Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

KML KONGRESSE

Expert:innen berichten zu Lymphomen & Leukämien

EHA 2025

MAILAND, ITALIEN

12. – 15. Juni 2025

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PD Dr. med. Othman Al-Sawaf
Uniklinik Köln

Chronische lymphatische Leukämie (CLL)

Offenlegung potentieller Interessenskonflikte

LymphomKompetenz KOMPAKT – EHA 2025 Mailand, Italien wird in Kooperation mit fünf unterstützenden Firmen durchgeführt.
Meine persönlichen Disclosures betreffen:

Anstellungsverhältnis, Führungsposition	Uniklinik Köln
Beratungs-/ Gutachtertätigkeit	AbbVie, Adaptive, Ascentage, AstraZeneca, BeiGene, Eli Lilly, Genmab, Gilead, Janssen, Roche
Besitz von Geschäftsanteilen, Aktien oder Fonds	
Patent, Urheberrecht, Verkaufslizenz	
Honorare	AbbVie, Adaptive, Ascentage, AstraZeneca, BeiGene, Eli Lilly, Genmab, Gilead, Janssen, Roche
Finanzierung wissenschaftlicher Untersuchungen	AbbVie, BeiGene, Janssen, Roche
Andere finanzielle Beziehungen	
Immaterielle Interessenkonflikte	

Kapitel 1

MRD-gesteuerte Therapie

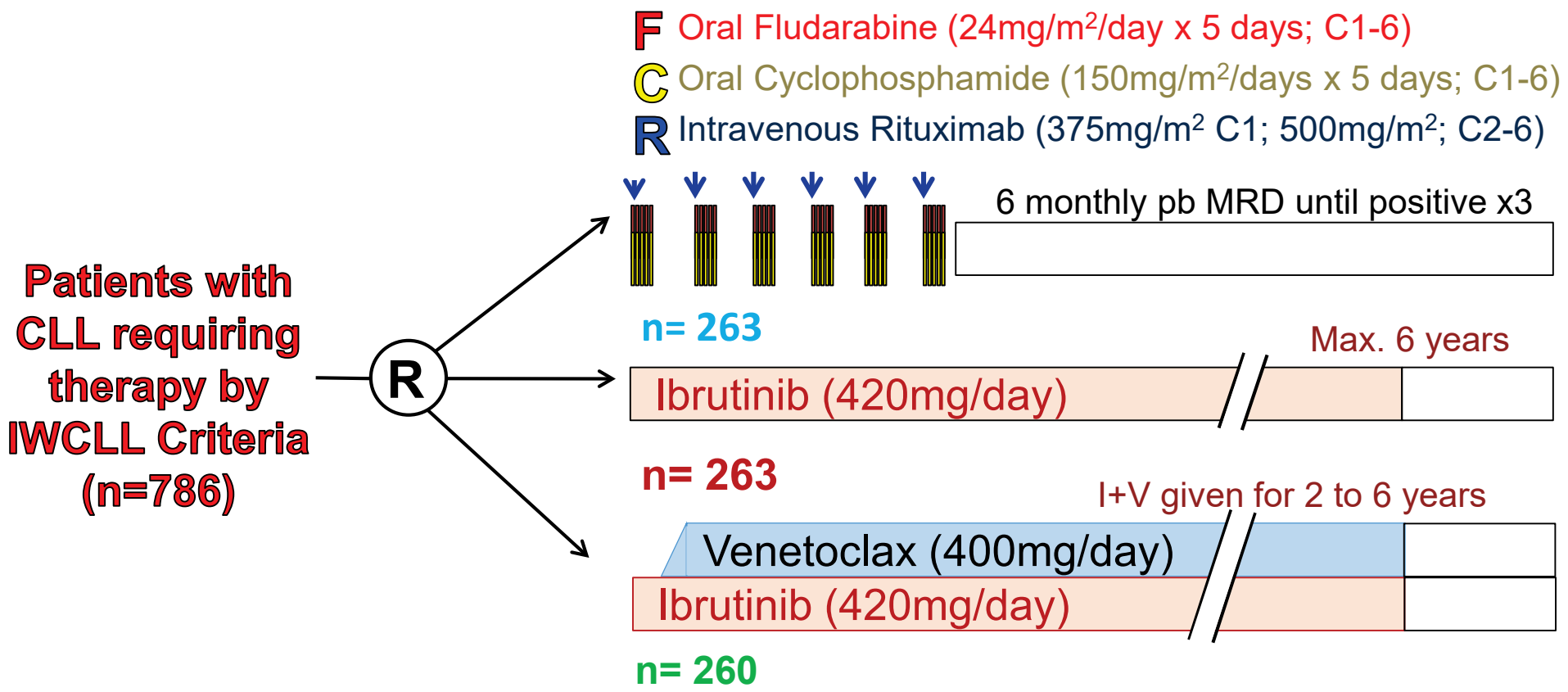
MRD-gesteuerte Therapie

S155: IBRUTINIB PLUS VENETOCLAX WITH MRD-GUIDED DURATION OF TREATMENT IS SUPERIOR TO BOTH CONTINUOUS IBRUTINIB MONOTHERAPY AND FCR FOR PREVIOUSLY UNTREATED CLL REPORT OF THE PHASE III UK FLAIR STUDY

