Mannheimer Onkologie Praxis

Dr. Phil nat. Jürgen Brust
Prof. Dr. Manfred Hensel
Dr. Nicolai Härtel
Dr. med. Christoph Plöger
PD. Dr. med. Roger Vogelmann

Onkologische Tagesklinik
am Diakonissenkrankenhaus
OTD

Makroglobulinämie Waldenström
Was gibt es Neues?

Prof. Dr. Manfred Hensel

16.11.22

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11th International Workshop on Waldenstrom's Macroglobulinemia

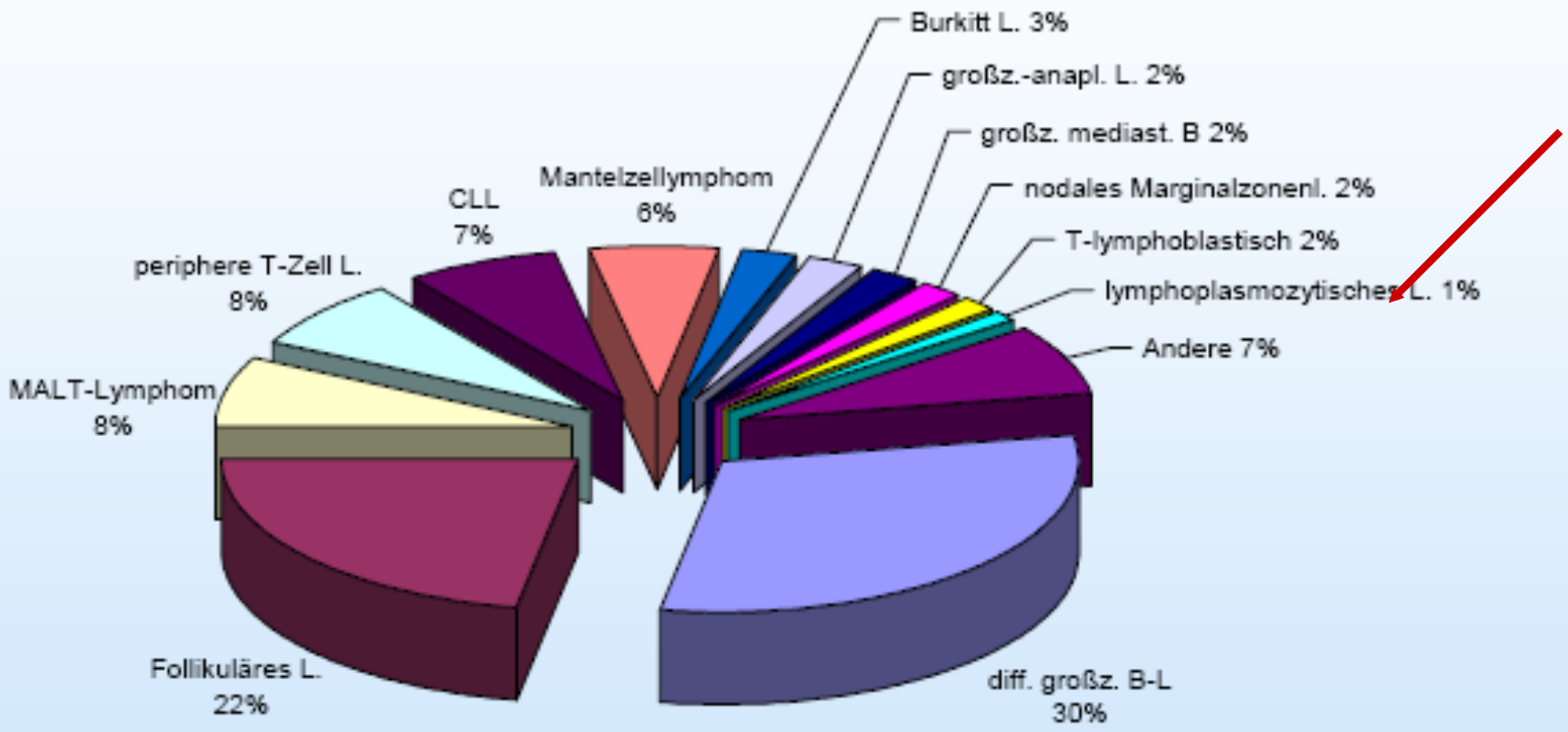
Thursday, October 27 through Sunday, October 30, 2022

Agenda

Mannheimer Onkologie Praxis

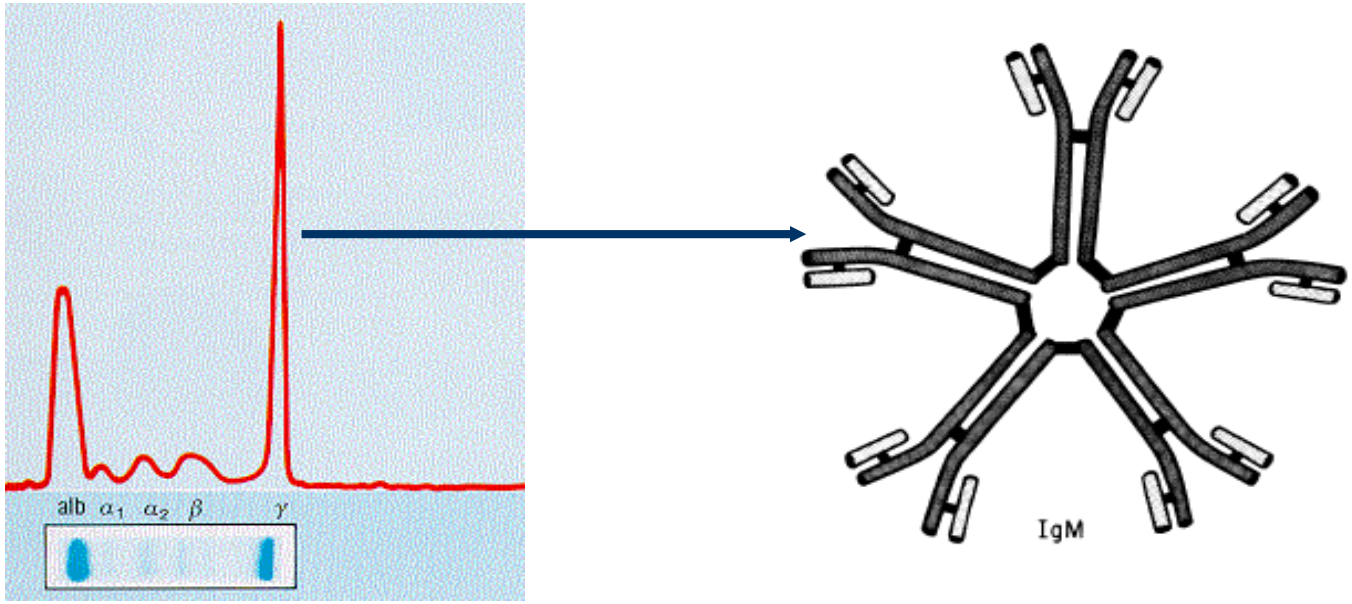
- Ein paar Grundlagen
  - Therapieprinzipien
    - wann?
    - wie
    - warum?
- Kongress
  - Programm
  - Daten zu bekannten Therapien
  - Blick in die Zukunft: neue Substanzen und Verfahren

WHO-Klassifikation maligner Lymphome: häufige Entitäten (ohne Hodgkin-Lymphom und Myelom)



M. Waldenström: *Definition*

Knochenmarkinfiltration durch
lymphoplasmozytisches Lymphom
+
Monoklonales IgM



Hensel et al., 2007, Deutsches Ärzteblatt

Wann Therapiebeginn?

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-Kein Vorteil für frühzeitige Therapie

- Asymptomatische Patienten sollten nur beobachtet werden

- IgM alleine ist nicht entscheidend

-einen definierten Grenzwert gibt es nicht (6000 mg/dl ?)

-Beginn erst bei:

-Auftreten von Symptomen, z.B. Nachtschweiß
- Abfall Hb-Wert < 10 g/dl, Thrombo < 100/nl
- Schwere Neuropathie
- symptomatische Milzvergrößerung
- große Lymphome
- starker Gewichtsverlust
-symptomatische Hyperviskosität
-Amyloidose
-Kryoglobulinämie
-Kälteagglutininkrankheit

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Ziel der Behandlung?

- Besserung der Symptome

- Normalisierung der Blutwerte

- Normalisierung von LK und Milz

- Verbesserung der Lebensqualität

- Verlängerung der Lebenserwartung

Welche Therapieform?

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- Chemoimmuntherapie:	Rituximab-Bendamustin (R-B) Rituximab-Cyclophosphamid-Dexamethason (RCD)
- Kinaseinhibitoren	Ibrutinib (Imbruvica©) Zanubrutinib (Brukinsa ©) Acalabrutinib, Venetoclax
-Neue Substanzen	bispezifische Antikörper CAR-T-Zellen

Deutsche Leitlinien

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onkopedia

onkopedia leitlinien

COVID-19
bei Krebspatienten

Inhaltsverzeichnis

Morbus Waldenström (Lymphoplasmozytisches Lymphom)

Hinweise zu COVID-19 finden Sie in der COVID-19-Leitlinie

ICD-10: C88.0

Stand: Januar 2022
Dies ist die aktuell gültige Version des Dokuments

Erstellung der Leitlinie: Regelwerk Interessenkonflikte

Autoren: Christian Buske, Dominik Heim, Michael Herold, Philipp Bernhard Staber, Martin Dreyling

