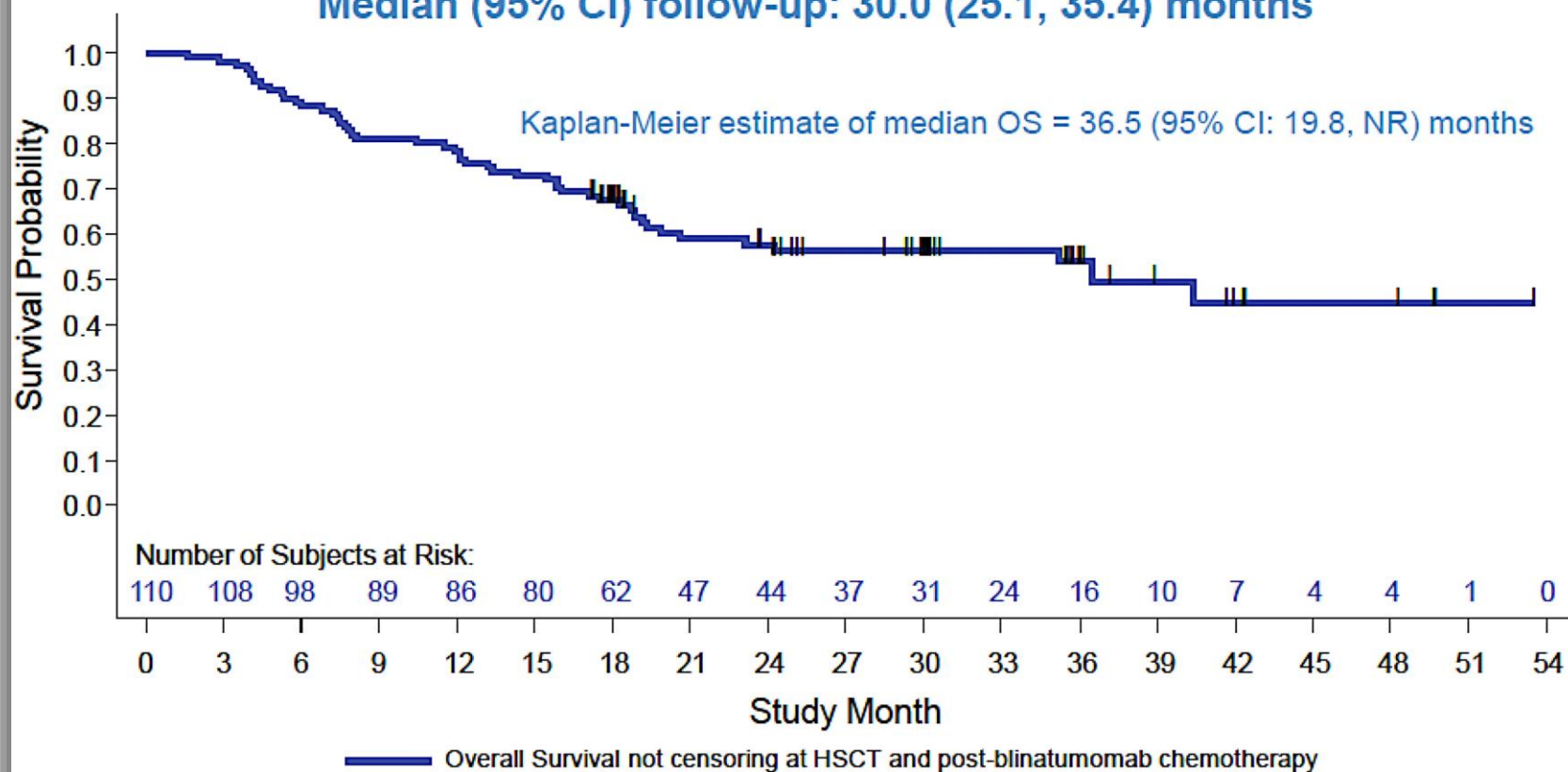
Paris,
iversity
elgium;
lizinische
d Medical
, University
ital
Germany;

Open-label, Multicenter, Confirmatory Phase 2 Study in MRD-positive B-precursor ALL

Overall Survival

Median age: 45 (18-76) yrs

Philadelphia-negative patients in hematologic CR
Median (95% CI) follow-up: 30.0 (25.1, 35.4) months