Talha Munir, Leeds, Vereinigtes Königreich

MRD-gesteuerte Therapie

FLAIR-Studiendesign



Primary objectives

PFS: To assess whether I+V is superior to FCR

MRD negativity: To assess whether I+V is superior to I

Key Secondary objectives

PFS of I+V in comparison with I

PFS of I in comparison with FCR

Overall survival

Proportion of participants obtaining undetectable MRD

IWCLL Response to therapy

Safety and toxicity

Health-related quality of life

Cost-effectiveness

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)

MRD-gesteuerte Therapie

Patientencharakteristika

		FCR (n=263)	Ibrutinib (n=263)	Ibrutinib+venetoclax (n=260)	Total (n=786)
Age	Median (years)	62	62	62	62
	>65 years	82 (31.2%)	84 (31.9%)	81 (31.2%)	247 (31.4%)
Gender	Male	187 (71.1%)	186 (70.7%)	186 (71.5%)	559 (71.1%)
Binet stage	Prog A or B	152 (57.8%)	153 (58.2%)	151 (58.1%)	461 (58.7%)
	C	111 (42.2%)	110 (41.8%)	109 (41.9%)	325 (41.3%)
Duration of CLL prior to randomisation	Median (months)	33.7	36.2	37.9	35.9
B symptoms	Yes	121 (46.5%)	126 (47.9%)	128 (49.2%)	375 (47.7%)

MRD-gesteuerte Therapie

Patientencharakteristika

		FCR (n=263)	Ibrutinib (n=263)	Ibrutinib+venetoclax (n=260)	Total (n=786)*
IGHV	Mutated	82 (31.2%)	87 (33.1%)	97 (37.3%)	266 (33.2%)
	Unmutated	139 (52.8%)	129 (49%)	123 (47.3%)	391 (49.9%)
	BCR Subset 2 mutated	6 (2.3%)	15 (5.7%)	11 (4.2%)	32 (4.1%)
	BCR Subset 2 Unmutated	8 (3.0%)	8 (3.0%)	5 (1.9%)	21 (2.7%)
	Not available	28 (10.6%)	24 (9.1%)	24 (9.2%)	76 (9.7%)
FISH Hierarchy	17p deletion*	0 (0%)	0 (0%)	1 (0.4%)	1 (0.1%)
	11q deletion	50 (19%)	36 (13.7%)	45 (17.3%)	131 (16.7%)
	Trisomy 12	29 (11%)	45 (17.1%)	57 (21.9%)	131 (16.7%)
	Normal	69 (26.2%)	64 (24.3%)	52 (20%)	185 (23.5%)
	13q deletion	100 (38%)	106 (40.3%)	87 (33.5%)	295 (37.5%)
	Failed/incomplete	15 (5.7%)	12 (4.6%)	16 (6.2%)	43 (5.5%)

MRD-gesteuerte Therapie

PFS – MRD-gesteuertes Ibrutinib+Venetoclax versus kontinuierliches Ibrutinib

Signifikant längeres PFS mit MRD-gesteuertem I+V im Vergleich zu kontinuierlichem I

MRD-gesteuerte Therapie

OS – MRD-gesteuertes Ibrutinib+Venetoclax versus kontinuierliches Ibrutinib

Signifikant längeres OS mit MRD-gesteuertem I+V im Vergleich zu kontinuierlichem I

Kapitel 2

Langzeit-Beobachtungen nach zeitlich-begrenzter Therapie

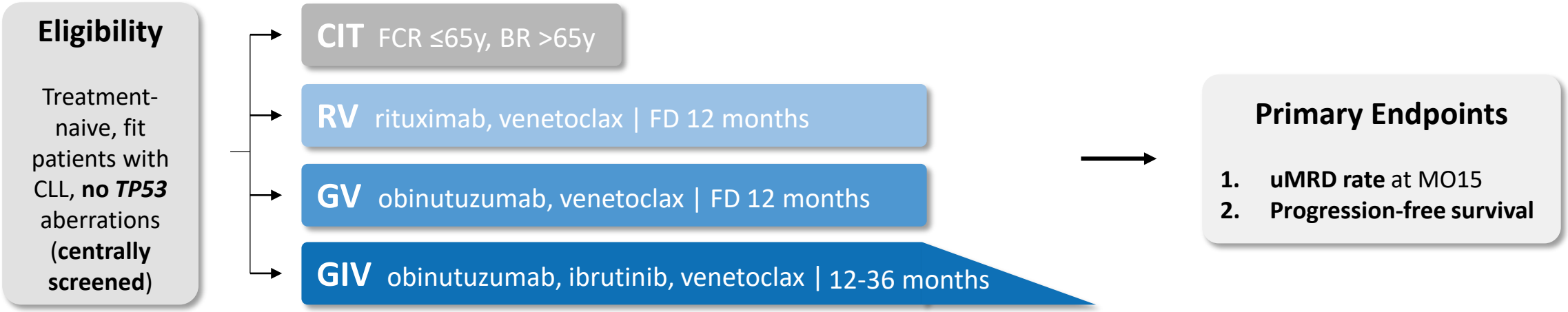
Fixed-duration Venetoclax-basierte Therapie