Vorherige Autoren: Mathias J. Rummel

Beteiligte Fachgesellschaften: DGHO, ÖGHO, SGH+SSH, SSMO SSOM SGMO

Buske et al, Onkopedia-Leitlinie 2022

Primärtherapie

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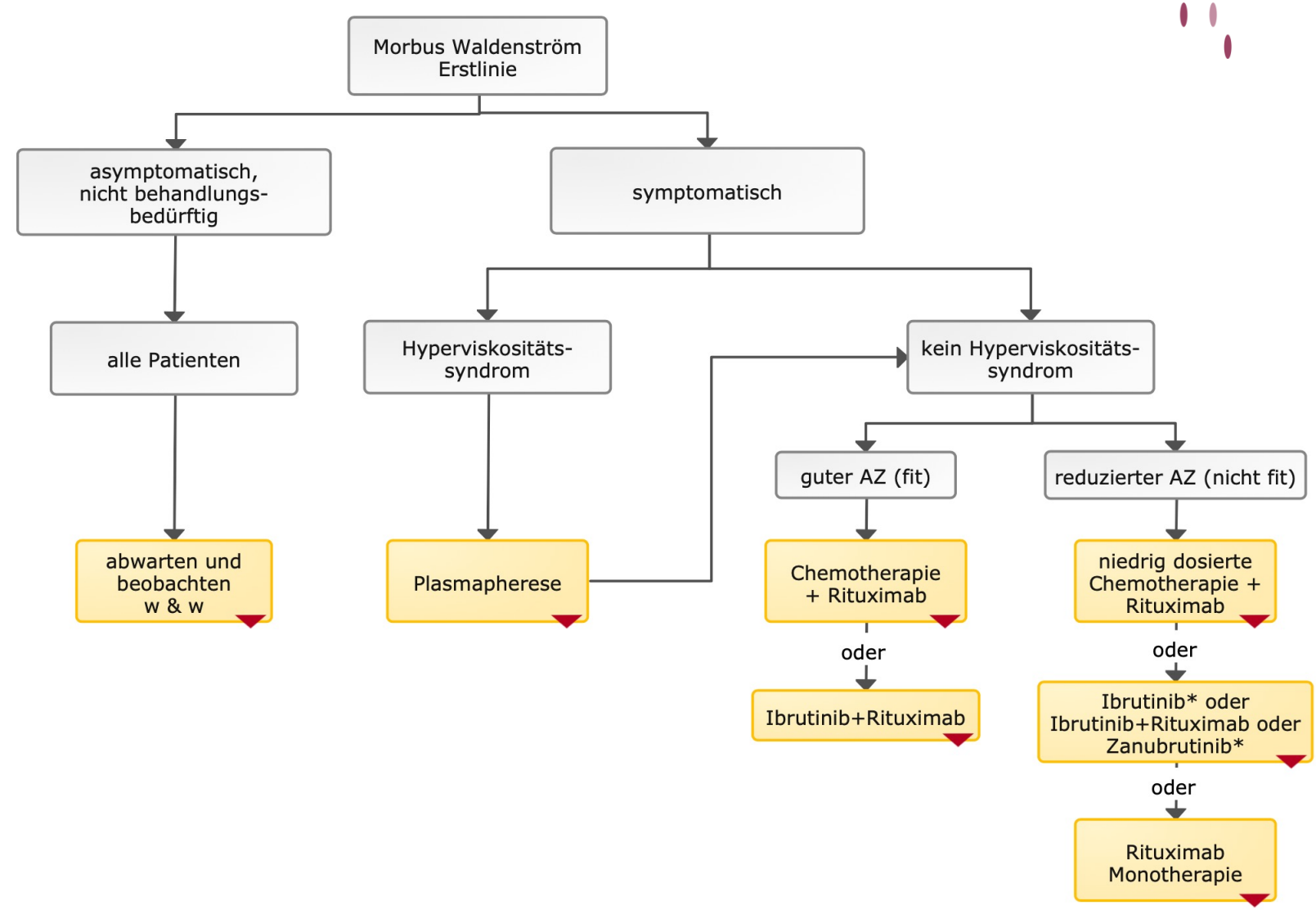

Legende: kurative Intention; palliative Intention;

*AZ – Allgemeinzustand, * nicht geeignet für Immunchemotherapie*

Buske et al, Onkopedia-Leitlinie 2022

Agenda

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Donnerstag, [17:45-18:00] Keynote Lecture

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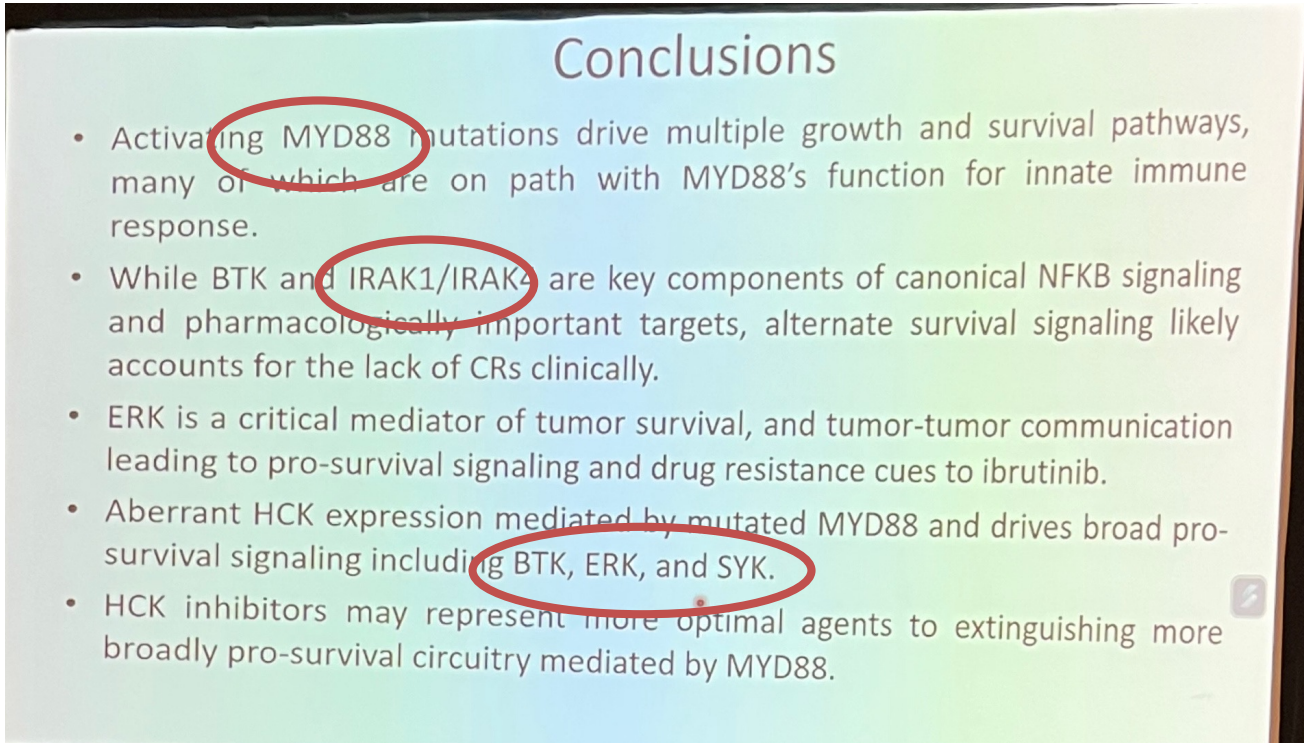
What the genomics of WM tells us about its curability

Keynote Speaker: Steve Treon, Dana Farber, USA



Friday, 28.10.22

Mannheimer Onkologie Praxis

[9:15-10:45] Session VIII
Chemoimmunotherapy
Veronique Leblond, Jorge Castillo [Chairs]

B-RCD vs. RCD Randomized Trial in WM
Pierre Morel, Centre Hospitalier Universitaire Amiens Picardie, France

RCD vs BCD Randomized Trial
Lugui Qiu, National Clinical Research Center for Blood Diseases, China

Bendamustine/Rituximab: Dose Intensity and Patient Outcomes
Suzanne Arulogun, UC London Hospitals NHS, UK

FILO Bendamustine Rituximab Study
Véronique Leblond, Hôpital Pitié Salpêtrière, France

STIL Maintenance Rituximab
Mathias Rummel, University of Giessen, Germany

BRB: Bendamustine, Rituximab, Bortezomib Study: Fondazione Italiana Linfomi Study
Giulia Benevolo, University of Torino, Italy

