ASH 2024

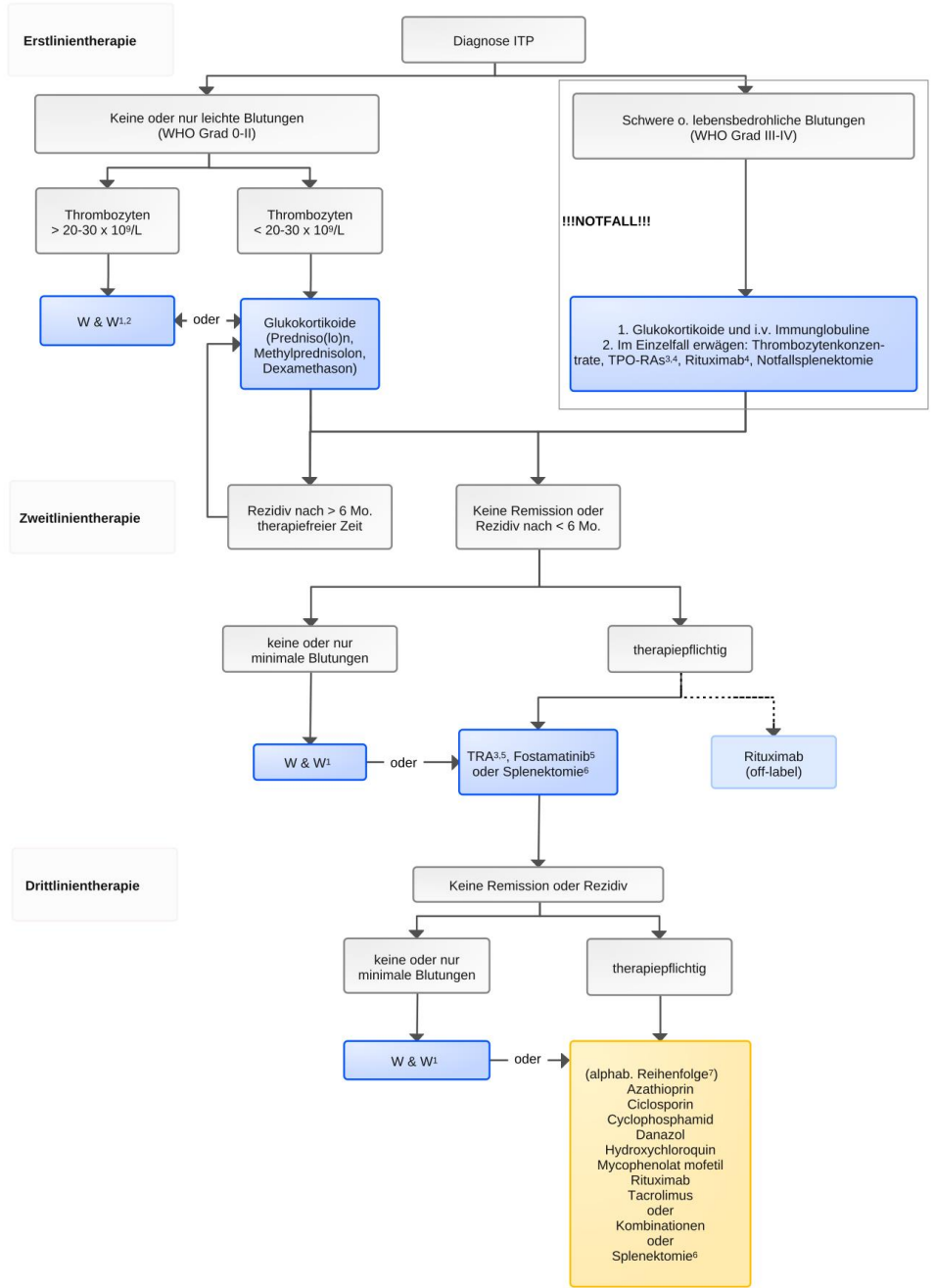
Wichtig zu wissen

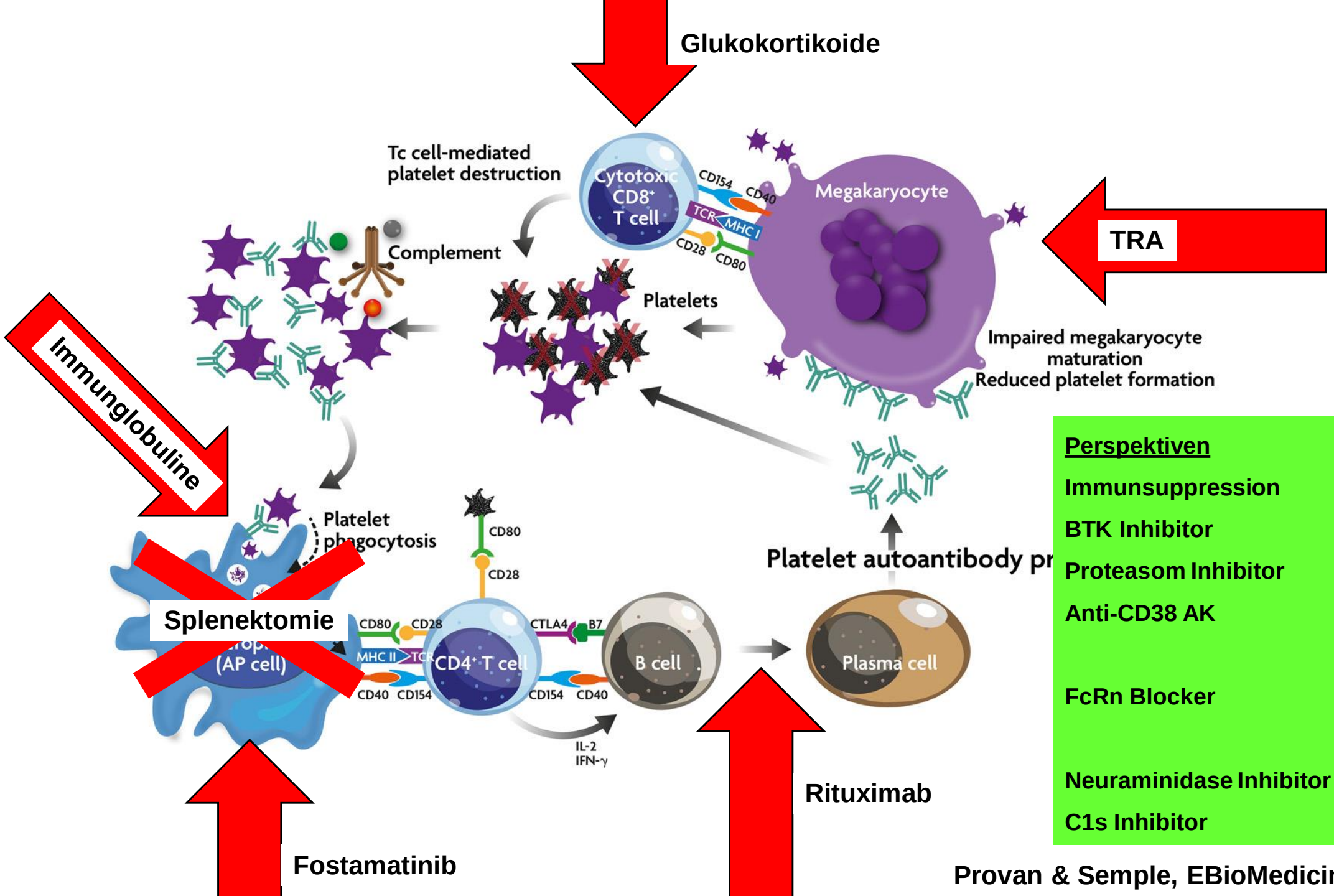
ASH Kongress 2024

wichtig zu wissen

- Immunthrombozytopenie
- Sichelzellkrankheit
- Venöse Thromboembolien
- Multiples Myelom
- Chronische Lymphatische Leukämie
- Mantelzell-Lymphom
- Follikuläres Lymphom
- Akute Lymphatische Leukämie
- Akute Myeloische Leukämie

Algorithmus zu Therapieempfehlungen bei Immunthrombozytopenie





Perspektiven	
Immunsuppression	MMF
BTK Inhibitor	
Proteasom Inhibitor	Bortezomib
Anti-CD38 AK	Daratumumab
	Mezagitamab
FcRn Blocker	Efgartigimod
	Rozanolixizumab
Neuraminidase Inhibitor	Oseltamivir
C1s Inhibitor	Sutimlimab

Provan & Semple, EBioMedicine, 2022

Bruton's Tyrosine Kinase inhibitors

Autoimmune cytopenias often improved with ibrutinib

Rogers et al, Leukemia 2016; Montillo et al, Blood Cancer Journal 2017; Hampel et al, Br J Haematol 2018.

Increased risk of bleeding (up to 40%) with 1st and 2nd generation BTKi

Inhibition of platelet aggregation

Tullemans et al, EJHaem 2021; Ninomoto J et al, Hematology 2020.

Goal: Treat the autoimmune cytopenia; avoid the off-target effects

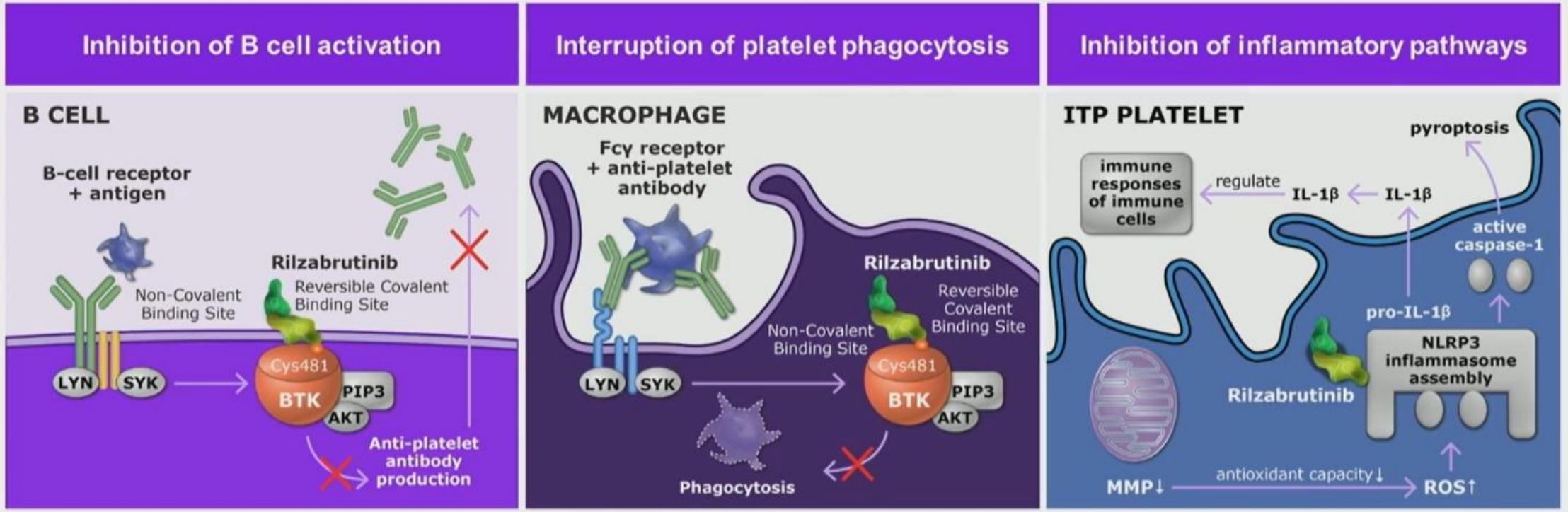
Efficacy and Safety of Oral Bruton Tyrosine Kinase Inhibitor Rilzabrutinib in Adults With Previously Treated Immune Thrombocytopenia: A Phase 3, Placebo-Controlled, Parallel-Group, Multicenter Study (LUNA 3)

David J. Kuter,[1] Waleed Ghanima,[2] Nichola Cooper,[3] Howard A. Liebman,[4] Lei Zhang,[5] Yu Hu,[6] Yoshitaka Miyakawa,[7] Luisa Elena Morales Galindo,[8] Ana Lisa Basquiera,[9] Chuen Wen Tan,[10] Güray Saydam,[11] Marie Luise Hütter-Krönke,[12] Chatree Chai-Adisaksopha,[13] David Gómez Almaguer,[14] Huy Tran,[15] Ho-Jin Shin,[16] Maria Cristina Pascual Izquierdo,[17] Ilya Kirgner,[18] Elisa Lucchini,[19] Ganna Kuzmina,[20] Sylvain Audia,[21] Matias Cordoba,[22] Remco Diab,[23] Mengjie Yao,[24] Michelle J. Lee,[22] and Ahmed Daak[22] (LUNA 3 Trial Group)

[1]Hematology Division, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA; [2]Østfold Hospital Trust, Grålum, Norway and Institute of Clinical Medicine, University of Oslo, Oslo, Norway; [3]Hammersmith Hospital, London, United Kingdom; [4]University of Southern California, Los Angeles, CA, USA; [5]Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin, China; [6]Wuhan Xie'he Hospital, Wuhan, China; [7]Department of Hematology, Saitama Medical University, Saitama, Japan; [8]IC La Serena Research SpA, La Serena, Chile; [9]Hospital Privado Universitario de Córdoba-Instituto Universitario de Ciencias Biomédicas de Córdoba (IUCBC), Cordoba, Argentina; [10]Department of Hematology, Singapore General Hospital, Singapore; [11]Internal Medicine and Hematıology, Faculty of Medicine, Ege University, İzmir Türkiye; [12]Department of Hematology, Oncology and Tumorimmunology, Charité - Universitätsmedizin Berlin, Freie Universität Berlin and Humboldt Universität zu Berlin, Berlin, Germany; [13]Maharaj Nakorn Chiang Mai Hospital, Chiang Mai, Thailand; [14]Hospital Universitario Dr. Jose Eleuterio Gonzalez, Monterrey, Mexico; [15]Peninsula Private Hospital, Frankston, Victoria, Australia; [16]Division of Hematology-Oncology, Department of Internal Medicine, Biochemical Research Institution, Pusan National University Hospital, Pusan National University School of Medicine, Busan, Republic of Korea; [17]Instituto de Investigación Gregorio Marañon, Madrid, Spain; [18]Tel Aviv Sourasky Medical Center, Tel Aviv, Israel; [19]UCO Ematologia, Azienda Sanitaria Universitaria Giuliano-Isontina, Trieste, Italy; [20]Municipal Enterprise Kryvyi Rih City Clinical Hospital #2 of Kryvyi Rih City Council, SI Dnipropetrovsk Medical Academy under the Ministry of Health of Ukraine, Kryvyi Rih, Ukraine; [21]CHU Dijon Bourgogne - Hopital Francois Mitterrand, Dijon, France; [22]Sanofi, Cambridge, MA, USA; [23]Sanofi, Rotkreuz, Zug, Switzerland; [24]Sanofi, Bridgewater, NJ, USA

#5

Rilzabrutinib: Oral, Reversible, BTK Inhibitor



Kuter DJ, et al. Ther Adv Hematol. 2023; ***Langrish CL, et al. J Immunol. 2021; Wang S, et al. Thromb Res. 2021; Daak A, et al. Blood. 2024 (abstract 2482).***

Does not cause platelet dysfunction

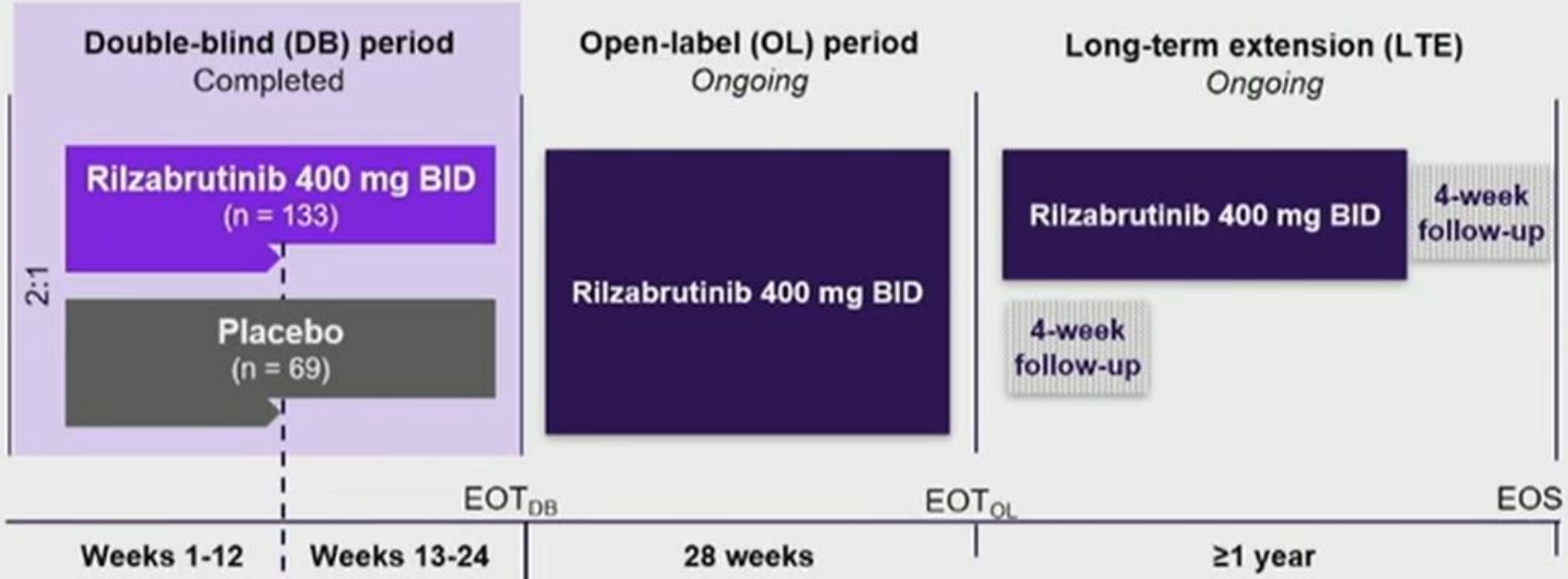
LUNA-2: Open-label, dose-finding, Phase 1–2 trial of Rilzabrutinib in ITP *Kuter et al, NEJM 2022*

LUNA-3: Phase 3 trial, Rilzabrutinib vs. Placebo for previously treated ITP

LUNA 3 Study Design

Adult patients (*pediatric ongoing*)

- Age ≥18 years
- Persistent or chronic primary ITP
- Prior IVIg/anti-D or CS but not sustained
- Qualifying platelet counts <30×10^9/L
- Allowed stable concomitant CS and/or TPO-RA



Platelet response (week 13)

- Platelet count ≥50×10^9/L or ≥30–<50×10^9/L and doubled from baseline
- Non-responders: option to discontinue or proceed to open-label on rilzabrutinib only

Durable response (week 25)

Primary endpoint

- Platelet count ≥50×10^9/L for ≥ two-thirds of last 12 weekly visits in the absence of rescue therapy

NCT04562766; EudraCT 2020-002063-60.

Baseline Demographics and Prior Therapy

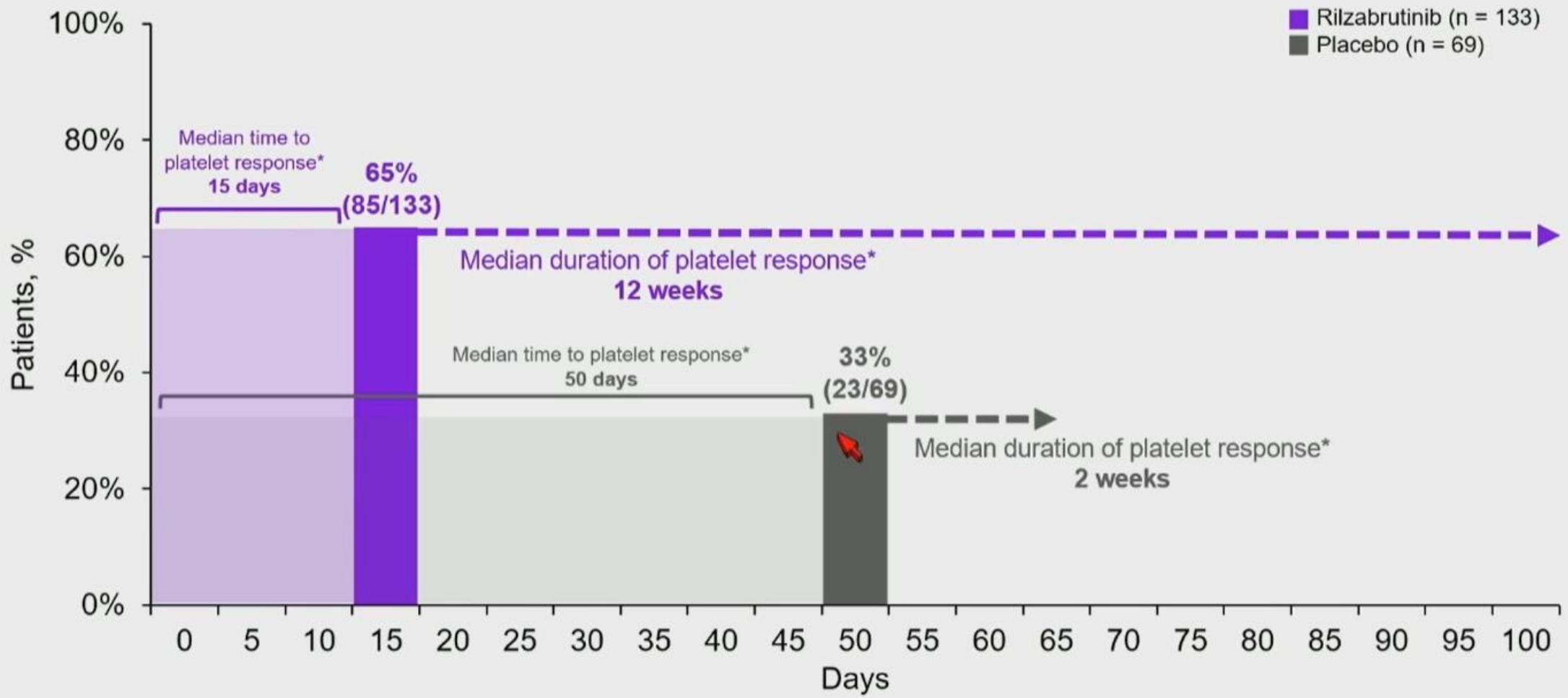
Generally balanced between arms

	Rilzabrutinib (n = 133)	Placebo (n = 69)
Median age, y (range)	47 (18–80)	46 (19–79)
Females, n (%)	78 (59)	49 (71)
Median duration of ITP, y (range)	8.1 (0.3–52.2)	6.2 (0.3–35.8)
Median baseline platelet count, $\times 10^9$/L (range)*	15 (1-32)	15 (1-54)
Median number of unique prior ITP therapies (range)†	4 (1-15)	5 (1-12)
≥5 prior therapies, n (%)	57 (43)	36 (52)
Prior splenectomy, n (%)	37 (28)	19 (28)
Prior TPO-RA, n %)	88 (66)	51 (74)

Data cutoff 14 March 2024.
*Averaged first and second qualifying screening platelet counts and study day 1 platelet count.
†Identified using standard medication term, different corticosteroids counted as one therapy, and splenectomy could be counted as one prior ITP therapy. Patients could receive more than one therapy.

Initial Platelet Response

Platelet count >50×10⁹/L or 30-<50×10⁹/L and at least doubled from baseline

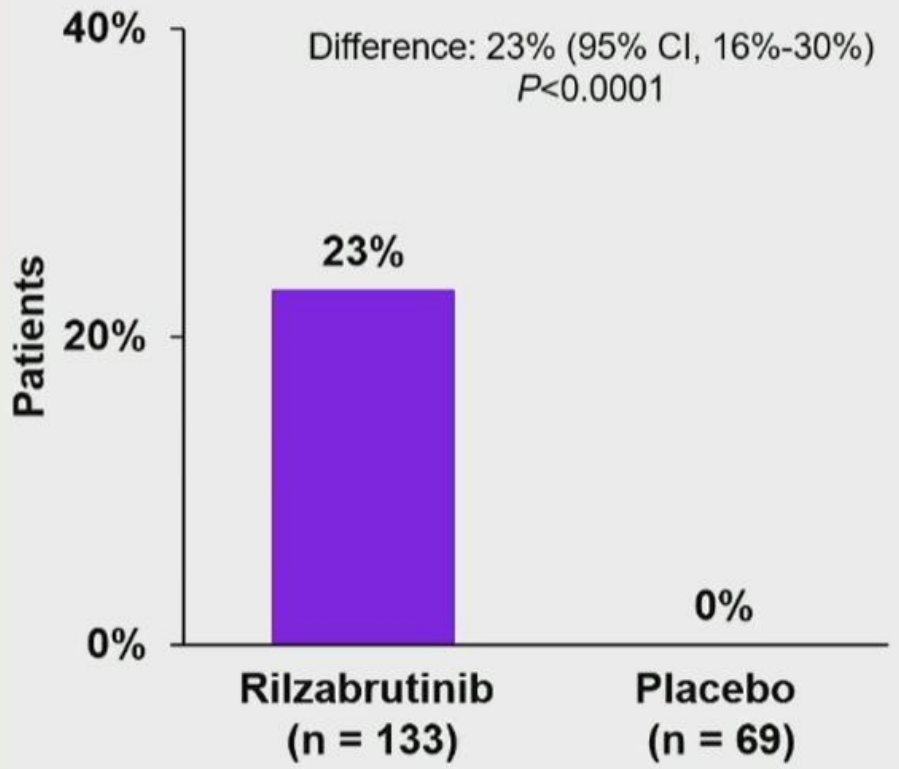


Data cutoff 14 March 2024.

*Response was at any during the double-blind period. Time to and duration of platelet response values were in patients achieving response at any point during the double-blind period.