S191: Venetoclax-ibrutinib-obinutuzumab prolongs PFS compared to venetoclax-CD20 combinations and chemoimmunotherapy in treatment-naive CLL: Final analysis of the phase 3 GAIA/CLL13 trial

Moritz Fürstenau, Köln, Deutschland

Finale Analyse CLL13

Studiendesign



Key patient characteristics

Randomized patients (=ITT population): **n= 926**

Median age:	**61 years** (range: 27-84)
Median CIRS score:	**2** (range: 0-7)
Unmutated IGHV:	**56%** of all patients
Complex karyotype:	**17%** of all patients

Final analysis (data cut-off: 02/2024)

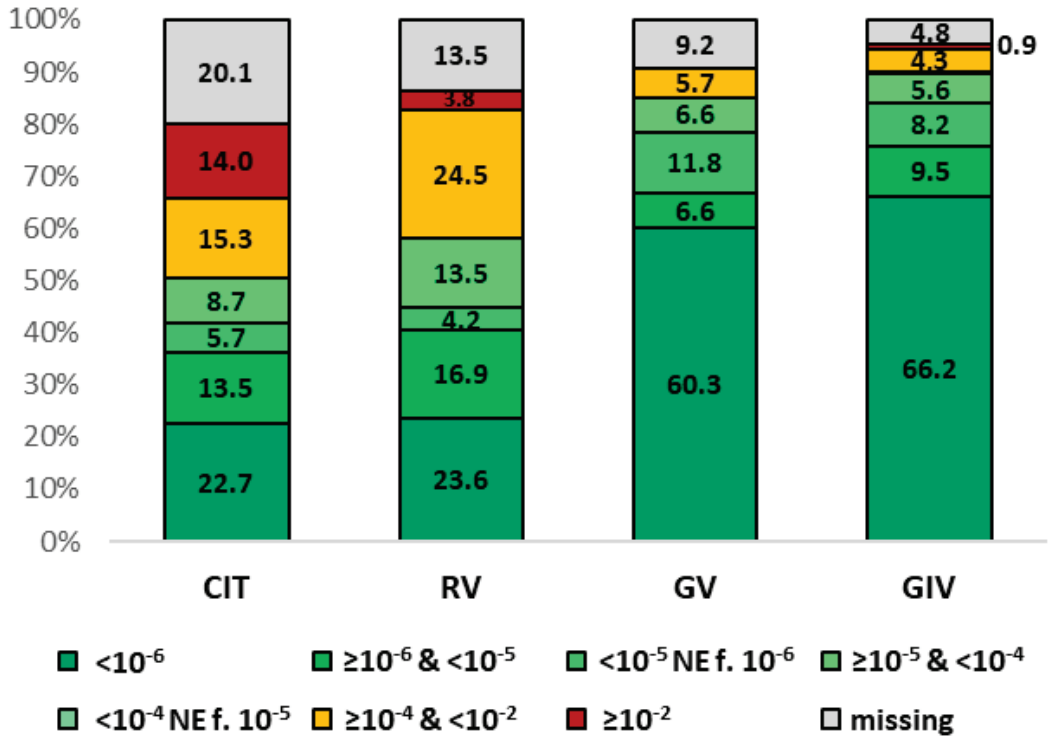
Median observation time
63.8 months (IQR: 57.4-71.3)

Median observation time after end of treatment
54.0 months (IQR: 47.3-61.1)

