Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

KML KONGRESSE

Expert:innen berichten zu Lymphomen & Leukämien

65th ASH Meeting 2023

San Diego & virtuell

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Expert:innen berichten zu Lymphomen & Leukämien

Prof. Dr. med. Barbara Eichhorst
Klinik I für Innere Medizin | Uniklinik Köln

Chronische lymphatische Leukämie (CLL)

Offenlegung potentieller Interessenskonflikte

LymphomKompetenz KOMPAKT – ASH2023 wird in Kooperation mit acht unterstützenden Firmen durchgeführt.
Meine persönlichen Disclosures betreffen:

Anstellungsverhältnis, Führungsposition	-
Beratungs-/ Gutachtertätigkeit	AbbVie, AstraZeneca, BeiGene, Kite, Lilly, Janssen, MSD
Besitz von Geschäftsanteilen, Aktien oder Fonds	-
Patent, Urheberrecht, Verkaufslizenz	-
Honorare	AbbVie, AstraZeneca, BeiGene, Kite, Janssen, MSD, Roche
Finanzierung wissenschaftlicher Untersuchungen	AbbVie, Astra Zeneca, BeiGene, Janssen, Roche
Andere finanzielle Beziehungen	-
Immaterielle Interessenkonflikte	Cochair DCLLSG

Therapie der CLL

Übersicht

Erstlinie:

- Dauertherapie: Acalabrutinib +/- Obi, Zanubrutinib, Ibrutinib +/- Obi
- Zeitlich begrenzte Therapie:
  - Venetoclax + Obinutuzumab
  - Ibrutinib + Venetoclax

Rezidiv:

- Dauertherapie: Acalabrutinib, Zanubrutinib, Ibrutinib
- Zeitlich begrenzte Therapie:
  - Venetoclax + Rituximab

Richter-Transformation: RCHOP, RDHAP, allo SCTx in fit

Kapitel 1

Zeitliche begrenzte Therapien in der Erstlinientherapie der CLL:

Ibrutinib + Venetoclax

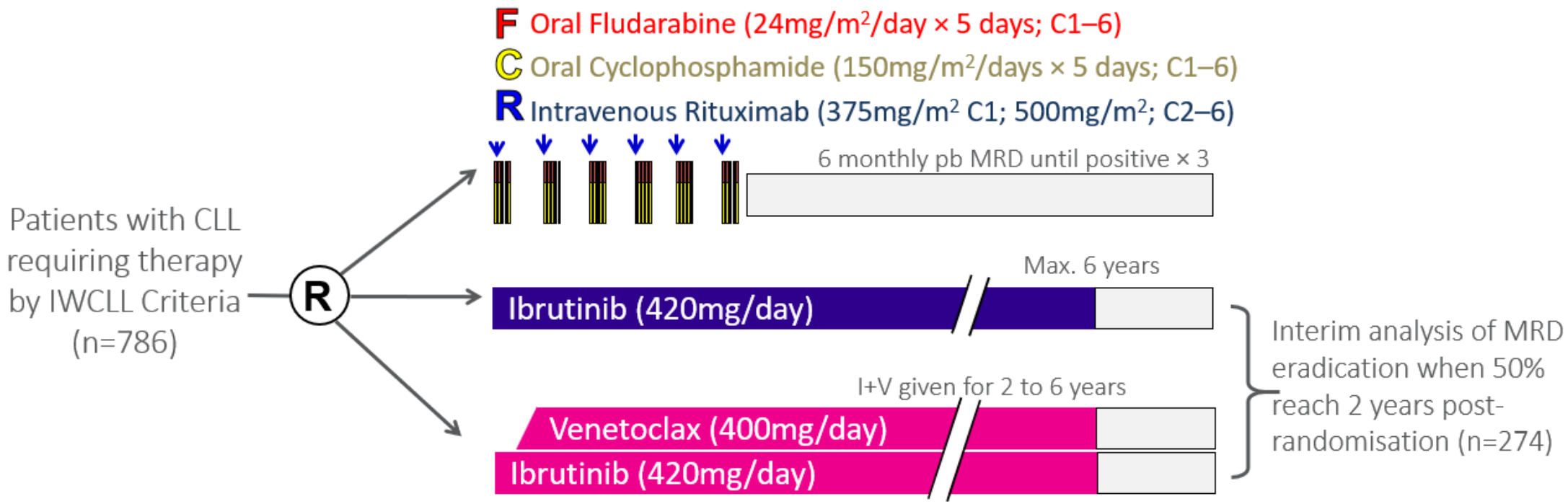
FLAIR-Studie: Ibrutinib + Venetoclax (IV) MRD gesteuert vs. FCR

631 - Ibrutinib Plus Venetoclax with MRD-Directed Duration of Treatment Is Superior to FCR and Is a New Standard of Care for Previously Untreated CLL: Report of the Phase III UK NCRI FLAIR Study

Peter Hillmen, Leeds, UK

FLAIR: IV vs. FCR

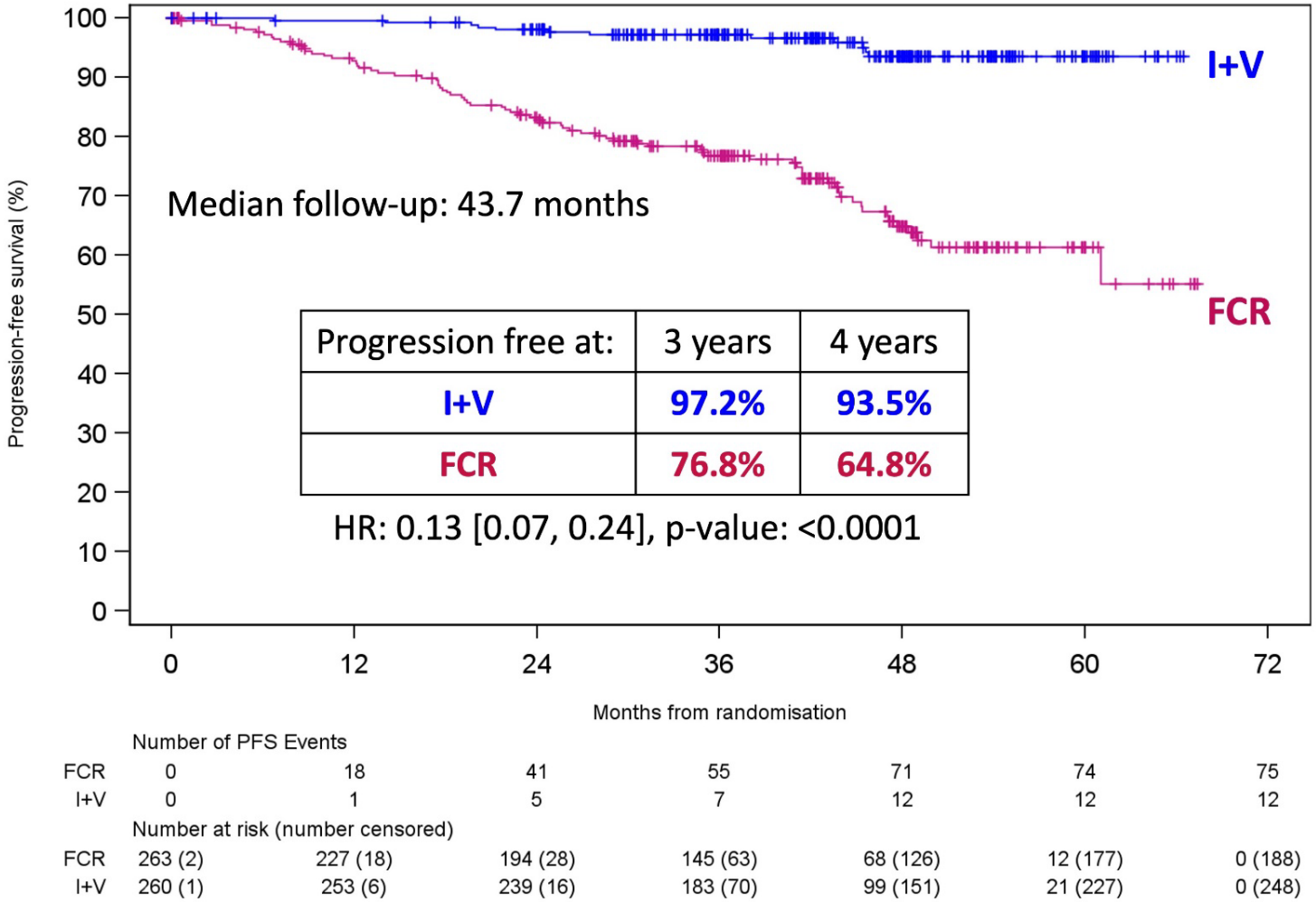
Phase III Studie des NCRI aus UK: Design