Friday, 28.10.22

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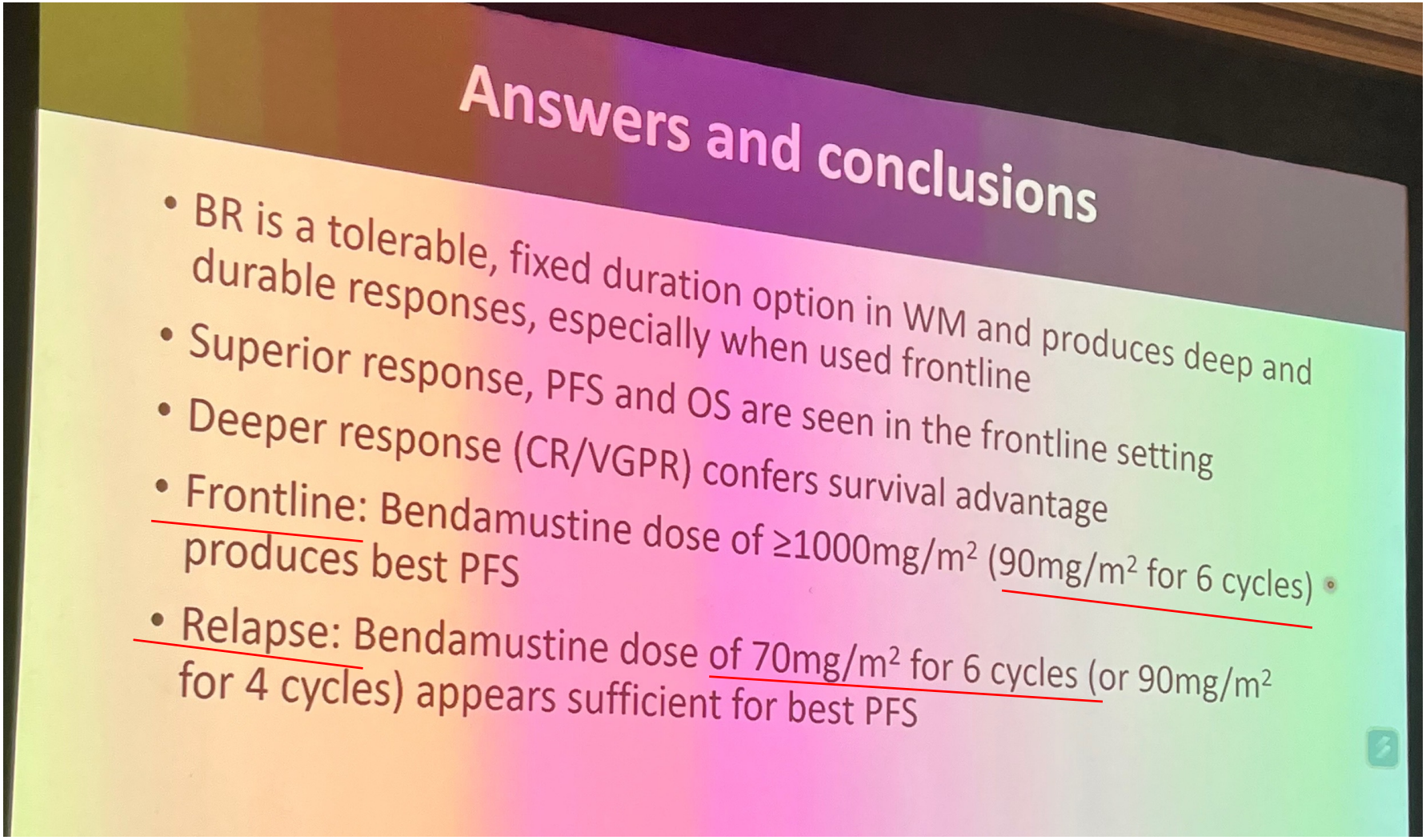
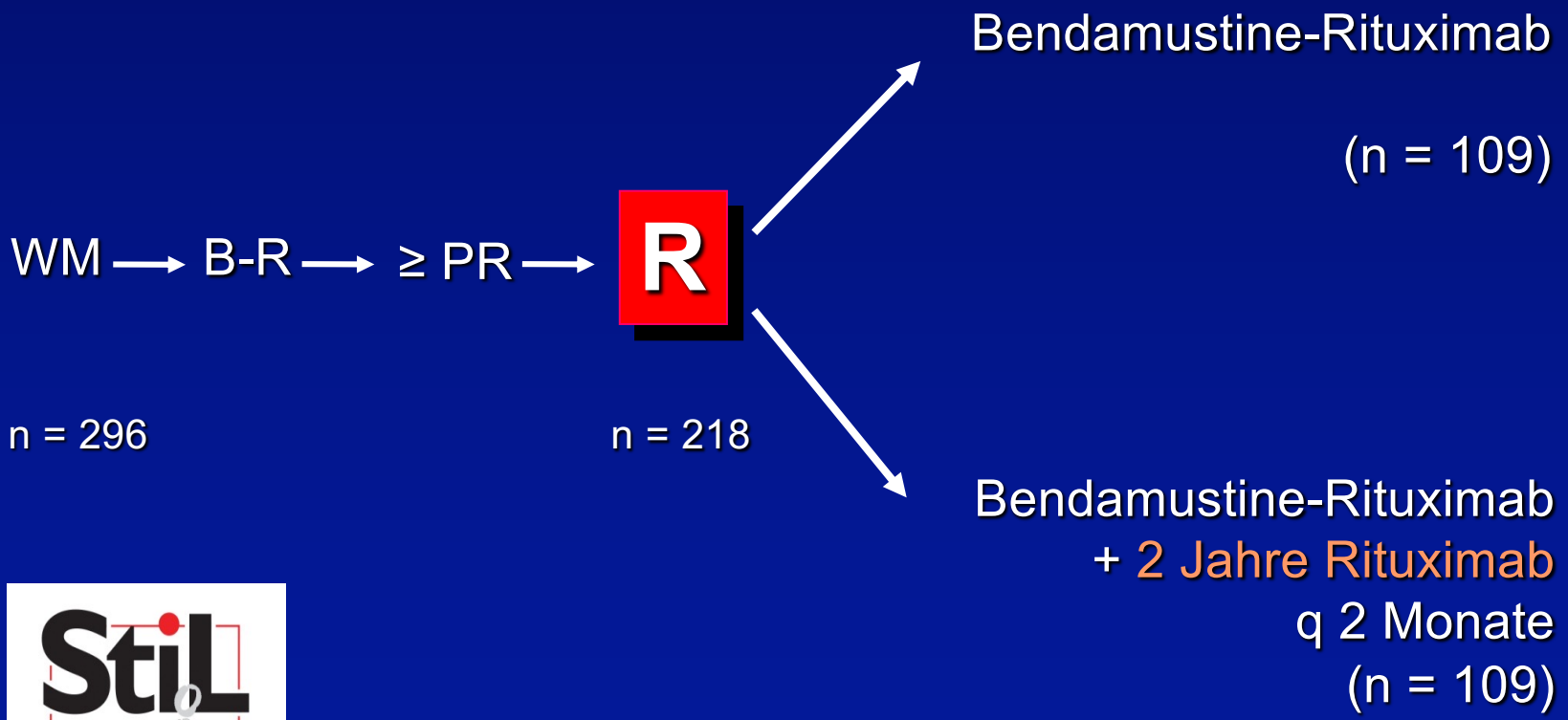
Bendamustine/Rituximab: Dose Intensity and Patient Outcomes
Suzanne Arulogun, UC London Hospitals NHS, UK



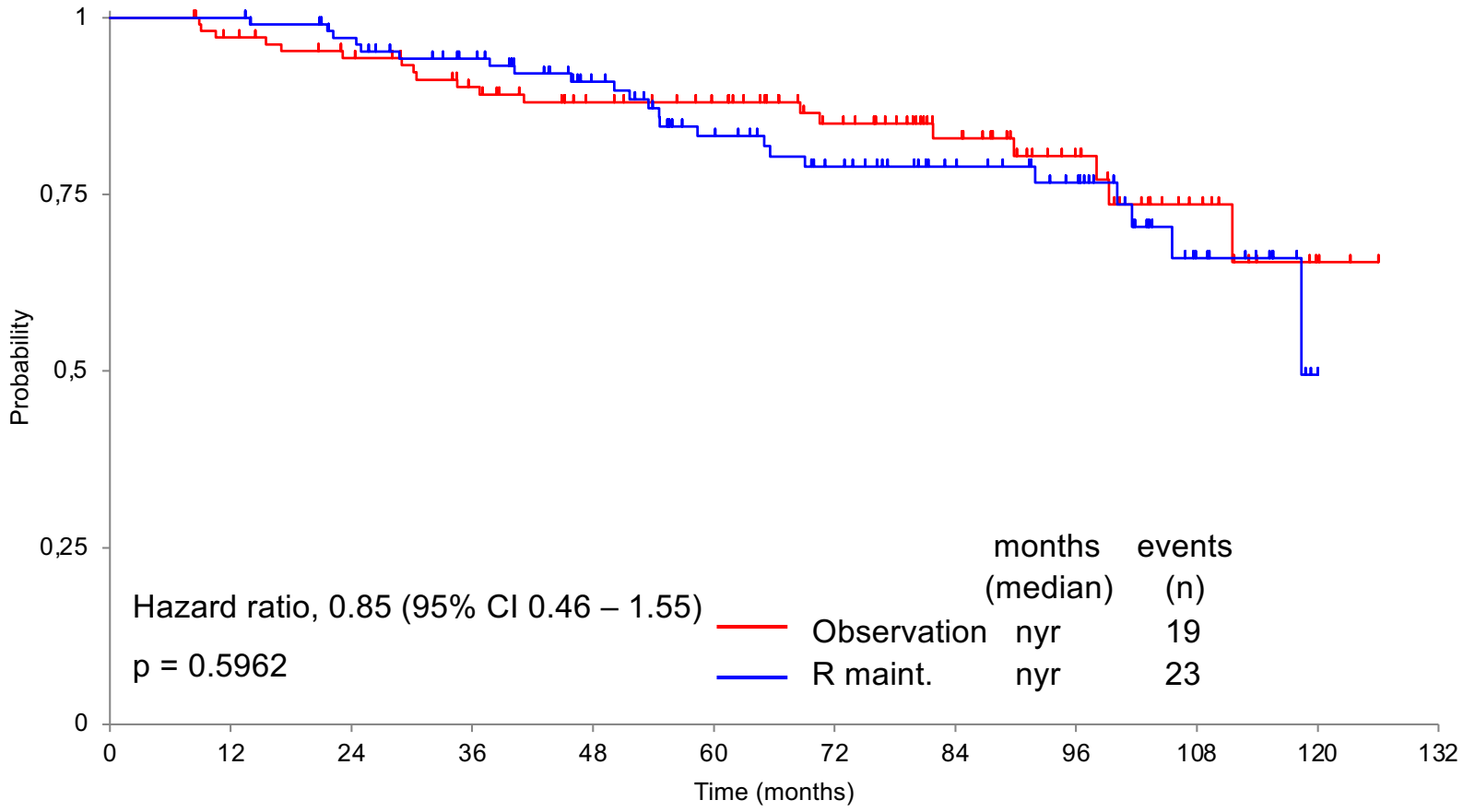
B-R + Watch & Wait vs. B-R + 2 years Rituximab

StiL NHL 7-2008 - MAINTAIN



StiL
Studiengruppe indolente Lymphome

Lebensdauer nach Beginn der Erhaltungstherapie



Pts at risk											
Observ.	109	103	96	86	75	69	55	40	26	12	3
R maint.	109	109	101	91	75	61	51	40	32	12	1

Erhaltungstherapie nicht Standard!

Friday, 28.10.22

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STIL Maintenance Rituximab

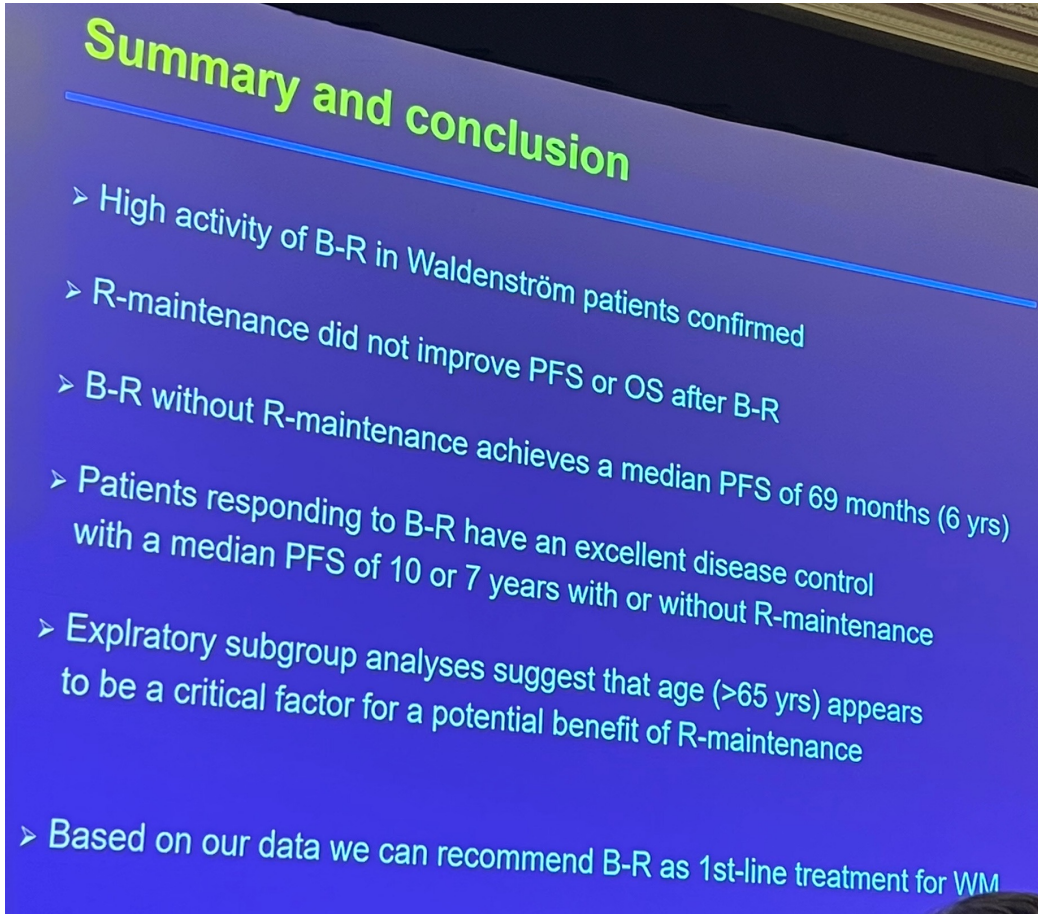
Mathias Rummel, University of Giessen, Germany

Kernaussagen:

- B-R sehr wirksam

- B-R Wirkdauer 7-10 Jahre Median (PFS)
  mit/ohne Erhaltung

- Erste Wahl!