Durable Platelet Response

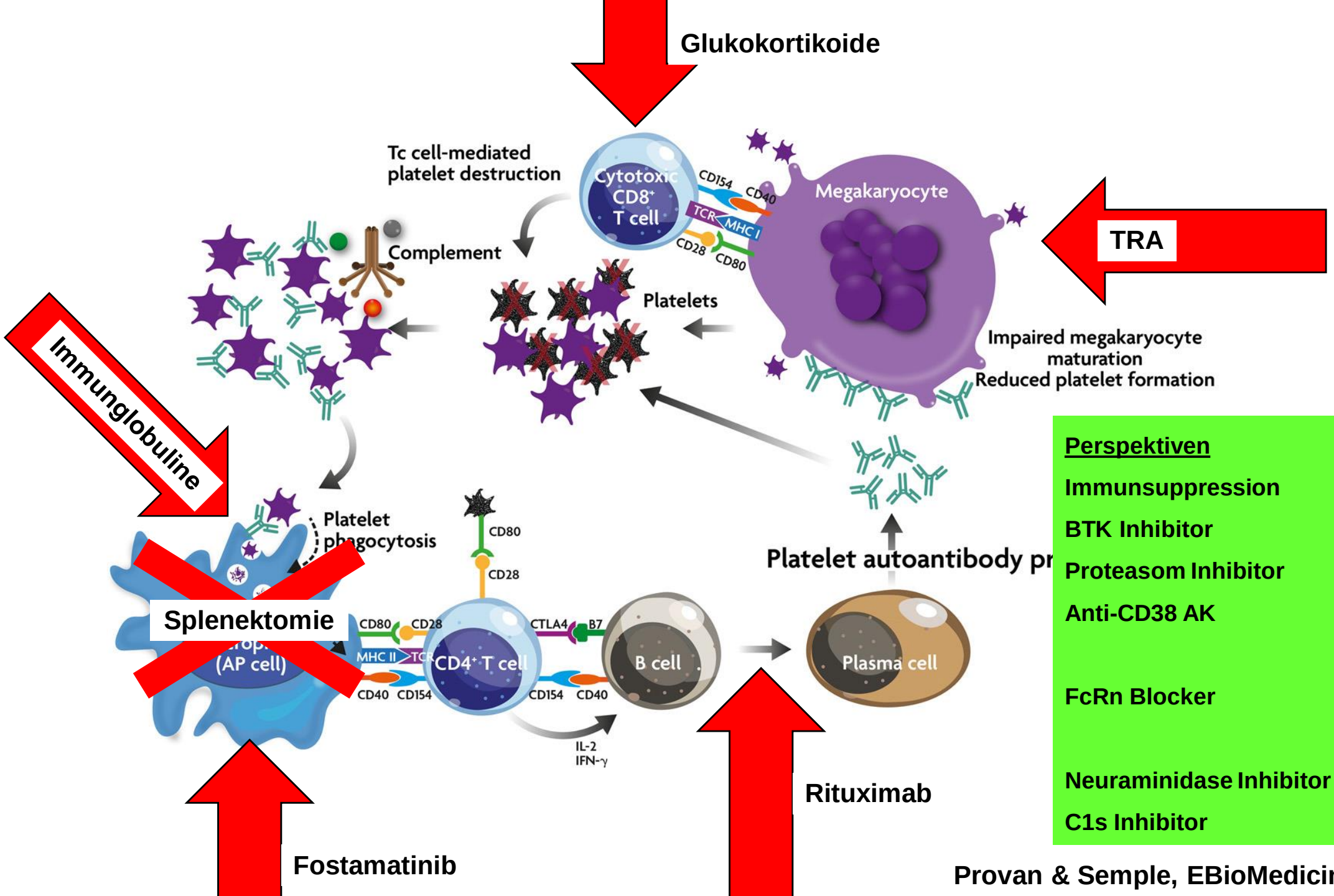
Durable Response
Week 25 Primary Endpoint Was Met



Durable Response

Defined as platelet counts ≥50×10^9/L for ≥two-thirds of ≥8 of the last 12 of 24 weeks without receiving rescue therapy

Data cutoff 14 March 2024.



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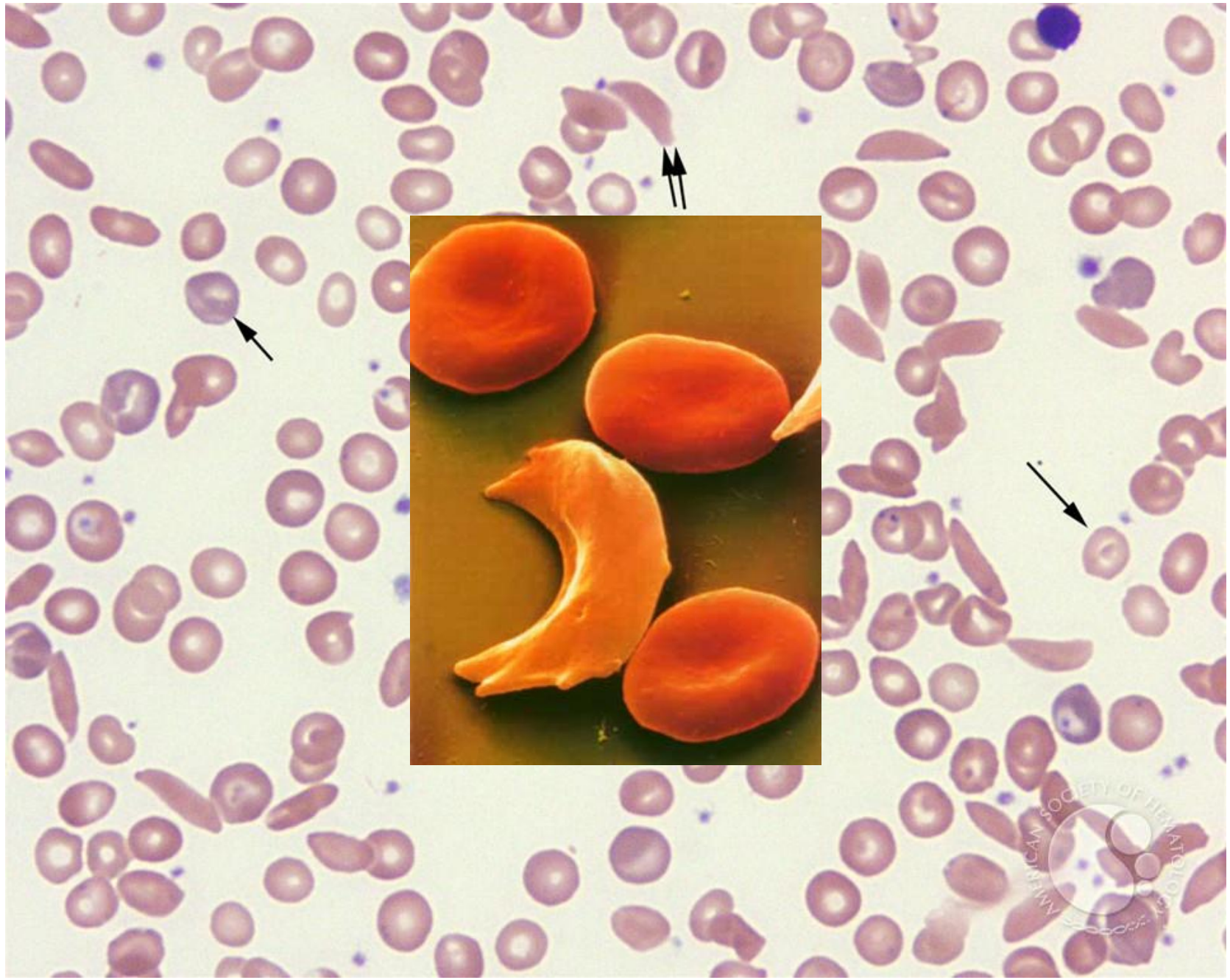
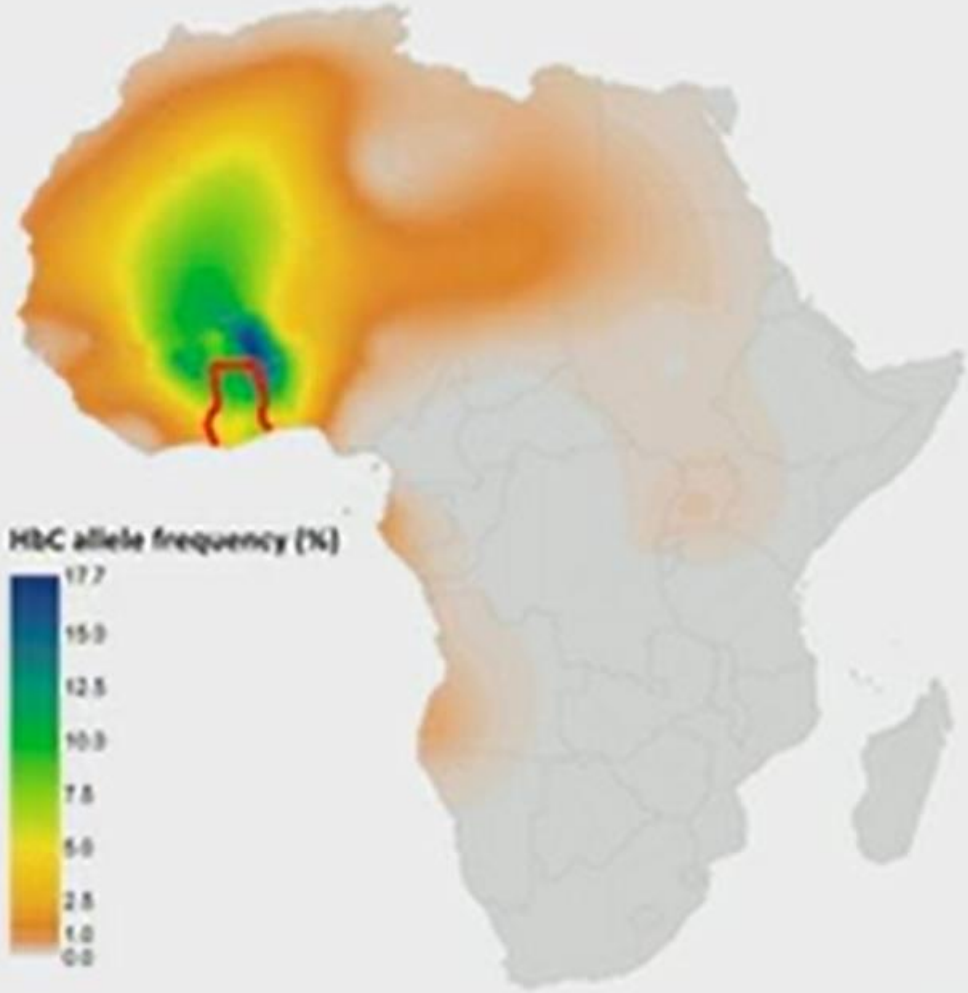
Provan & Semple, EBioMedicine, 2022



Hemoglobin SC is the second most common sickle cell disease genotype

Hb S β6Glu-Val	Hb S β6Glu-Val	Hemoglobin SS disease Sickle Cell Anemia
Hb S β6Glu-Val	Hb C β6Glu-Lys	Hemoglobin SC disease



Piel F, *et al. Sci Rep*, 2013.
Bachir D and Galacteros F. Orphanet Encyclopedia, 2004.

In Deutschland lebende HbSC-Patienten stammen aus Ghana, Burkina-Faso, Togo, Kamerun, Nigeria - aber auch aus der Karibik und Nord-und Südamerika. Diese Form der Erkrankung wird zu Unrecht oft als "leichte Form der Sichelzell-Anämie" bezeichnet (keine ZNS-Infarkte, selten ATS, selten Niereninsuffizienz, höhere Lebenserwartung als HbSS-Patienten) Die Erkrankung ist weder leicht noch trifft der Begriff "Sichelzellanämie" zu: die Lebensqualität der HbSC-Patienten kann extrem beeinträchtigt werden durch Blindheit und / oder Taubheit und >90% der erwachsenen Patienten haben keine Anämie sondern Hb-Werte im unteren Bereich der Altersnorm.

Prospective Identification of Variables as Outcomes for Treatment (PIVOT)

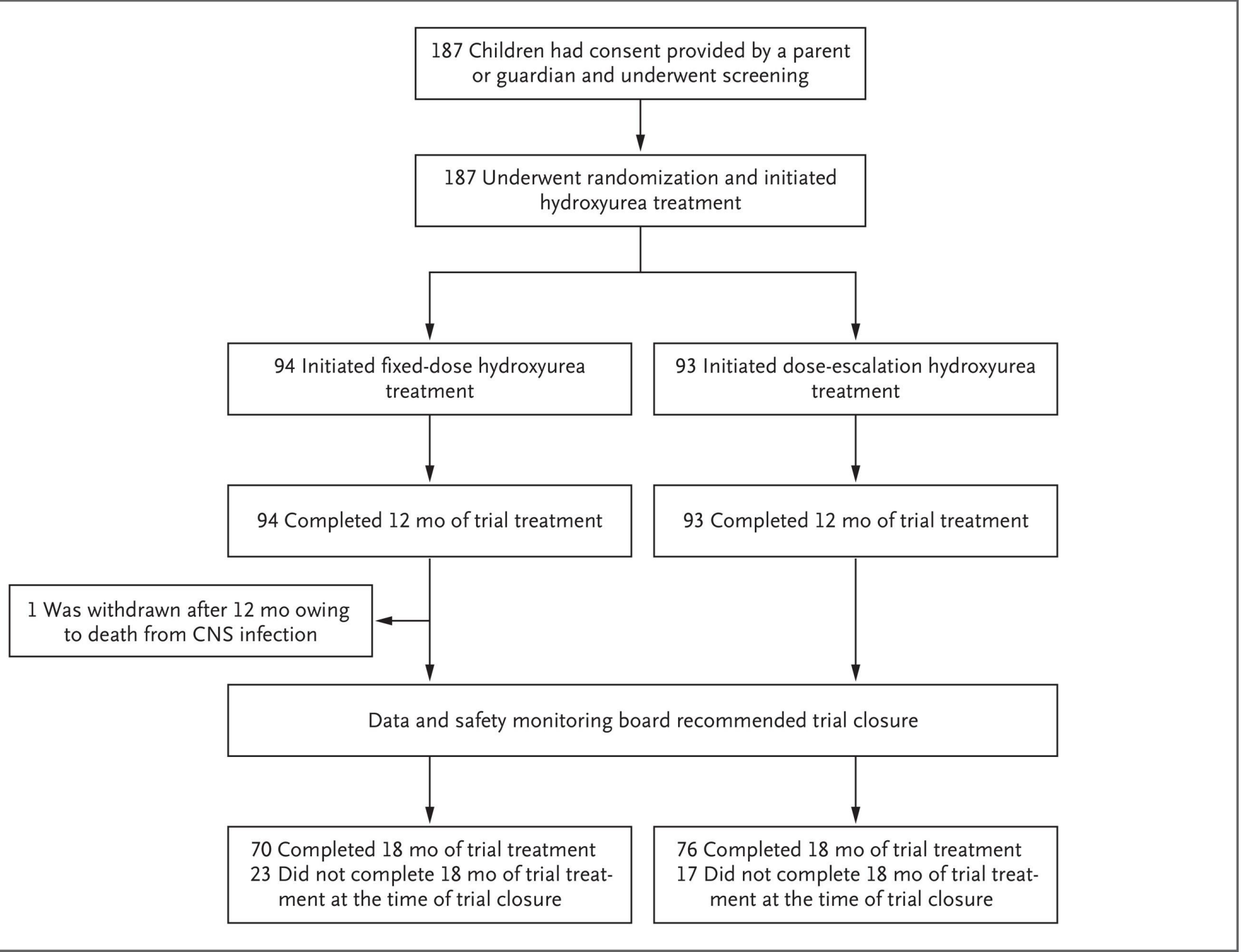
- Double-blind, placebo-controlled Phase 2 trial
- 100 children, 100 adults with HbSC disease
- Age 5-50 years
- 20 mg/kg hydroxyurea vs placebo for 12 months
- Two opportunities for dose escalation
- Open-label continuation if deemed safe

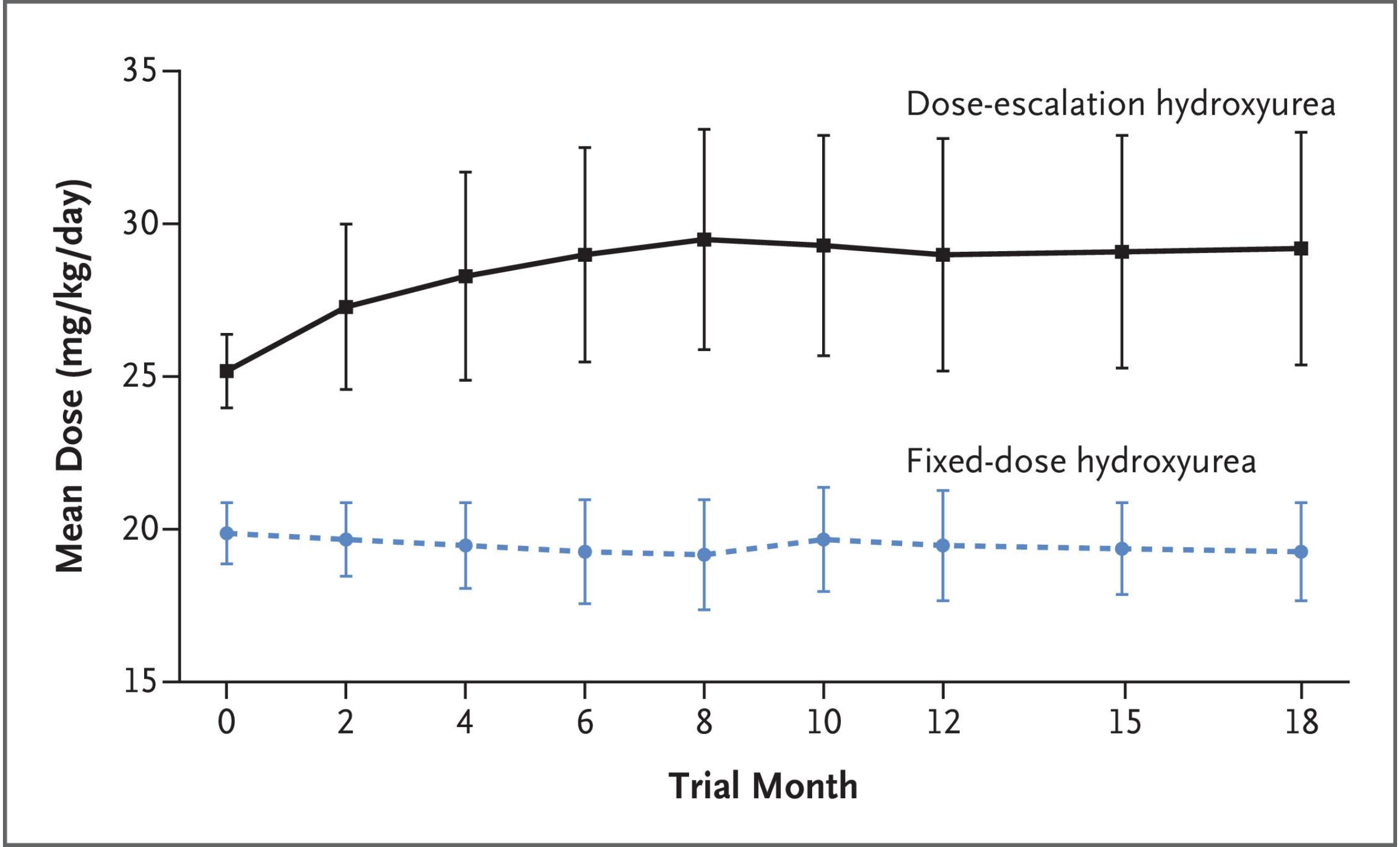
Cincinnati Children's
changing the outcome together

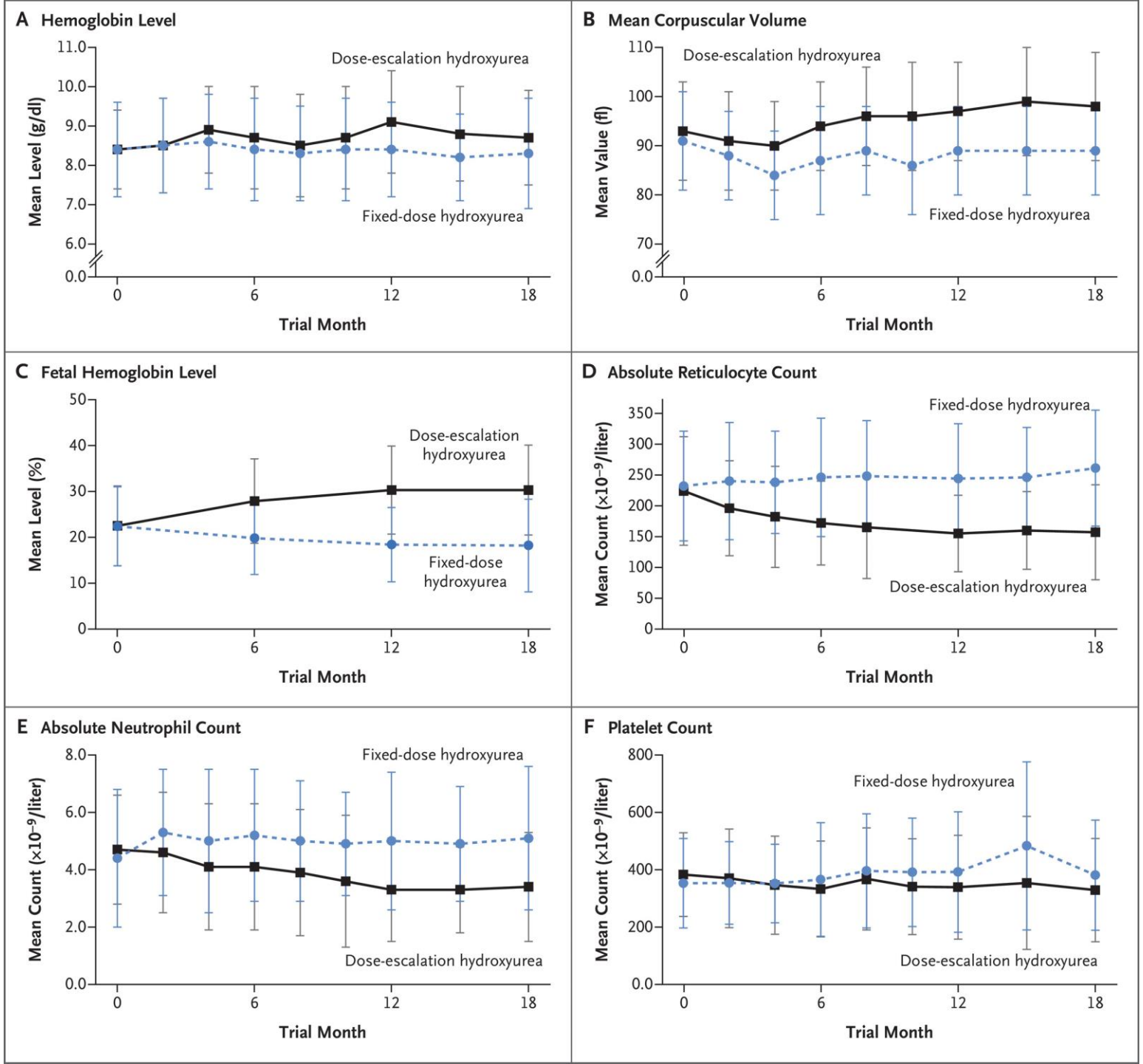
theravia

Study Endpoints

- Primary: dose-limiting toxicities in each treatment arm
  - Non-inferiority design (15% threshold)
  - Cytopenia and high hemoglobin (> 12.0 g/dL, ≥ 1.0 g/dL increase)
- Secondary: laboratory effects, clinical adverse events
  - CBC, reticulocytes, Hb quantification (HbF, S, C)
  - Sickle cell-related events, hospitalizations, malaria


187 Children had consent provided by a parent or guardian and underwent screening
187 Underwent randomization and initiated hydroxyurea treatment
94 Initiated fixed-dose hydroxyurea treatment
93 Initiated dose-escalation hydroxyurea treatment
94 Completed 12 mo of trial treatment
93 Completed 12 mo of trial treatment
1 Was withdrawn after 12 mo owing to death from CNS infection
Data and safety monitoring board recommended trial closure
70 Completed 18 mo of trial treatment
23 Did not complete 18 mo of trial treatment at the time of trial closure
76 Completed 18 mo of trial treatment
17 Did not complete 18 mo of trial treatment at the time of trial closure


Dose-escalation hydroxyurea
Fixed-dose hydroxyurea
Mean Dose (mg/kg/day)
35
30
25
20
15
0
2
4
6
8
10
12
15
18
Trial Month


A Hemoglobin Level
Mean Level (g/dl)
11.0
10.0
9.0
8.0
7.0
6.0
0.0
Dose-escalation hydroxyurea
Fixed-dose hydroxyurea
0
6
12
18
Trial Month
B Mean Corpuscular Volume
Mean Value (fl)
110
100
90
80
70
0.0
Dose-escalation hydroxyurea
Fixed-dose hydroxyurea
0
6
12
18
Trial Month
C Fetal Hemoglobin Level
Mean Level (%)
50
40
30
20
10
0
Dose-escalation hydroxyurea
Fixed-dose hydroxyurea
0
6
12
18
Trial Month
D Absolute Reticulocyte Count
Mean Count (×10⁻⁹/liter)
350
300
250
200
150
100
50
0
Fixed-dose hydroxyurea
Dose-escalation hydroxyurea
0
6
12
18
Trial Month
E Absolute Neutrophil Count
Mean Count (×10⁻⁹/liter)
8.0
6.0
4.0
2.0
0.0
Fixed-dose hydroxyurea
Dose-escalation hydroxyurea
0
6
12
18
Trial Month
F Platelet Count
Mean Count (×10⁻⁹/liter)
800
600
400
200
0.0
Fixed-dose hydroxyurea
Dose-escalation hydroxyurea
0
6
12
18
Trial Month