In ibrutinib and ibrutinib+venetoclax arms: PB MRD every 6 months. If PB MRD negative repeat after 3 months and then PB and BM at 6 months – if all MRD negative, then first PB MRD negative result is time to MRD negativity.
Duration of therapy – double time to MRD negativity (minimum 2 years; maximum 6 years)

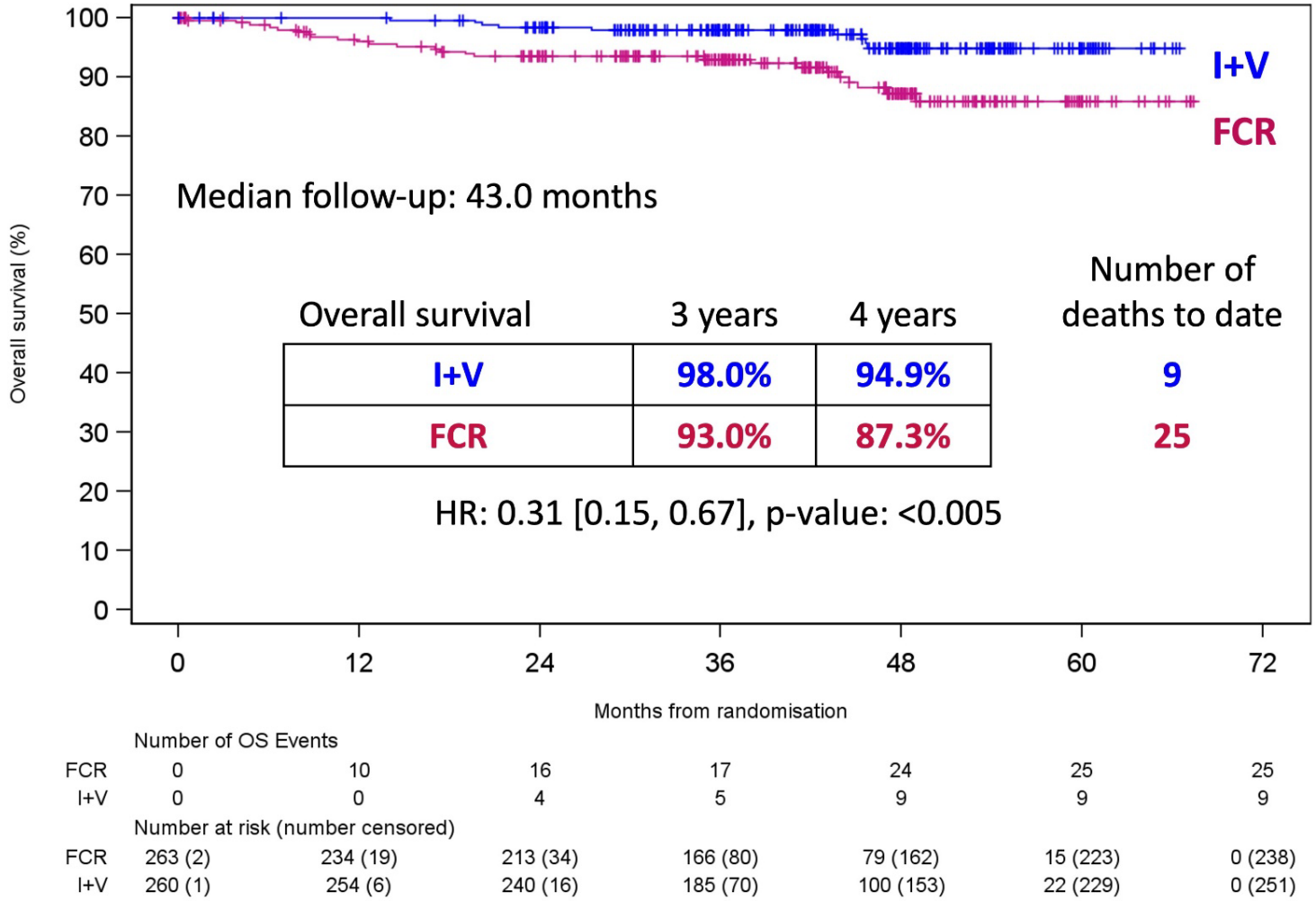
FLAIR: IV vs. FCR

Phase III Studie des NCRI aus UK: PFS



FLAIR: IV vs. FCR

Phase III Studie des NCRI aus UK: OS



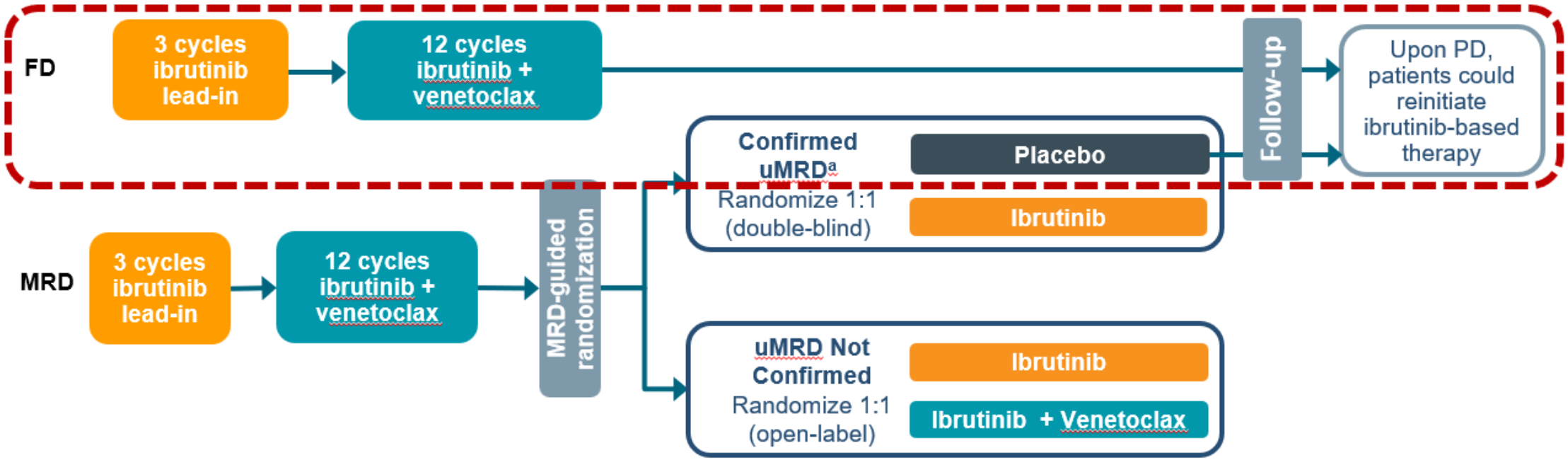
CAPTIVATE-Studie / Phase II Studie:
Zeitlich begrenzte Ibrutinib + Venetoclax Therapie

633: Relapse after First-Line Fixed Duration Ibrutinib + Venetoclax: High Response Rates to Ibrutinib Retreatment and Absence of BTK Mutations in Patients with Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) with up to 5 Years of Follow-up in the Phase 2 Captivate Study