Welche Therapieform?

Mannheimer Onkologie Praxis

- Chemoimmuntherapie: Rituximab-Bendamustin (R-B)
  Rituximab-Cyclophosphamid-Dexamethason (RCD)

- Kinaseinhibitoren Ibrutinib (Imbruvica©)

  Zanubrutinib (Brukinsa ©)

  Acalabrutinib, Venetoclax

Friday, 28.10.22

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[13:30-14:30] Session X
BTK-Inhibitors II
Alessandra Tedeschi, Constantine Tam [Chairs]

*Long Term Follow-up-**Acalabrutinib** Phase II*
Roger Owen, Leeds Hospital NHS Trust, UK

*Long Term Follow-Up **Zanubrutinib**-Phase II*
Judith Trotman, University of Sydney, Australia

*Phase II **Zanubrutinib** in relapsed/refractory WM: **Chinese experience***
Lugui Qui, National Clinical Research Center for Blood Diseases, China

*Phase II study of **Zanubrutinib, Ixazomib and Dexamethasone***
Shuhua Yi, Institute of Hematology and Blood Diseases Hospital
Chinese Academy of Medical Sciences

Friday, 28.10.22

Mannheimer Onkologie Praxis

[14:30-15:30] Session: XI
Plenary Session II
M.J. Kersten, Christian Buske [Chairs]

WM004 Final results of the Phase I/II Hovon 124/ECWM-R2 Study including 2 year rituximab maintenance after induction with ixazomib, rituximab and dexamethasone in relapsed Waldenstrom's Macroglobulinemia.
Karima Amaador, UMC Medical Center, University of Amsterdam, Netherlands

WM042 ASPEN: Long term follow-up results of a Phase 3 randomized trial of zanubrutinib versus ibrutinib in patients with Waldenstrom Macroglobulinemia.
Meletios Dimopoulos, University of Athens, Greece

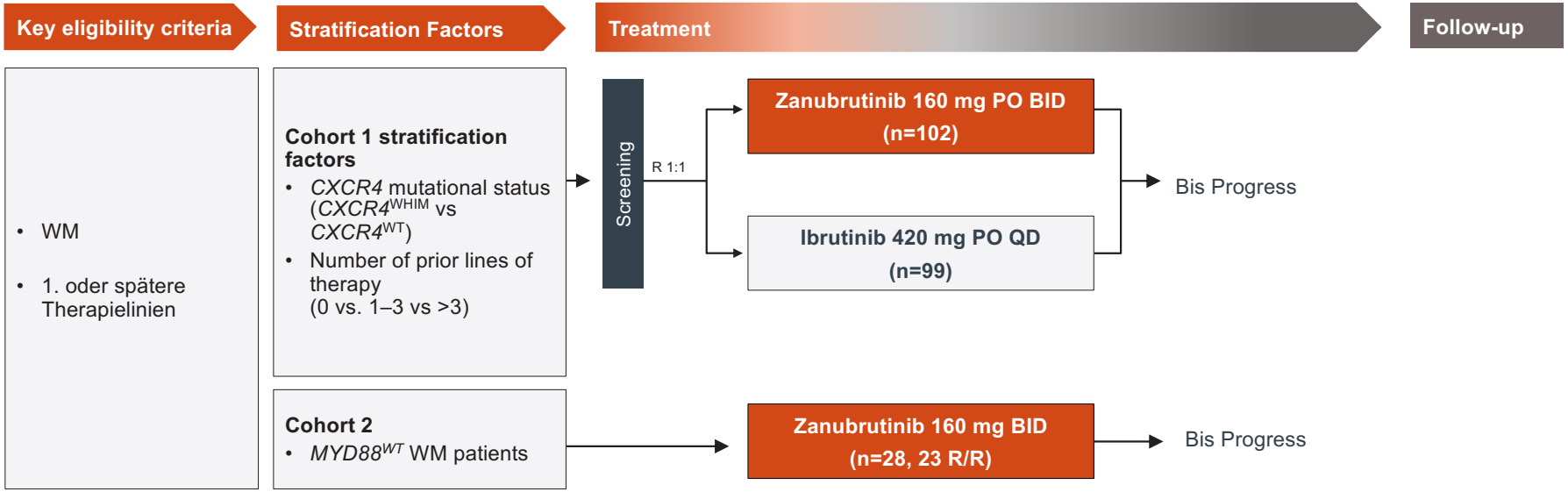
WM041 ASPEN Biomarker analysis: Response to BTK inhibitor treatment in patients with Waldenstrom Macroglobulinemia harboring CXCR4, TP53, and TERT mutations.
Constantine Tam, Peter MacCallum Cancer Center, Australia

WM024 Identification of robust predictors for ibrutinib response by multi-omic genomics in MYD88 mutated Waldenstrom's Macroglobulinemia.
Kris Richardson, Dana Farber Cancer Institute, USA

ASPEN Studie

ASPEN
Phase 3 Waldenström Macroglobulinemia

Phase 3



ASPEN-Studie

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Ergebnisse:

-Ibrutinib und Zanubrutinib ähnlich effektiv

-höhere Rate an VGPR, Gesamtansprechen gleich

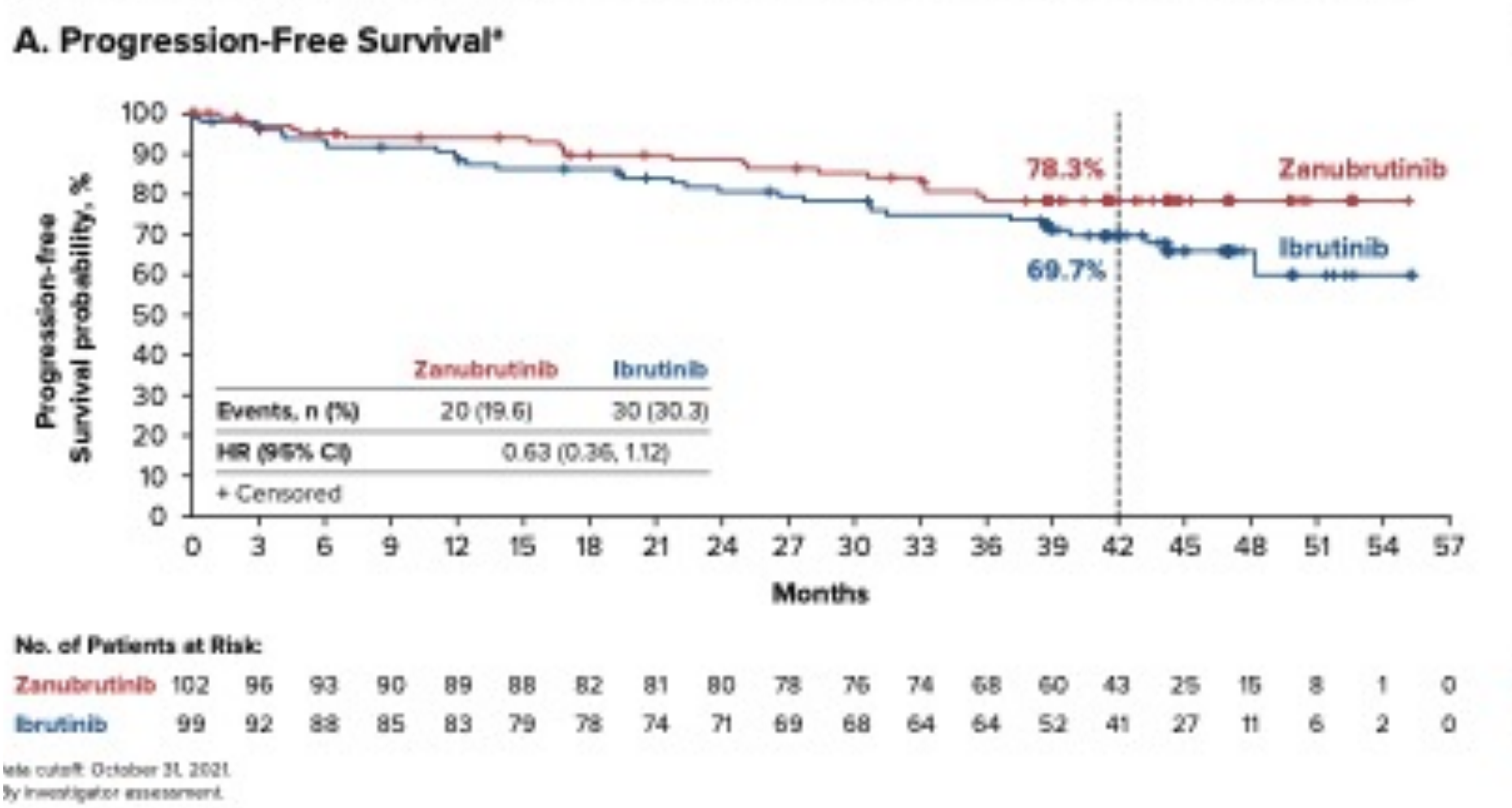
-Dauer bis zum Rückfall in beiden Armen fast gleich

-leicht verminderte Rate an Nebenwirkungen, insbesondere Vorhofflimmern (18 vs.3%) und Blutungen (60 vs. 50%)

BeiGene

WM042 ASPEN: Long term follow-up results of a Phase 3 randomized trial of zanubrutinib versus ibrutinib in patients with Waldenstrom Macroglobulinemia.