Summary and Conclusions

- The placebo-controlled Phase 2 PIVOT trial was successfully conducted in Ghana, where HbSC is prevalent and causes morbidity and mortality
- Hydroxyurea treatment at 20mg/kg/day was associated with more DLT than placebo, all asymptomatic, mild, transient and reversible
- Measurable benefits were observed in hematological parameters
- Associated with fewer clinical adverse events
- Hydroxyurea may provide effective disease-modifying therapy for HbSC

American Society of Hematology
Helping hematologists conquer blood diseases worldwide

66th ASH Annual Meeting
San Diego,
LBA-3, December 10, 2024

EXTENDED TREATMENT OF VENOUS THROMBOEMBOLISM WITH REDUCED- VS FULL-DOSE DIRECT ORAL ANTICOAGULANTS IN PATIENTS AT HIGH RISK OF RECURRENCE. THE RENOVE TRIAL

Francis Couturaud, M.D., Ph.D., Jeannot Schmidt, M.D., Ph.D., Olivier Sanchez, M.D., Ph.D., Alice Ballerie, M.D., Marie-Antoinette Sevestre, M.D., Ph.D., Nicolas Meneveau, M.D., Ph.D., Laurent Bertoletti, M.D., Ph.D., Jérôme Connault, M.D., Ph.D., Ygal Benhamou, M.D., Ph.D., Joël Constans, M.D., Ph.D., Thomas Quemeneur, M.D., François-Xavier Lapébie, M.D., Ph.D., Gilles Pernod, M.D., Ph.D., Gaël Picart, M.D., Antoine Elias, M.D., Ph.D., Caroline Doutrelon, M.D., Claire Neveux, M.D., Lina Khider, M.D., Ph.D., Pierre-Marie Roy, M.D., Ph.D., Stéphane Zuily, M.D., Ph.D., Nicolas Falvo, M.D., Philippe Lacroix, M.D., Ph.D., Joseph Emmerich, M.D., Ph.D., Isabelle Mahé, M.D., Ph.D., Julien Boileau, M.D., Azzedine Yaici, M.D., Sylvain Le Jeune, M.D., Dominique Stéphan, M.D., Ph.D., Pierre Plissonneau Duquene, M.D., Valérie Ray, M.D., Marc Danguy des Déserts, M.D., Rafik Belhadj-Chaidi, M.D., Bouchra Lamia, M.D., Ph.D., Gruel Yves, M.D., Ph.D., Emilie Presles, M.S., Philippe Girard, M.D., Cécile Tromeur, M.D., Ph.D., Moustapha Farès, M.D., Ph.D., Vincent Rothstein, M.D., Karine Lacut, M.D., Ph.D., Solen Melac, R.N., Sophie Barillot, M.S., Patrick Mismetti, M.D., Ph.D., Silvy Laporte, M.S., Ph.D., Dominique Mottier, M.D., Ph.D., Guy Meyer, M.D., and Christophe Leroyer, M.D., Ph.D., for the RENOVE Investigators*

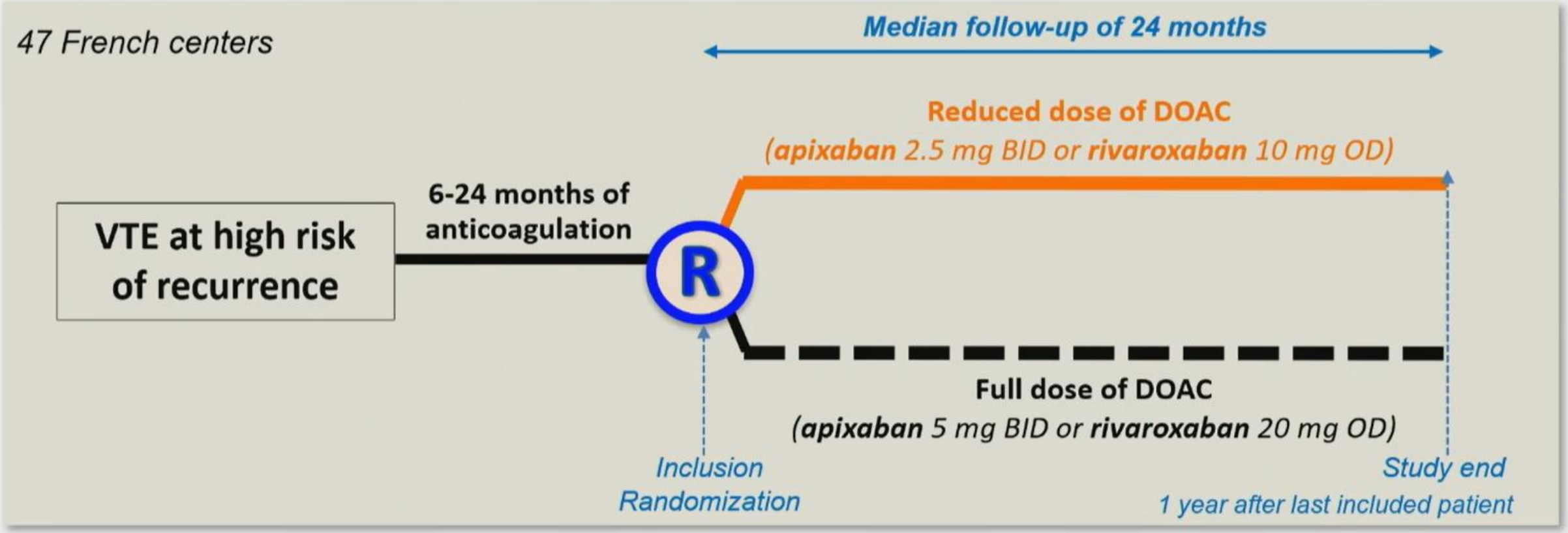
CLINICALTRIALS.GOV #: NCT03285438
EudraCT #: 2017-002433-31

RENOVE - trial

Design

- **Design**: academic, multicenter, randomized, open, blinded end-point (PROBE) trial.

- **Randomization**: central, stratified by center, DOAC (apixaban/rivaroxaban) and antiplatelet agent use.



Sponsor: Brest University Hospital, Brest, France
Funding: French Ministry of Health, PHRC N

1/ Stevens SM, et al. Chest 2021;160(6):e545-e608.
2/ Konstantinides SV, et al. Eur Heart J 2014;35(43):3033-69, 3069a-3069k.

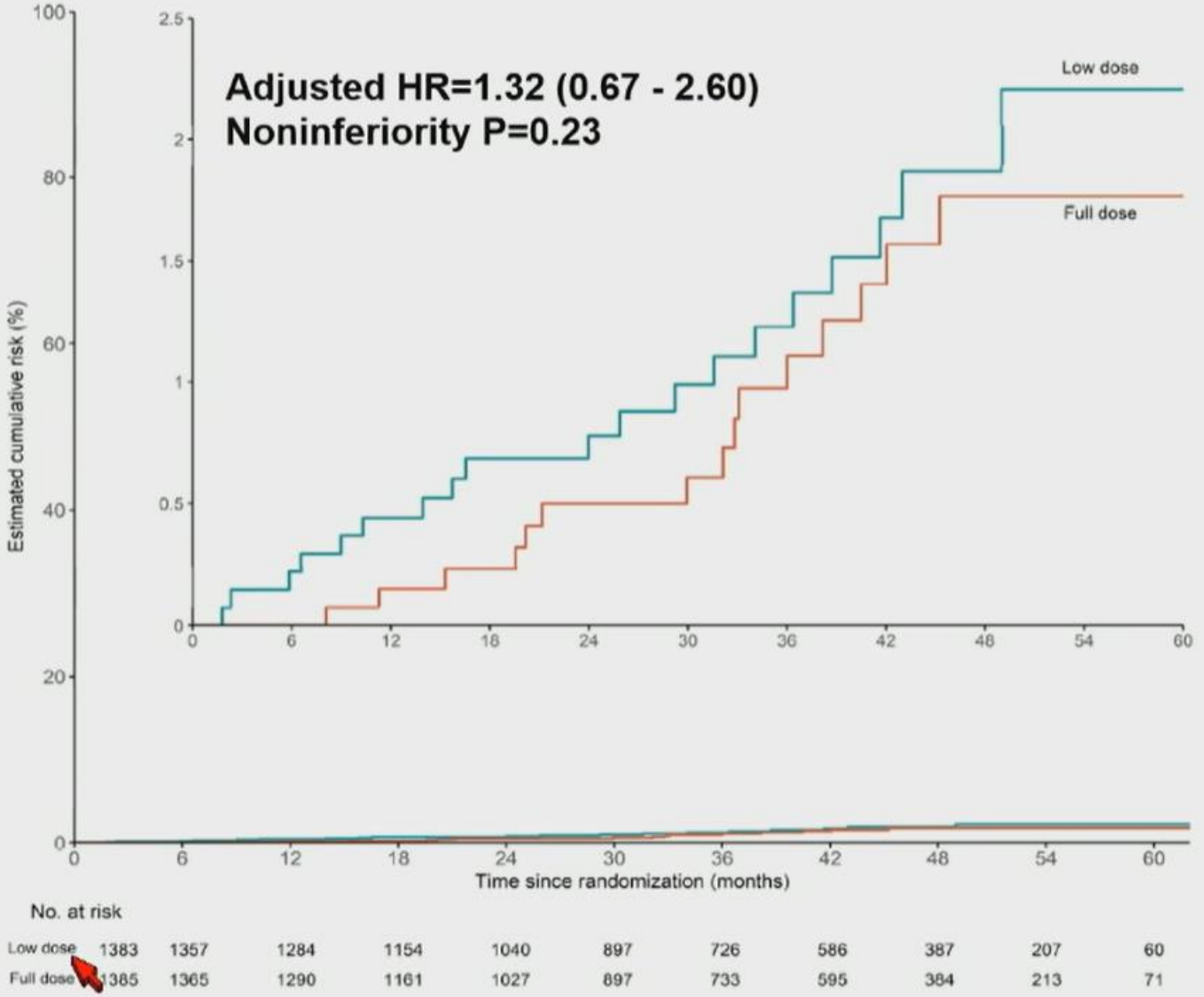
RENOVE - trial

Study population

	Reduced Dose (N=1383)	Full Dose (N=1385)
Age - mean (SD), yr	62.2 (14.3)	63.1 (14.3)
Female sex - no. (%)	489 (35.4)	481 (34.7)
BMI ≥30 kg/m² - no. (%)	428 (31.0)	416 (30.0)
Previous cancer (≥6 m before index event) - no. (%)	140 (10.1)	129 (9.3)
Family history of VTE - no. (%)	499 (36.1)	481 (34.7)
Characteristics of index event - no. (%)		
Symptomatic PE with or without DVT	1178 (85.4)	1192 (86.3)
PE at intermediate-high or high risk of death	230 (19.5)	247 (20.7)
Symptomatic isolated proximal DVT	201 (14.6)	189 (13.7)

RENOVE - trial

Cumulative incidence of symptomatic recurrent VTE during the treatment period (primary outcome)



RENOVE - trial

Secondary outcomes

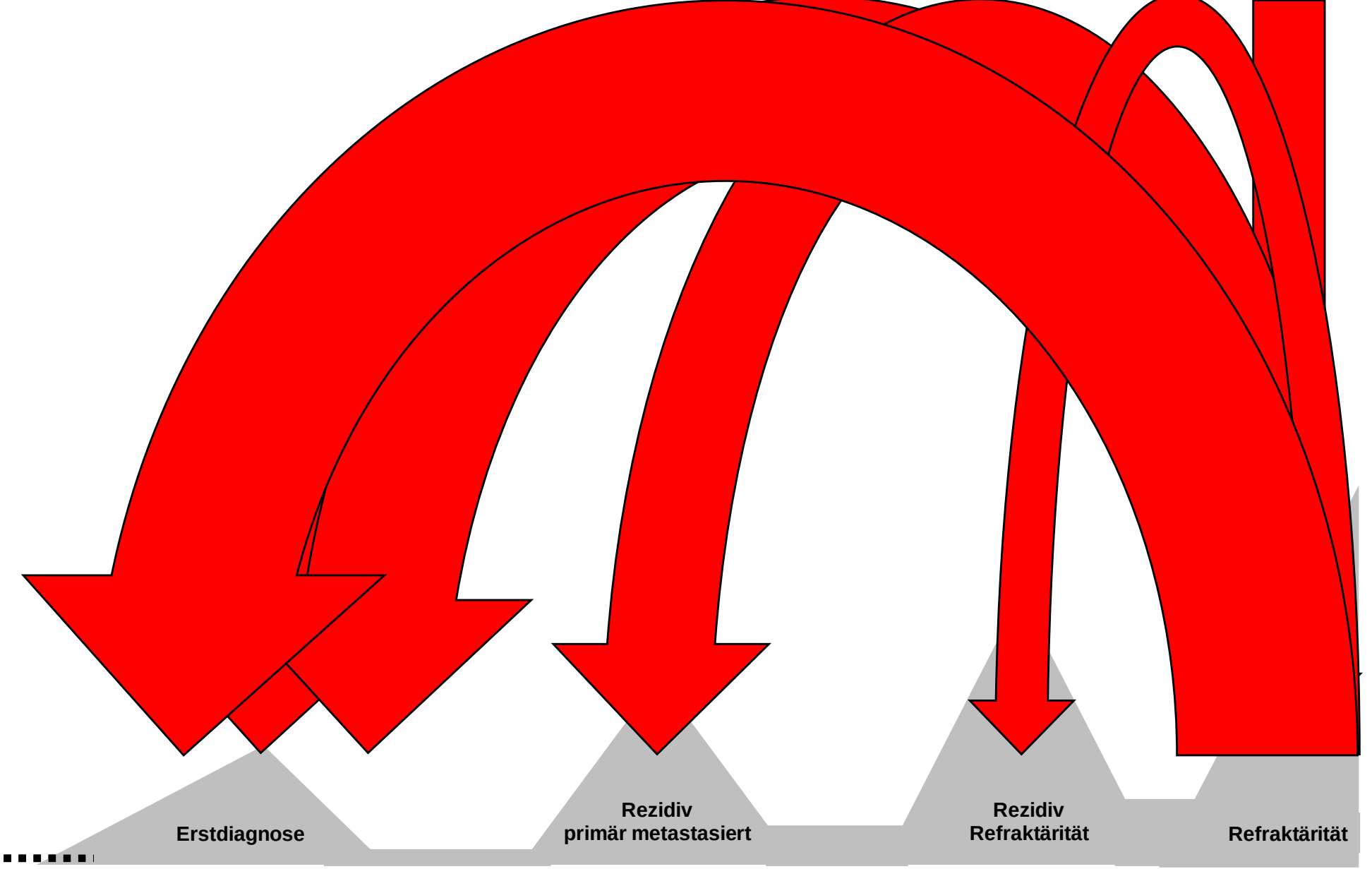
5-year cumulative incidence

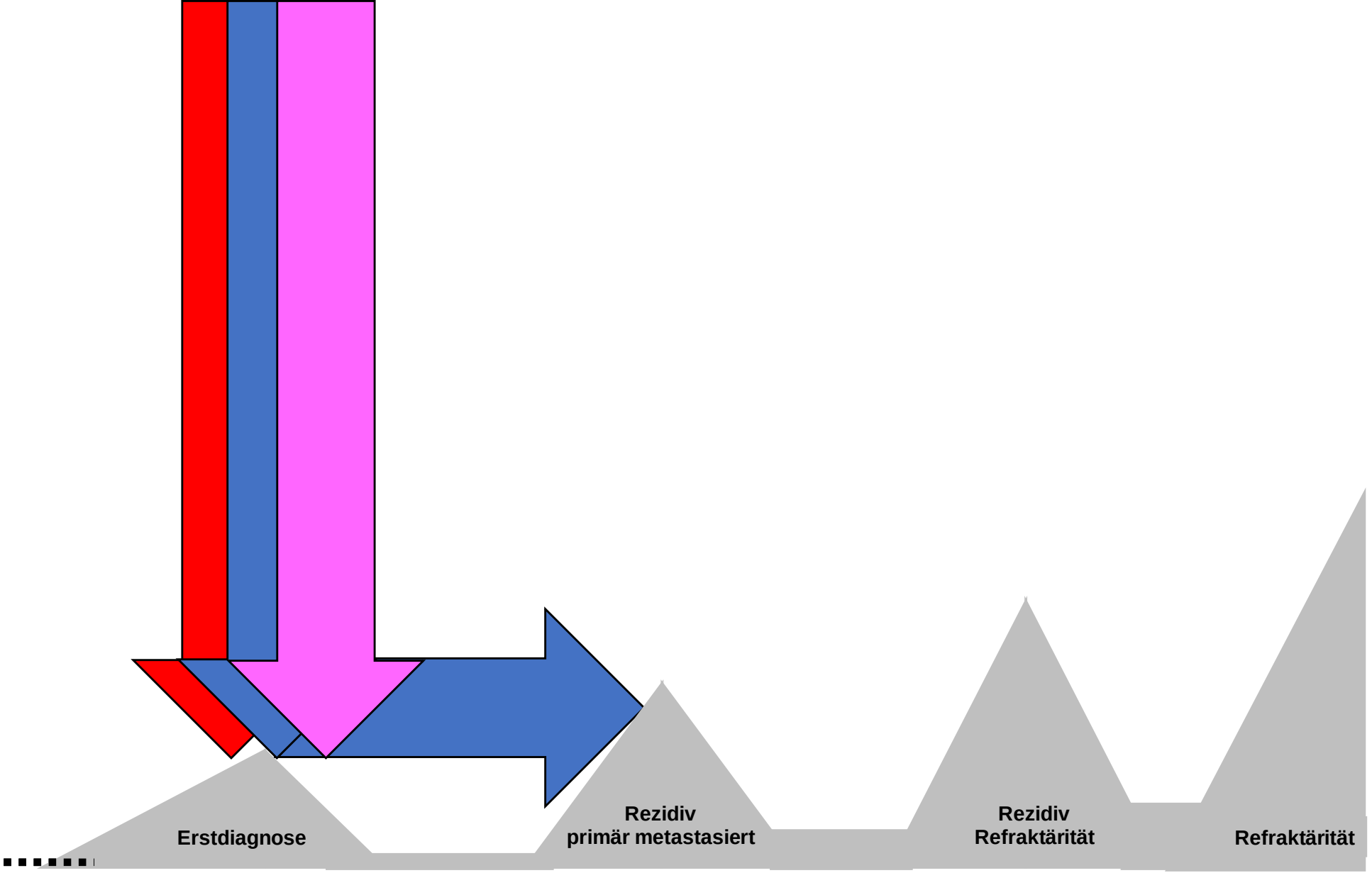
	Reduced Dose (N=1383)	Full Dose (N=1385)	Adjusted HR (95% CI)	P-Value
Key secondary outcomes				
Clinically relevant bleeding - no. (%)	**96** (9.9)	**154** (15.2)	**0.61** (0.48 - 0.79)	
Major bleeding	15 (2.1)	38 (4.0)	0.40 (0.22 - 0.72)	
Fatal	2	3		
Clinically relevant non major bleeding	84 (8.6)	118 (11.5)	0.70 (0.53 - 0.93)	
Composite (recurrent VTE, or clinically relevant bleeding) - no. (%)	**113** (11.8)	**166** (16.5)	**0.67** (0.53 - 0.86)	

RENOVE - trial

Conclusions

- DOAC dose reduction, in patients with VTE who need extended anticoagulation, **did not meet the study noninferiority** criteria.
- **Rates of recurrent VTE were low** in both the reduced- and full-dose groups.
- In the reduced-dose group, **clinically relevant bleeding** and **the composite** of recurrent VTE or clinically relevant bleeding **were lower** than in the full-dose group and did not appear to be offset by an increased risk of death or arterial thromboembolic events.
- These findings will be useful to **strengthen future guidelines and enrich shared-decision making process** for patients with VTE who need extended anticoagulation.

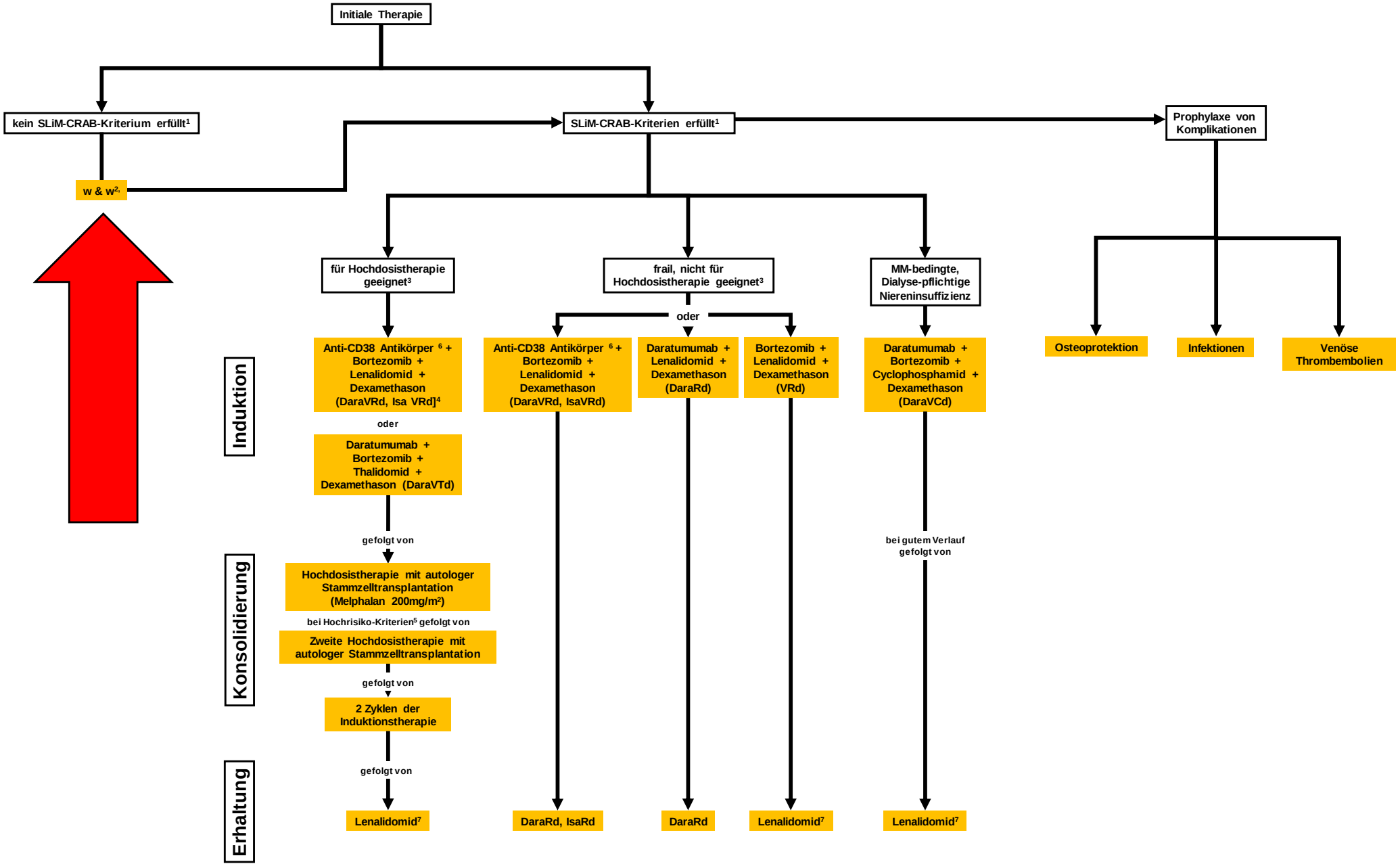

Erstdiagnose
Rezidiv
primär metastasiert
Rezidiv
Refraktärität
Refraktärität


Erstdiagnose
Rezidiv
primär metastasiert
Rezidiv
Refraktärität
Refraktärität

Multiples Myelom

Smouldering Myeloma

Diagnose	MGUS[1]	Schwelendes Myelom (smouldering myeloma)	Multiples Myelom		Solitäres Plasmozytom	Plasmazell-Leukämie
Kriterien						
Klonale Plasmazellen im Knochenmark	< 10 %	≥ 10 – 60 %	≥ 10 %	≥ 60 %	< 10 %	
	und	und / oder	und / oder	oder	und	
Monoklonales Protein im Serum	< 30 g / l	≥ 30 g / l	nachweisbar		nicht obligat nachweisbar	
	und	und / oder	und / oder		und	
Monoklonales Protein im Urin	< 500 mg / 24 h[3]	≥ 500 mg / 24 h[3]	nachweisbar		nicht obligat nachweisbar	
	und	und	und		und	
Endorganschäden[2]	nicht nachweisbar	nicht nachweisbar	nachweisbar		nicht nachweisbar	
	und				und	
	abnormaler freier Leichtketten-Quotient[3]			abnormaler freier Leichtketten-Quotient ≥ 100 und betroffene Leichtkette ≥ 100mg/L	singuläre Knochen-manifestation oder extramedulläre Manifestation in MRT / CT	≥ 2 x 10^9 / l klonale Plasmazellen im peripheren Blut
				oder	und	und / oder
				≥ 1 Herdbefund im MRT	klonale Plasmazellen bioptisch gesichert	≥ 5% klonale Plasmazellen im Differentialblutbild[4]


Initiale Therapie
kein SLiM-CRAB-Kriterium erfüllt[1]
SLiM-CRAB-Kriterien erfüllt[1]
Prophylaxe von Komplikationen
w & w[2]
für Hochdosistherapie geeignet[3]
frail, nicht für Hochdosistherapie geeignet[3]
MM-bedingte, Dialyse-pflichtige Niereninsuffizienz
oder
Osteoprotektion
Infektionen
Venöse Thrombembolien
Induktion
Anti-CD38 Antikörper [6] + Bortezomib + Lenalidomid + Dexamethason (DaraVRd, Isa VRd][4]
oder
Daratumumab + Bortezomib + Thalidomid + Dexamethason (DaraVTd)
Anti-CD38 Antikörper [6] + Bortezomib + Lenalidomid + Dexamethason (DaraVRd, IsaVRd)
Daratumumab + Lenalidomid + Dexamethason (DaraRd)
Bortezomib + Lenalidomid + Dexamethason (VRd)
Daratumumab + Bortezomib + Cyclophosphamid + Dexamethason (DaraVCd)
gefolgt von
Konsolidierung
Hochdosistherapie mit autologer Stammzelltransplantation (Melphalan 200mg/m²)
bei Hochrisiko-Kriterien[5] gefolgt von
Zweite Hochdosistherapie mit autologer Stammzelltransplantation
gefolgt von
2 Zyklen der Induktionstherapie
gefolgt von
bei gutem Verlauf gefolgt von
Erhaltung
Lenalidomid[7]
DaraRd, IsaRd
DaraRd
Lenalidomid[7]
Lenalidomid[7]

Phase 3 Randomized Study of Daratumumab Monotherapy Versus Active Monitoring in Patients With High-risk Smoldering Multiple Myeloma: Primary Results of the AQUILA Study

Meletios A Dimopoulos[1], Peter M Voorhees[2], Fredrik Schjesvold[3], Yael C Cohen[4], Vania Hungria[5], Irwindeep Sandhu[6], Jindriska Lindsay[7], Ross I Baker[8], Kenshi Suzuki[9], Hiroshi Kosugi[10], Mark-David Levin[11], Meral Beksac[12], Keith Stockerl-Goldstein[13], Albert Oriol[14], Gabor Mikala[15], Gonzalo Garate[16], Koen Theunissen[17], Ivan Spicka[18], Anne K Mylin[19], Sara Bringhen[20], Katarina Uttervall[21], Bartosz Pula[22], Eva Medvedova[23], Andrew J Cowan[24], Philippe Moreau[25], Maria-Victoria Mateos[26], Hartmut Goldschmidt[27], Tahamtan Ahmadi[28], Linlin Sha[29], Els Rousseau[30], Liang Li[29], Robyn M Dennis[31], Robin Carson[32], S Vincent Rajkumar[33]

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Presented by MA Dimopoulos at the 66th American Society of Hematology (ASH) Annual Meeting & Exposition; December 7-10, 2024; San Diego, CA, USA

AQUILA: Study Design

AQUILA enrollment period: December 2017 to May 2019 at 124 sites in 23 countries

Screening

Key eligibility criteria:

- ≥18 years of age
- Confirmed SMM diagnosis (per IMWG criteria) for ≤5 years
- ECOG PS score of 0 or 1
- Clonal BMPCs ≥10% and ≥1 of the following risk factors:
  - Serum M-protein ≥30 g/L
  - IgA SMM
  - Immunoparesis with reduction of 2 uninvolved Ig isotypes
  - Serum involved:uninvolved FLC ratio ≥8 and <100
  - Clonal BMPCs >50% to <60%

All patients were required to have CT/PET-CT and MRI imaging during screening

1:1 randomization (N = 390)

Stratified by number of risk factors[a] for progression to MM (<3 vs ≥3)

Treatment/active monitoring phase

DARA monotherapy

1800 mg SC[b] QW Cycles 1-2, Q2W Cycles 3-6, Q4W thereafter in 28-day cycles until 39 cycles/36 months*

Active monitoring

No disease-specific treatment, with AE monitoring up to 36 months*

*Or confirmed disease progression (whichever occurred first).