Paolo Ghia et al., Mailand, Italien

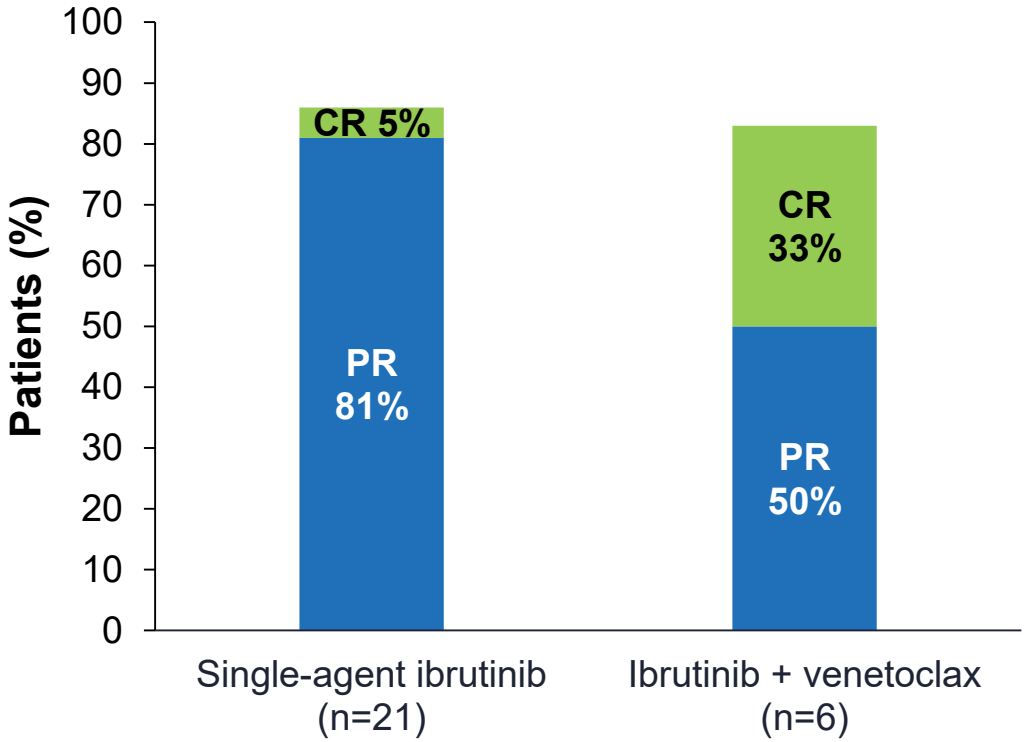
CAPTIVATE: Zeitlich begrenzte Ibrutinib + Venetoclax Therapie

Studiendesign der 2 Kohorten: zeitlich begrenzt und MRD gesteuert



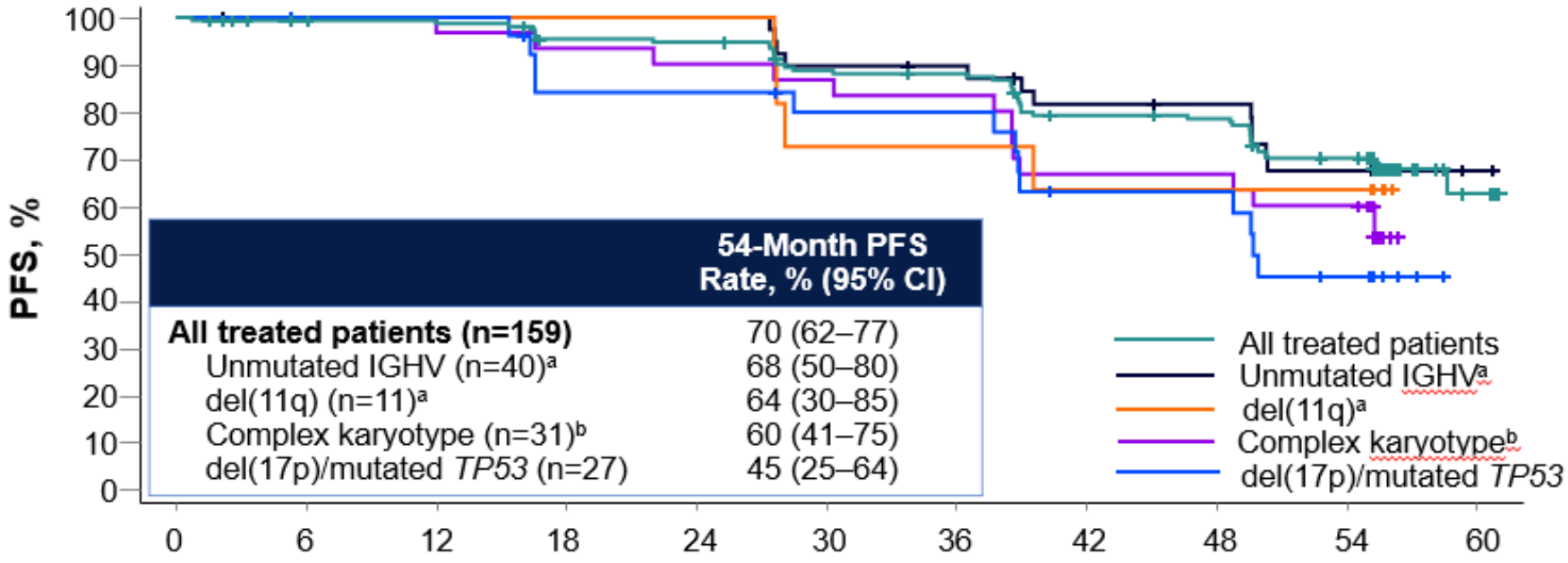
CAPTIVATE: Zeitlich begrenzte Ibrutinib + Venetoclax Therapie

Ibrutinib + Venetoclax zeitliche begrenzt: Ansprechen auf Therapie im Rezidiv



CAPTIVATE: Zeitlich begrenzte Ibrutinib + Venetoclax Therapie

Ibrutinib + Venetoclax zeitliche begrenzt: PFS



Patients at risk

All treated patients	159	153	152	144	143	132	130	115	113	99	11
Unmutated IGHV[a]	40	39	39	39	39	35	34	30	29	24	1
del(11q)[a]	11	11	11	11	11	8	8	7	7	7	0
Complex karyotype[b]	31	31	31	28	27	26	25	20	20	18	0
del(17p)/mutated *TP53*	27	26	26	21	21	19	19	14	14	9	0

Kapitel 2

Zeitliche begrenzte Therapien in der Erstlinientherapie der CLL:

Venetoclax + CD20-Antikörper

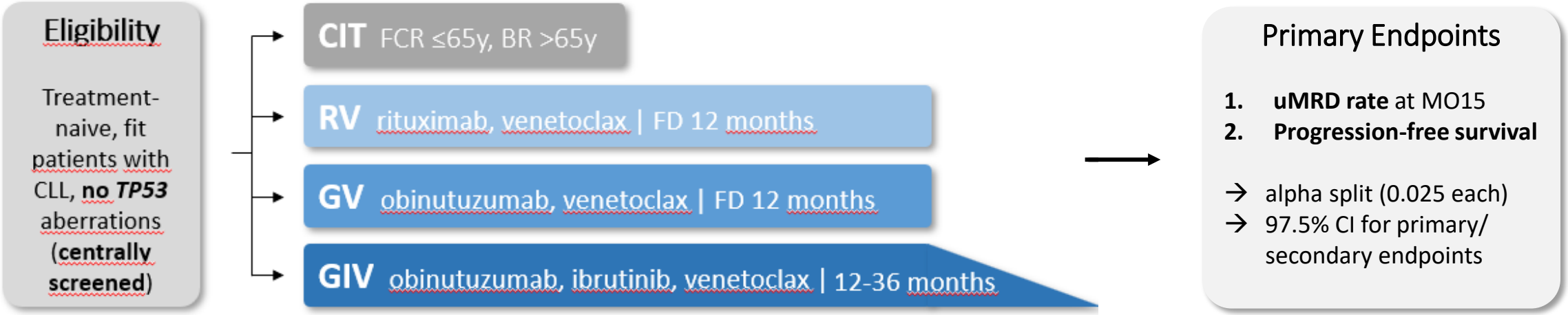
CLL13/GAIA-Studie

635 - First-Line Venetoclax Combinations in Fit Patients with CLL: 4-Year Follow-up and NGS-Based MRD Analysis from the Phase 3 GAIA/CLL13 Trial