Meletios Dimopoulos, University of Athens, Greece



WM042 ASPEN: ***Nebenwirkungen***

Meletios Dimopoulos, University of Athens, Greece

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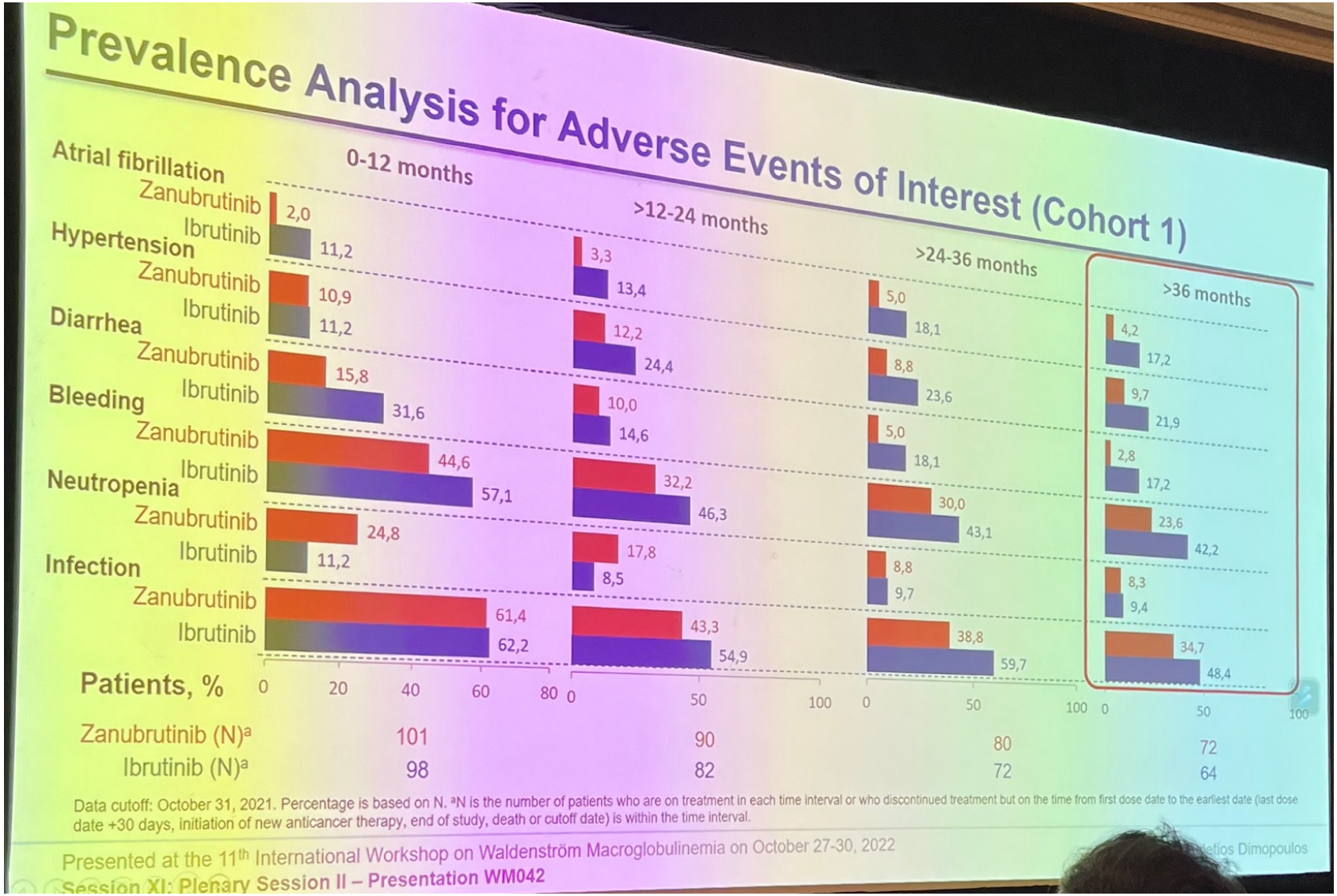

Auswirkung von Dosisreduktion Ibrutinib auf die Krankheit

Shayna Sarosiek, Dana Farber Cancer Institute, US

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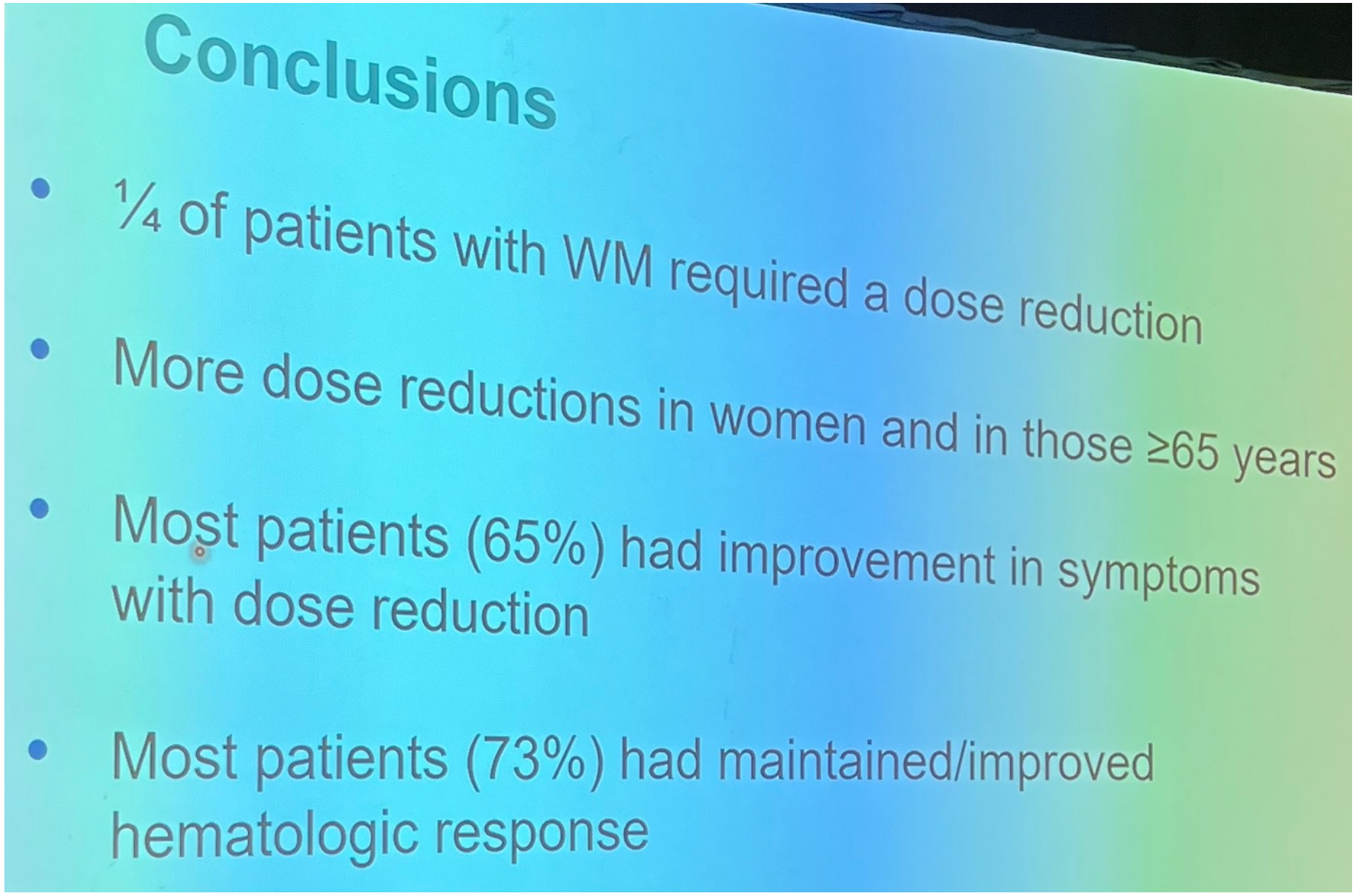

Falls Ibrutinib nicht vertragen wird: Zanubrutinib?

Mazyar Shadman, Fred Hutchinson Cancer Res Center, USA

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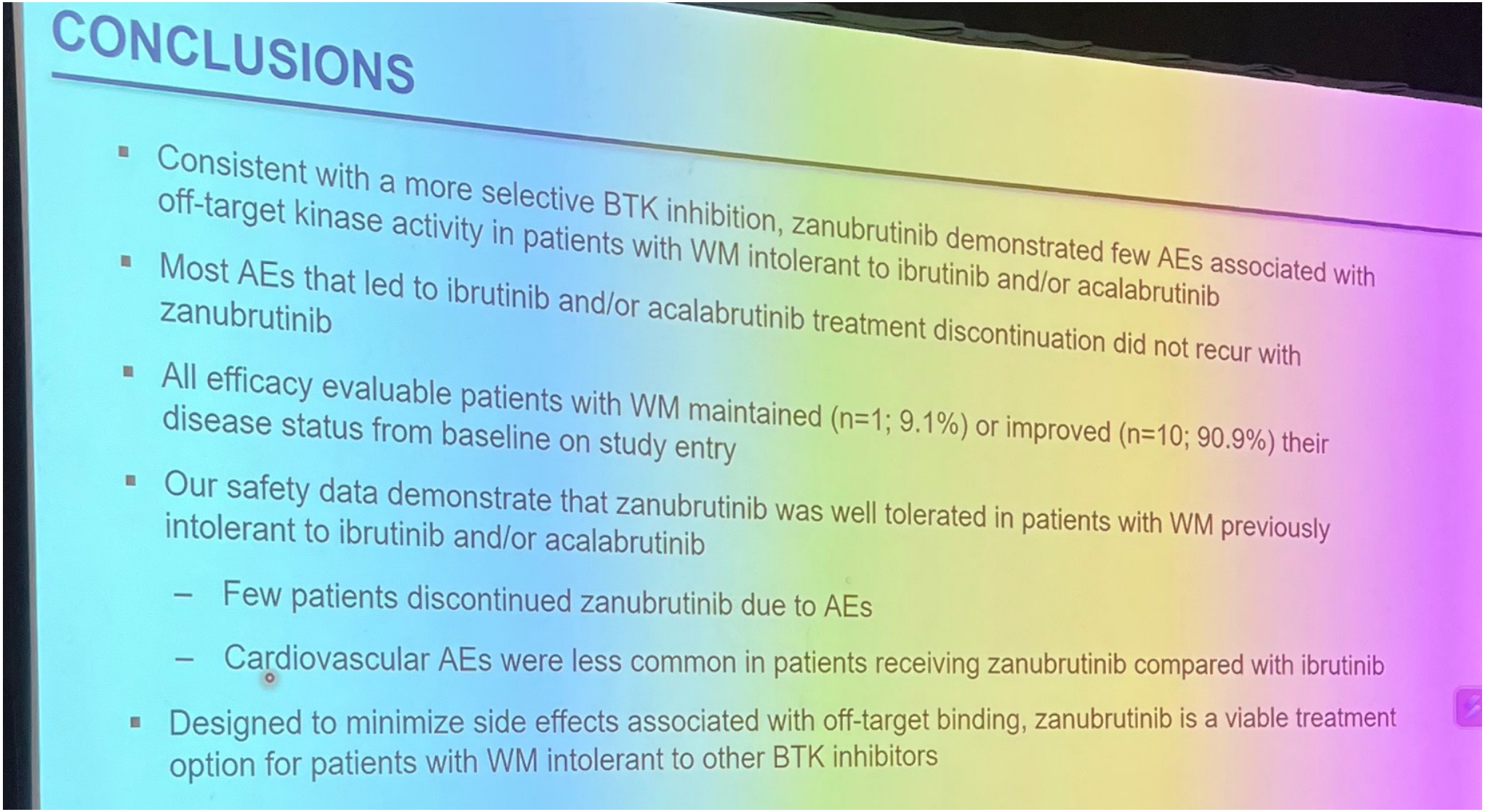