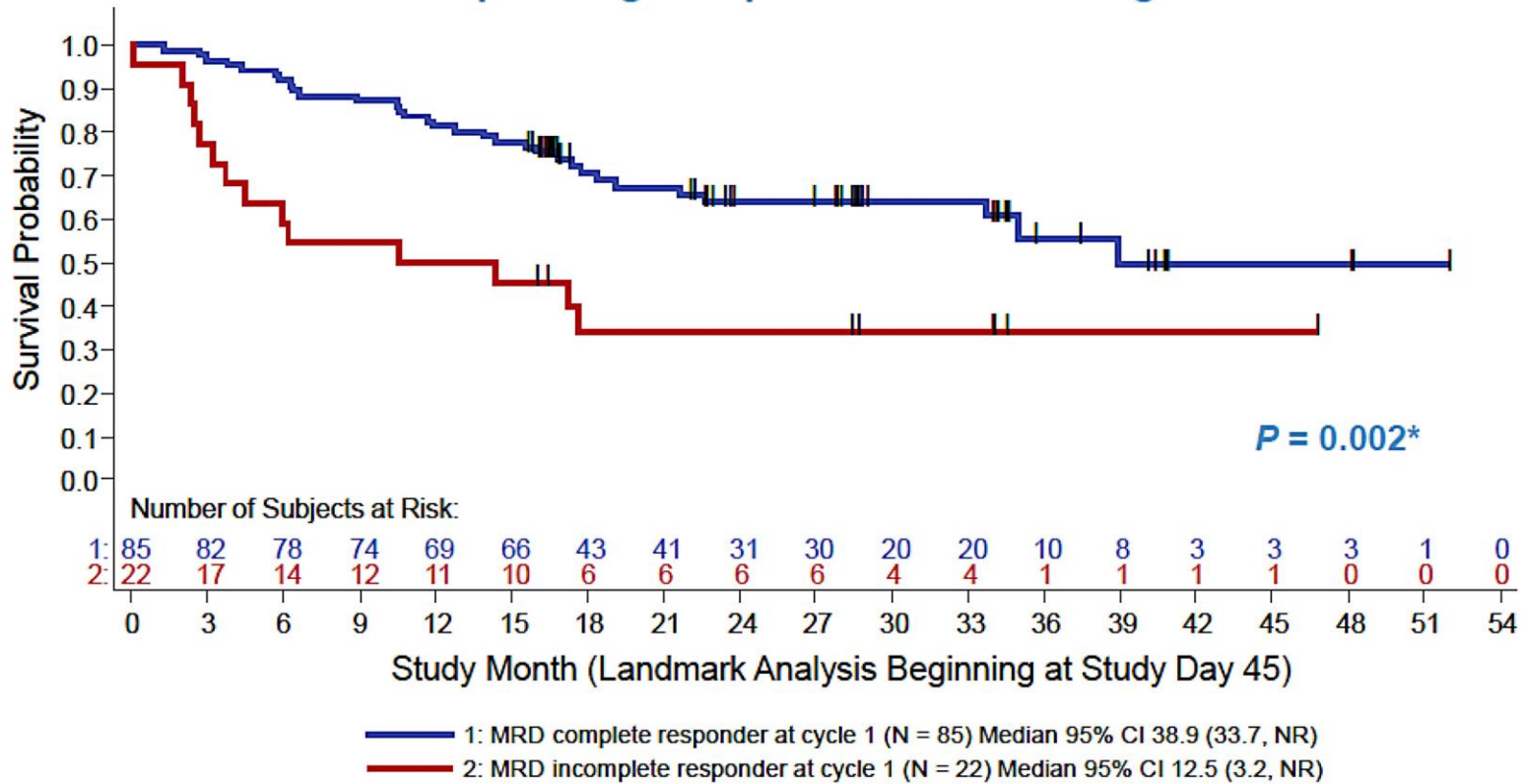


NR = not reached.

Open-label, Multicenter, Confirmatory Phase 2 Study in MRD-positive B-precursor ALL

Overall Survival by Complete MRD Response

Philadelphia-negative patients in hematologic CR



Complete MRD response (primary endpoint): MRD negative, no amplification in PCR (minimum sensitivity 10⁻⁴)

NR = not reached. The landmark analysis by MRD response included patients with overall survival of ≥ 45 days

*Log rank P value for association between OS and MRD response; causality not implied for both outcomes.

9th Edition, Firenze 2016

ALL: HOT ISSUES

Qual è il timing ideale dell'impiego di Blinatumomab nella ALL ?