Follow-up phase

- **Efficacy follow-up until progression by SLiM-CRAB**
- **Survival follow-up every 6 months until end of study**

Primary endpoint:

- PFS by IRC per IMWG SLiM-CRAB criteria[c]

Key secondary endpoints:

- ORR
- Time to first-line treatment for MM
- PFS on first-line treatment for MM
- Overall survival

Disease evaluation schedule

- Laboratory efficacy – Every 12 weeks by central lab until disease progression
- Imaging (CT/PET-CT, MRI) – Yearly (central review)
- Bone marrow – At least every 2 years

IMWG, International Myeloma Working Group; ECOG PS, Eastern Cooperative Oncology Group performance status; BMPC, bone marrow plasma cell; FLC, free light chain; CT, computed tomography; MRI, magnetic resonance imaging; QW, weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; AE, adverse event; IRC, independent review committee; ORR, overall response rate. [a]Risk factors included involved:uninvolved FLC ratio ≥8 (yes vs no), serum M-protein ≥30 g/L (yes vs no), IgA SMM (yes vs no), immunoparesis (reduction of 2 uninvolved immunoglobulins vs other), or clonal BMPCs (>50% to <60% vs ≤50%). [b]DARA SC (1800 mg co-formulated with recombinant human hyaluronidase PH20 [rHuPH20; 2,000 U/mL; ENHANZE® drug delivery technology; Halozyme, Inc.]). [c]PFS was defined as duration from randomization to initial documented progression to active MM or death due to any cause, whichever occurred first.

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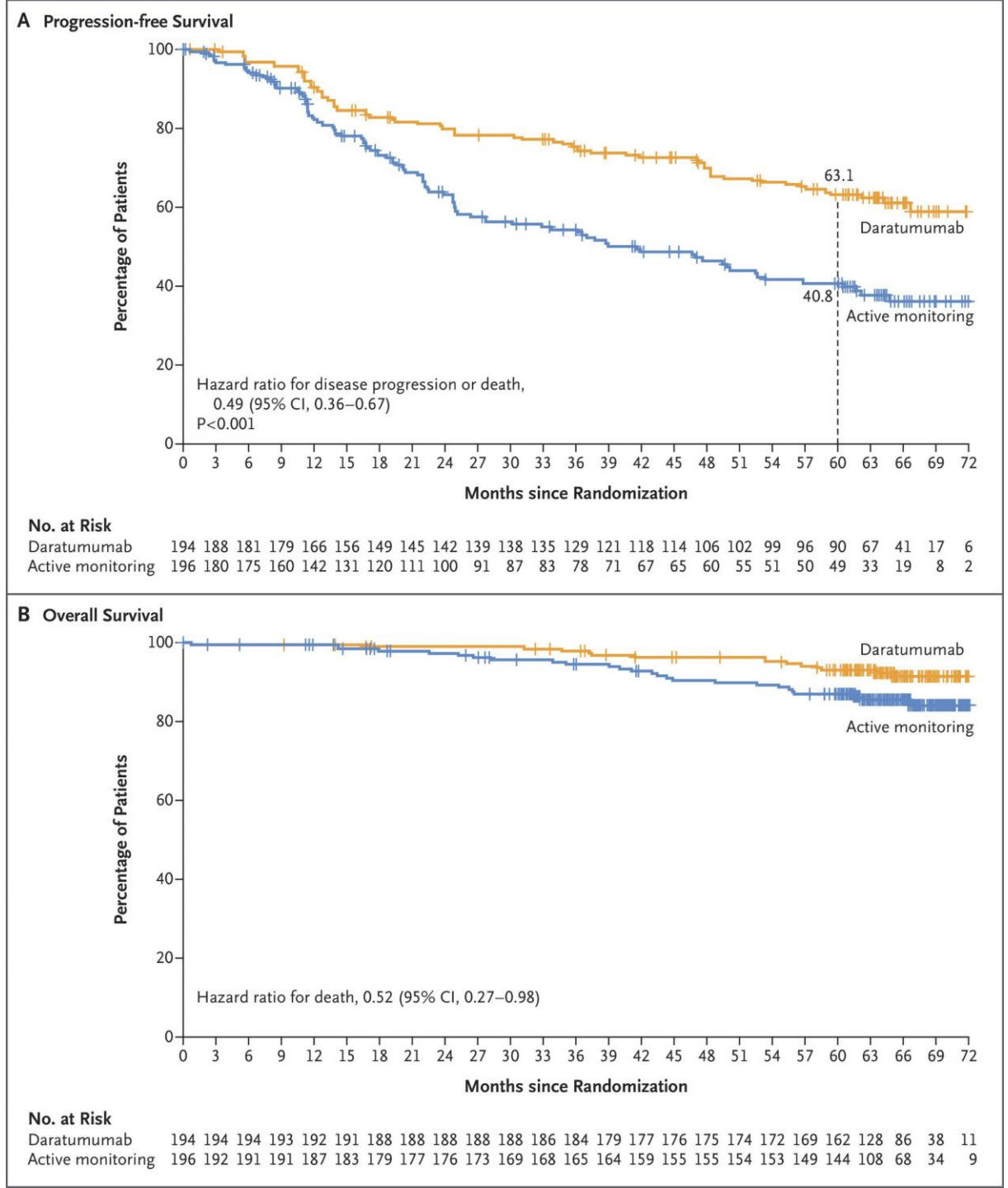
A Progression-free Survival
Percentage of Patients
100
80
60
40
20
0
63.1
Daratumumab
40.8
Active monitoring
Hazard ratio for disease progression or death,
0.49 (95% CI, 0.36–0.67)
P<0.001
0 3 6 9 12 15 18 21 24 27 30 33 36 39 42 45 48 51 54 57 60 63 66 69 72
Months since Randomization
No. at Risk
Daratumumab 194 188 181 179 166 156 149 145 142 139 138 135 129 121 118 114 106 102 99 96 90 67 41 17 6
Active monitoring 196 180 175 160 142 131 120 111 100 91 87 83 78 71 67 65 60 55 51 50 49 33 19 8 2
B Overall Survival
Percentage of Patients
100
80
60
40
20
0
Daratumumab
Active monitoring
Hazard ratio for death, 0.52 (95% CI, 0.27–0.98)
0 3 6 9 12 15 18 21 24 27 30 33 36 39 42 45 48 51 54 57 60 63 66 69 72
Months since Randomization
No. at Risk
Daratumumab 194 194 194 193 192 191 188 188 188 188 188 186 184 179 177 176 175 174 172 169 162 128 86 38 11
Active monitoring 196 192 191 191 187 183 179 177 176 173 169 168 165 164 159 155 155 154 153 149 144 108 68 34 9

AQUILA: AEs of Special Interest

Event, n (%)	DARA (n = 193)	Active monitoring (n = 196)
Systemic infusion-related reactions	32 (16.6)	–
Grade 3 or 4	2 (1.0)	–
Local injection-site reactions	53 (27.5)	–
Grade 3 or 4	0	–
Second primary malignancies	18 (9.3)	20 (10.2)
Noncutaneous	9 (4.7)	11 (5.6)
Cutaneous	7 (3.6)	3 (1.5)
Hematologic	3 (1.6)	6 (3.1)

Event, n (%)	DARA (n = 193)	Active monitoring (n = 196)
Cytopenias (all grades)	23 (11.9)	24 (12.2)
Neutropenia	13 (6.7)	5 (2.6)
Anemia	9 (4.7)	19 (9.7)
Thrombocytopenia	4 (2.1)	3 (1.5)
Lymphopenia	3 (1.6)	1 (0.5)
Grade 3 or 4 infections	31 (16.1)	9 (4.6)
Number of grade 3 or 4 infections	37	11
Recovered or resolved	35 (94.6)	8 (72.7)
Median duration of infection	9 days	5 days

- **Grade 3 or 4 infections were of short duration, and the majority recovered or resolved**
- **Comparable frequency of second primary malignancies**

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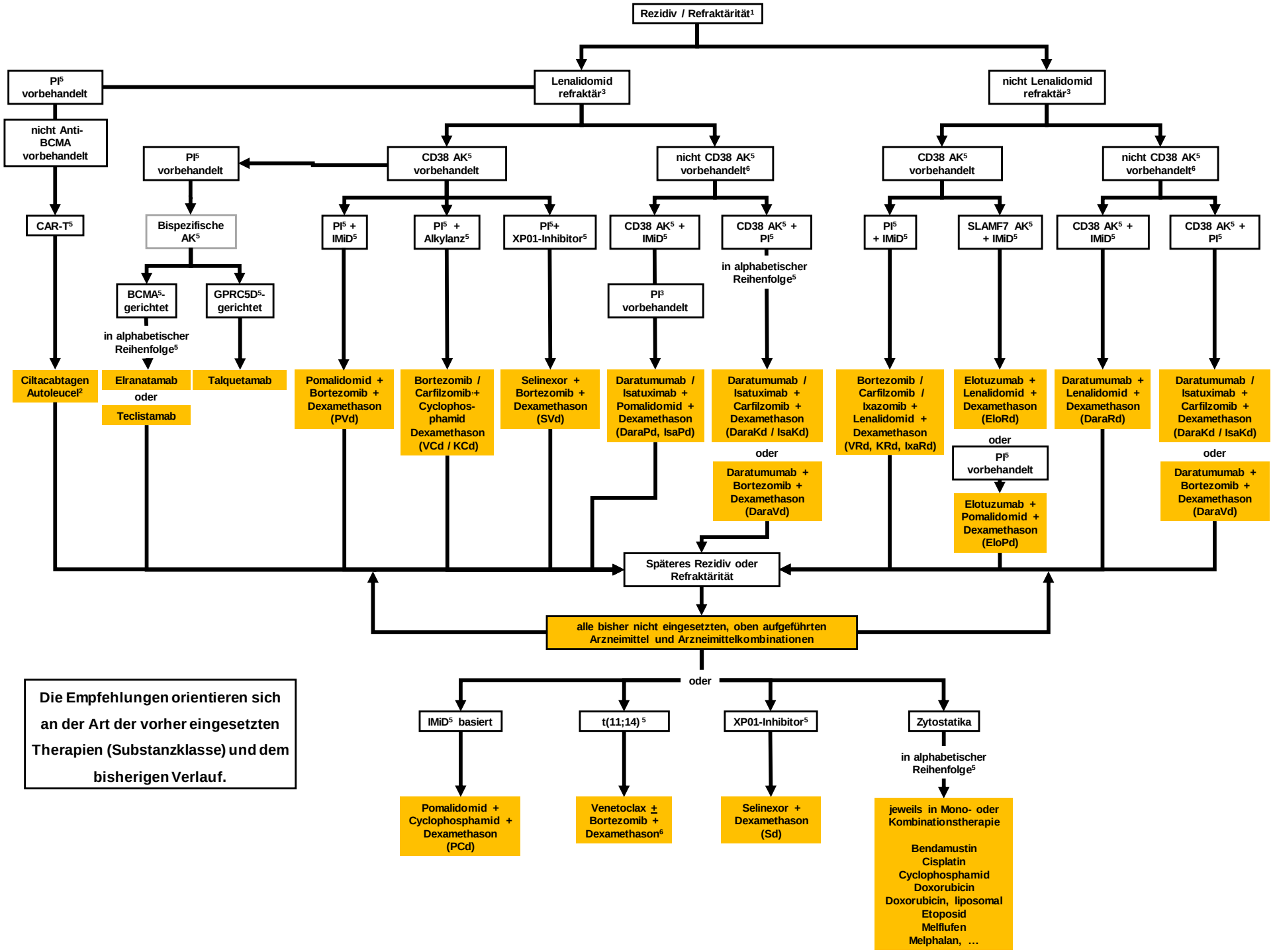
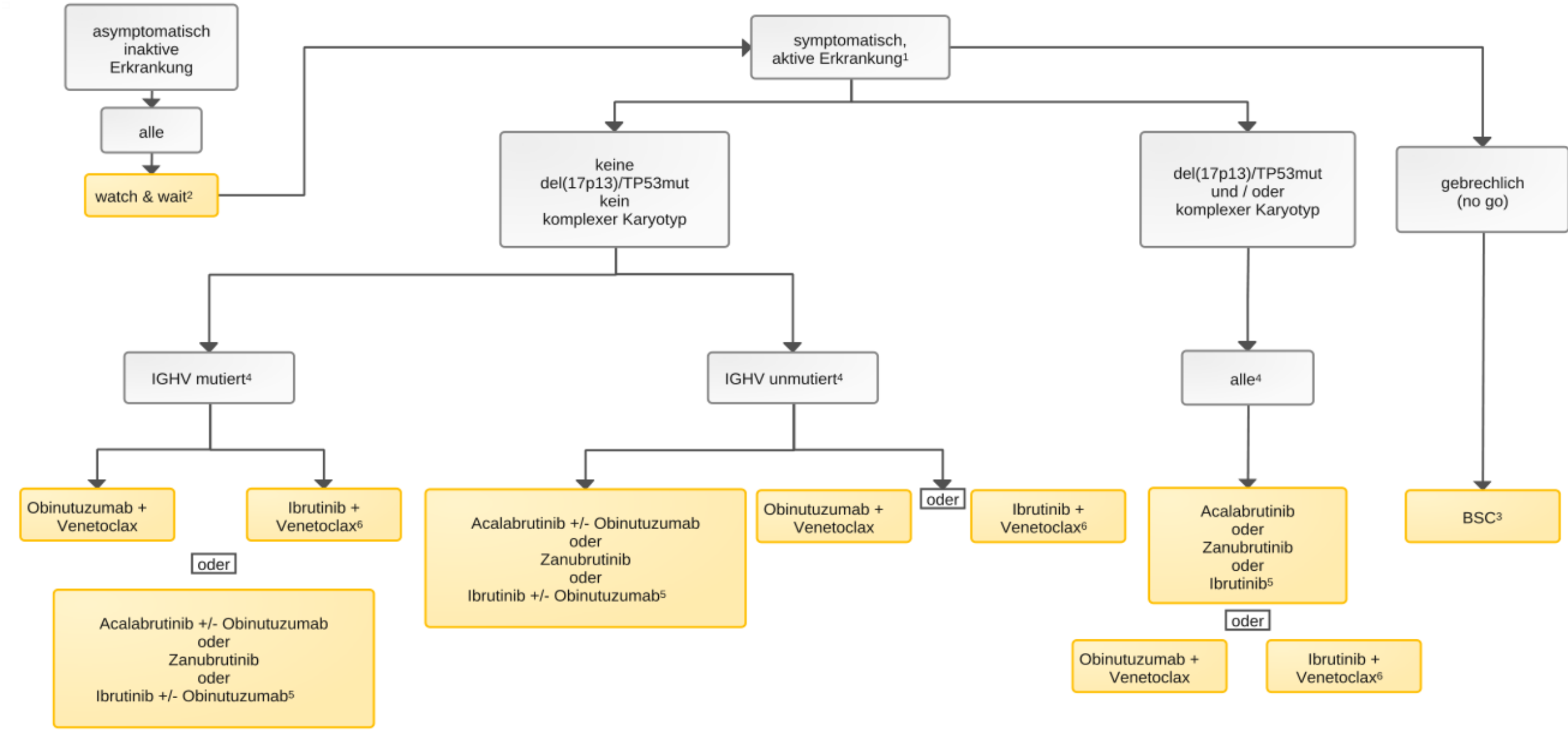

Rezidiv / Refraktärität[1]
PI[5] vorbehandelt
Lenalidomid refraktär[3]
nicht Lenalidomid refraktär[3]
nicht Anti-BCMA vorbehandelt
PI[5] vorbehandelt
CD38 AK[5] vorbehandelt
nicht CD38 AK[5] vorbehandelt[6]
CD38 AK[5] vorbehandelt
nicht CD38 AK[5] vorbehandelt[6]
CAR-T[5]
Bispezifische AK[5]
PI[5] + IMiD[5]
PI[5] + Alkylanz[5]
PI[5]+ XP01-Inhibitor[5]
CD38 AK[5] + IMiD[5]
CD38 AK[5] + PI[5]
PI[5] + IMiD[5]
SLAMF7 AK[5] + IMiD[5]
CD38 AK[5] + IMiD[5]
CD38 AK[5] + PI[5]
BCMA[5]-gerichtet
GPRC5D[5]-gerichtet
in alphabetischer Reihenfolge[5]
PI[3] vorbehandelt
in alphabetischer Reihenfolge[5]
Ciltacabtagen Autoleucel[2]
Elranatamab
oder
Teclistamab
Talquetamab
Pomalidomid + Bortezomib + Dexamethason (PVd)
Bortezomib / Carfilzomib + Cyclophos-phamid Dexamethason (VCd / KCd)
Selinexor + Bortezomib + Dexamethason (SVd)
Daratumumab / Isatuximab + Pomalidomid + Dexamethason (DaraPd, IsaPd)
Daratumumab / Isatuximab + Carfilzomib + Dexamethason (DaraKd / IsaKd)
oder
Daratumumab + Bortezomib + Dexamethason (DaraVd)
Bortezomib / Carfilzomib / Ixazomib + Lenalidomid + Dexamethason (VRd, KRd, IxaRd)
Elotuzumab + Lenalidomid + Dexamethason (EloRd)
oder
PI[5] vorbehandelt
Elotuzumab + Pomalidomid + Dexamethason (EloPd)
Daratumumab + Lenalidomid + Dexamethason (DaraRd)
Daratumumab / Isatuximab + Carfilzomib + Dexamethason (DaraKd / IsaKd)
oder
Daratumumab + Bortezomib + Dexamethason (DaraVd)
Späteres Rezidiv oder Refraktärität
alle bisher nicht eingesetzten, oben aufgeführten Arzneimittel und Arzneimittelkombinationen
oder
IMiD[5] basiert
t(11;14) [5]
XP01-Inhibitor[5]
Zytostatika
in alphabetischer Reihenfolge[5]
Pomalidomid + Cyclophosphamid + Dexamethason (PCd)
Venetoclax ± Bortezomib + Dexamethason[6]
Selinexor + Dexamethason (Sd)
jeweils in Mono- oder Kombinationstherapie
Bendamustin
Cisplatin
Cyclophosphamid
Doxorubicin
Doxorubicin, liposomal
Etoposid
Melflufen
Melphalan, ...
Die Empfehlungen orientieren sich an der Art der vorher eingesetzten Therapien (Substanzklasse) und dem bisherigen Verlauf.

Erstlinientherapie der CLL



AMPLIFY: Studiendesign

TN CLL (N=867)

Key inclusion criteria
- Age ≥18 years
- TN CLL requiring treatment per iwCLL 2018 criteria[1]
- Without del(17p) or *TP53*[a]
- ECOG PS ≤2

Key exclusion criteria
- CIRS-Geriatric >6
- Significant cardiovascular disease

Stratification
- Age (>65 vs ≤65 years)
- IGHV mutational status
- Rai stage (≥3 vs <3)
- Geographic region

AMPLIFY: randomized, multicenter, open-label, Ph 3 trial

RANDOMIZE 1:1:1

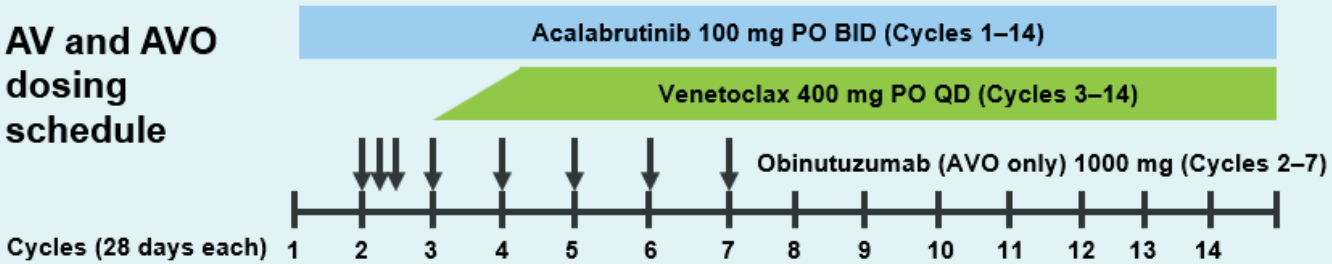
- AV (14 cycles)
- AVO (14 cycles)
- FCR/BR (6 cycles)

***Crossover** not built into protocol*

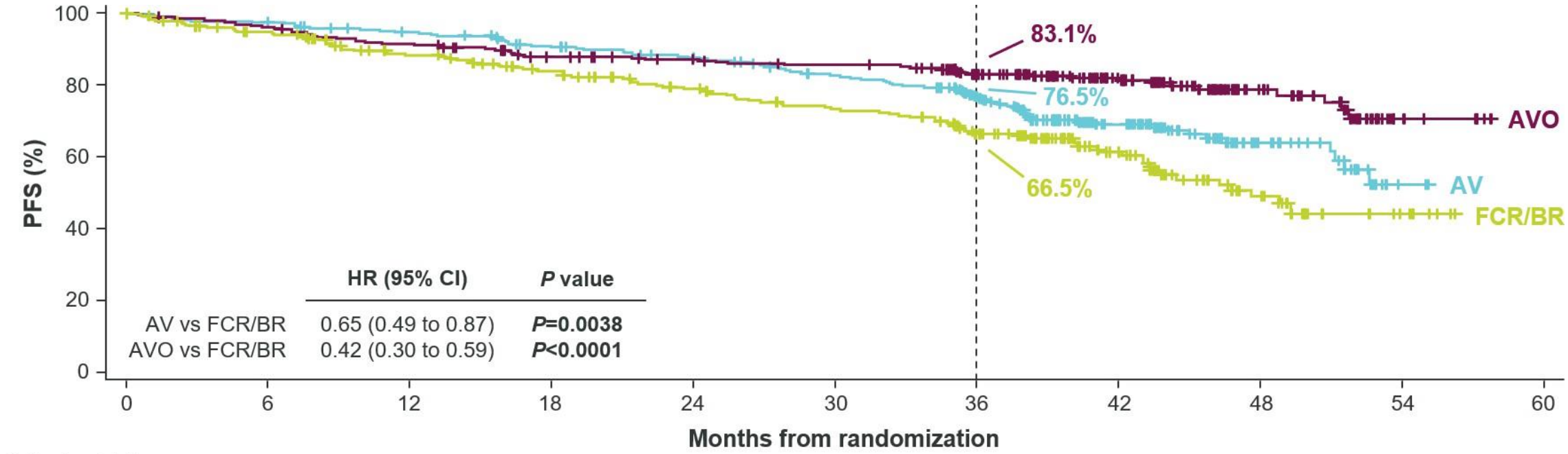
Primary endpoint: IRC-assessed PFS (AV vs FCR/BR)

If primary endpoint met, secondary endpoints tested in fixed sequential hierarchy:
1) IRC-PFS (AVO vs FCR/BR)
2) uMRD (AV vs FCR/BR)
3) uMRD (AVO vs FCR/BR)
4) OS (AV vs FCR/BR)
5) OS (AVO vs FCR/BR)