CONCLUSIONS

- Consistent with a more selective BTK inhibition, zanubrutinib demonstrated few AEs associated with off-target kinase activity in patients with WM intolerant to ibrutinib and/or acalabrutinib
- Most AEs that led to ibrutinib and/or acalabrutinib treatment discontinuation did not recur with zanubrutinib
- All efficacy evaluable patients with WM maintained (n=1; 9.1%) or improved (n=10; 90.9%) their disease status from baseline on study entry
- Our safety data demonstrate that zanubrutinib was well tolerated in patients with WM previously intolerant to ibrutinib and/or acalabrutinib
  - Few patients discontinued zanubrutinib due to AEs
  - Cardiovascular AEs were less common in patients receiving zanubrutinib compared with ibrutinib
- Designed to minimize side effects associated with off-target binding, zanubrutinib is a viable treatment option for patients with WM intolerant to other BTK inhibitors

Samstag, 29.10.22, Tag der Debatten!

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[8:00-11:15] Session XIII
Great Debates in WM
Eva Kimby, Jesus San Miguel [Chairs]

[8:00-8:30] Great Debate I
Should we treat smoldering WM? -No
Prashant Kapoor, Mayo Clinic, USA

Should we treat smoldering WM? -Yes
Irene Ghobrial, Dana Farber Cancer Institute

[8:30-9:00] Great Debate II
Should BTK-I or Benda-R be the standard frontline induction regimen? -for Benda-R
Christian Buske, University Hospital Ulm, Germany

Should BTK-I or Benda-R be the standard frontline induction regimen? -for BTK-I
Meletios Dimopoulos, University of Athens, Greece

[9:00-9:45] Great Debate III
Does the choice of BTK-inhibitor matter? -for Ibrutinib
Ranjana Advani, Stanford University Medical Center, USA

Does the choice of BTK-inhibitor matter? -for Acalabrutinib
Roger Owen, Leeds Hospital NHS Trust, UK

Does the choice of BTK-inhibitor matter? -for Zanubrutinib
Judith Trotman, University of Sydney, Australia

Sollen asymptomatische Patienten schon behandelt werden?

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[8:00-8:30] Great Debate I

No

Prashant Kapoor, Mayo Clinic, USA

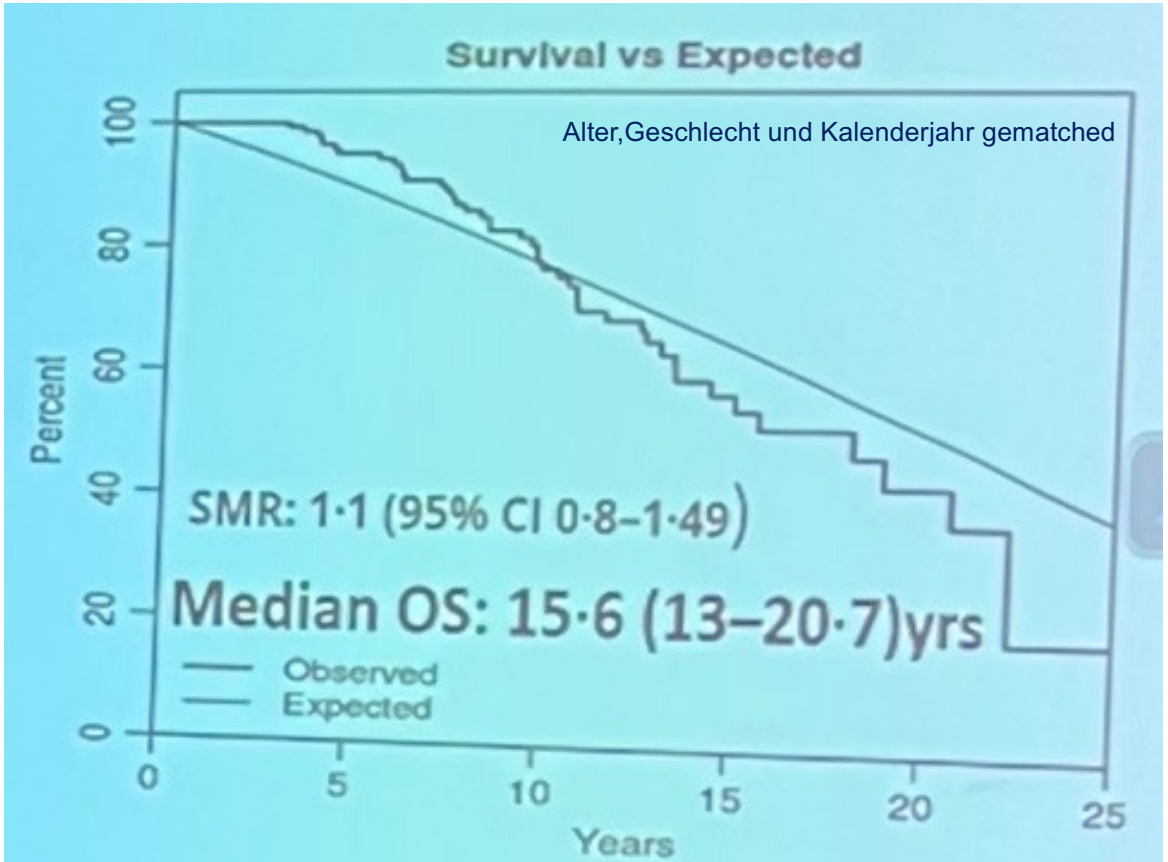
smouldering MW hat normale Lebenserwartung,
Kein Überlebensvorteil durch frühe Therapie,

Yes

Irene Ghobrial, Dana Farber Cancer Institute

früh die besten Chancen auf Heilung
mit den besten Medikamenten:
bispezifische Antikörper,
CAR-T-Zellen

Abstimmung:
Gewinnerin: Kapoor: Abwarten
Aber: Ghobrial: Trials for early treatment



Gobbi Clin Cancer research, 2005; Zanwar BJH,2021

BTK-I oder Benda-R die beste Erstlinientherapie?

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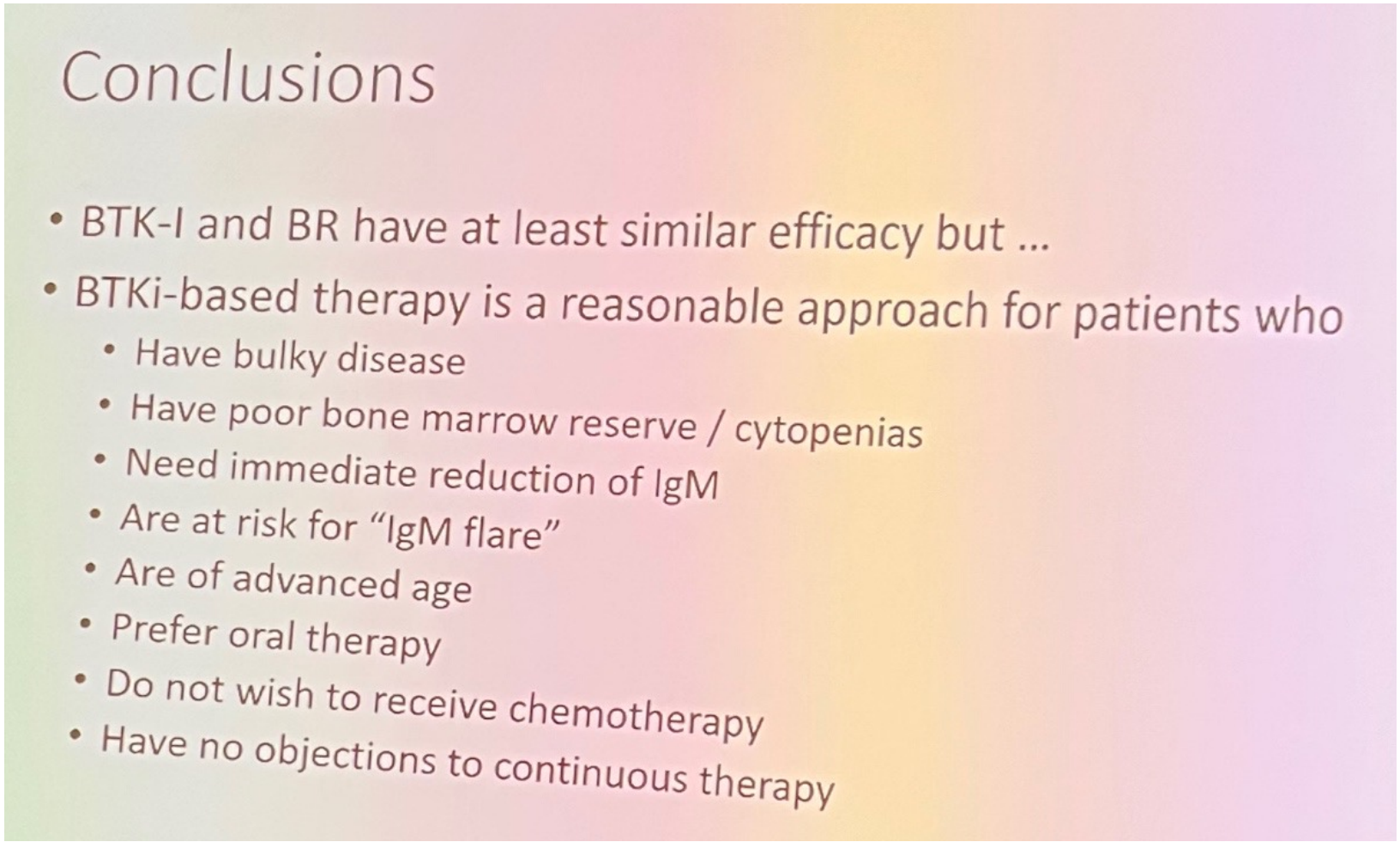
[8:30-9:00] Great Debate II

für BTK-I

Meletios Dimopoulos, University of Athens, Greece#



BTK-I oder Benda-R die beste Erstlinientherapie?