1

- Quanti hanno fatto esperienza con BLINA?
- **7 Centri, circa 45 Pazienti**
- **negli MRD+ (ma l'indicazione per ora sarà x R/R)**
 - MRD+ come bridge to transplant
 - Negli MRD+ a prescindere dall'ALLO
- In prima linea? **STUDI GIMEMA A BREVE**
- **Nei recidivati dopo ALLO**

8th Edition, Firenze 2016

ALL: HOT ISSUES

Qual è il timing ideale dell'impiego di Blinatumomab nella ALL ?

- 2** • Necessario approccio creativo alla comprensione dei fenomeni biologici/implicazioni sottesi a certi aspetti (numero cellule T pre-infusione, perdita del CD19 alla ricaduta, altro)



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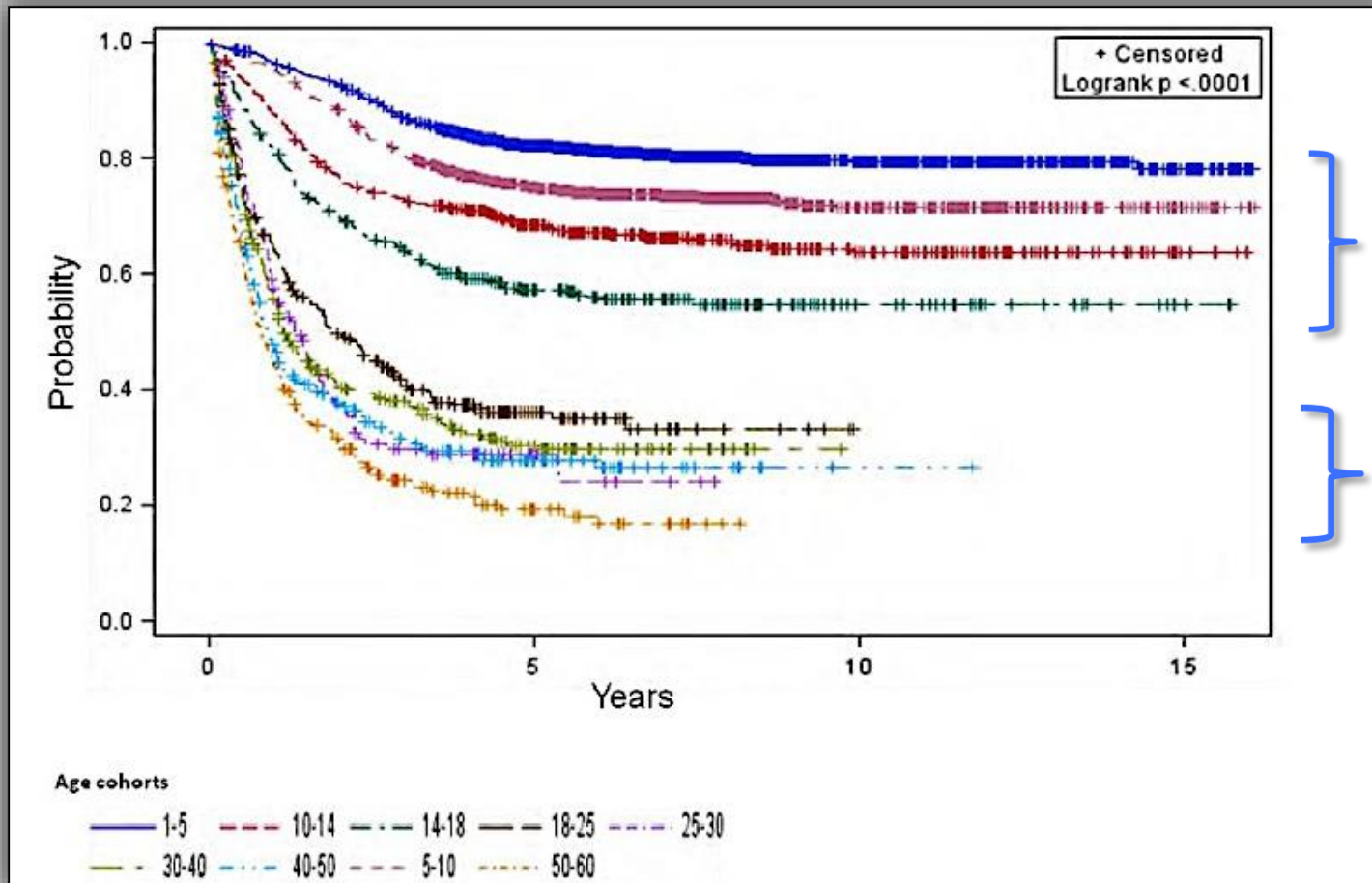
Highlights from EHA

8th Edition, Firenze 2016

ALL: HOT ISSUES

Quale età e quali comorbidità vanno considerate nell'approccio "pediatric-like" nella ALL ?