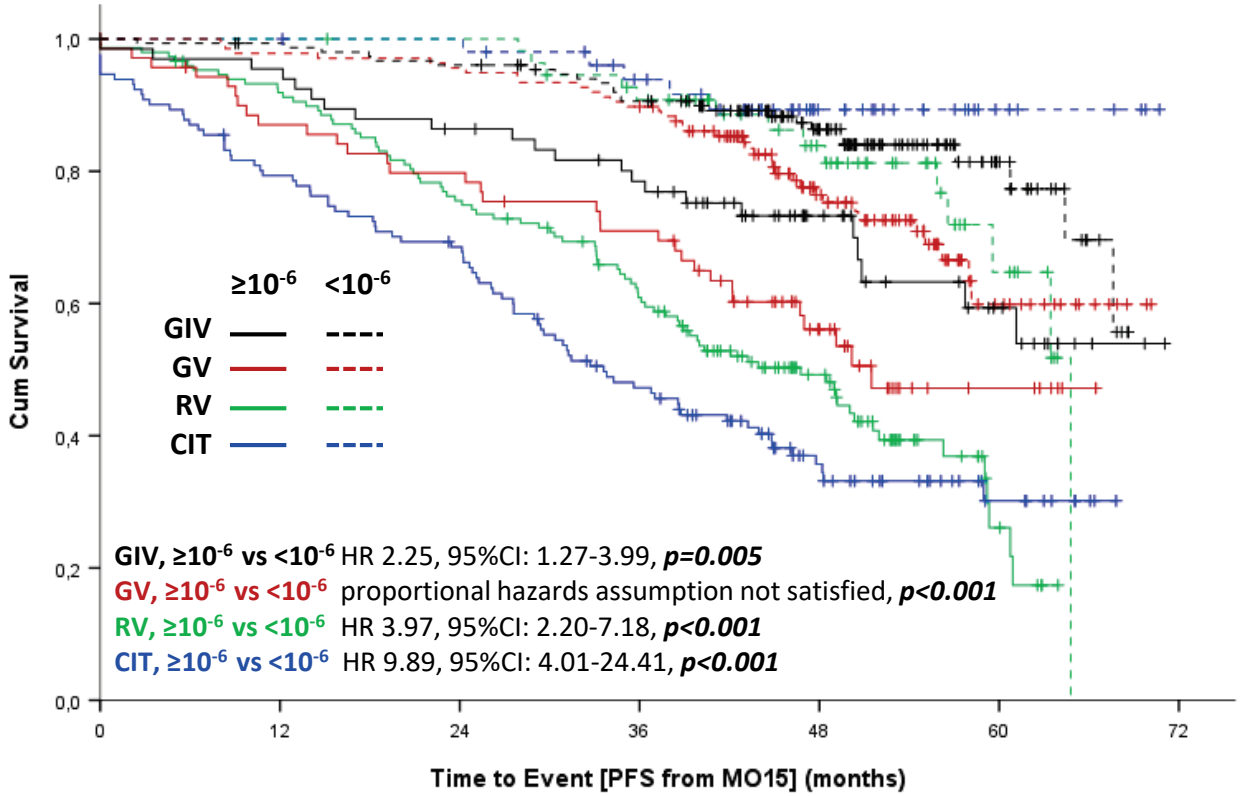
Finale Analyse CLL13

MRD Ergebnisse

NGS MRD level in PB at MO15



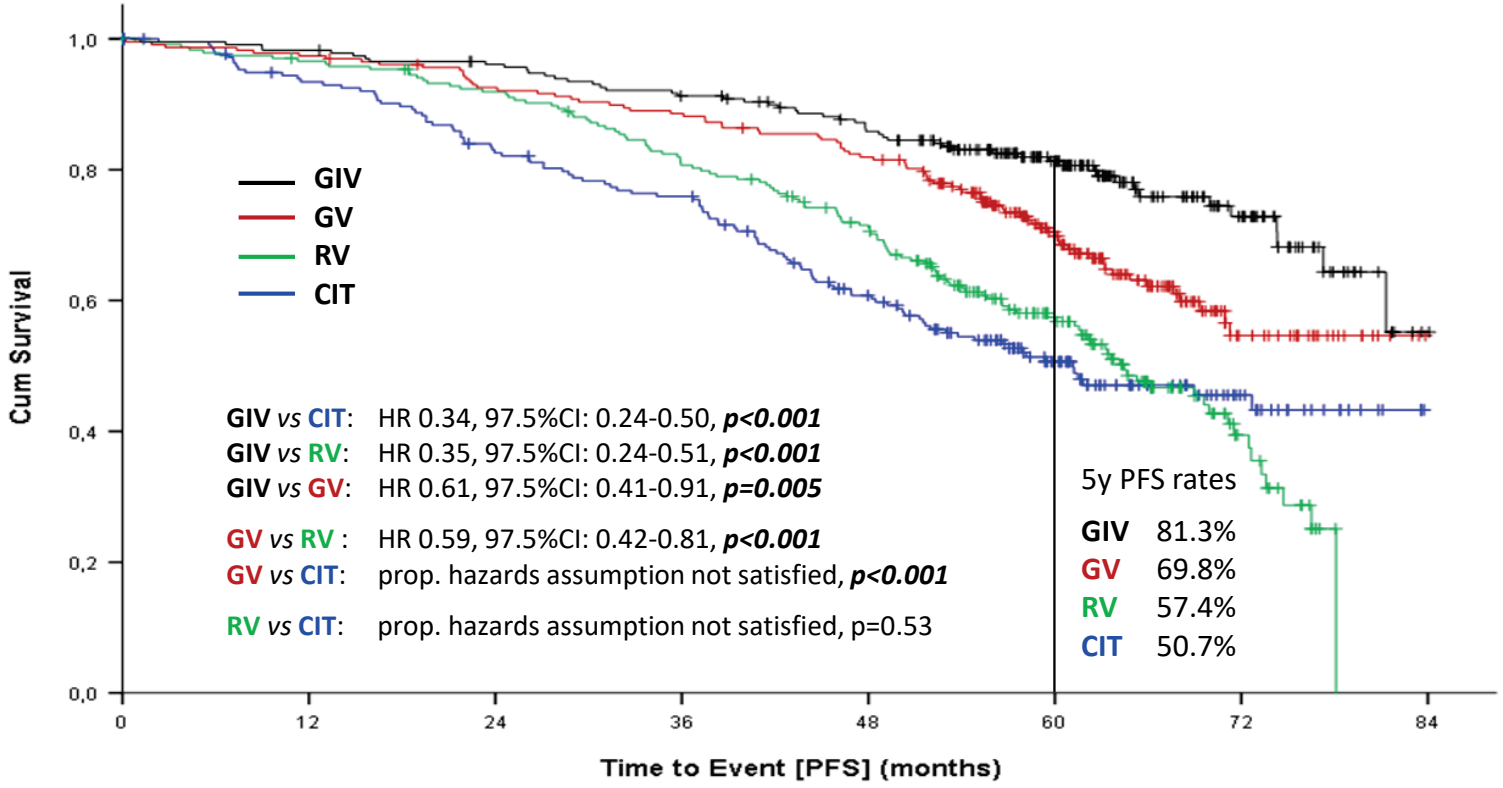
PFS according to MO15 uMRD6 (PB) status



Finale Analyse CLL13

PFS

Progression-free survival



Patients at risk

CIT	229	198	174	159	119	67	21
RV	237	227	214	187	160	89	20
GV	229	223	210	201	185	109	25
GIV	231	227	219	207	189	126	44

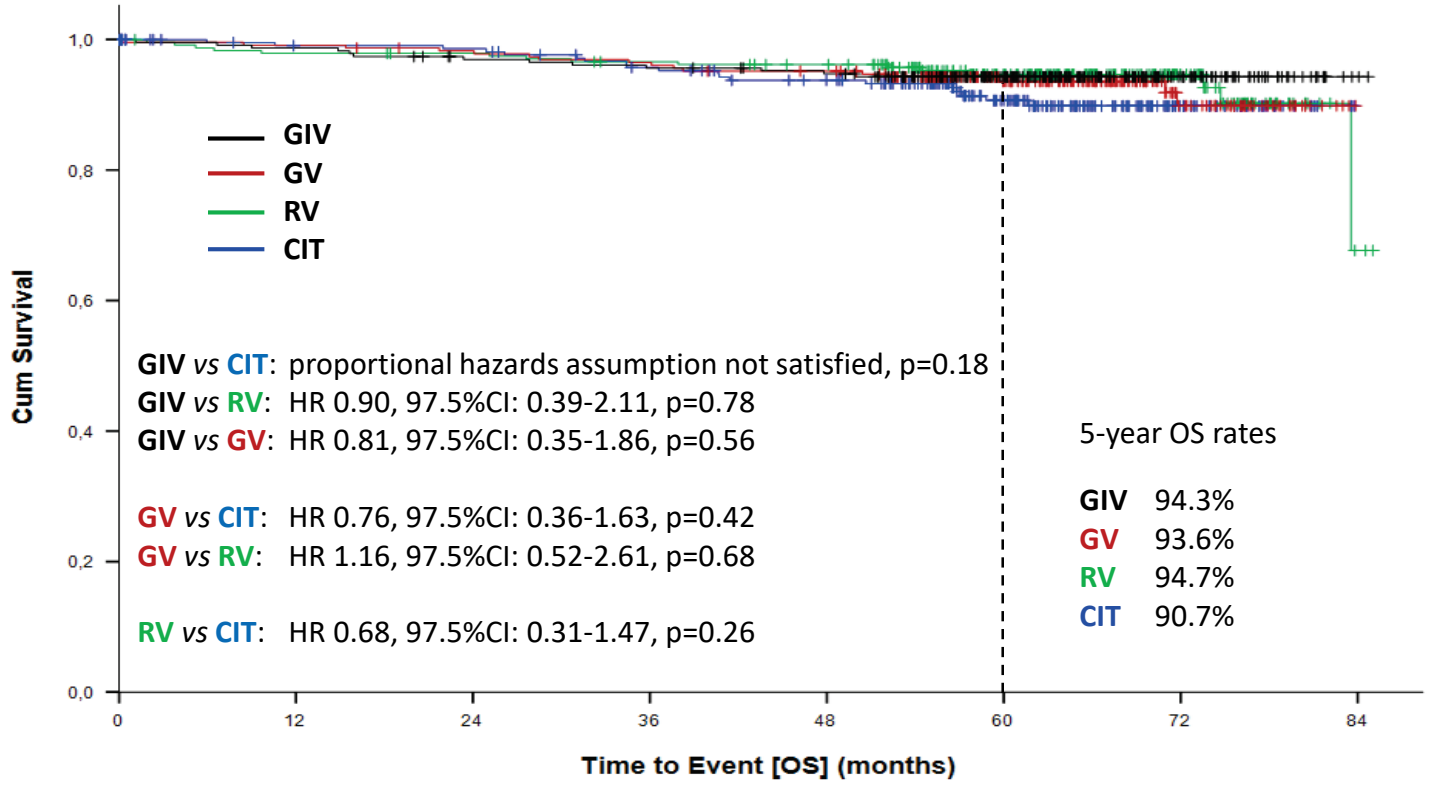
Independent prognostic factors, PFS (MVA)

Variable	HR	95% CI	P value
GIV			
Trisomy 12 (yes vs no)	2.12	1.14-3.94	0.02
IGHV (unmut vs mut)	2.07	1.13-3.78	0.02
GV			
ECOG (≥1 vs 0)	1.72	1.08-2.72	0.02
IGHV (unmut vs mut)	2.68	1.60-4.49	<0.001
RV			
B symptoms (yes vs no)	1.47	1.01-2.12	0.04
Co. karyotype (≥3 vs <3)	1.64	1.05-2.55	0.03
IGHV (unmut vs mut)	2.17	1.45-3.26	<0.001
CIT			
Age (>65 vs ≤65 years)	2.16	1.43-3.26	<0.001
Bulky disease (yes vs no)	1.55	1.01-2.37	0.046
Co. karyotype (≥3 vs <3)	1.69	1.09-2.61	0.02
IGHV (unmut vs mut)	3.55	2.20-5.75	<0.001