Moritz Fürstenau, Köln

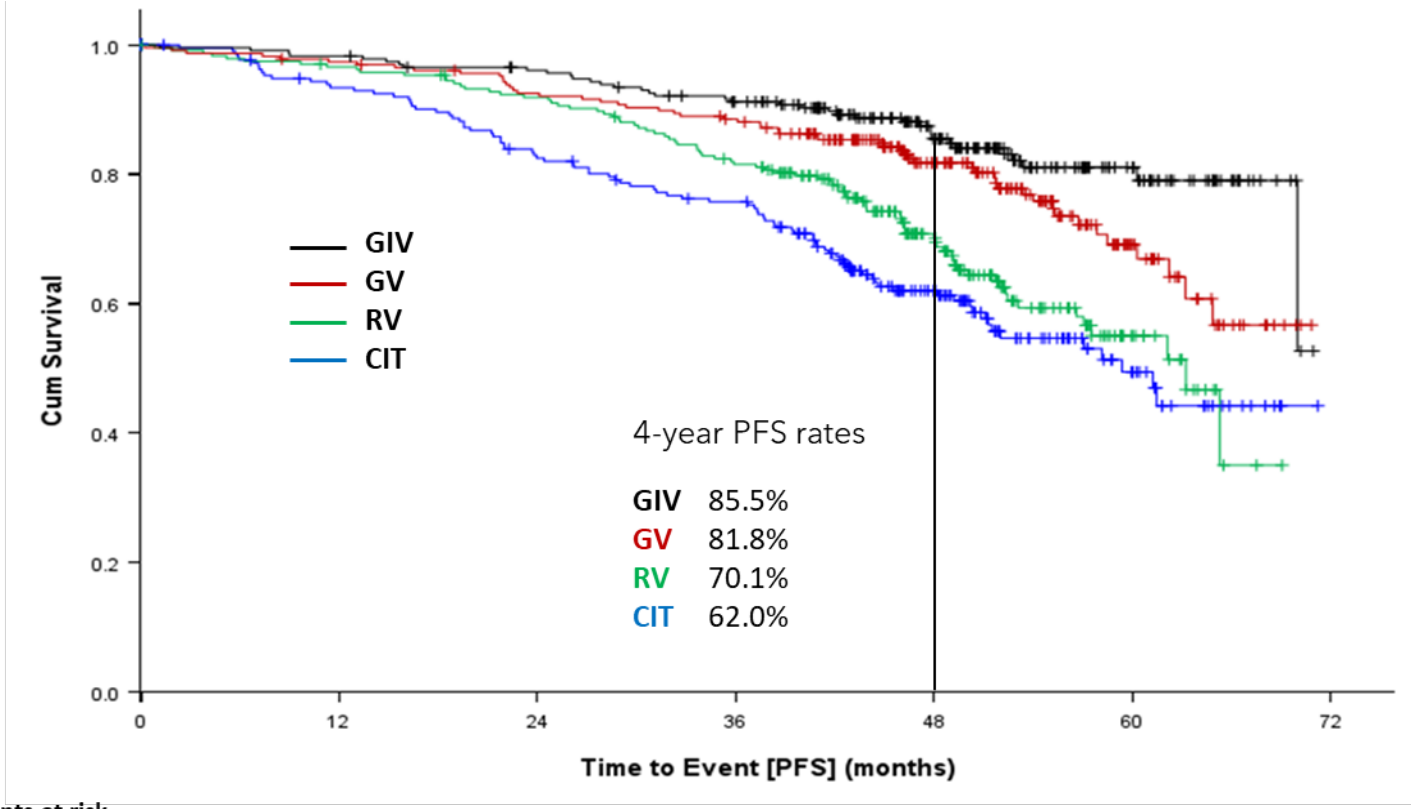
CLL13/GAIA Studie

Phase III: Venetoclax + Obinutuzumab + Ibrutinib vs Venetoclax + Obinutuzumab vs Venetoclax + Rituximab vs FCR/BR



CLL13/GAIA Studie

PFS nach 50.7 Monaten Beobachtungszeit für Venetoclax + Obinutuzumab (GIV + Ibrutinib vs Venetoclax + Obinutuzumab vs Venetoclax + Rituximab vs FCR/BR



Patients at risk

CIT	229	197	173	156	84	24
RV	237	227	214	188	106	21
GV	229	222	209	198	121	32
GIV	231	227	218	201	130	44

PFS comparisons

GIV *vs* **CIT**: HR 0.30, 97.5%CI: 0.19-0.47, ***p<0.001***
GIV *vs* **RV**: HR 0.38, 97.5%CI: 0.24-0.59, ***p<0.001***
GIV *vs* **GV**: HR 0.63, 97.5%CI: 0.39-1.02, p=0.03

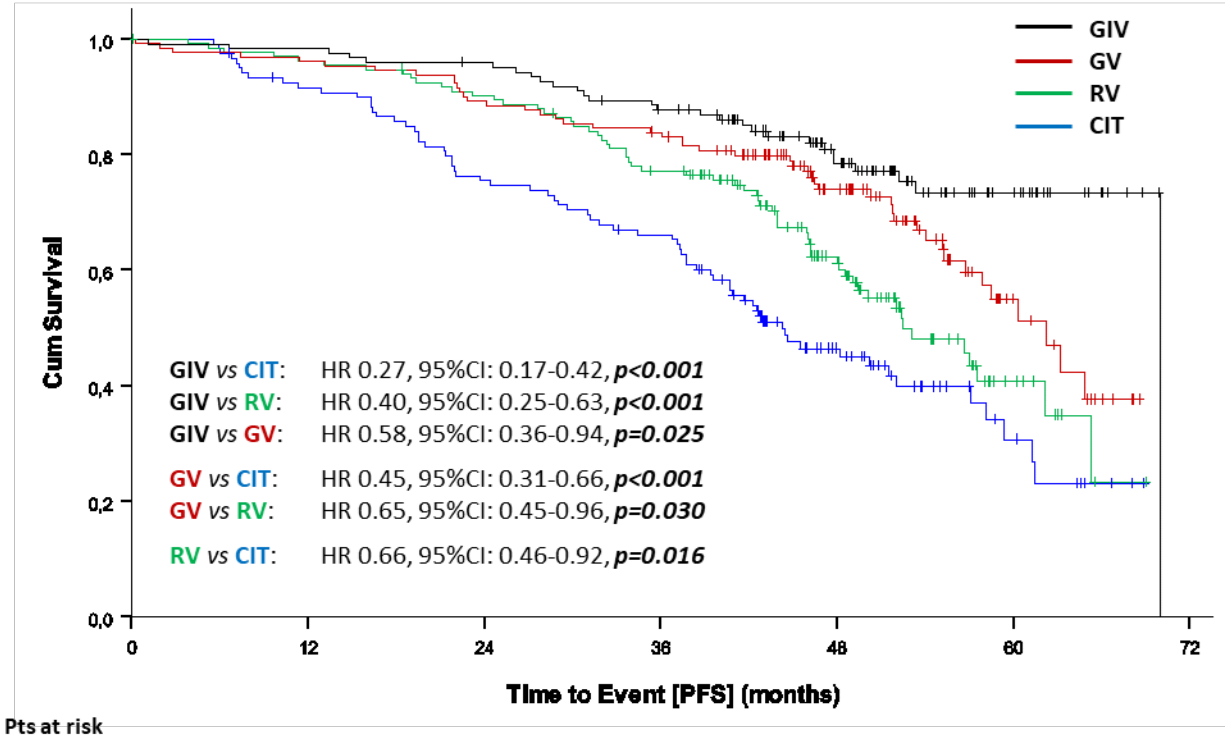
GV *vs* **CIT**: HR 0.47, 97.5%CI: 0.32-0.69, ***p<0.001***
GV *vs* **RV**: HR 0.57, 97.5%CI: 0.38-0.84, ***p=0.001***