Studi **GIMEMA** e **AIEOP** 1995-2009: 5.202 pazienti, risultati per età



<18 anni

>18 anni

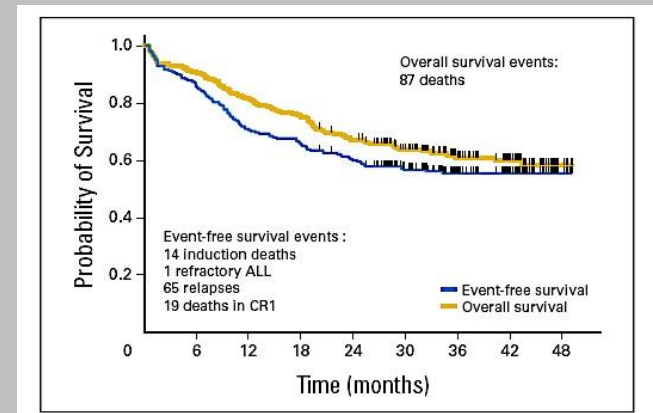
Schemi terapeutici "pediatric-like" nell'adulto

Study Group	Protocol	Patients	CR (%)	OS (%)	DFS (%)
GMALL ¹	07/2003	1,226 (age 15-55)	91	60-67 at 3-years	61-74 at 3-years
GRAALL ²	2003	225 (age 15-60)	93	60 at 42-months	55% at 42-months
NILG ³	10/07	205 (age 18-65)	88	54 at 4-years	56 at 4-years

¹Goekbuget N et al, ASH 2010 (abstr 494)

²Huguet F et al, J Clin Oncol 2009

³Bassan R et al, ASH 2013



8th Edition, Firenze 2016

ALL: HOT ISSUES

Quale età e quali comorbidità vanno considerate nell'approccio "pediatric-like" nella ALL ?

1

Quanti adottiamo cosa

- approccio "true": **tutti**
- approccio "like": **nessuno**

Fino a quale età?

- **fino a 45 anni** (Ferrara & Co)
- **fino a 60 anni con le precauzioni del caso**

8th Edition, Firenze 2016

ALL: HOT ISSUES

Quale età e quali comorbidità vanno considerate nell'approccio "pediatric-like" nella ALL ?

2

Con quali **precauzioni**?

- "danno epatico"
- "danno" respiratorio
- BMI elevato
- altre comorbidità rilevanti

Problema "**sopportazione**" asparaginasi

Impatto sull'outcome della **non aderenza** alla tempistica?