Finale Analyse CLL13

OS

Overall survival



GIV *vs* **CIT**: proportional hazards assumption not satisfied, p=0.18
GIV *vs* **RV**: HR 0.90, 97.5%CI: 0.39-2.11, p=0.78
GIV *vs* **GV**: HR 0.81, 97.5%CI: 0.35-1.86, p=0.56

GV *vs* **CIT**: HR 0.76, 97.5%CI: 0.36-1.63, p=0.42
GV *vs* **RV**: HR 1.16, 97.5%CI: 0.52-2.61, p=0.68

RV *vs* **CIT**: HR 0.68, 97.5%CI: 0.31-1.47, p=0.26

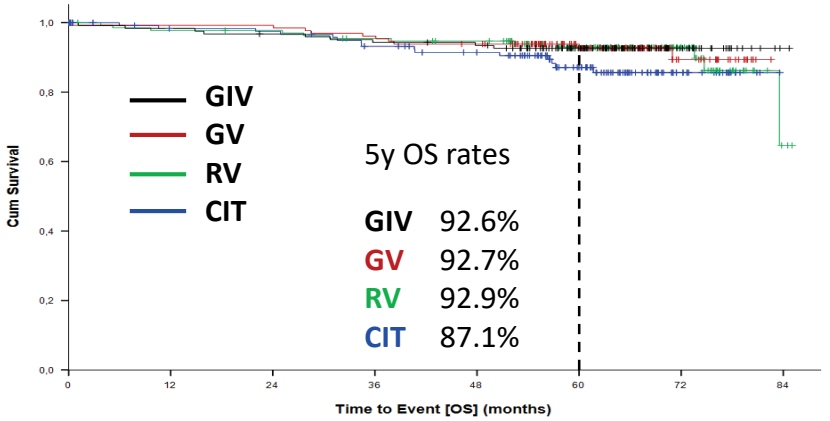
5-year OS rates

GIV	94.3%
GV	93.6%
RV	94.7%
CIT	90.7%

Patients at risk

CIT	229	210	209	198	186	123	38
RV	237	231	229	224	219	153	55
GV	229	227	223	219	214	138	44
GIV	231	228	220	217	212	152	53