AV and AVO dosing schedule



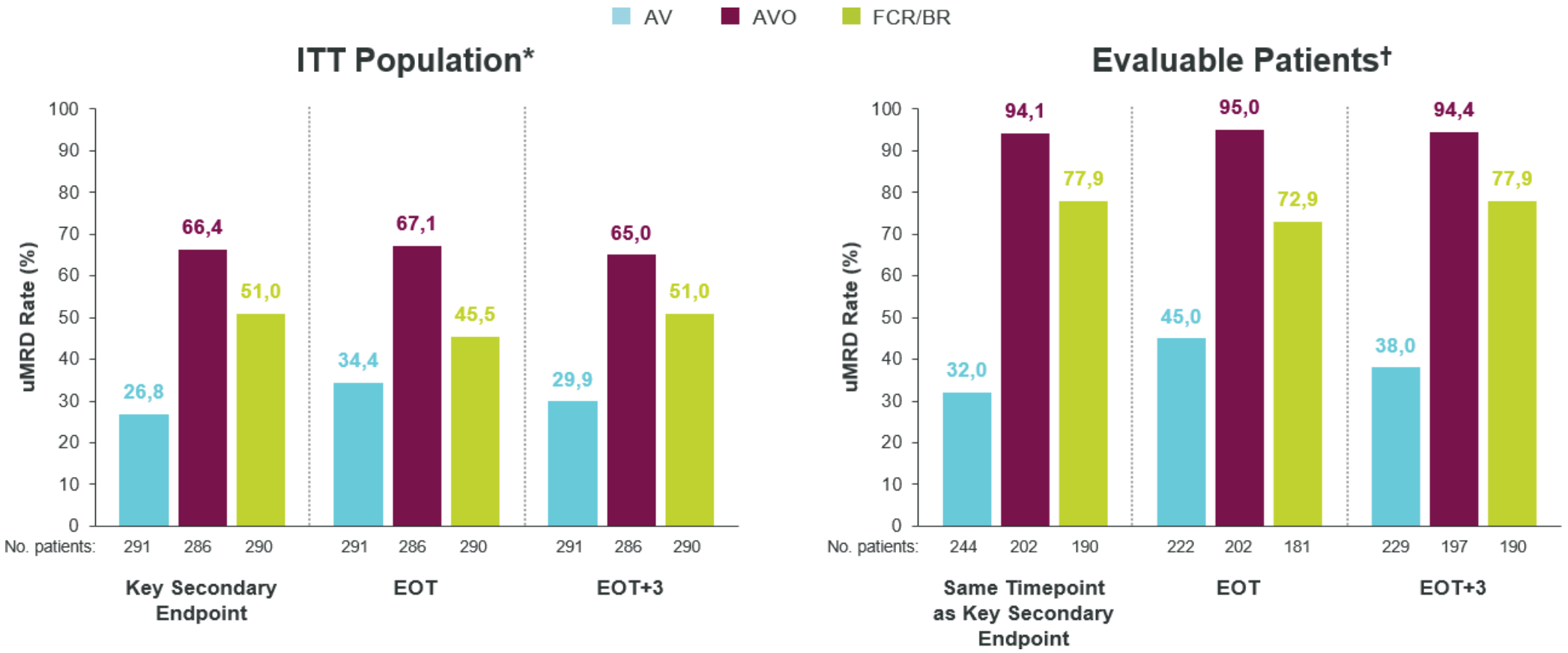
AMPLIFY: Primärer Endpunkt: PFS



Patients at risk

AV	291	282	269	251	237	219	177	102	35	3	0
AVO	286	272	258	237	225	219	191	116	51	7	0
FCR/BR	290	236	208	189	170	154	127	66	28	6	0

AMPLIFY: Minimal residual disease (MRD) nach Durchflusszytometrie

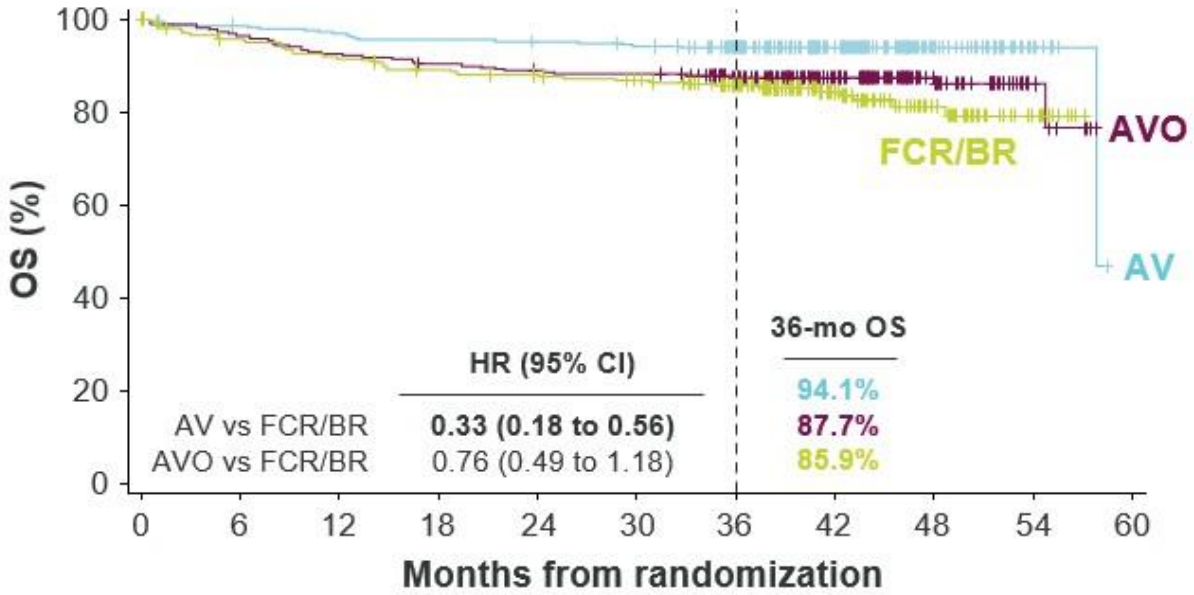


AMPLIFY: Nebenwirkungen: alle

	AV (n=291)		AVO (n=284)		FCR/BR (n=259)	
Preferred Term	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Neutropenia	90 (30.9)	78 (26.8)	114 (40.1)	100 (35.2)	99 (38.2)	84 (32.4)
Diarrhea	95 (32.6)	5 (1.7)	103 (36.3)	4 (1.4)	28 (10.8)	1 (0.4)
Headache	102 (35.1)	4 (1.4)	80 (28.2)	1 (0.4)	20 (7.7)	1 (0.4)
Nausea	43 (14.8)	0	62 (21.8)	2 (0.7)	93 (35.9)	0
Infusion-related reaction	0	0	56 (19.7)	6 (2.1)	85 (32.8)	9 (3.5)
COVID-19	55 (18.9)	8 (2.7)	58 (20.4)	19 (6.7)	6 (2.3)	4 (1.5)
Pyrexia	17 (5.8)	1 (0.3)	44 (15.5)	5 (1.8)	47 (18.1)	6 (2.3)
Contusion	40 (13.7)	0	44 (15.5)	0	4 (1.5)	0
Neutrophil count decreased	18 (6.2)	16 (5.5)	29 (10.2)	29 (10.2)	27 (10.4)	22 (8.5)
Thrombocytopenia	13 (4.5)	4 (1.4)	24 (8.5)	17 (6.0)	33 (12.7)	22 (8.5)
COVID-19 pneumonia	21 (7.2)	16 (5.5)	35 (12.3)	33 (11.6)	7 (2.7)	7 (2.7)
Febrile neutropenia	5 (1.7)	5 (1.7)	7 (2.5)	7 (2.5)	24 (9.3)	24 (9.3)
Anemia	20 (6.9)	11 (3.8)	13 (4.6)	6 (2.1)	25 (9.7)	17 (6.6)

AMPLIFY: Ergebnisse

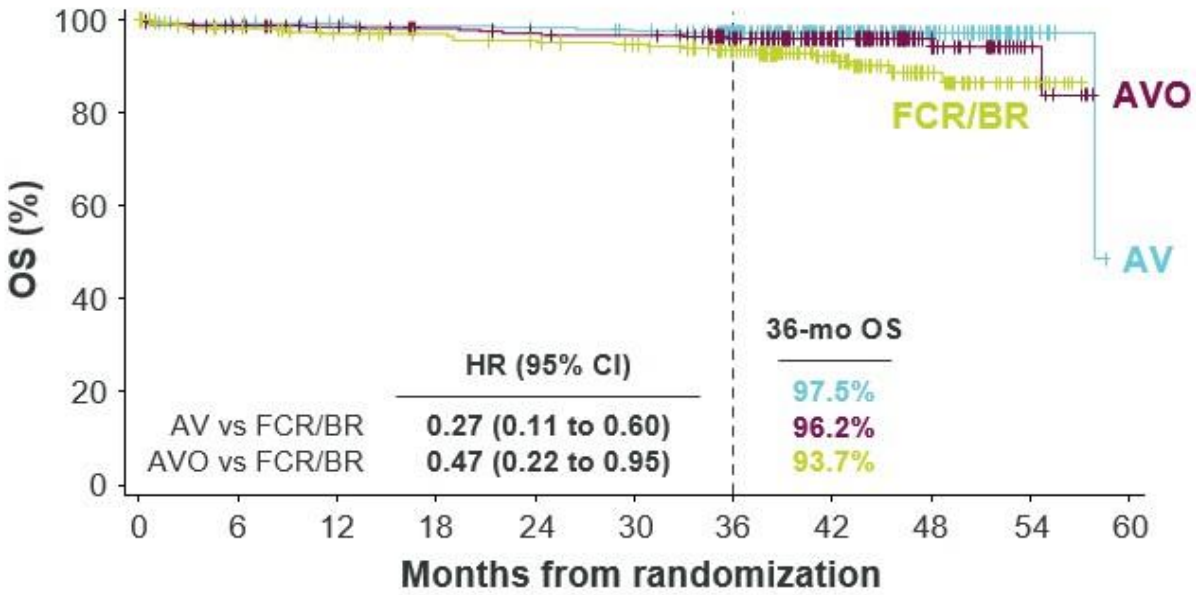
With AV vs FCR/BR



Patients at risk

AV	291	286	281	277	275	270	233	142	58	10	0
AVO	286	276	265	257	252	250	223	143	64	10	0
FCR/BR	290	247	236	228	223	217	182	98	45	13	0

With AV and AVO vs FCR/BR (COVID-19 Deaths Censored)



Patients at risk

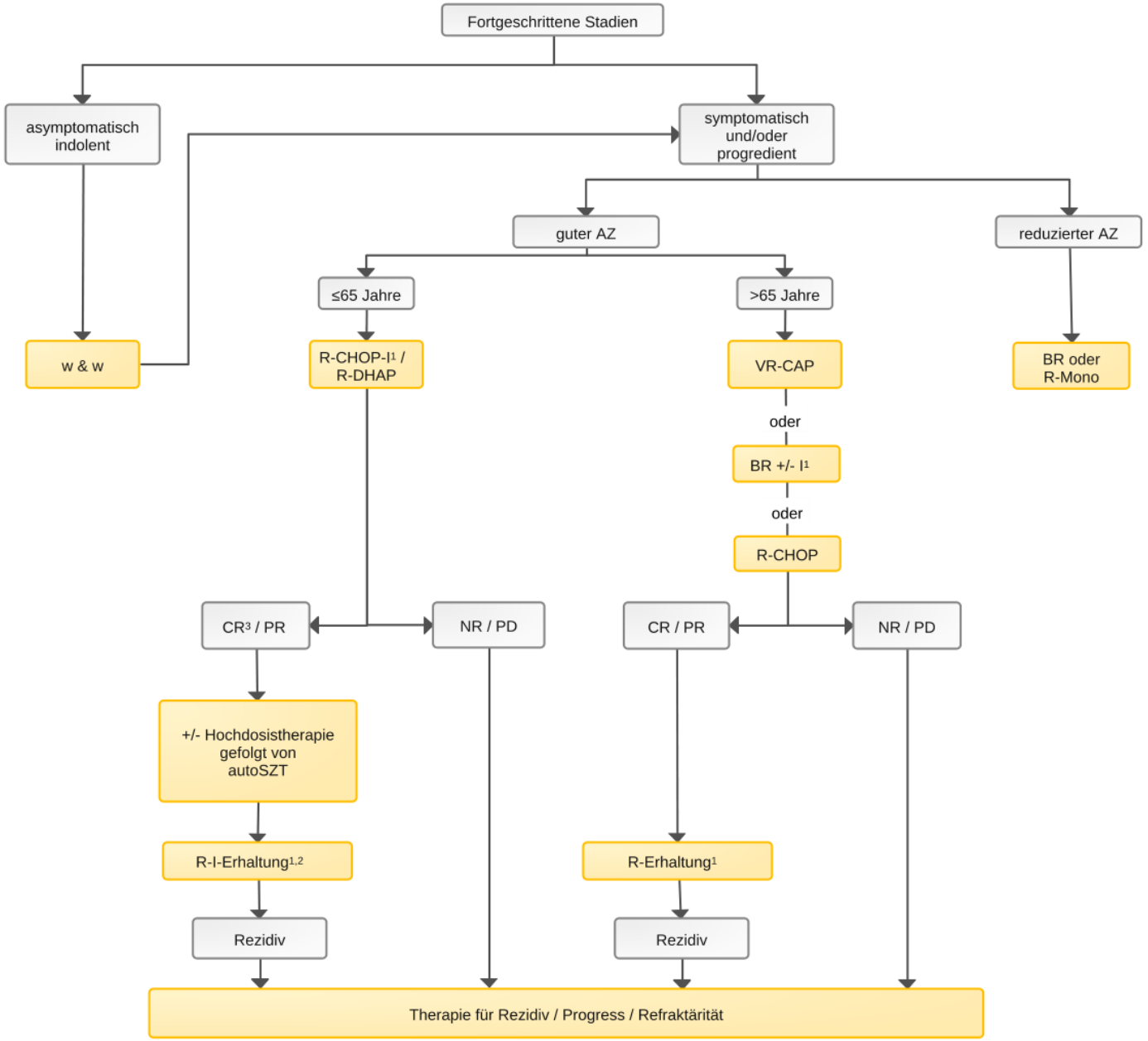
AV	291	286	281	277	275	270	233	142	58	10	0
AVO	286	276	265	257	252	250	223	143	64	10	0
FCR/BR	290	247	236	228	223	217	182	98	45	13	0

COVID-19 deaths: 10 (AV), 25 (AVO), 21 (FCR/BR)

ITT population

Therapiealgorithmus für die Erstlinientherapie

Mantelzell-Lymphom

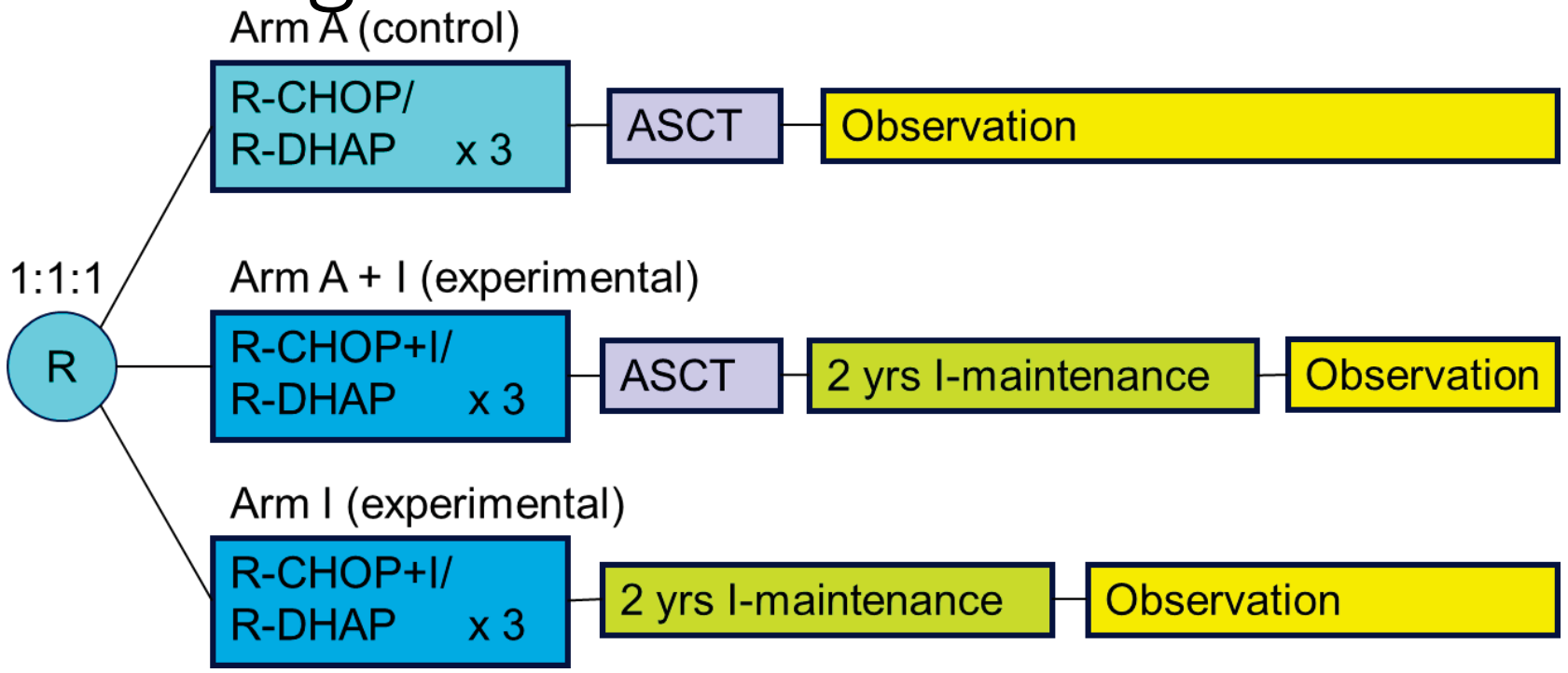


TRIANGLE: Trial Design

- MCL patients
- previously untreated
- stage II-IV
- younger than 66 years
- suitable for HA and ASCT
- ECOG 0-2

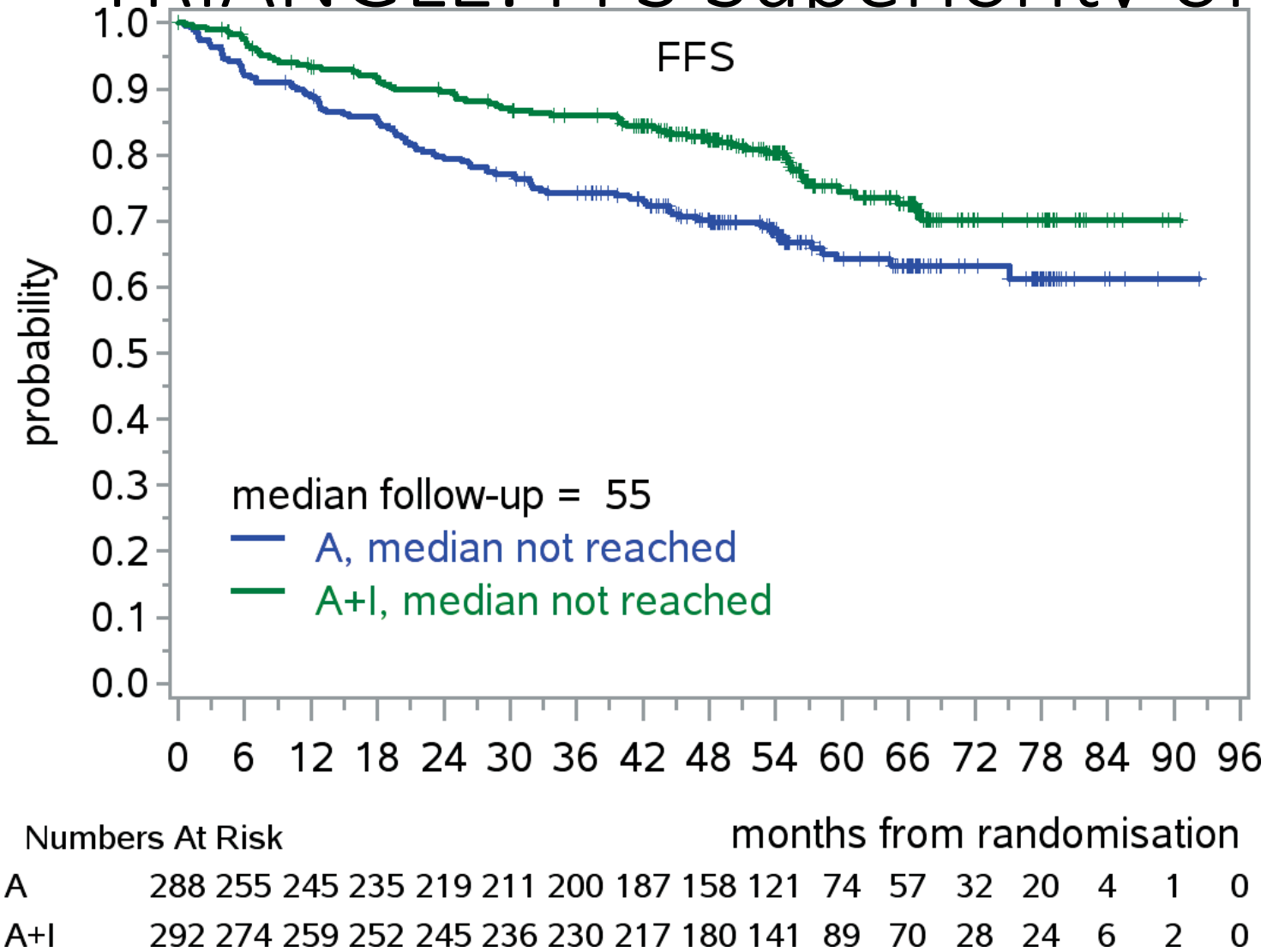
- Primary outcome: FFS

- Secondary outcomes:
  - Response rates
  - PFS, RD
  - OS
  - Safety



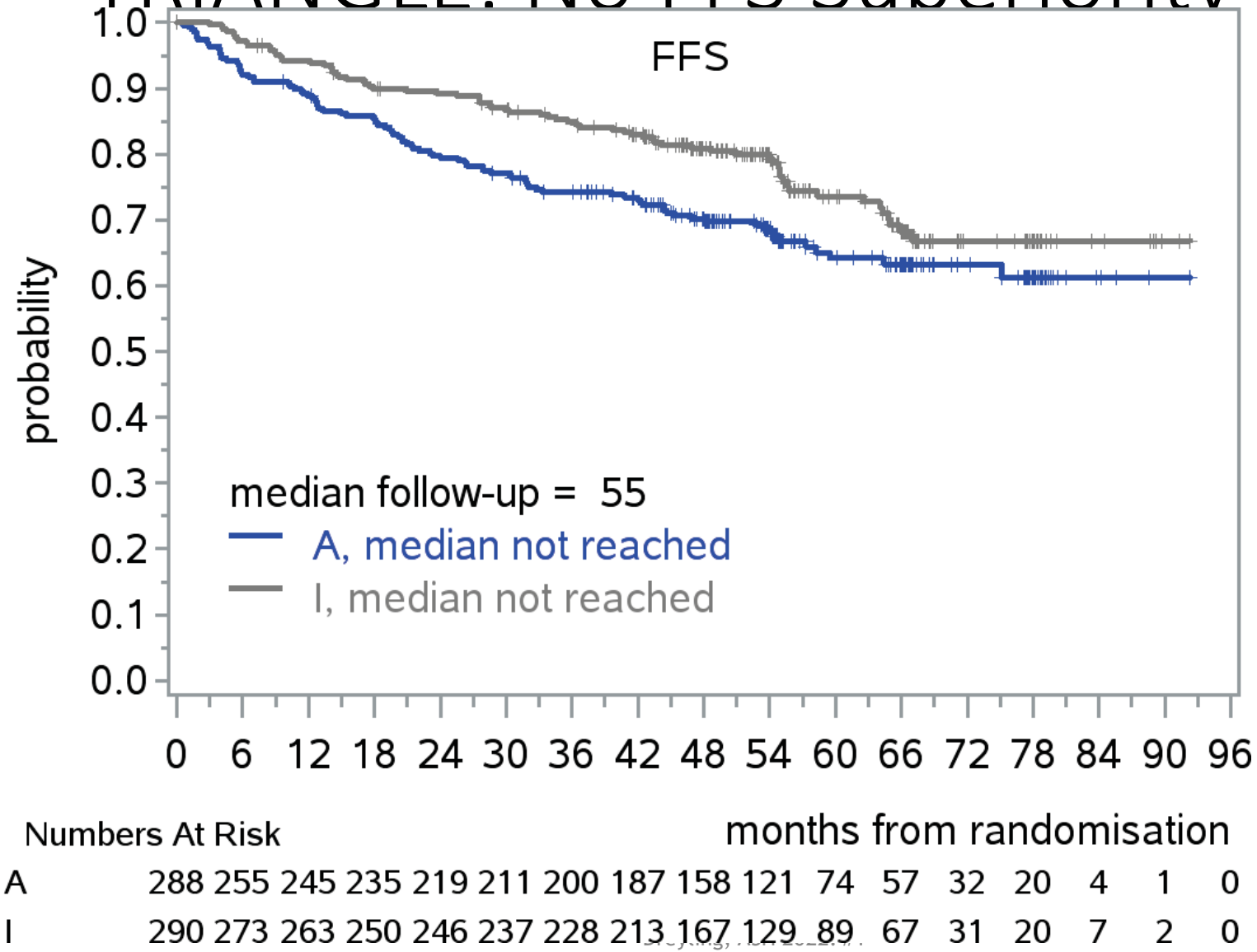
- R maintenance was added following national guidelines in all 3 trial arms
- Rituximab maintenance (without or with Ibrutinib) was started in 168 (58 %)/165 (57 %)/158 (54 %) of A/A+I/I randomized patients.