RV *vs* **CIT**: HR 0.78, 97.5%CI: 0.55-1.10, p=0.1

CLL13/GAIA Studie

PFS nach IGHV Status

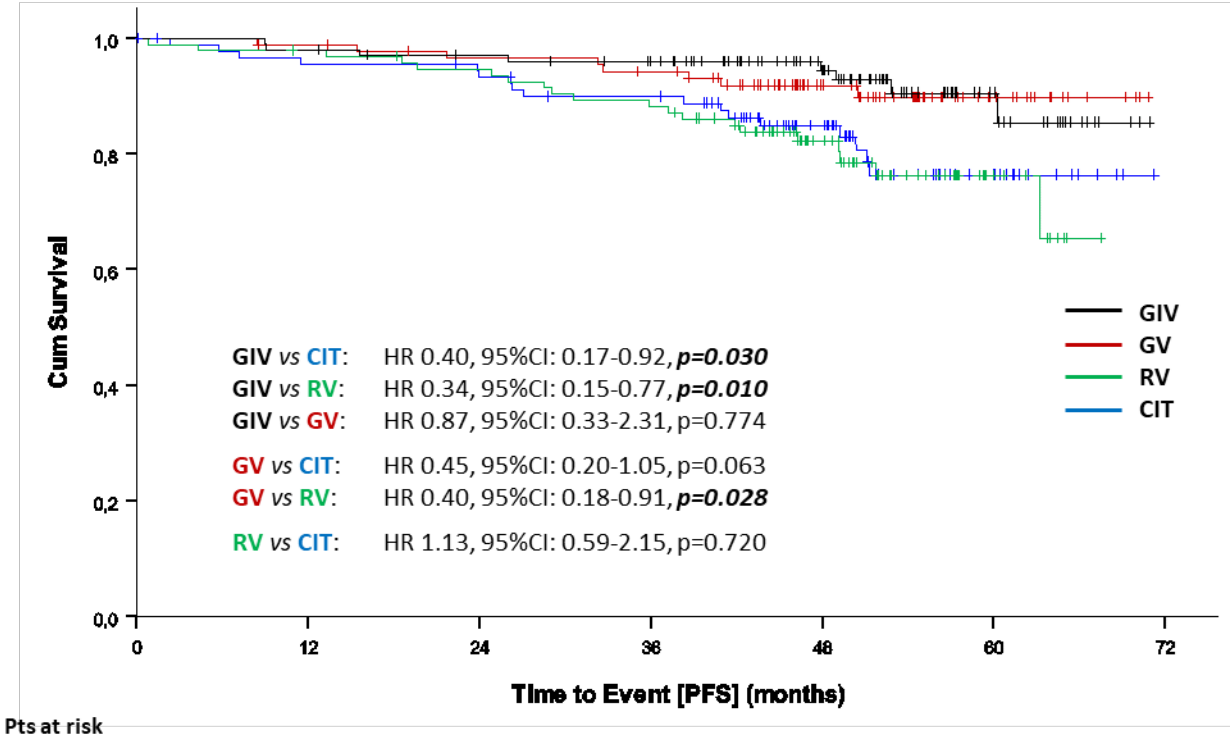
PFS, patients with unmutated IGHV



Pts at risk

CIT	131	108	89	77	34	9
RV	134	128	119	100	56	10
GV	130	125	116	108	67	15
GIV	123	121	117	105	65	24

PFS, patients with mutated IGHV

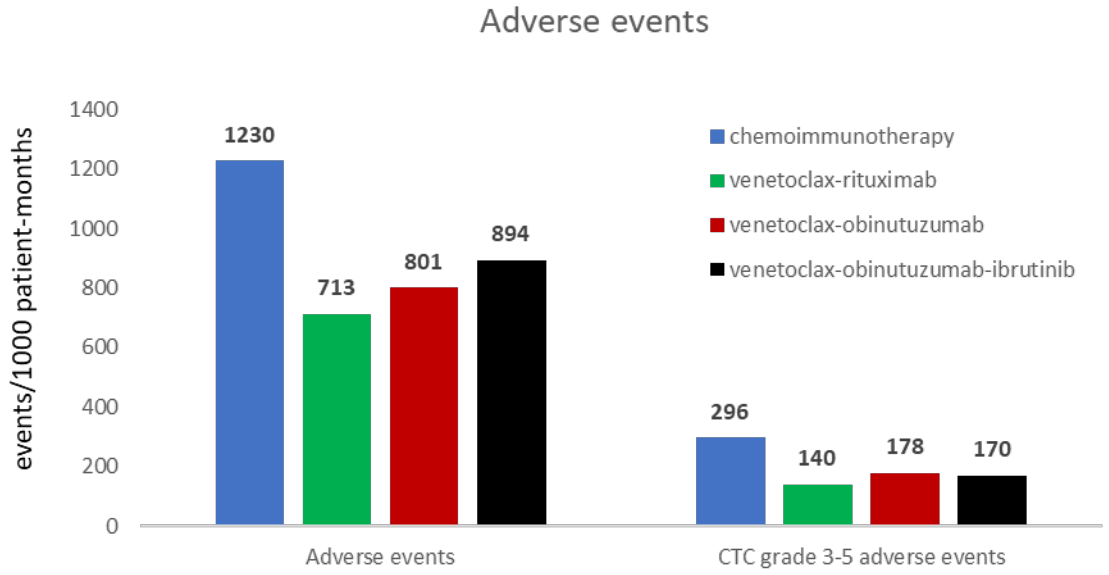


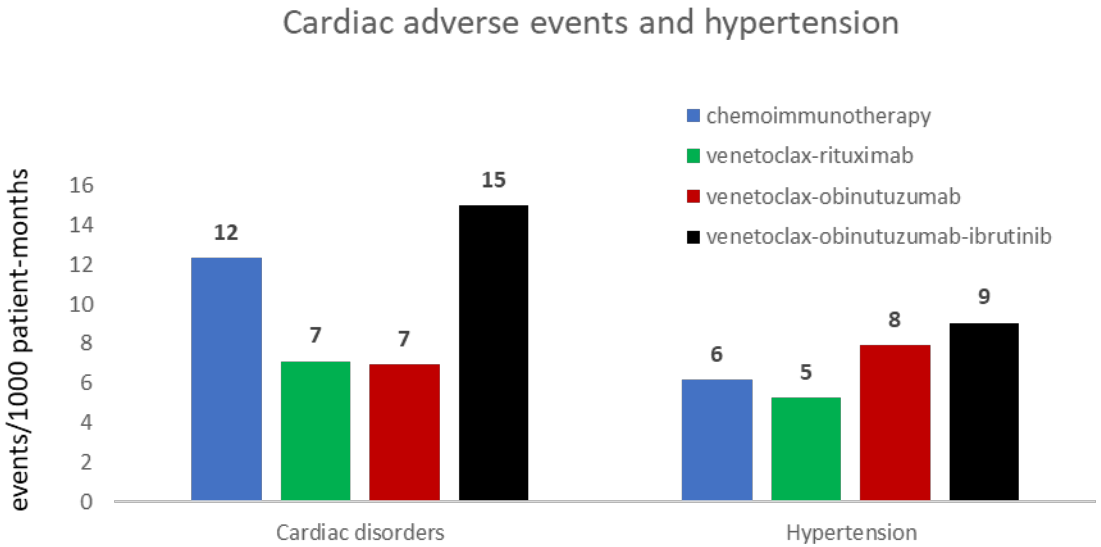
Pts at risk

CIT	95	86	83	78	50	15
RV	95	92	88	82	47	11
GV	89	87	83	80	48	15
GIV	101	99	95	90	60	20

CLL13/GAIA Studie

Nebenwirkungen kumulativ berechnet





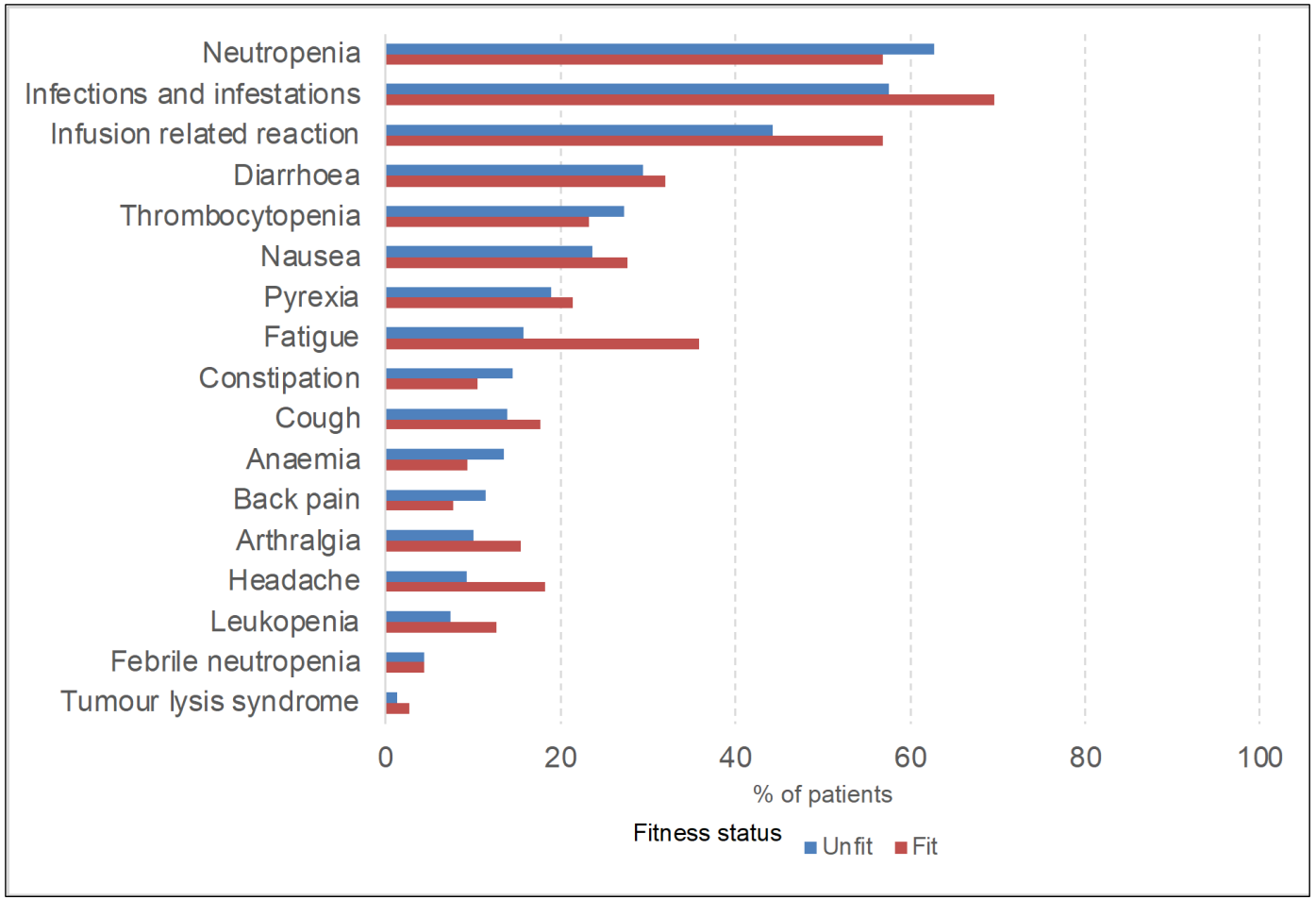
Vergleich CLL13 und CLL14 zum Outcome von Ven+Obi bei fitten/unfitten Patienten