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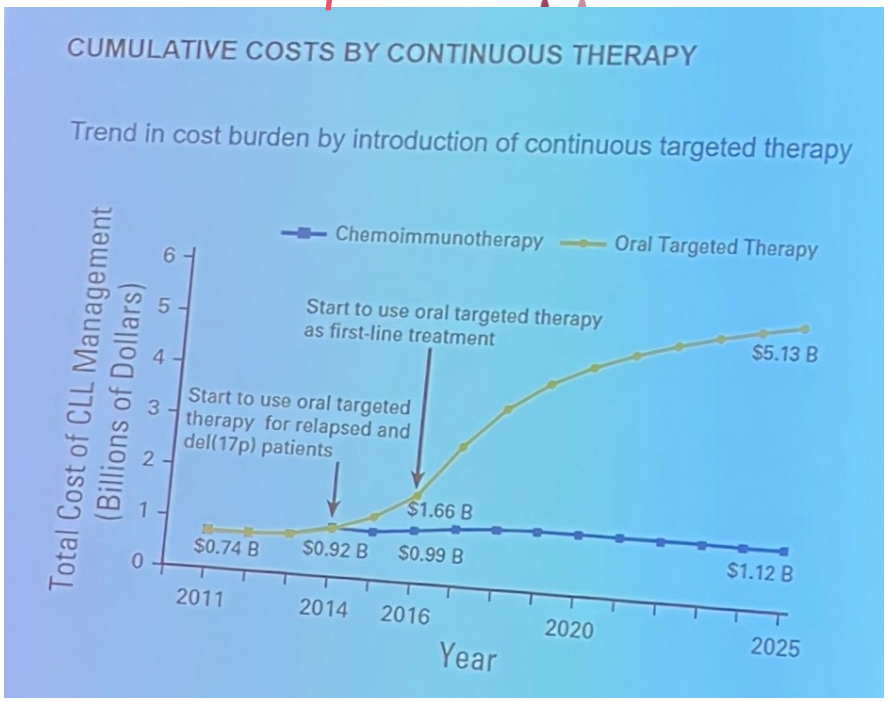
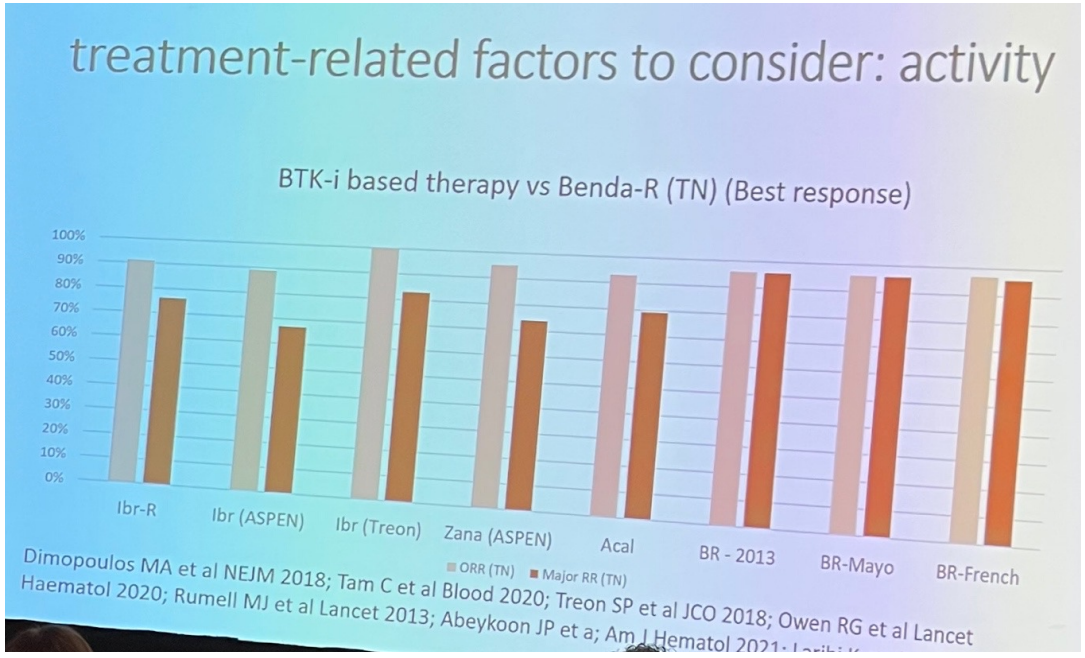
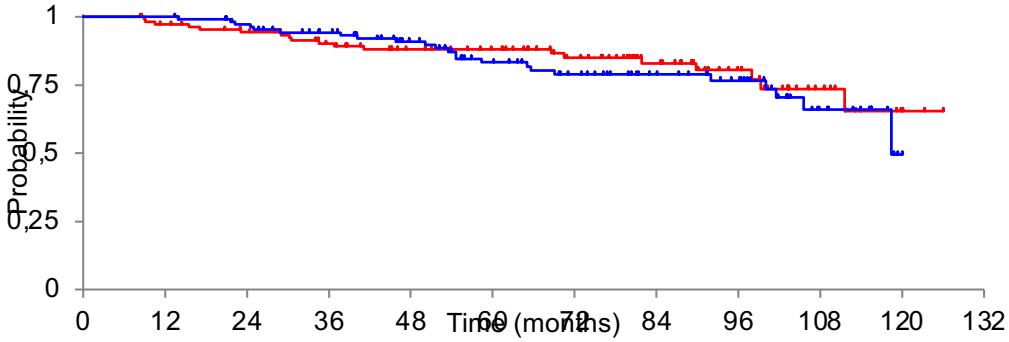
für Benda-R

Christian Buske, University Hospital Ulm, Germany







Abstimmung:
Gewinner: Buske (R-Benda

Samstag, 29.10.22

Mannheimer Onkologie Praxis

[11:15-12:15] Session XIV
Novel Treatment Approaches to WM-Clinical I
Sheeba Thomas, Moshe Gatt [Chairs]

Venetoclax in combination with ibrutinib for WM
Jorge Castillo, Dana Farber Cancer Institute, USA

Zu toxisch, Studienabbruch

Targeting mutated CXCR4 in WM
Steven Treon, Dana Farber Cancer Institute, USA

Vielversprechend, ganz neue Substanzen

Obinutuzumab and Idelalisib in WM
Véronique Leblond, Hôpital Pitié Salpêtrière, France

m.E. keine Zukunft

Acalabrutinib and Rituximab for WM and IGM RD PN
Shayna Sarosiek, Dana Farber Cancer Institute, USA

Studie bei Polyneuropathie, startet gerade

Samstag, 29.10.22

Mannheimer Onkologie Praxis

[14:00-15:00] Session XVI
Novel Treatment Approaches to WM-Clinical III

Bispecifics in WM-CD3XCD20 RGN1979
Stephen Ansell, Mayo Clinic, USA

Phase II Study of Loncastuximab in WM
Shayna Sarosiek, Dana Farber Cancer Institute, USA

Idiotype DNA Vaccine Therapy for WM
Sheeba Thomas, MD Anderson, USA

CD20 CAR-T therapy for WM and other B-NHLs
Mazyar Shadman, Fred Hutchinson Cancer Res Center, USA