TRIANGLE: FFS Superiority of A+I vs. A



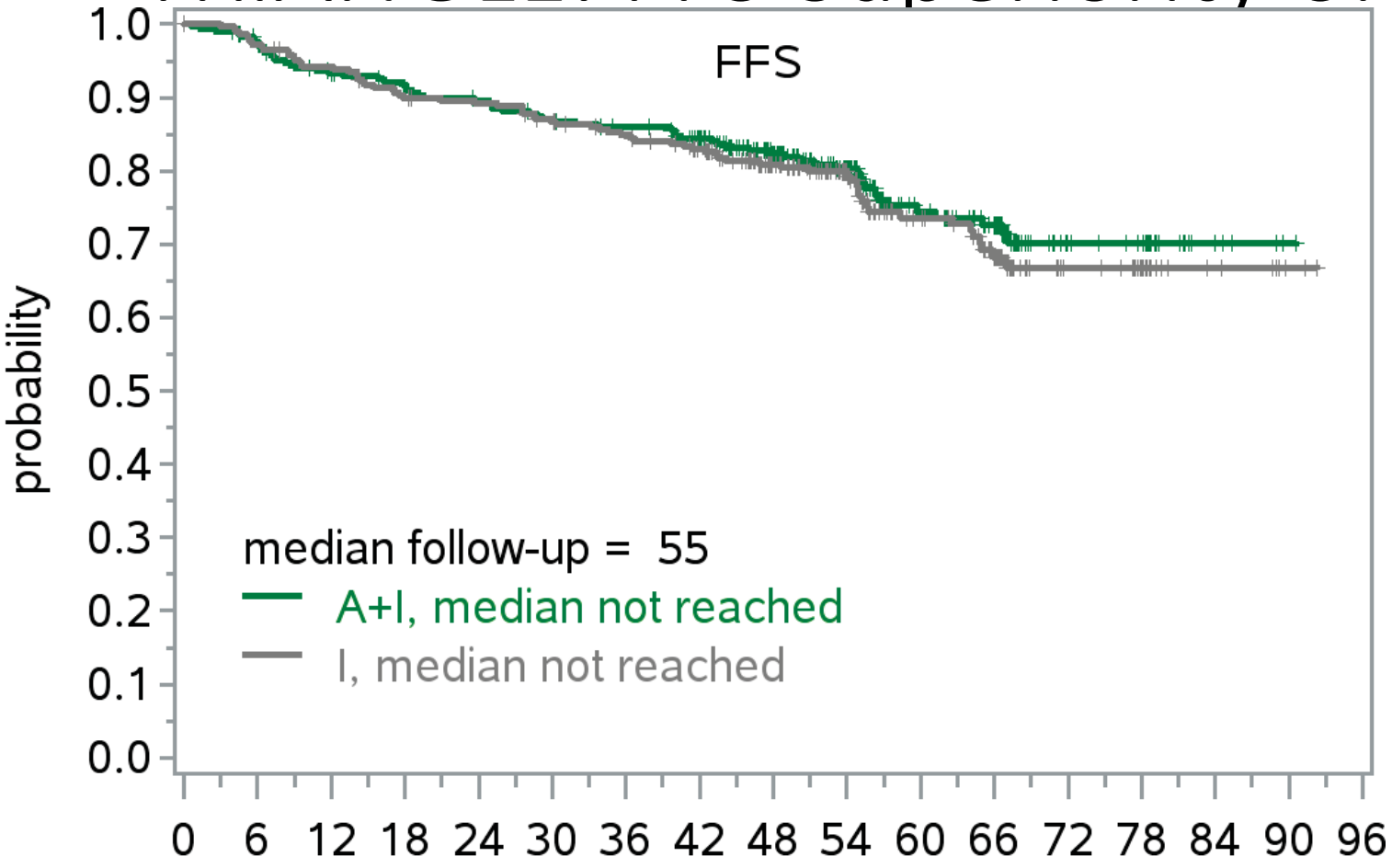
- Superiority of A+I vs. A
  - 4-year FFS A+I: 82%
  - 4-year FFS A: 70%
- p-value (overrunning, one-sided): p=0.0026
- HR (A+I vs. A): HR=0.64

TRIANGLE: No FFS Superiority of A vs. I



- Superiority of A vs. I rejected
  - 4-year FFS A: 70% (MCL Younger: 70%)
  - 4-year FFS I: 81%
- p-value (overrunning, one-sided): p=0.9890
- HR (A vs. I): HR=1.29
- Superiority of I (two-sided, retrospective) p=0.0208

TRIANGLE: FFS Superiority of A+I vs. I ?

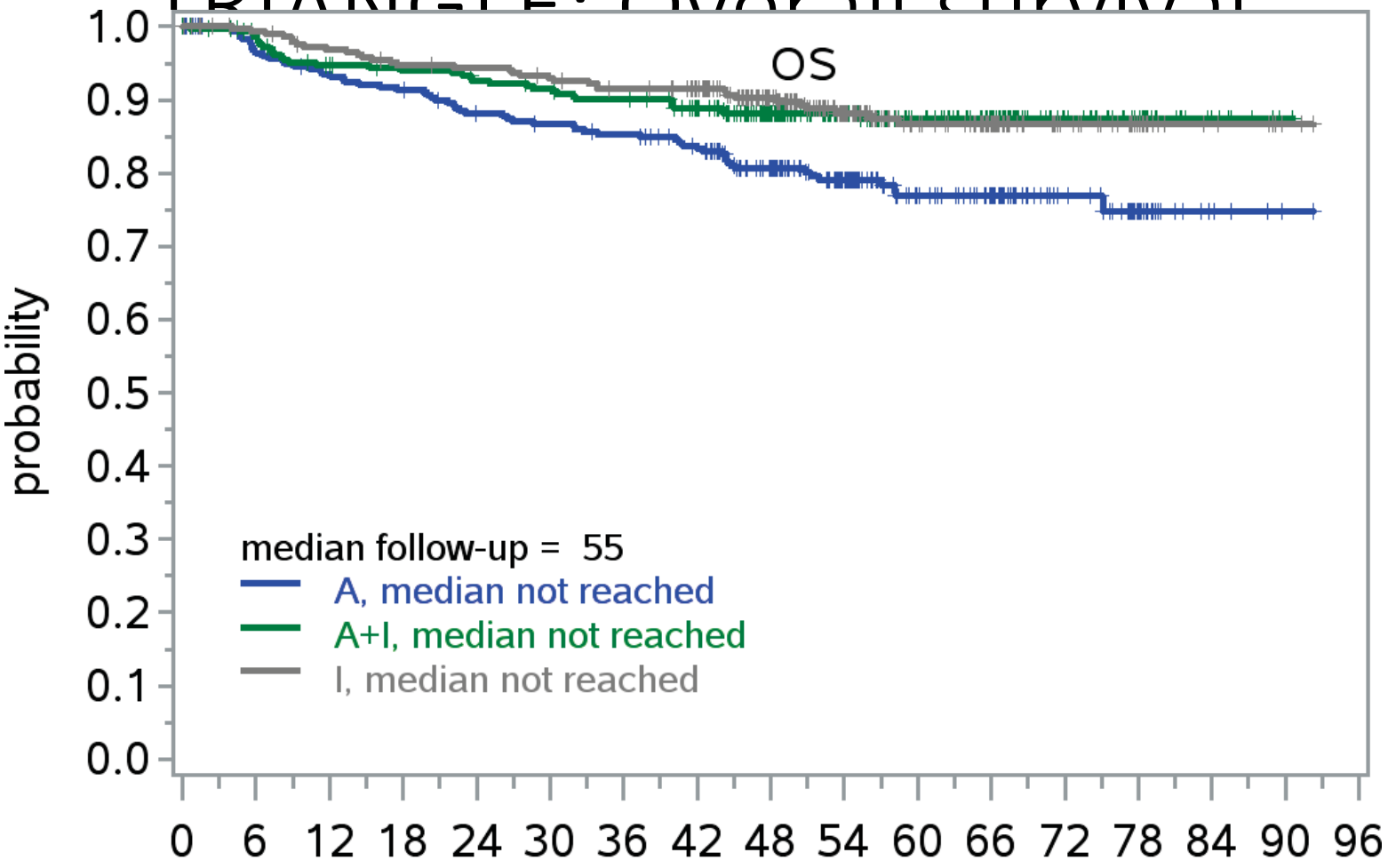


Numbers At Risk

A+I	292	274	259	252	245	236	230	217	180	141	89	70	28	24	6	2	0
I	290	273	263	250	246	237	228	213	167	129	89	67	31	20	7	2	0

- Superiority of A+I vs. I rejected
  - 4-year FFS A+I: 82%
  - 4-year FFS I: 81%
- p-value (overrunning, one-sided): p=0.21
- HR (A+I vs. I): HR=0.83

TRIANGLE: Overall survival



Numbers At Risk

A	288	270	260	255	243	238	233	222	186	145	92	73	41	23	5	1
A+I	292	281	267	262	257	253	248	235	201	160	107	83	39	26	8	2
I	290	282	273	266	264	259	253	243	194	147	101	78	41	21	7	2

- 4-year OS:
  - A: 81%
    (MCL Younger exp.: 80%)
  - A+I: 88%
  - I: 90%

- two-sided test, (a = 5%):
  - A vs. I: p=0.0019, HR: 0.565
  - A vs. A+I: p=0.0036, HR I: 0.587
  - A+I vs. I: ongoing

Ibrutinib-rituximab versus Immunochemotherapy in previously untreated mantle cell lymphoma

Dr David J Lewis [1], Prof Mats Jerkeman [2], Dr Lexy Sorrell [3], Prof David Wright [4], Prof Ingrid Glimelius [5], Dr Christian B Poulsen [6], Dr Annika Pasanen [7], Prof Andrew Rawstron [8], Dr Karin Wader [9], Dr Nick Morley [10], Dr Catherine Burton [8], Prof Andrew J Davies [11], Dr. Ingemar Lagerlöf [12], Dr Surita Dalal [8], Dr Ruth De Tute [8], Dr Chris McNamara [13], Mrs Nicola Crosbie [1], Mrs Helle Erbs Toldbod [14], Dr Jeanette Sanders [3], Prof Victoria Allgar [3], Dr Sree Aroori [3], Mr Mark Warner [3], Ms Claire Scully [3], Mr Brian Wainman [3], Dr Jacob Haber Christensen [15], Dr Jon Riise [16], Dr Kristina Sonnevi [17], Dr Mark J Bishton [18], Dr Toby A Eyre [19], Prof Simon Rule [20] on behalf of the ENRICH investigators

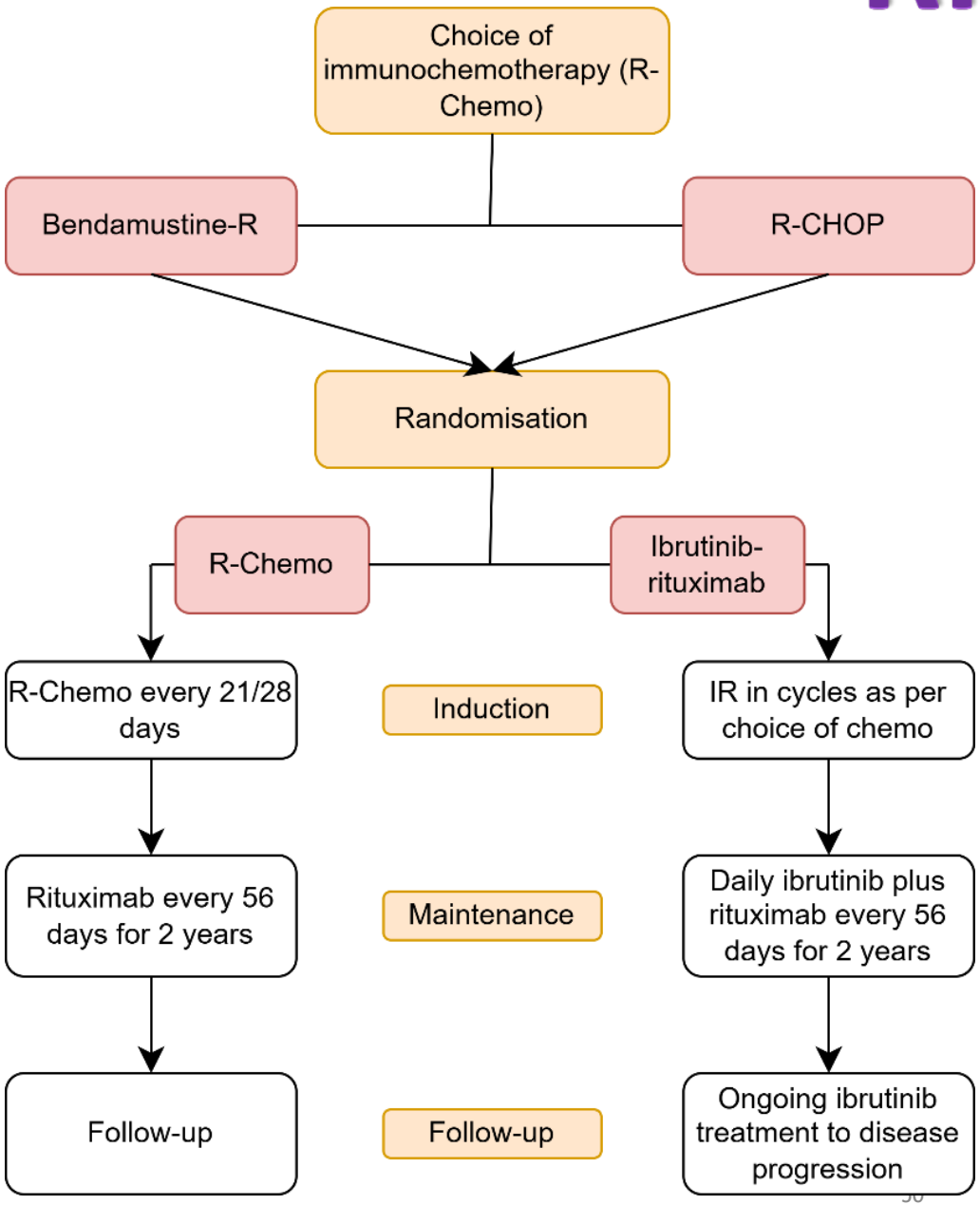
1 University Hospitals Plymouth NHS Trust, Plymouth, UK, PL6 8DH, 2 Lund University Hospital, 3University of Plymouth, 4University of Exeter, 5 Dept of Immunology, Genetics and Pathology, Uppsala University, 6 Zealand University Hospital Roskilde, 7 HUS Helsinki University Hospital, Helsinki, Finland, 8 Leeds Teaching Hospitals NHS Trust, 9 St Olav's Hospital HF, Trondheim, Norway, NO 700, 10 Sheffield Teaching Hospitals NHS Foundation Trust, 11 University of Southampton, 12 Linköping University Hospital, 13 University College London, 14 Aarhus University Hospital, 15 Odense Universitetshospital, 16 Oslo University Hospital,17 Karolinska University Hospital, 18 University of Nottingham, 19 Oxford University Hospitals NHS Trust, 20 AstraZeneca Mississaug

Trial design

Inclusion criteria
- 60 years or older
- Pathologically confirmed MCL, including either cyclin D1 overexpression or t(11;14)(q13;q32)
- Previously untreated, measurable (>1.5cm), stage II-IV MCL in need of treatment
- ECOG 0-2

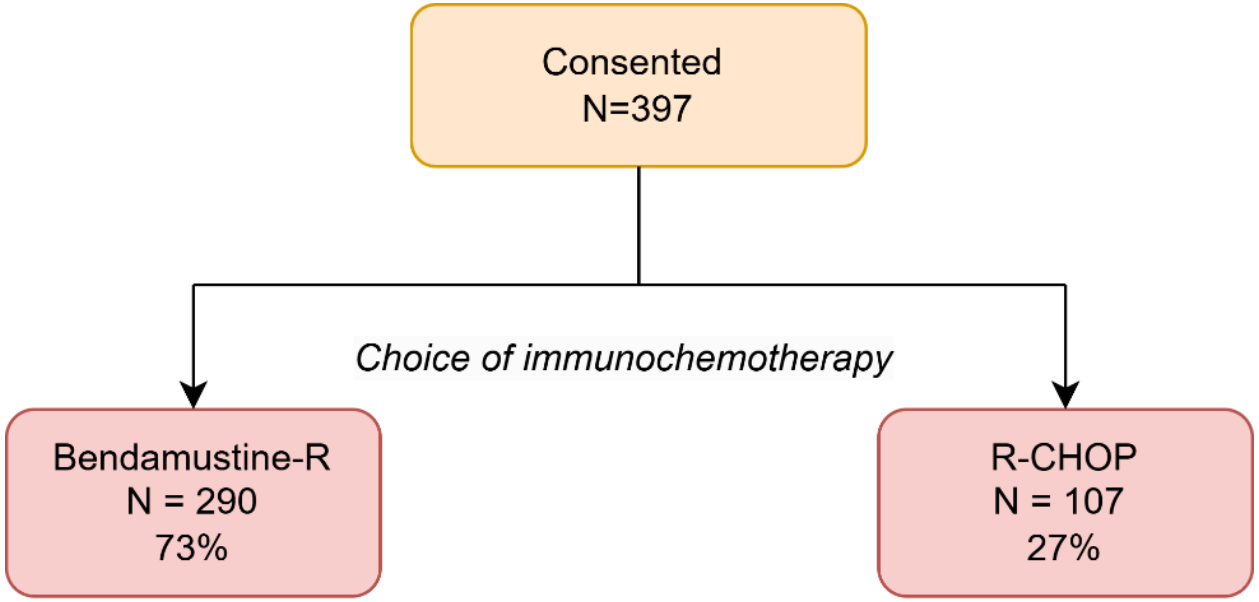
Exclusion criteria
- Considered fit for stem cell transplantation
- CNS involvement
- Known serological positivity for HBC/HCV/HIV

Rituximab 375mg/m^2
Ibrutinib – 560 mg od
Bendamustine 90 mg/m^2 D1+D2 of 28 day cycle
CHOP - (Cyclophosphamide 750 mg/m^2, Doxorubicin 50mg/m^2, Vincristine 1.4 mg/m^2, Prednisolone 100mg *5 days) 21 day cycle
Maintenance rituximab - 1400mg sc every 56 days

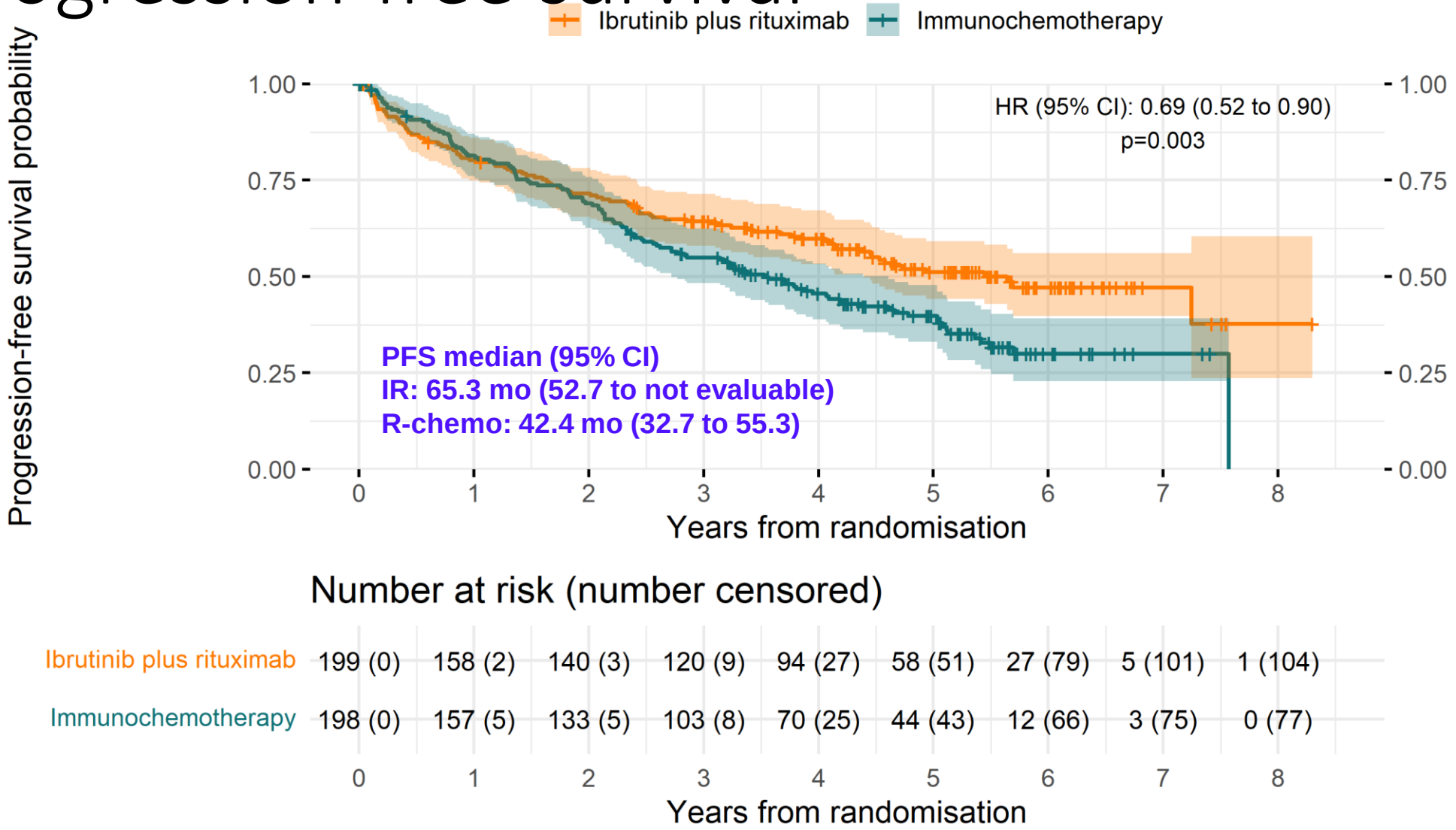


Patients

- Recruitment open December 2015 - June 2021
- Patients from 66 sites in UK, Sweden, Norway, Finland and Denmark