4639: The impact of fitness and dose intensity on safety and efficacy outcomes after venetoclax-obinutuzumab in previously untreated chronic lymphocytic leukemia

Florian Simon, Köln

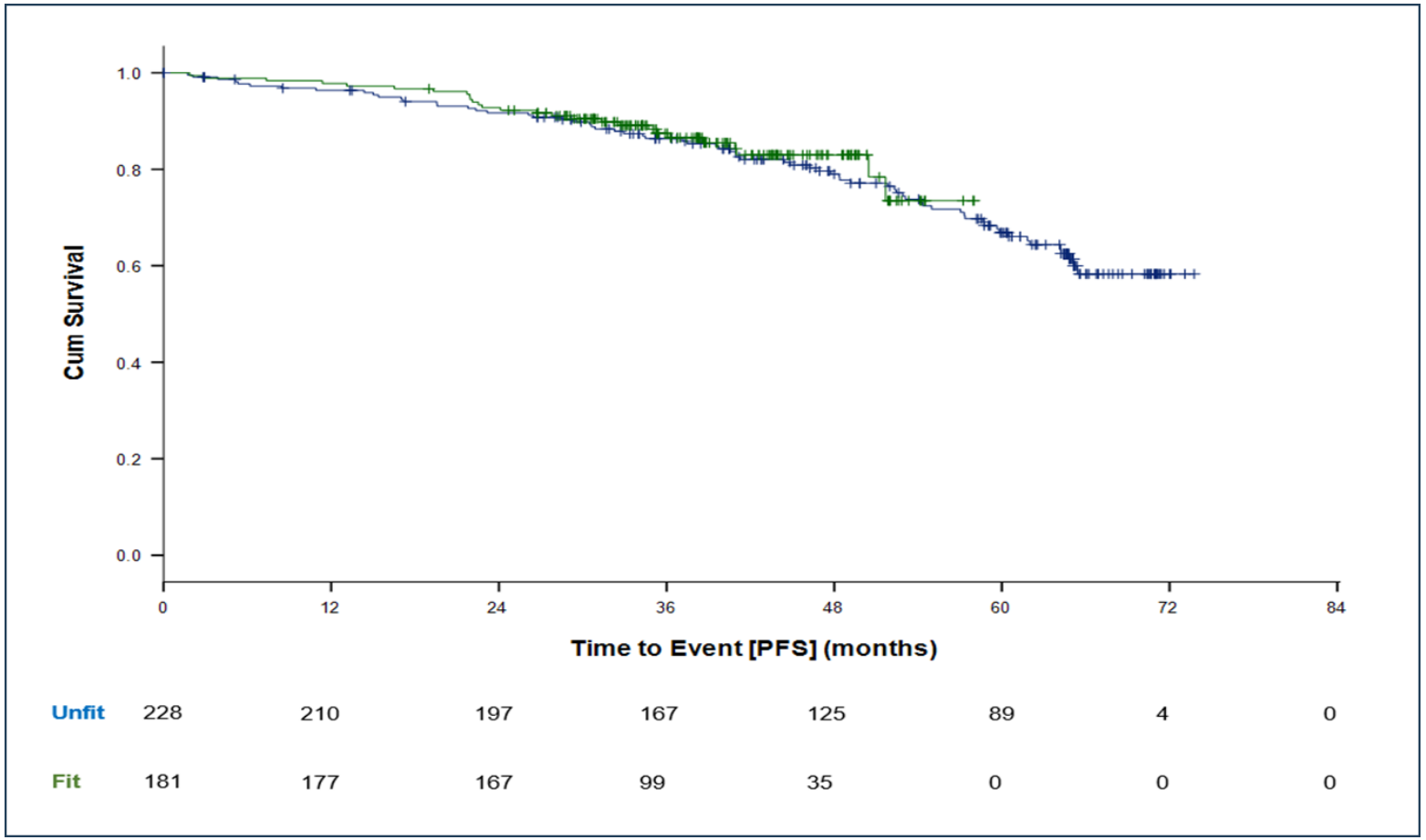
Vergleich CLL13 und CLL14 Studie: Outcome Ven + Obi

Evaluation von 181 fitten und 228 unfitten Patienten, die Ven + Obi erhielten: Verträglichkeit



Vergleich CLL13 und CLL14 Studie: Outcome Ven + Obi

Evaluation von 181 fitten und 228 unfitten Patienten, die Ven + Obi erhielten: PFS



Kapitel 3

Herausforderung: Behandlung der Richter-Transformation

Anti-CD19-CART cells in Richter Transformation

108: Anti-CD19 Chimeric Antigen Receptor T-Cell Therapy for Richter's Transformation: An International Multicenter Retrospective Study