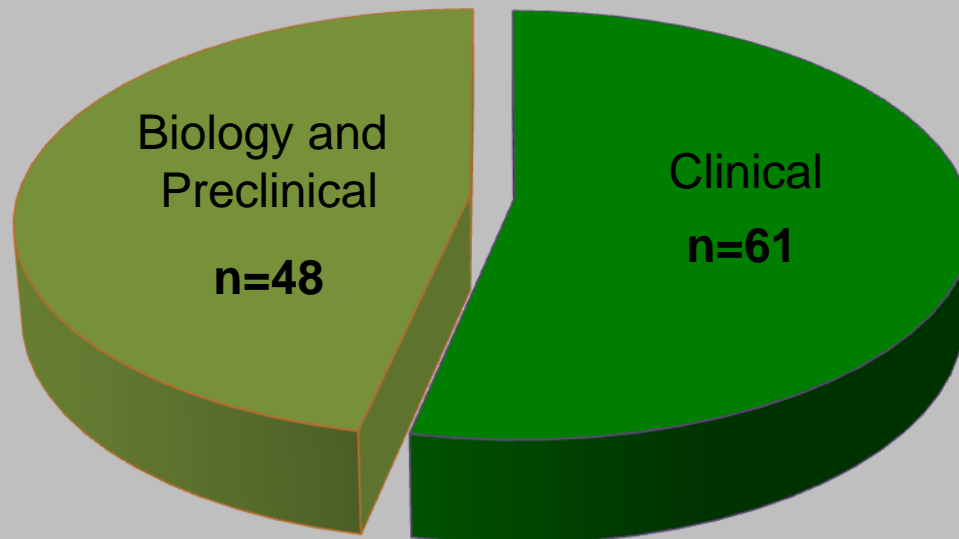


COPENHAGEN
21ST CONGRESS
JUNE 9 - 12 | 2016

European Hematology Association

Acute lymphoblastic leukemia: **109/2174 abstracts**

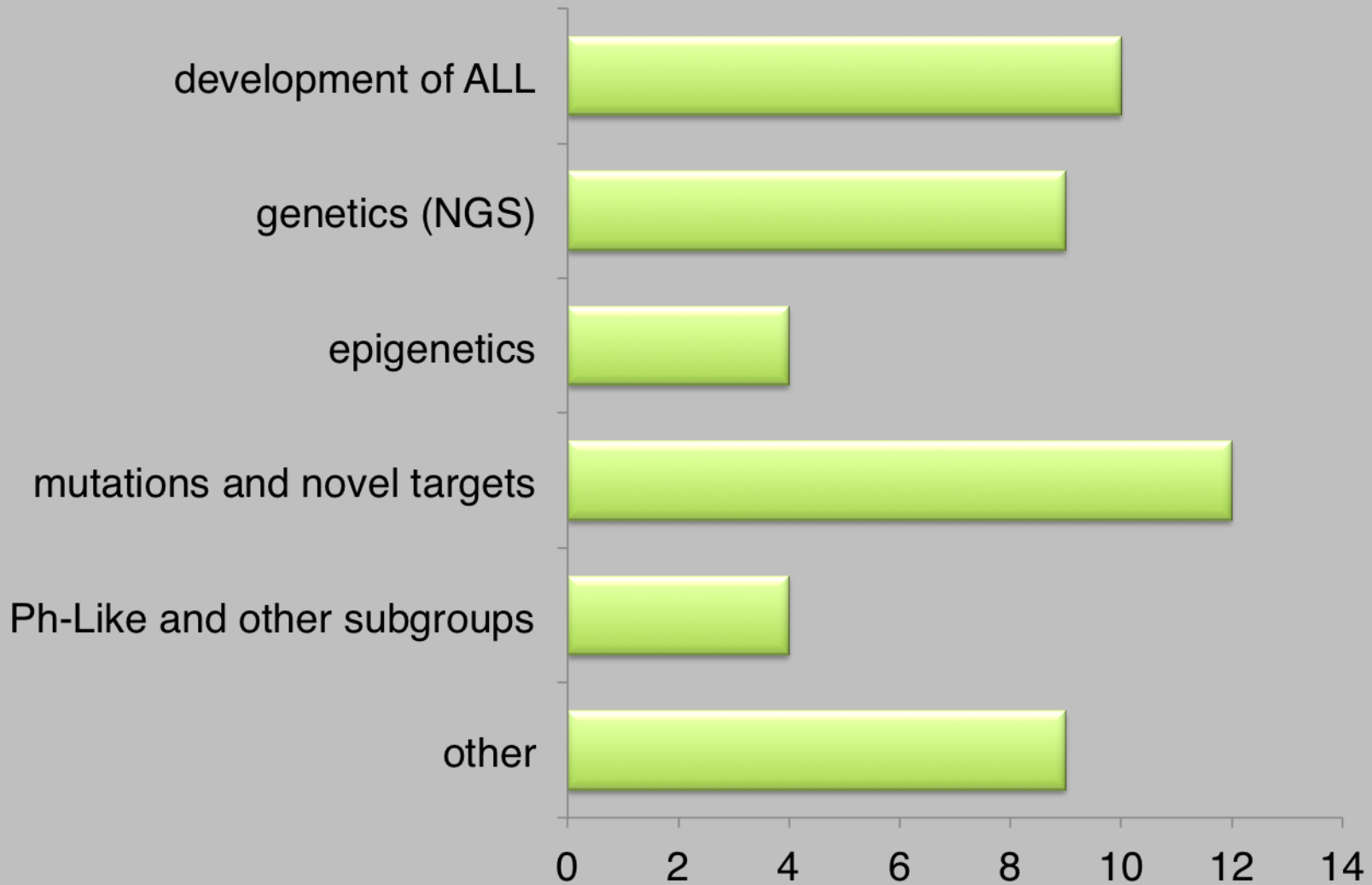
17 oral presentation
43 poster
49 e-poster