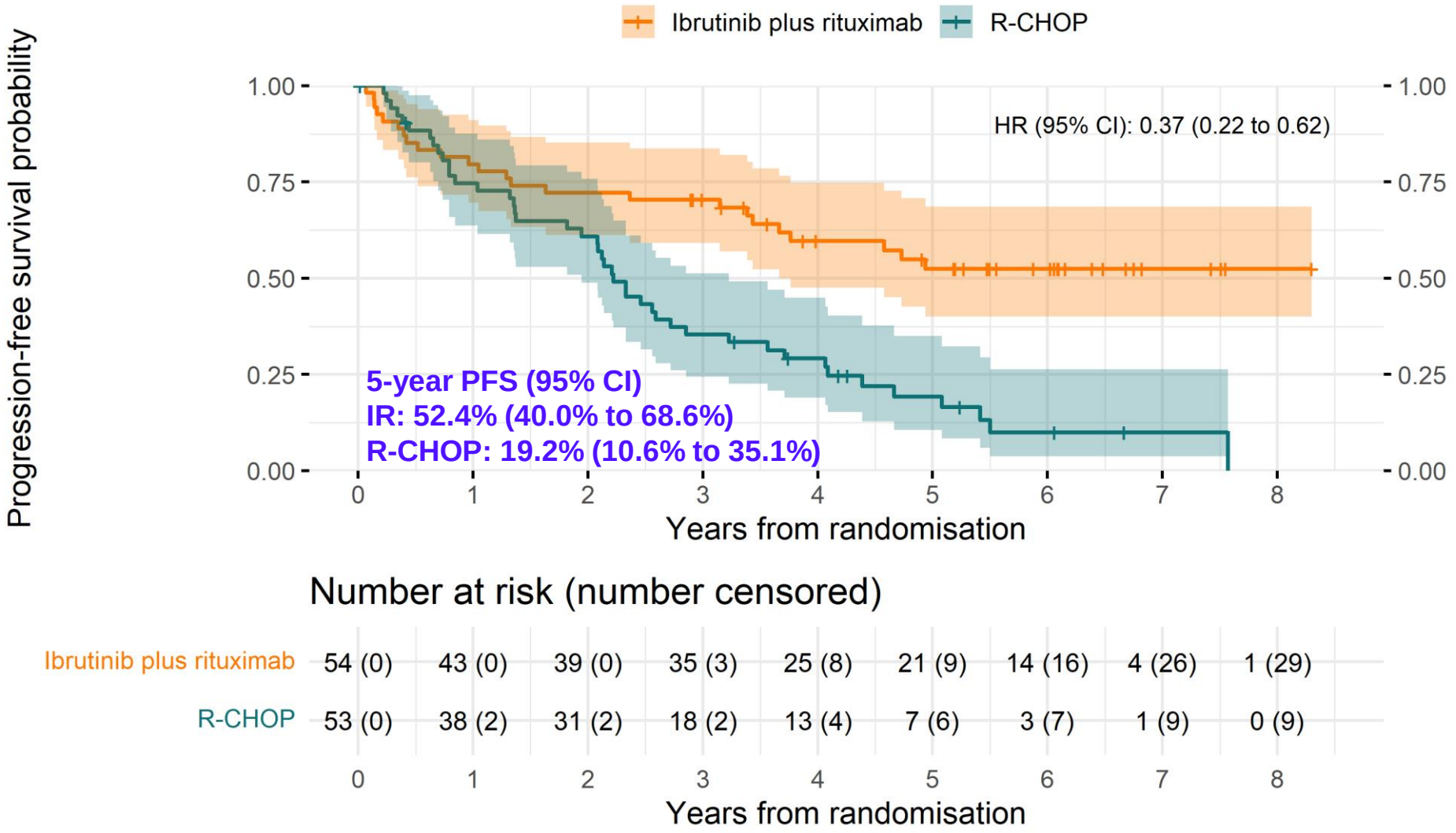


Progression-free survival

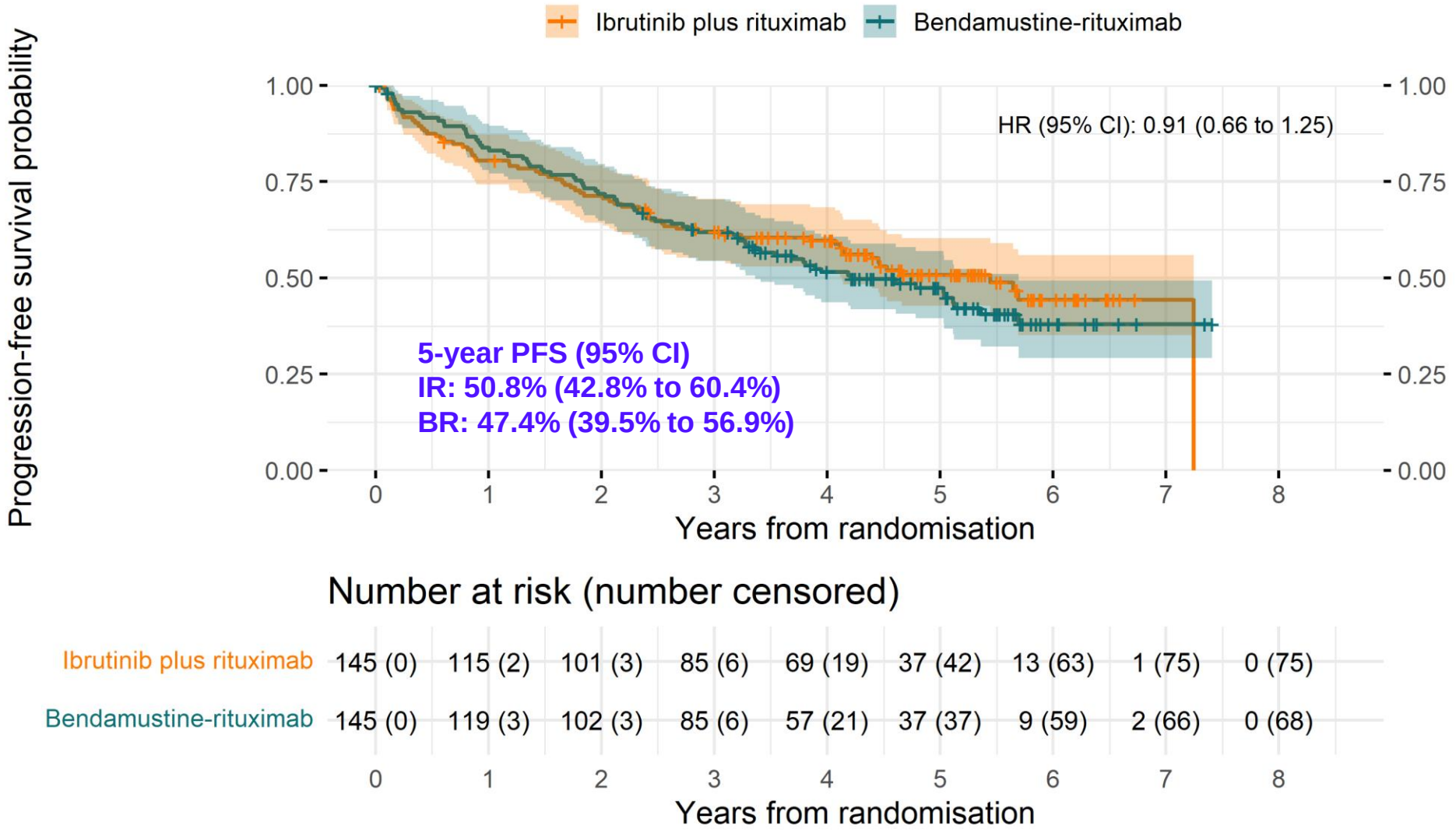


Median Follow up 47.9 months

PFS for R-CHOP choice



PFS for BR choice



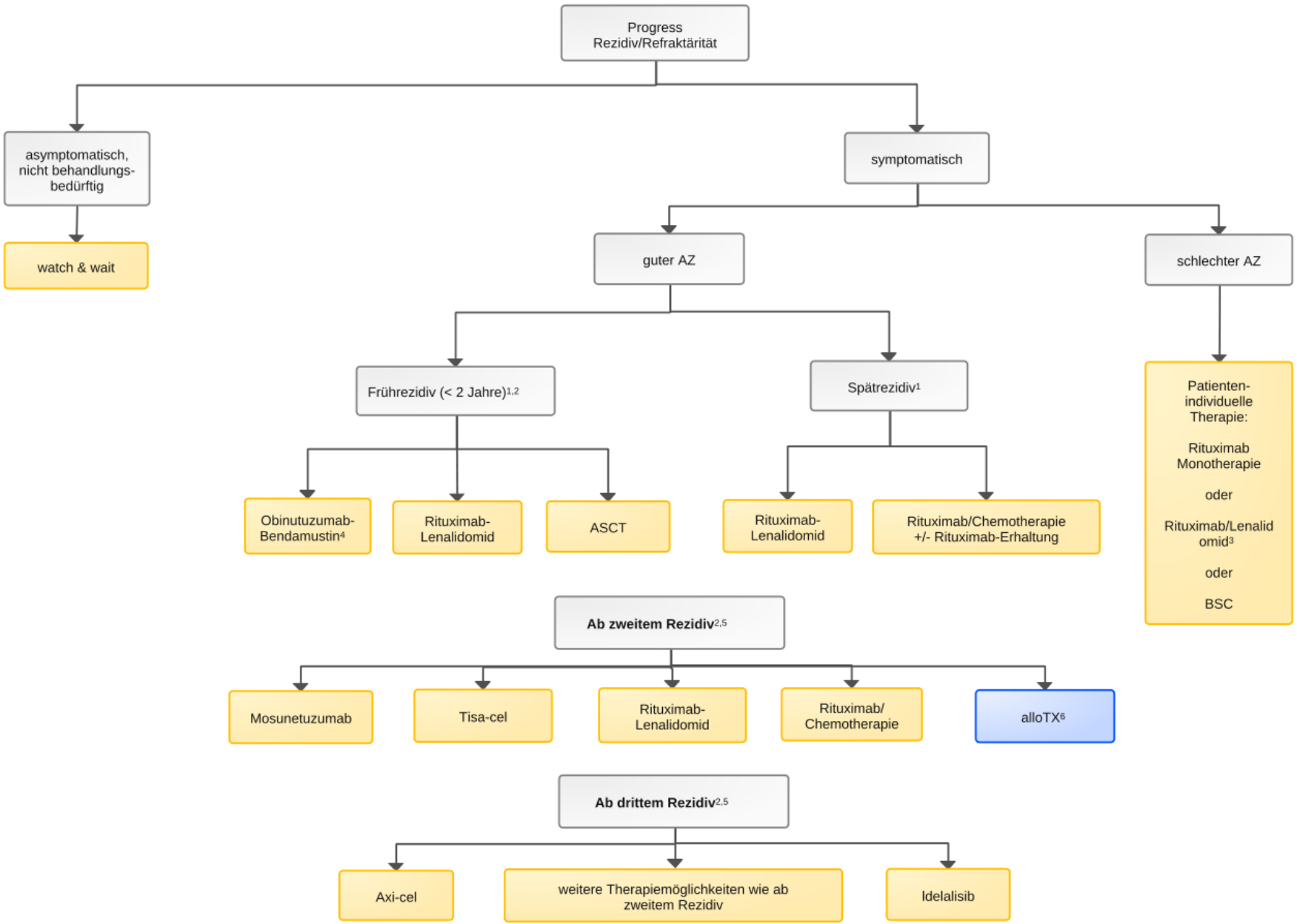
Grade 3-4 Adverse events

N participants (% of safety population)	**Ibrutinib plus rituximab, N=198**	**Bendamustine-rituximab, N=143**	**R-CHOP, N=52**
Total	125 (63.1%)	97 (67.8%)	36 (69.2%)
All Cardiac AEs	44 (22.2%)	7 (4.9%)	7 (13.5%)
All bleeding AEs	10 (5.1%)	3 (2.1%)	3 (5.8%)
Atrial Fibrillation	12 (6.1%)	1 (0.7%)	0
Neutropenia	18 (9.1%)	27 (18.9%)	11 (21.2%)
Neutropenic sepsis	6 (3.0%)	2 (1.4%)	8 (15.4%)
Corona virus infection	10 (5.1%)	10 (7.0%)	0

Grade 3 and 4 adverse events during induction treatment and maintenance

Safety population - patients who had at least one cycle of treatment

Rezidivtherapie des Follikulären Lymphoms



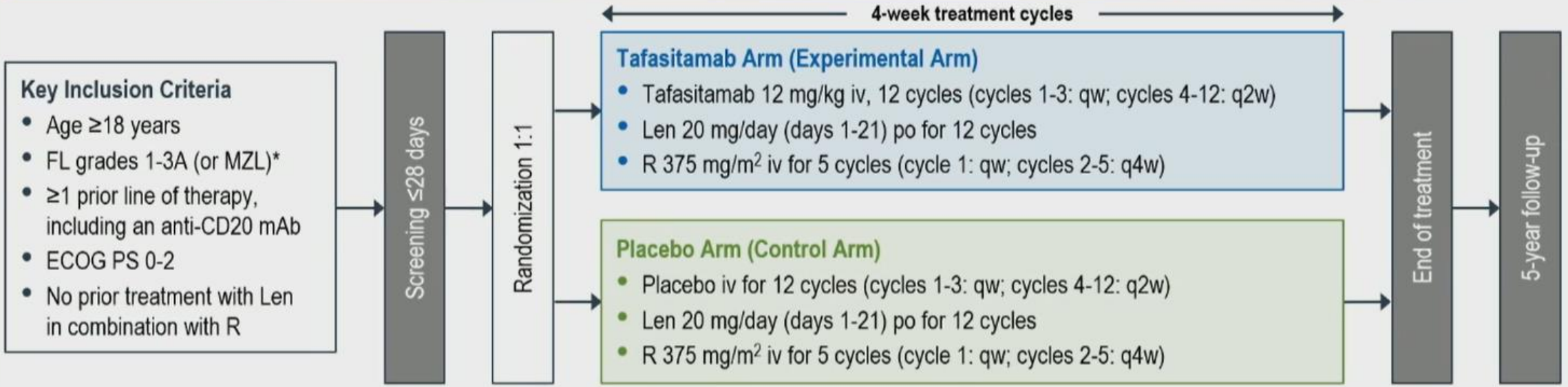
Tafasitamab Plus Lenalidomide and Rituximab for Relapsed or Refractory Follicular Lymphoma: Results From a Phase 3 Study (inMIND)

Laurie H. Sehn,[1] Stefano Luminari,[2,3] Christian W. Scholz,[4] Kai Hübel,[5] Antonio Salar,[6] Shankara Paneesha,[7,8] Björn E. Wahlin,[9] Panayiotis Panayiotidis,[10] Hui Peng Lee,[11] Ana Jimenez Ubieto,[12] Juan-Manuel Sancho,[13] Tae Min Kim,[14] Eva Domingo Domenech,[15] Takahiro Kumode,[16] Christina Poh,[17] Catherine Thieblemont,[18] Dries Deeren,[19] Edwin de Wit,[20] Michael Arbushites,[21] Marie-Laure Casadebaig[20] and Marek Trneny[22]

[1]BC Cancer Centre for Lymphoid Cancer and The University of British Columbia, Vancouver, BC, Canada; [2]Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy; [3]Surgical, Medical and Dental Department of Morphological Sciences related to Transplant, Oncology and Regenerative Medicine, University of Modena and Reggio Emilia, Reggio Emilia, Italy; [4]Vivantes Klinikum Am Urban, Berlin, Germany; [5]University of Cologne and Faculty of Medicine and University Hospital of Cologne, Cologne, Germany; [6]Hospital del Mar-IMIM, Barcelona, Spain; [7]University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK; [8]University of Birmingham, Birmingham, UK; [9]Karolinska University Hospital, Stockholm, Sweden; [10]National and Kapodistrian University of Athens Medical School, General Hospital LAIKO, Athens, Greece; [11]Flinders Medical Centre, Adelaide, South Australia, Australia; [12]Servicio de Hematología, Hospital 12 de Octubre, Madrid, Spain; [13]ICO-IJC-Hospital Germans Trias i Pujol, Badalona, Universitat Autònoma de Barcelona, Barcelona, Spain; [14]Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Republic of Korea; [15]Institut Català d'Oncologia, Hospital Duran I Reynals, IDIBELL, Barcelona, Spain; [16]Kindai University, Osaka, Japan; [17]Fred Hutchinson Cancer Center/University of Washington, Seattle, WA, USA; [18]Saint-Paris Cité Université; Assistance Publique-Hôpitaux de Paris, Saint-Hospital, Paris, France; [19]AZ Delta General Hospital, Roeselare, Belgium; [20]Incyte International Biosciences Sàrl, Morges, Switzerland; [21]Incyte Corporation, Wilmington, DE, USA; [22]First Faculty of Medicine, Charles University, Prague, Czech Republic

Presented at the 66th ASH Annual Meeting & Exposition • San Diego, CA, USA • December 7-10, 2024 (Abstract #LBA-1)

inMIND: Phase 3, Double-Blind, Placebo-Controlled, International, Multicenter Randomized Study



Stratification Factors (Patients With FL)

- POD24
- Refractoriness to prior anti-CD20 mAb therapy
- Number of prior lines of therapy (1 or ≥2)

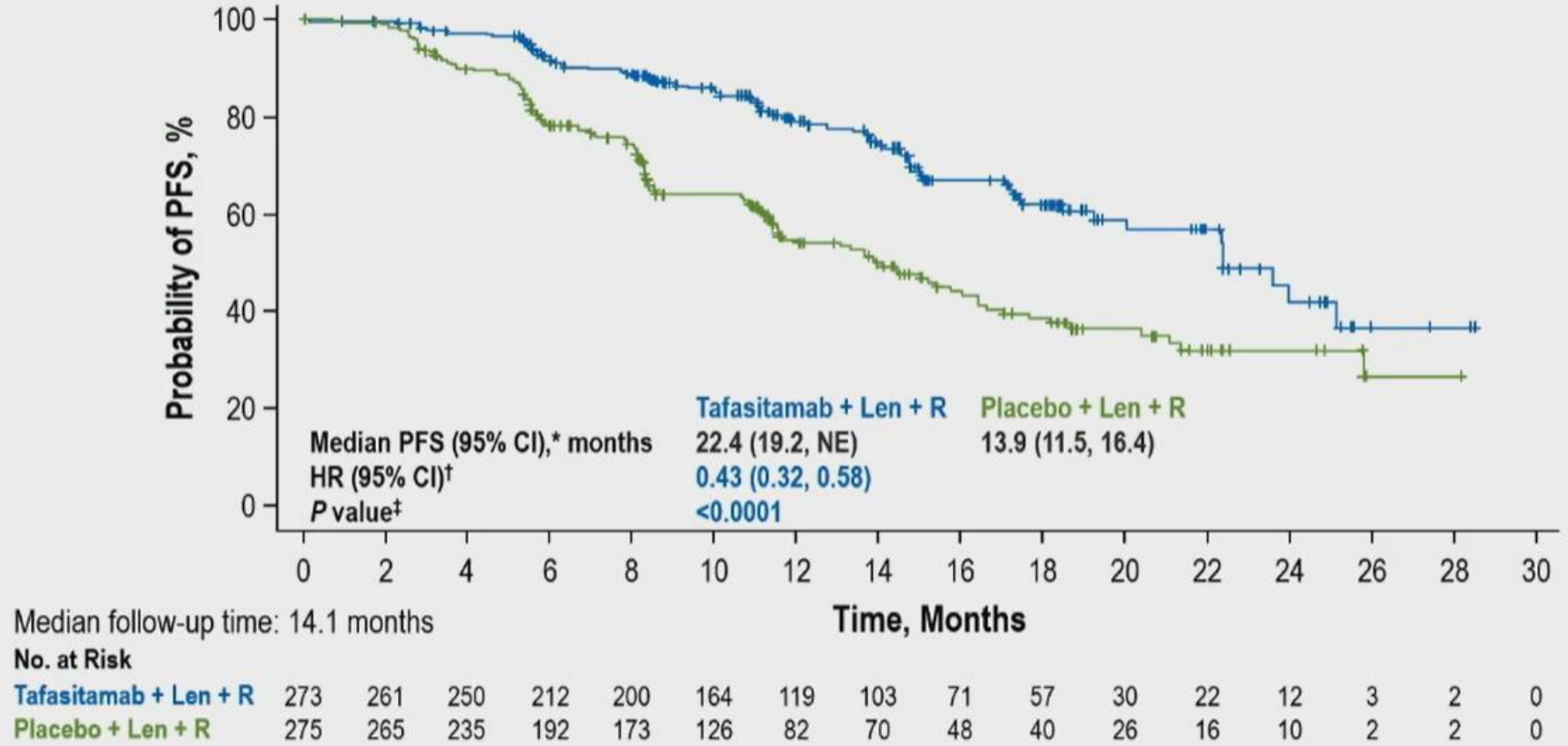
Study Endpoints in FL Population (Investigator Assessed Unless Specified)

- **Primary study endpoint:** PFS
- **Key secondary:** PET-CR rate in the FDG-avid population, OS
- **Select other secondary:** PFS by IRC, ORR, DOR, safety, QoL, MRD
- **Exploratory:** TTNT, B-cell recovery, Ig levels, CD19 expression

- Powered to assess PFS in the FL population, triggered when 174 investigator-assessed events occurred
- OS analysis planned after 5 years of follow-up

*Limited number of patients with MZL were enrolled but the study was not powered for this population; data for patients with MZL will be presented separately. DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FDG, fluorodeoxyglucose; FL, follicular lymphoma; Ig, immunoglobulin; IRC, independent review committee; iv, intravenous; Len, lenalidomide; mAb, monoclonal antibody; MRD, minimal residual disease; MZL, marginal zone lymphoma; ORR, overall response rate; OS, overall survival; PET-CR, positron emission tomography-complete response; PFS, progression-free survival; po, orally; POD24, disease progression within 24 months of initial diagnosis; QoL, quality of life; qw, weekly; q2w, every 2 weeks; q4w, every 4 weeks; R, rituximab; TTNT, time to next treatment.

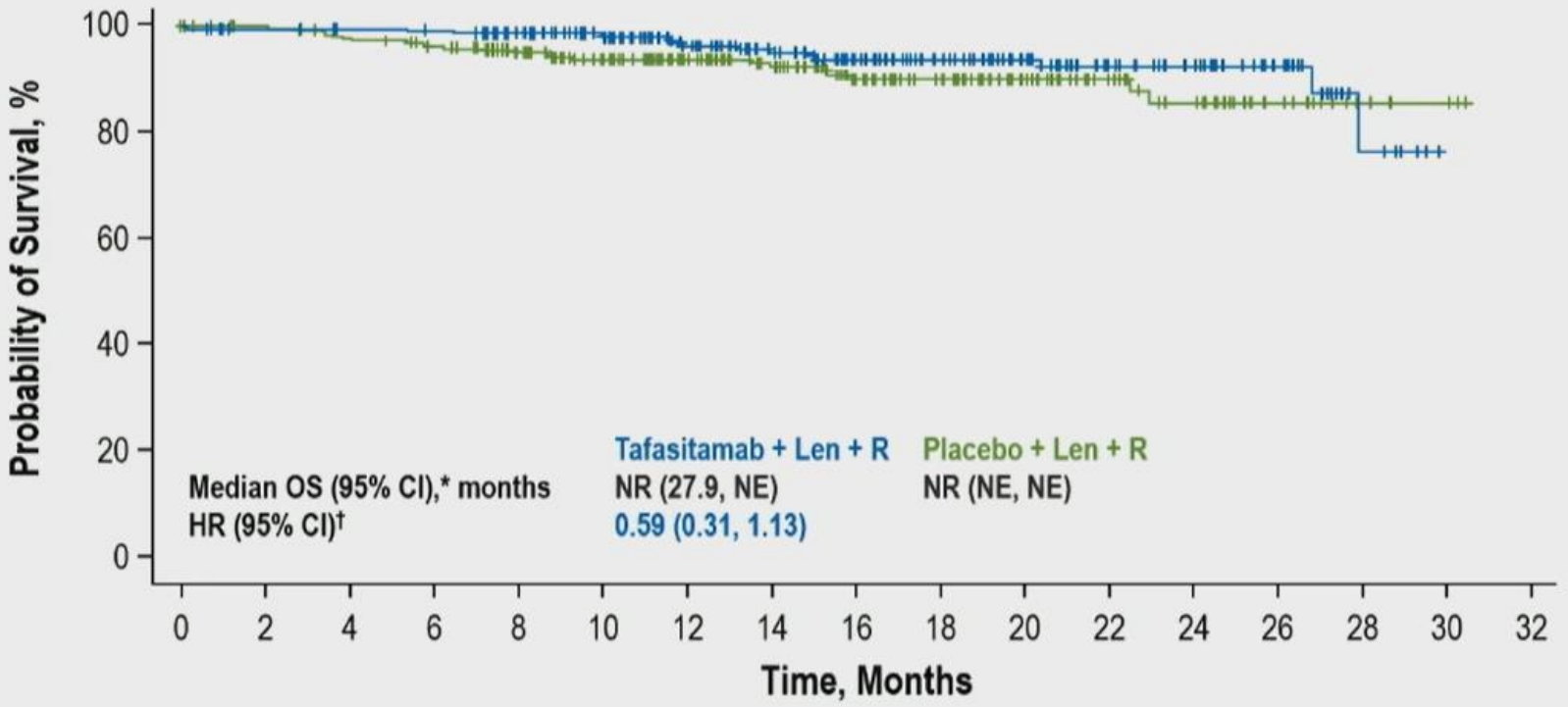
Primary Endpoint: PFS by Investigator Assessment



Significant improvement in PFS was observed with tafasitamab

ITT population. *Estimated using Kaplan-Meier method. †Estimated using a stratified Cox proportional hazard model. ‡Stratified log-rank test with a 2-sided significance level of 5%. CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; Len, lenalidomide; NE, not evaluable; PFS, progression-free survival; R, rituximab.

Overall Survival



No. at Risk																	
Tafasitamab + Len + R	273	266	263	261	240	216	178	149	124	103	80	53	42	26	7	0	0
Placebo + Len + R	275	268	260	252	230	203	164	138	108	90	66	46	34	15	6	3	0

- OS was tested only for futility at the time of the primary analysis
- After a median follow-up of 15.3 months, the futility threshold was not crossed and a positive trend was observed

ITT population. Analysis by investigator assessment. *Estimated using Kaplan-Meier method. †Estimated using a stratified Cox proportional hazard model. CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; Len, lenalidomide; NE, not evaluable; NR, not reached; OS, overall survival; R, rituximab.

Grade 3 or 4 TEAEs and Dose Modifications

Most Common Grade 3 or 4 TEAEs (≥5% in Any Group)

Preferred Term, n (%)	Tafasitamab + Len + R (n=274)*	Placebo + Len + R (n=272)†	Total (n=546)
Neutropenia	109 (39.8)	102 (37.5)	211 (38.6)
Pneumonia	23 (8.4)	14 (5.1)	37 (6.8)
Thrombocytopenia	17 (6.2)	20 (7.4)	37 (6.8)
Neutrophil count decreased	16 (5.8)	18 (6.6)	34 (6.2)
Anemia	12 (4.4)	16 (5.9)	28 (5.1)
COVID-19	16 (5.8)	6 (2.2)	22 (4.0)
COVID-19 pneumonia	13 (4.7)	3 (1.1)	16 (2.9)

- Tafasitamab and placebo dose interruptions or discontinuations due to TEAEs were similar between treatment arms, n (%):
  - Dose delay or interruption due to TEAEs: 203 (74%) vs 190 (70%)
  - Discontinued study treatment due to TEAEs: 30 (11%) vs 18 (7%)
- Len discontinuations due to TEAEs were similar between tafasitamab and placebo arms, n (%):
  - 39 (14%) vs 31 (11%)
- Len dose reductions were similar between tafasitamab and placebo arms
  - Median relative dose intensity: 86% vs 87%

Safety population. *One patient randomized to the placebo + len + R group is included in the tafasitamab + len + R safety population because the patient erroneously received tafasitamab. †Three patients randomized to the placebo + len + R group are not included in the safety population because they erroneously received tafasitamab (n=1), or did not receive any study treatment due to confirmation of R hypersensitivity (n=1), or the patient withdrew from the study (n=1). COVID-19, coronavirus disease 2019; Len, lenalidomide; R, rituximab; TEAE, treatment-emergent adverse event.