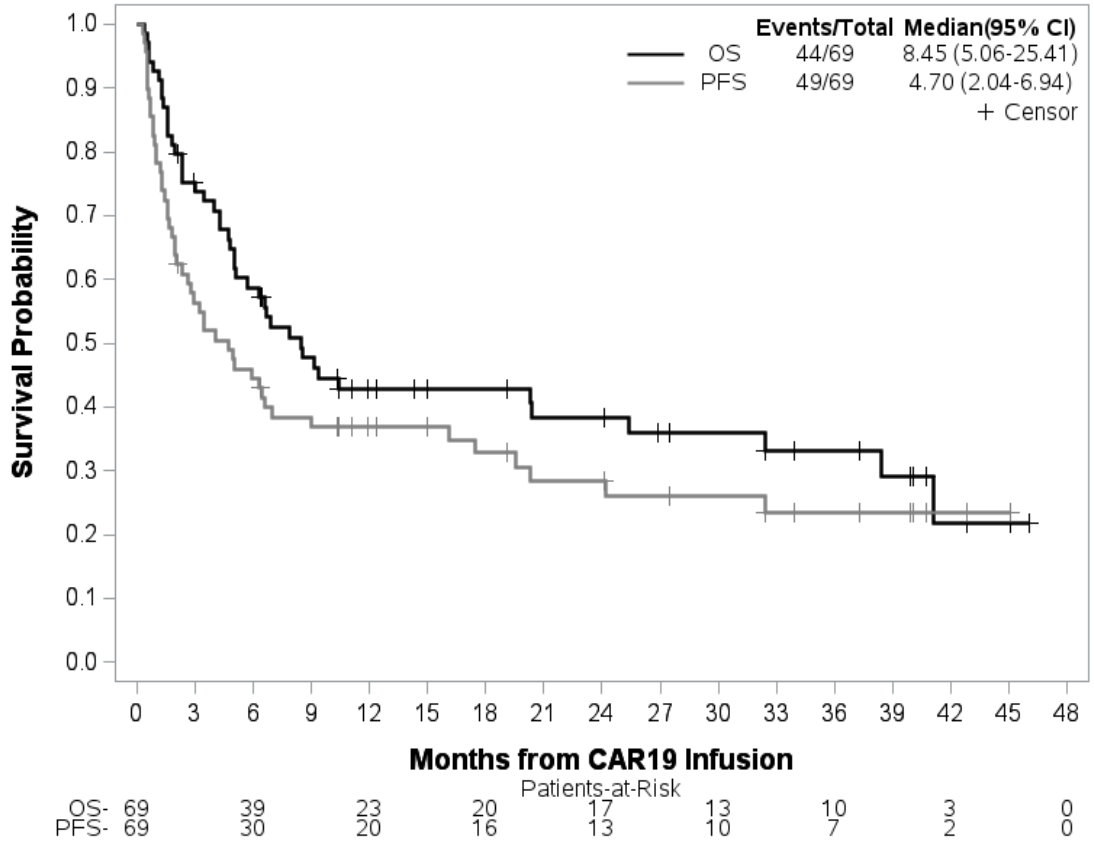
Adam Kittai at al., Columbus, Ohio; USA

CART cells in Richter Transformation

Retrospektive multizentrische Analyse

RT Characteristics and TRMT	N=69
Age at RT Dx, median (range)	63 (26-80)
Clonal relationship to CLL, N (%)	
Related	23 (100)
Unknown	46
Complex KT (≥3 abn) at RT, N (%)	19 (65.5)
Unknown	40
del17p (RT), N (%)	12 (41.4)
Unknown	40
TP53 mut (RT), N (%)	14 (58.3)
Unknown	45
NOTCH1 mut (RT), N (%)	4 (21.1)
Unknown	50
MYC translocation, N (%)	8 (20.0)
Unknown	29
Median Ki-67 (%)	80 (40-100)
Unknown	9
Prior BTKi alone or in combo for RT	46 (66.7)
Prior Ven alone or in combo for RT	35 (50.7)
Prior BTKi or Ven for RT or CLL, N (%)	58 (84%)

Median follow-up in months (range) – 24.13 (2.14-46.02)



CART cells in Richter Transformation

Retrospektive multizentrische Analyse: Toxizität

	N=69
Cause of Death (N=44), N (%)	
Disease	32 (72.7)
Non-disease	12 (27.3)
Non-relapse Mortality from CART Infusion, % (95% CI)	
Number of events	12
3-month estimate	7.3% (2.7-15.0)
6-month estimate	10.3% (4.5-18.9)
12-month estimate	13.4% (6.5-22.8)

CAR-T Outcomes	N=69
Grade 3-4 neutropenia, N (%)	60 (87.0)
Grade 3-4 thrombocytopenia, N (%)	49 (71.0)
Febrile neutropenia, N (%)	46 (66.7)
CRS max grade, N (%)	
0	8 (11.6)
1	24 (34.8)
2	26 (37.7)
3	9 (13.0)
4	2 (2.9)
ICANS max grade, N (%)	
0	23 (33.8)
1	12 (17.7)
2	8 (11.8)
3	17 (25.0)
4	8 (11.8)
Unknown	1
Grade 3-4 infection, N (%)	14 (20.3)

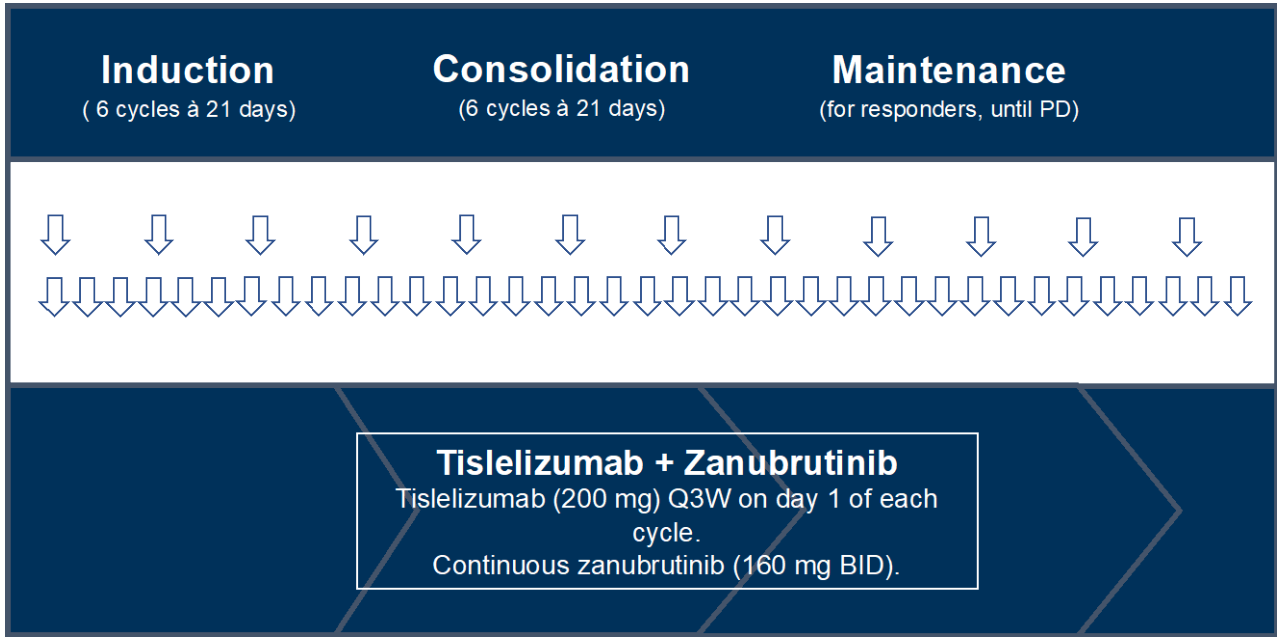
RT1-Studie der DCLLSG: Tislelizumab + Zanubrutinib bei Richter Transfromation

204: Tislelizumab Plus Zanubrutinib in Patients with Richter Transformation: Primary Endpoint Analysis of the Prospective, Multi-Center, Phase-II RT1 Trial of the German CLL Study Group