Bispezifische Antikörper und CAR-T-Zellen

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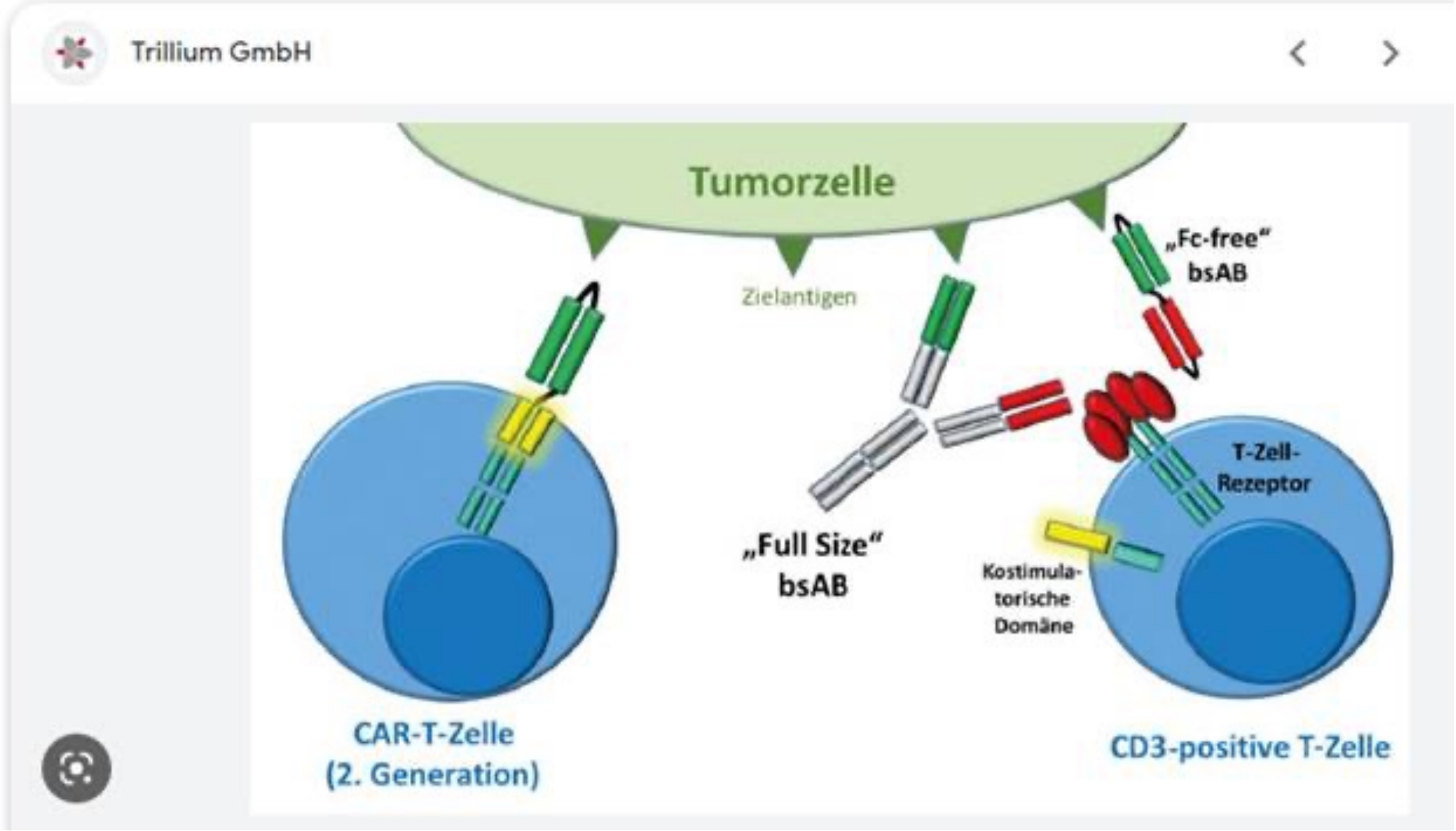
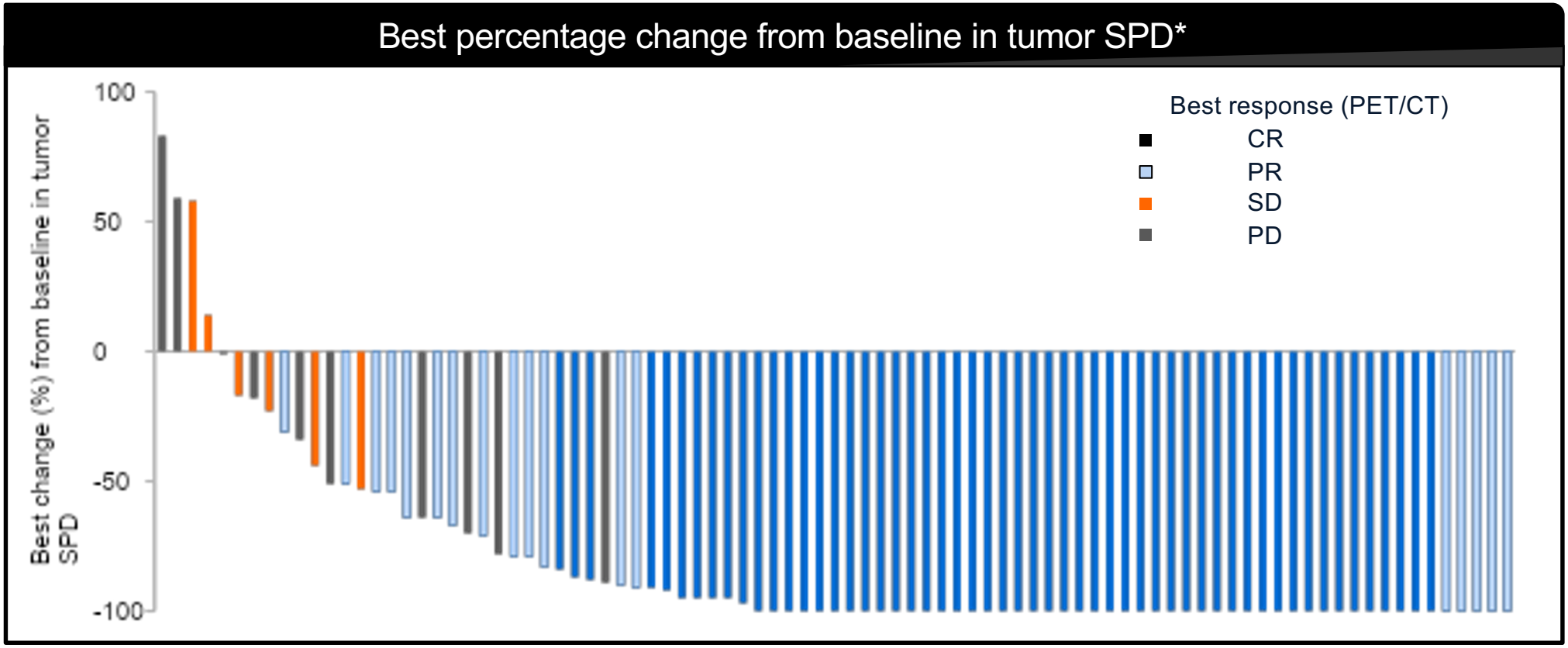


Anti-tumor efficacy

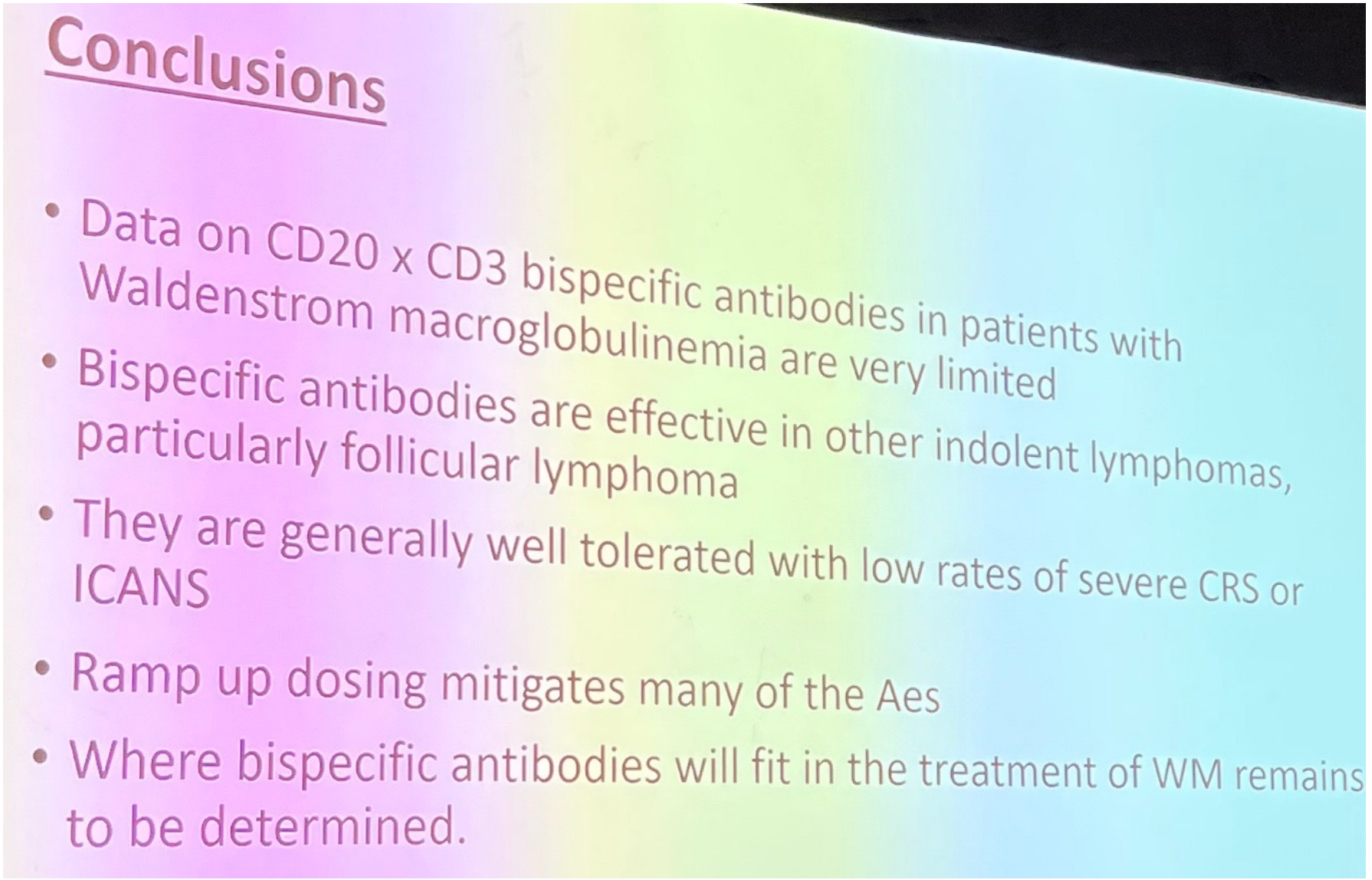


*in all patients with a baseline and ≥1 post-baseline SPD available; PD, progressive disease; SPD, sum of product diameters

Budde LE et al., ASH 2021

Bispecifics in WM-CD3XCD20 RGN1979

Stephen Ansell, Mayo Clinic, USA



Phase II Study of Loncastuximab in WM

Shayna Sarosiek, Dana Farber Cancer Institute, USA

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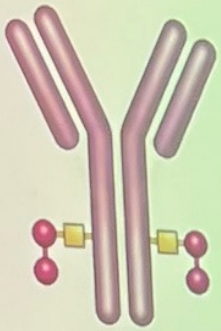
Loncastuximab tesirine



- Antibody drug conjugate
- Humanized monoclonal antibody directed against CD19, attached with a cleavable linker to SG3199, a pyrrolobenzodiazepine dimer cytotoxin
- Binds to the DNA minor groove and forms cytotoxic interstrand cross-links
- FDA approved for relapsed/refractory large B-cell lymphoma

Samstag, 29.10.22

Mannheimer Onkologie Praxis

[15:00-15:30] Keynote Lectures

Bi-specifics and Conjugated Antibodies: MM Experience
Keynote Speaker: Kenneth C. Anderson, Dana Farber Cancer Institute, USA

Bringing CART to WM: Which One?
Keynote Speaker: Nikhil Munshi, Dana Farber Cancer Institute, USA

Zusammenfassung

Mannheimer Onkologie Praxis
Dr. phil. nat. Jürgen Brust
Prof. Dr. Manfred Hensel
Dr. med. Christoph Plöger
Dr. med. Dieter Schuster

Onkopedia-Leitlinien sind aktualisiert und einsehbar

Mehrere sehr gute Therapien für die Primärtherapie zur Auswahl:

Rituximab und Bendamustin, 6 Zyklen, alle 4 Wochen
RCD
Ibrutinib +/- Rituximab
Zanubrutinib

Meine erste Wahl ist weiterhin Rituximab und Bendamustin

Bei Rückfall gegebenenfalls Wiederholung der Primärtherapie (bei langer Remissionsdauer, z.B. >3 J.) oder eine der anderen Substanzen

Viele neue Substanzen in der Erprobung

Wissenschaftliche Comunity ist sehr aktiv!

Mannheimer Onkologie Praxis

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Dr.med. Nicolai Härtel
Prof. Dr. Manfred Hensel
Dr. med. Christoph Plöger
PD. Dr. med. Roger Vogelmann

Onkologische Tagesklinik
am Diakonissenkrankenhaus
OTD

Vielen Dank für Ihre Aufmerksamkeit