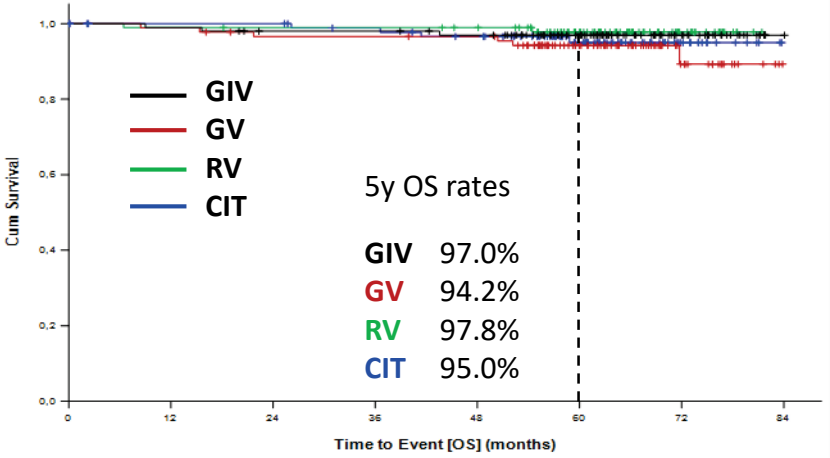
OS, unmutated IGHV



5y OS rates

GIV	92.6%
GV	92.7%
RV	92.9%
CIT	87.1%

OS, mutated IGHV



5y OS rates

GIV	97.0%
GV	94.2%
RV	97.8%
CIT	95.0%

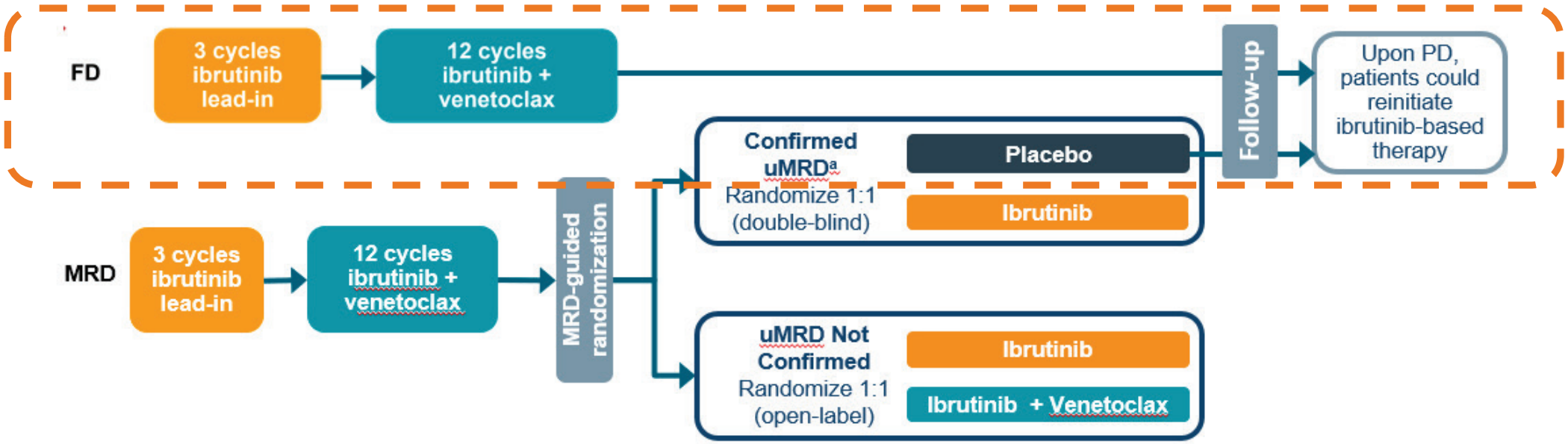
Fixed-duration Venetoclax-basierte Therapie

S156: Final Analysis of Fixed-Duration Ibrutinib + Venetoclax for Chronic Lymphocytic Leukemia/ Small Lymphocytic Lymphoma in the Phase 2 CAPTIVATE Study