Othman Al Sawaf et al., Köln

RT1: Tislelizumab + Zanubrutinib bei RT

Studiendesign



Primary endpoint

- Overall response rate (ORR) after induction therapy

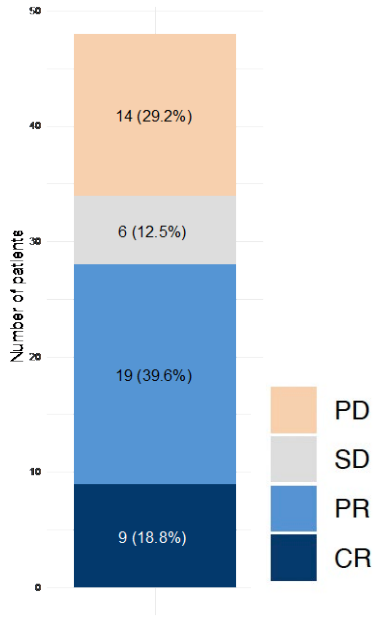
Key secondary endpoints

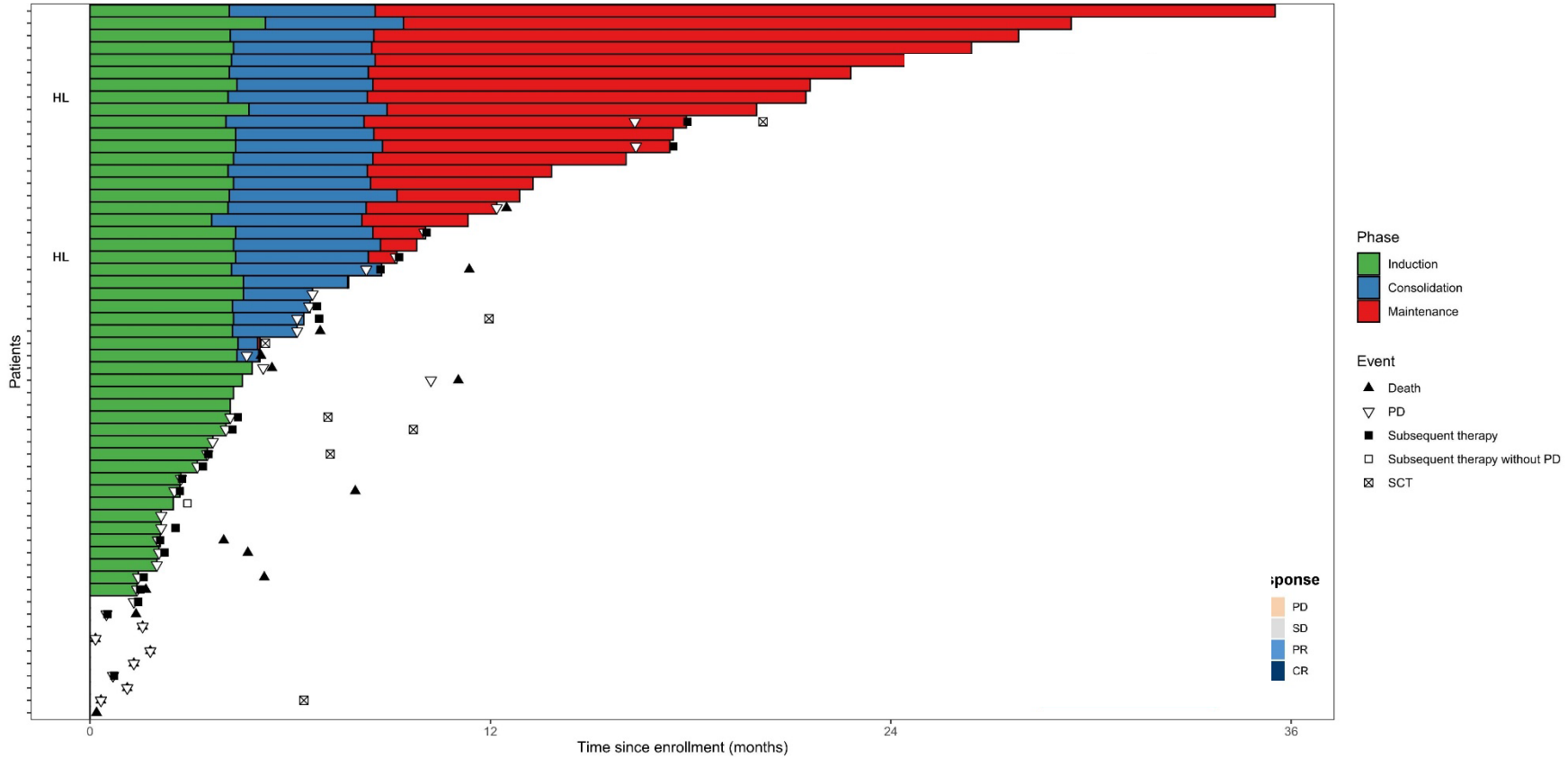
- PFS
- OS
- TTNT

RT1: Tislelizumab + Zanubrutinib bei RT

Ansprechen und Dauer des Ansprechens

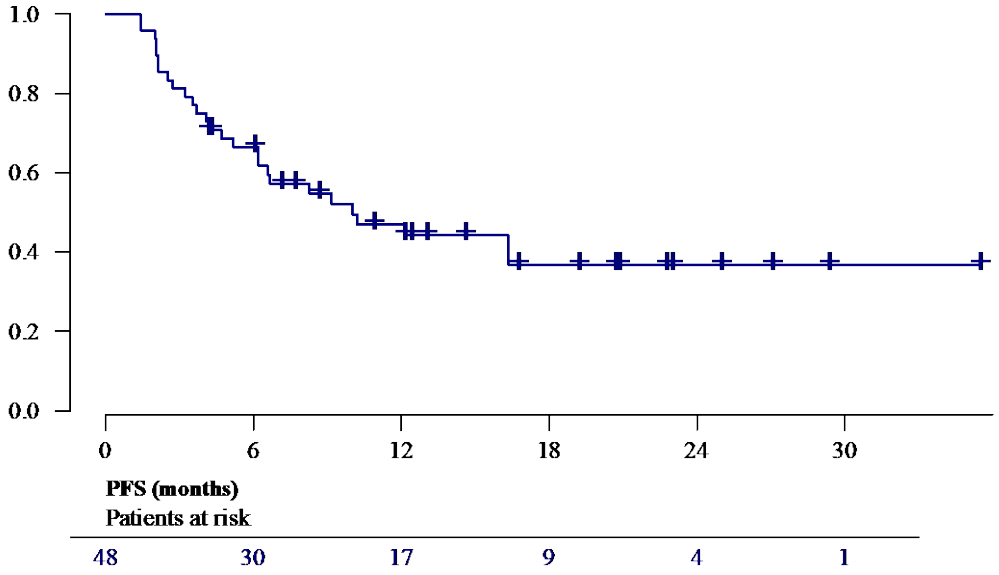
Primary endpoint met with
ORR of 58.3%
(95% CI 43.2-72.4)



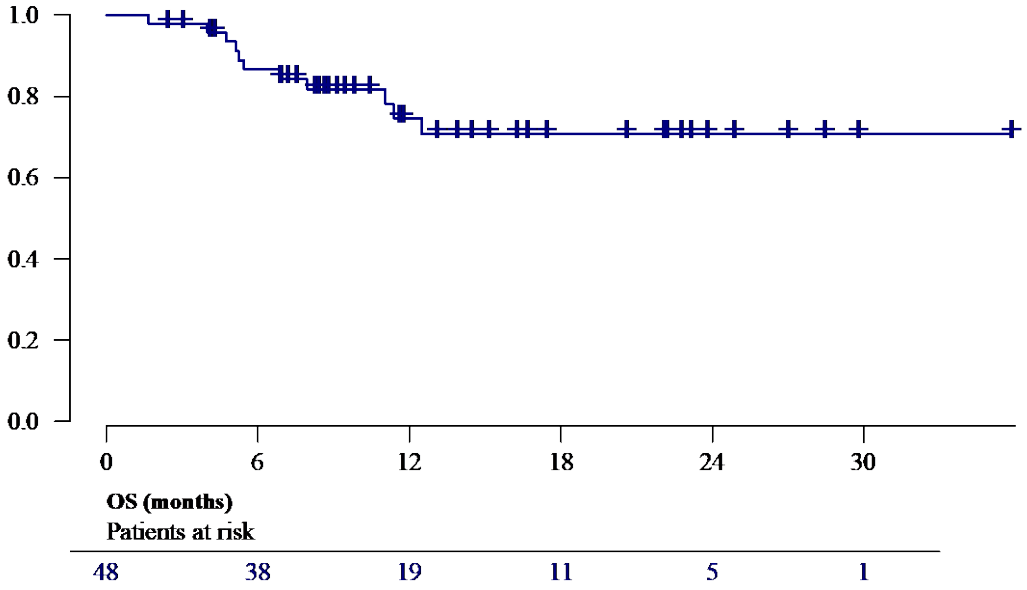


RT1: Tislelizumab + Zanubrutinib bei RT

PFS & Überleben



- Median PFS 10.0 months (95% CI 3.8 – 16.3)
- 12-month-PFS rate 46.9% (95% CI 29.4-64.5)



- Median OS not reached
- 12-month-OS rate 74.7% (95% CI 58.4-91.0)

Zusammenfassung | Take-Home-Messages

Neue Daten zur Kombination Ibrutinib + Venetoclax mit Überlebensvorteil:

- Ibrutinib+ Venetoclax V.a. bei Patienten mit unmutiertem IGHV und ohne cardiale Begleiterkrankungen erwägen
- Risiko der Resistenzentwicklung ist gering

Venetoclax + Obinutuzumab ist V.a. bei älteren Patienten gut verträglich

Hoffnung für Richter Transformation: Ziel – gerichtete Therapien und Zelluläre Therapien auf dem Vormarsch: Einschluss in Studien !

Die Kurzpräsentationen sind online unter

www.lymphome.de/ash2023

Für den Inhalt verantwortlich:

Prof. Dr. med. Barbara Eichhorst

Uniklinik Köln

Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

KML KONGRESSE

Expert:innen berichten zu Lymphomen & Leukämien

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