Blinatumomab added to chemotherapy improves disease-free survival in newly diagnosed NCI standard risk pediatric B-acute lymphoblastic leukemia: Results from Children's Oncology Group Study AALL1731

Study Chairs:
Rachel Rau
Sumit Gupta

Sr. Statistician:
John Kairalla

Vice Chair:
Karen Rabin

COG ALL Leads:
Mignon Loh
Elizabeth Raetz

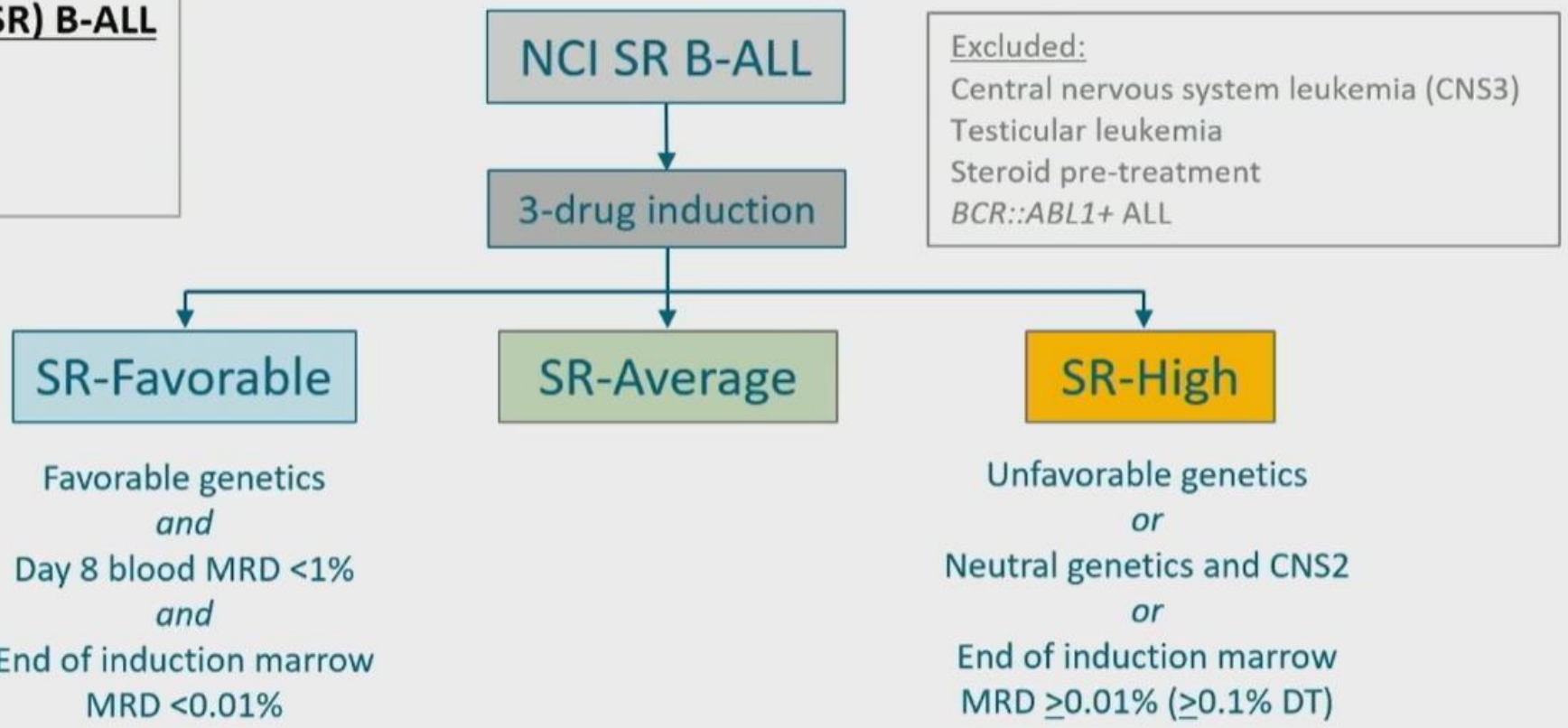
CHILDREN'S ONCOLOGY GROUP

Further progress in pediatric B-ALL has stalled

CHILDREN'S ONCOLOGY GROUP

AALL1731 risk stratification

NCI Standard Risk (SR) B-ALL
At diagnosis:
Age 1-<10 years
WBC <50,000/µL



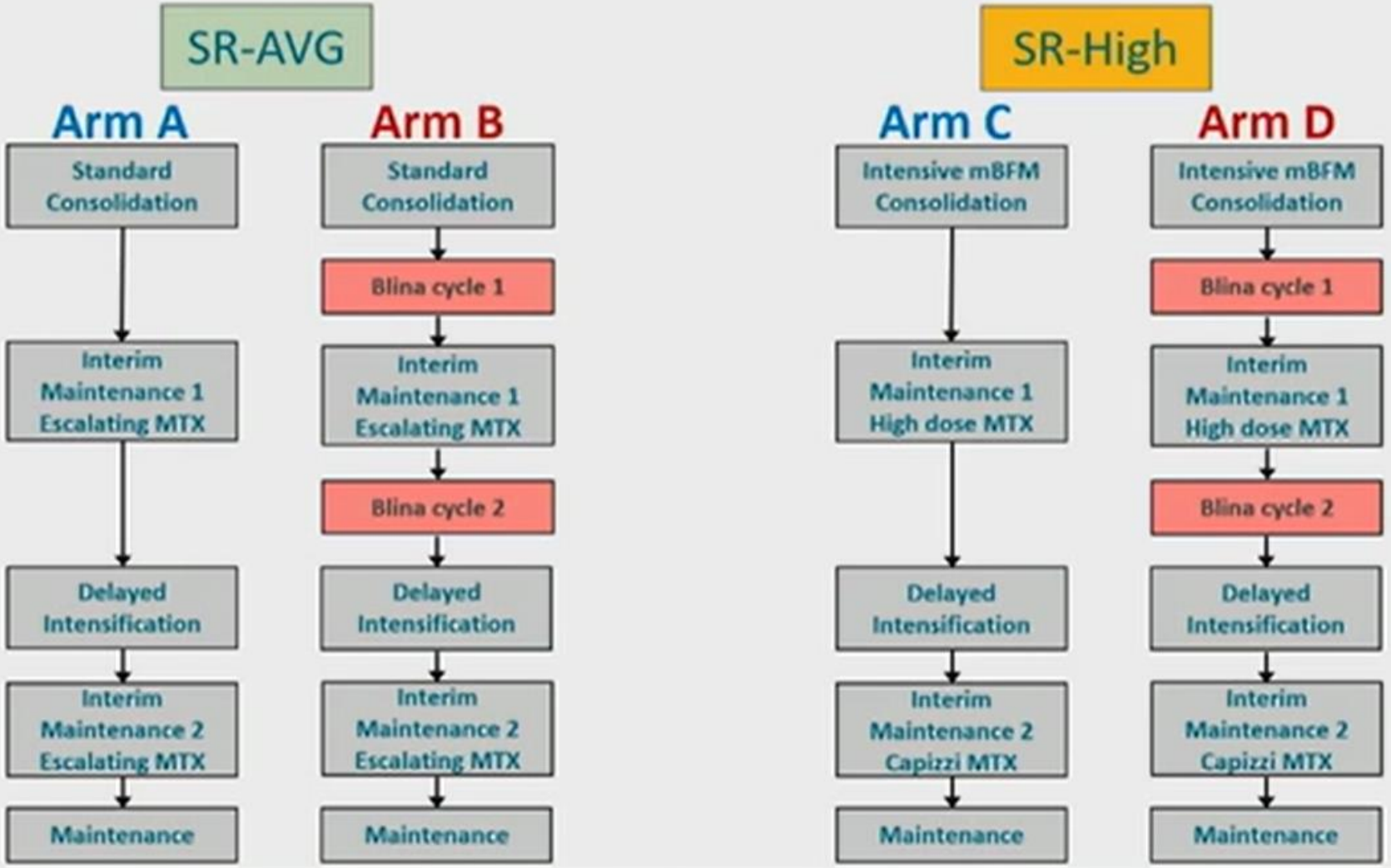
Excluded:
Central nervous system leukemia (CNS3)
Testicular leukemia
Steroid pre-treatment
BCR::ABL1+ ALL

MRD = minimal residual disease

CHILDREN'S ONCOLOGY GROUP

Favorable genetics = ETV6::RUNX1 or double trisomies chr 4 and 10 (DT)
Unfavorable genetics = iAMP21, KMT2Ar, hypodiploidy (<44chr), t(17;19)
Neutral genetics = no favorable or unfavorable lesions present

Randomization



MTX = methotrexate

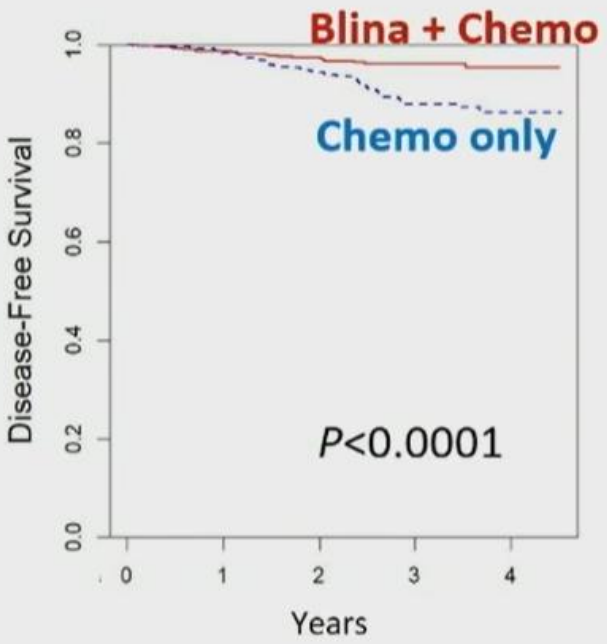
CHILDREN'S ONCOLOGY GROUP

Blinatumomab cycle

15mcg/m^2/day x 28 days via continuous IV infusion

Blinatumomab significantly improves DFS

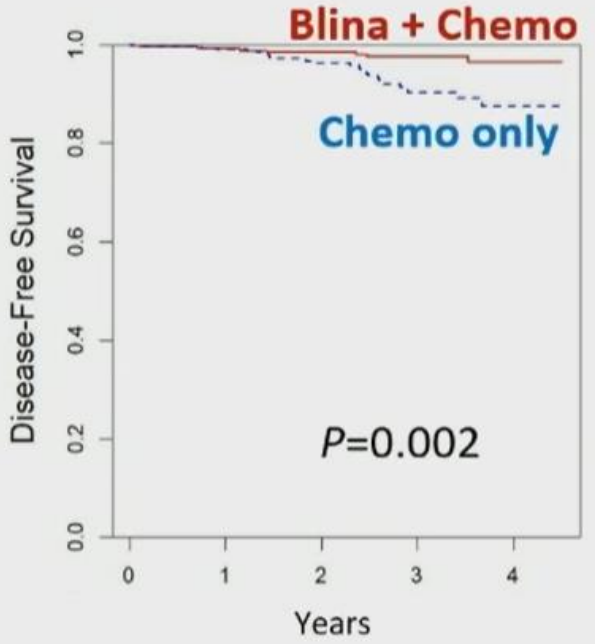
Overall cohort



3-yr DFS 87.9 vs 96%

Hazard ratio (HR) 0.39

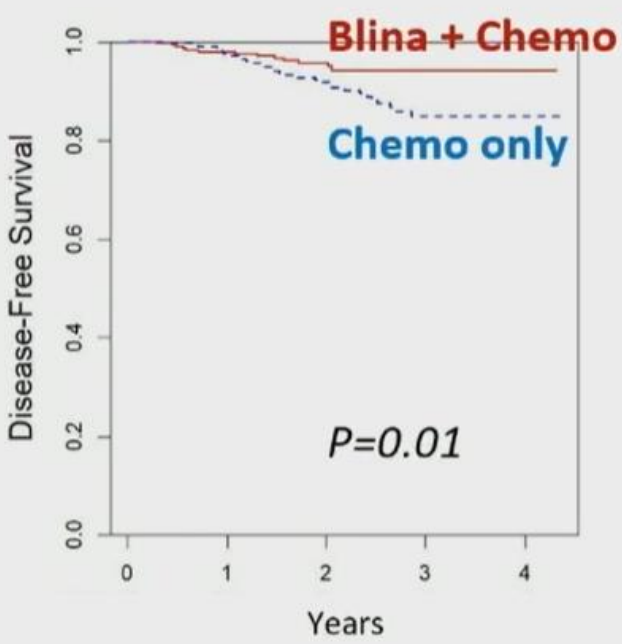
SR-Avg



3-yr DFS 90.2 vs 97.5%

HR 0.33

SR-High

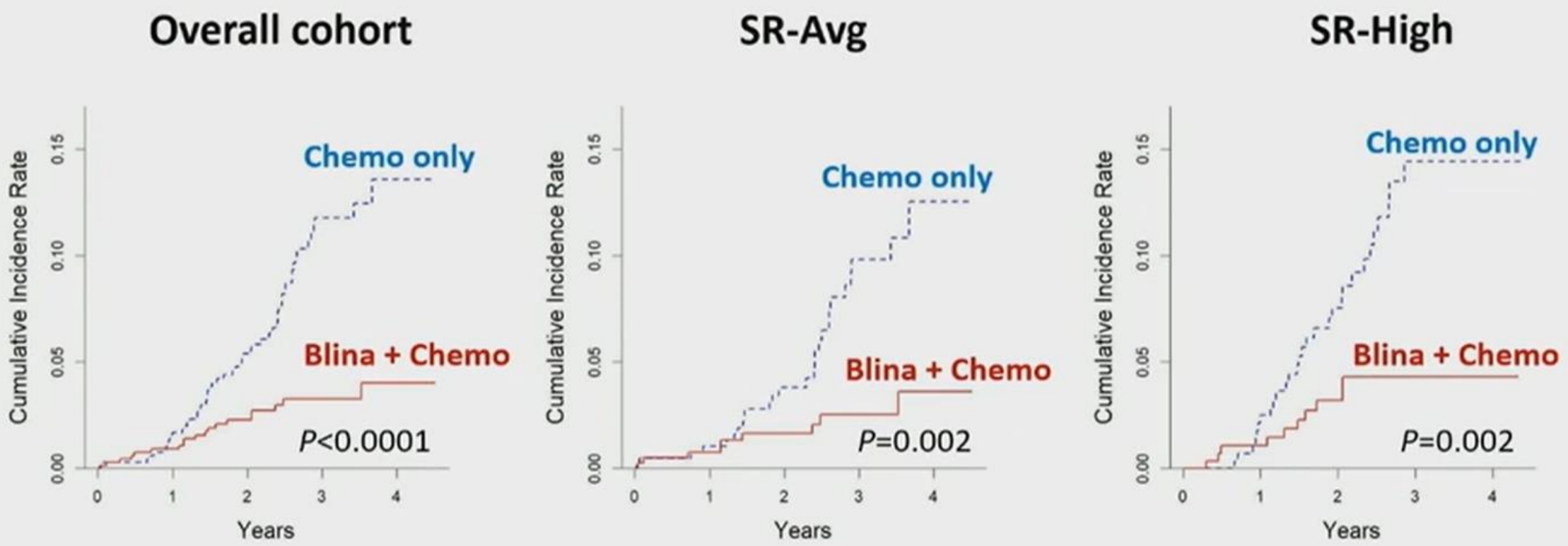


3-yr DFS 84.8 vs 94.1%

HR 0.45

CHILDREN'S ONCOLOGY GROUP

Blinatumomab reduces relapses



CHILDREN'S ONCOLOGY GROUP

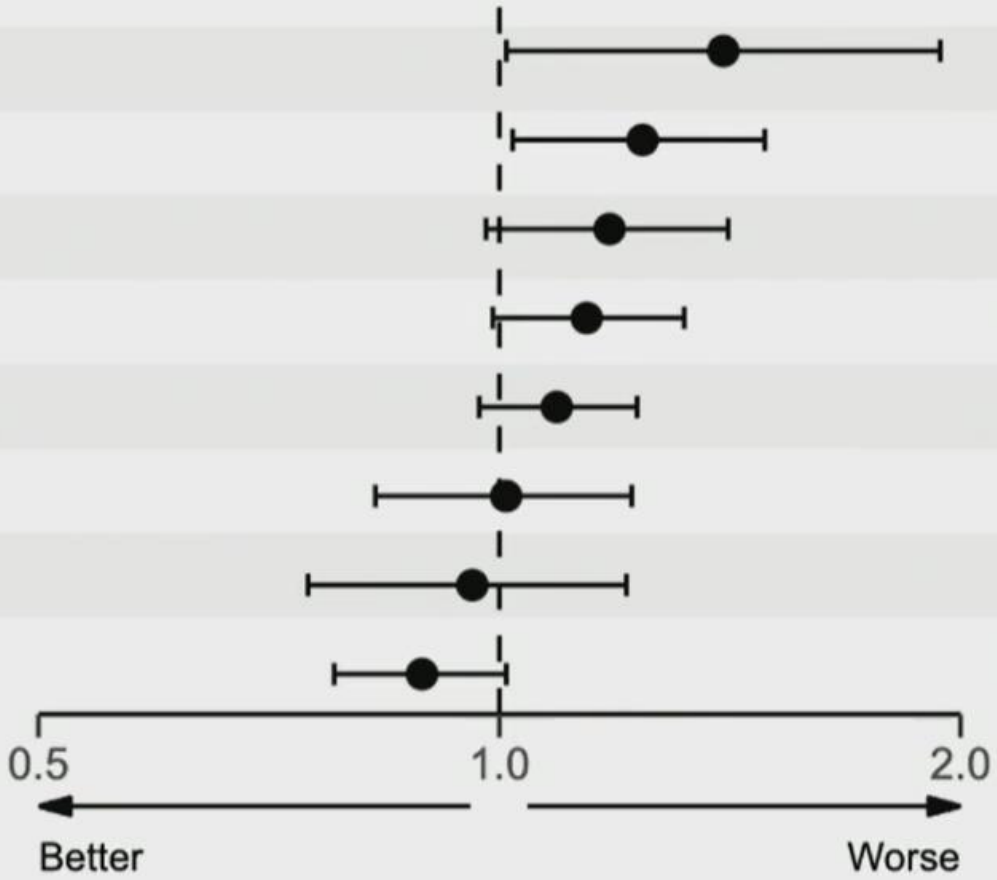
Fred Hutch Cancer Center

Impact of Socioeconomic Factors on Access to and Outcomes of Allogeneic Hematopoietic Cell Transplantation for Acute Myeloid Leukemia: A Multi-Center Observational Study

Natalie Wuliji, DO; Ted Gooley, PhD; Salene Jones, PhD; Aaron T. Gerds, MD, MS; Bruno C. Medeiros, MD; Paul Shami, MD; John Galvin, MD; Kehinde Adekola, MD; Selina Luger, MD; Maria R. Baer, MD; David Rizzieri, MD; Tanya Wildes, MD; Eunice S. Wang, MD; Mikkael A. Sekeres, MD, MS; Sudipto Mukherjee, MD, PhD; Julie Smith, MD; Mitchell Garrison, MD; Kiarash Kojouri, MD; Jacob Appelbaum, MD, PhD; Mary-Elizabeth Percival, MD ; Brenda M. Sandmaier; MD; Frederick R. Appelbaum, MD; Mohamed L. Sorror, MD, MSc

Mortality without allo-HCT

Characteristic	aHR (95% CI)
Proportion on SSI	1.4 (1.01-1.94)
Proportion with < high school education	1.24 (1.02-1.49)
Proportion below Federal Poverty Level	1.18 (0.98-1.41)
Proportion on SNAP	1.14 (0.99-1.32)
Proportion driving to work alone	1.09 (0.97-1.23)
Proportion spending ≥30% on housing	1.01 (0.83-1.22)
Proportion with a second mortgage	0.96 (0.75-1.21)
Median Income	0.89 (0.78-1.01)



Adjusted for age and HCT-CI, KPS, PHQ-9, ADL scale, 4MWT and quality of life per FACT, diagnosis and ELN risk

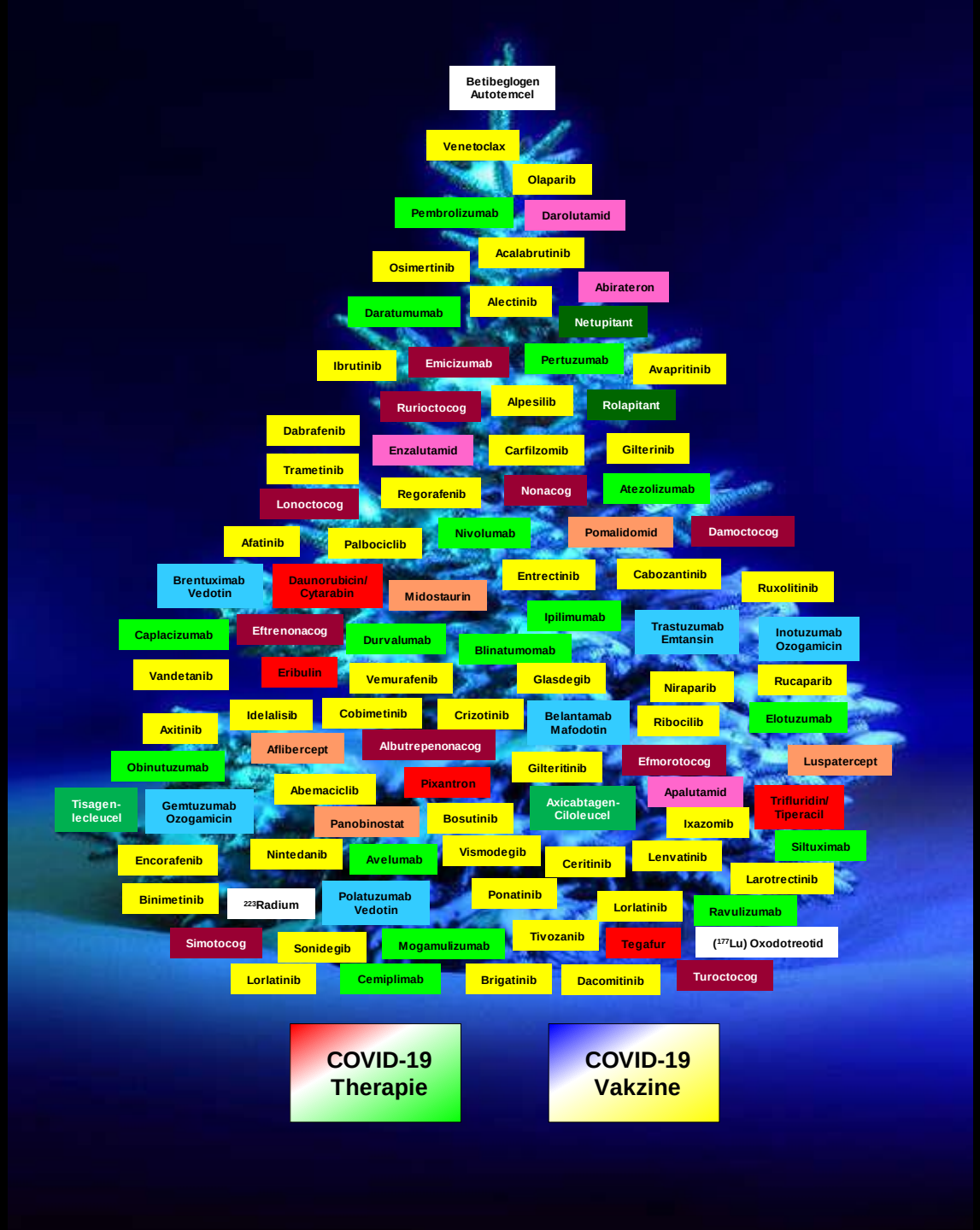
SDOH factors modeled with HRs per $25K increase in income, 10% increase in other factors

ASH Kongress 2024

nicht in der Zusammenfassung …

- Akute Myeloische Leukämie: Bedeutung von MRD
- CAR-T Zellen: Einfluss von ketogener Diät und b-Hydroxybutyrat
- Erythrozytose (Polyzythämie): Einfluss von Hepatic-like Erythropoietin
- Hämatopoetische Stammzellen: Einfluss von Plättchenfaktor 4 auf Altern
- Hämophilie A: Lentiviraler Gentransfer in CD34+ Stammzellen
- Sichelzelllkrankheit: Reduktion von Vaskulopathie post allo TX
- Sichelzellkrankheit: Gentherapie
- …

10.01.2025	14:00 - 15:00	Weichgewebstumoren	Prof. Dr. Sebastian Bauer
24.01.2025	14:00 - 15:00	Gentherapie bei hereditären hämatologischen Erkrankungen	Prof. Dr. Roland Meisel
07.02.2025	14:00 - 15:00	Paroxysmale Nächtliche Hämoglobinurie (PNH)	Prof. Dr. Jörg Schubert
21.02.2025	14:00 - 15:00	Ösophaguskarzinom	Prof. Dr. Sylvie Lorenzen
07.03.2025	14:00 - 15:00	Keimzelltumoren	Prof. Dr. Anja Lorch
21.03.2025	14:00 - 15:00	akute GvHD	Prof. Dr. Robert Zeiser
04.04.2025	14:00 - 15:00	Hepatozelluläres Karzinom	Prof. Dr. Sebastian Stintzing
25.04.2025	14:00 - 15:00	Urothelkarzinom	Prof. Dr. Maike de Wit
09.05.2025	14:00 - 15:00	Morbus Waldenström / …	Prof. Dr. Christian Buske, NN
23.05.2025	14:00 - 15:00	Febrile Neutropenie	PD Dr. Dr. Michael Sandherr
06.06.2025	14:00 - 15:00	Best of ASCO 2025	Prof. Dr. Bernhard Wörmann
20.06.2025	14:00 - 15:00	ZNS Infektionen	Prof. Dr. Martin Schmidt-Hieber
27.06.2025	14:00 - 15:00	Best of EHA, Best of Lugano	Prof. Dr. Bernhard Wörmann
11.07.2025	14:00 - 15:00	Speicheldrüsenkarzinome; Kopf-Hals-Plattenepithelkarzinome	Prof. Dr. Orlando Guntinas-Lichius, PD Dr. Konrad Klinghammer


Betibeglogen Autotemcel
Venetoclax
Olaparib
Pembrolizumab
Darolutamid
Acalabrutinib
Osimertinib
Abirateron
Alectinib
Daratumumab
Netupitant
Ibrutinib
Emicizumab
Pertuzumab
Avapritinib
Rurioctocog
Alpesilib
Rolapitant
Dabrafenib
Enzalutamid
Carfilzomib
Gilterinib
Trametinib
Regorafenib
Nonacog
Atezolizumab
Lonoctocog
Nivolumab
Pomalidomid
Damoctocog
Afatinib
Palbociclib
Brentuximab Vedotin
Daunorubicin/ Cytarabin
Midostaurin
Entrectinib
Cabozantinib
Ruxolitinib
Ipilimumab
Caplacizumab
Eftrenonacog
Durvalumab
Blinatumomab
Trastuzumab Emtansin
Inotuzumab Ozogamicin
Vandetanib
Eribulin
Vemurafenib
Glasdegib
Niraparib
Rucaparib
Idelalisib
Cobimetinib
Crizotinib
Belantamab Mafodotin
Ribocilib
Elotuzumab
Axitinib
Aflibercept
Albutrepenonacog
Efmorotocog
Luspatercept
Obinutuzumab
Gilteritinib
Abemaciclib
Pixantron
Apalutamid
Tisagen-lecleucel
Gemtuzumab Ozogamicin
Axicabtagen-Ciloleucel
Trifluridin/ Tiperacil
Panobinostat
Bosutinib
Ixazomib
Encorafenib
Nintedanib
Avelumab
Vismodegib
Ceritinib
Lenvatinib
Siltuximab
Larotrectinib
Binimetinib
223Radium
Polatuzumab Vedotin
Ponatinib
Lorlatinib
Ravulizumab
Simotocog
Sonidegib
Mogamulizumab
Tivozanib
Tegafur
(177Lu) Oxodotreotid
Lorlatinib
Cemiplimab
Brigatinib
Dacomitinib
Turoctocog
COVID-19 Therapie
COVID-19 Vakzine

2020

2024


Praxen
Ambulanzen
Intersektorale
Versorgung
KHVVG
Arzneimittel-
Versorgung