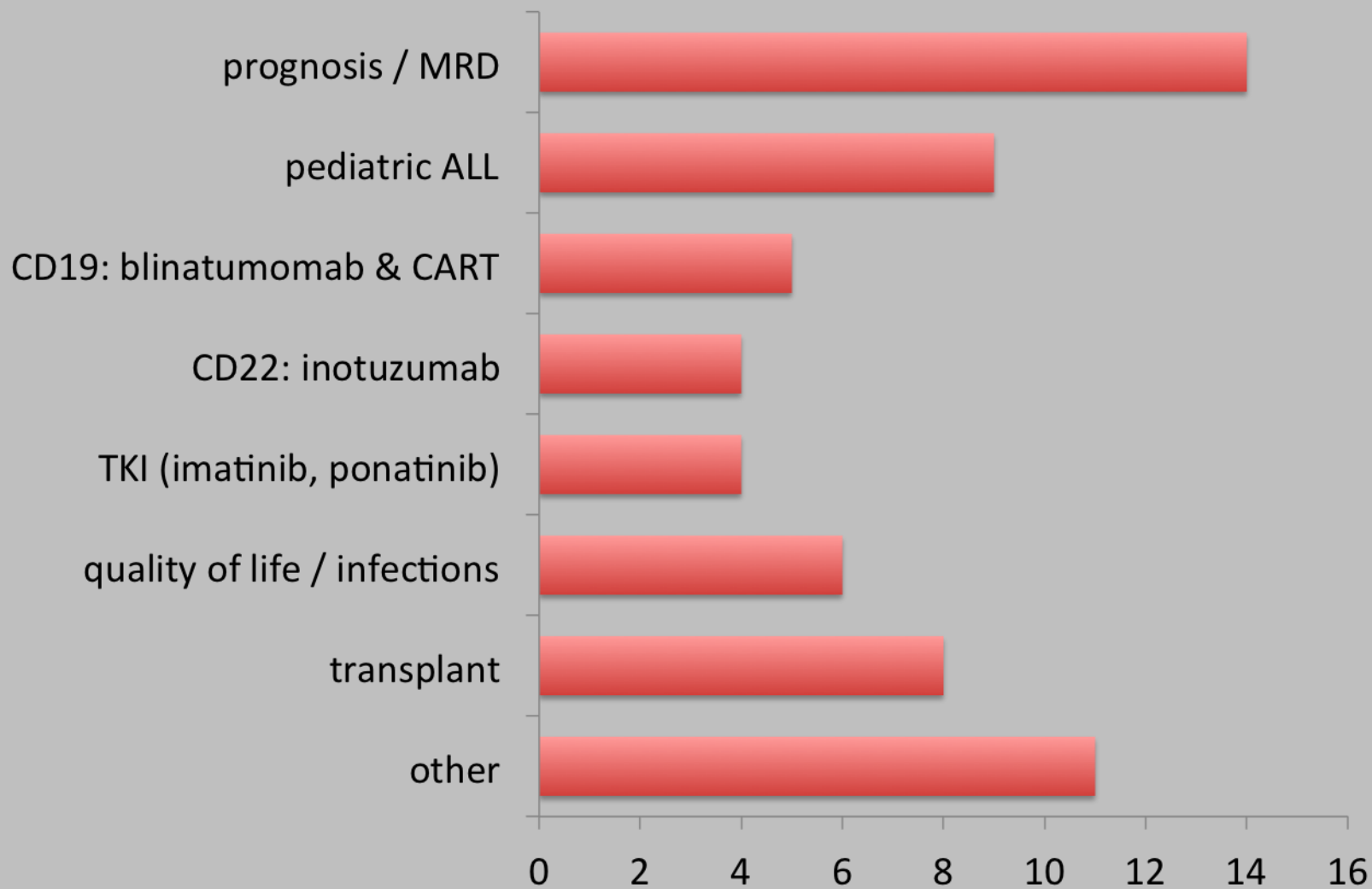
From:

ITALY	18 abstr.
US	13
Belgium	10
China	8
Netherlands	7
Germany	7
Spain	7
Other EU	25
Extra EU	14

Biology and preclinical topics



Clinical topics















EUROPEAN
HEMATOLOGY
ASSOCIATION

EHA Jean Bernard Lifetime Achievement Award 2016

has been awarded to

Clara Camaschella



In recognition of her significant contribution to the understanding of the pathophysiology of inherited disorders of iron metabolism, including hereditary hemochromatosis, genetic iron deficiency and iron-loading anemias.



12:50
Friday
June 10, 2016



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LAL: Report del gruppo di lavoro: 21!