Paolo Ghia, Mailand, Italien

Finale Analyse CAPTIVATE

Studiendesign



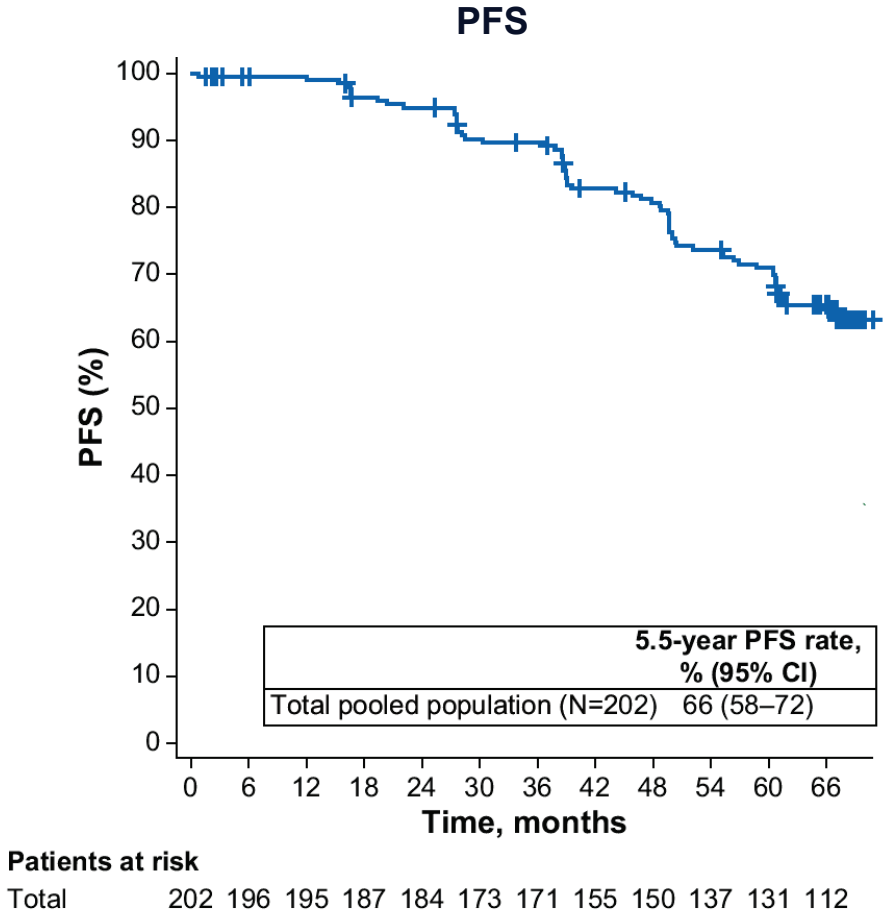
Finale Analyse CAPTIVATE

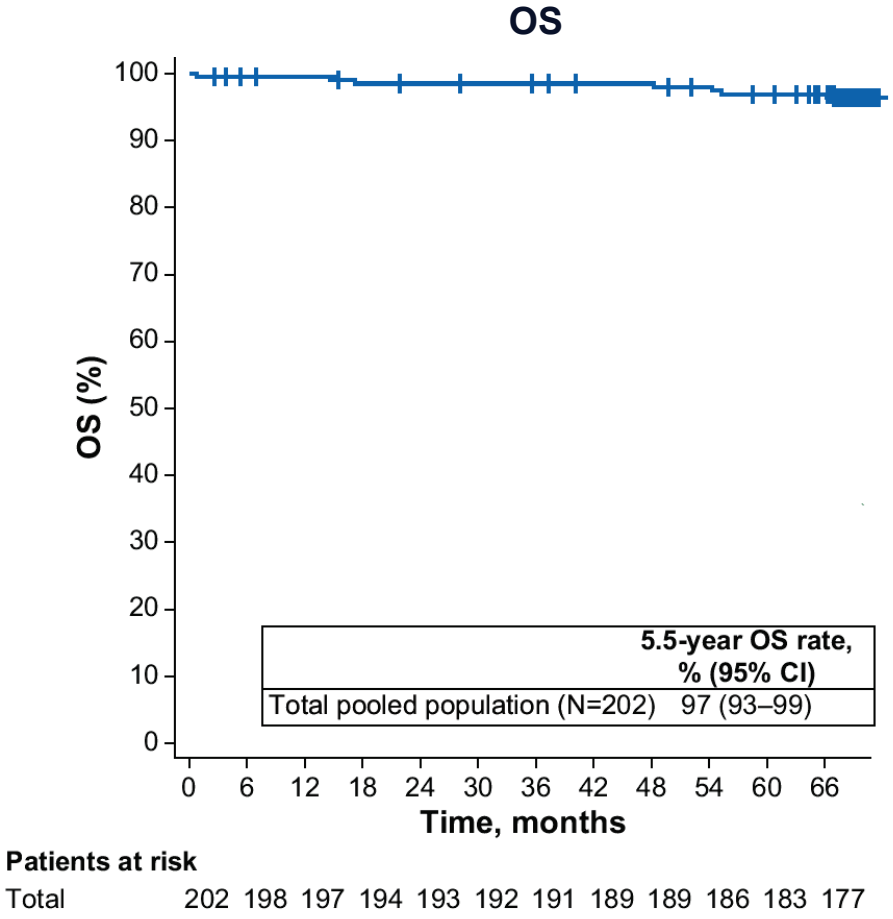
Patientencharakteristika

Characteristic	Total Pooled Population (N=202)	FD Cohort Only (N=159)
Median age (range), years	60.0 (33–71)	60.0 (33-71)
Male, n (%)	131 (65)	106 (67)
Rai stage III/IV, n (%)	59 (29)	44 (28)
High-risk genomic features, n (%)		
uIGHV	119 (59)	89 (56)
del(17p)/TP53	29 (14)	27 (17)
del(11q)[a]	36 (18)	28 (18)
CK (≥3 abnormalities)[b]	35 (17)	31 (20)
CK (≥5 abnormalities)[b]	19 (9)	16 (10)
Bulky LN disease, n (%)		
≥5 cm	66 (33)	48 (30)
≥10 cm	6 (3)	5 (3)

Finale Analyse CAPTIVATE

PFS und OS

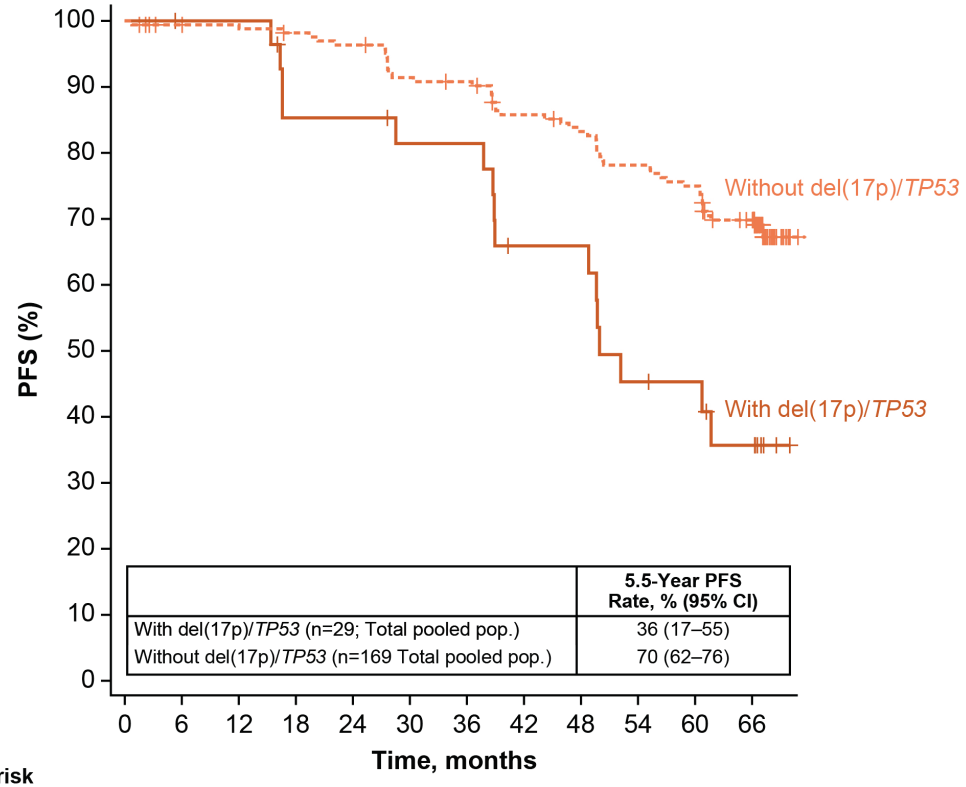




Finale Analyse CAPTIVATE

PFS nach TP53 und IGHV

PFS by del(17p)/*TP53* Mutation Status



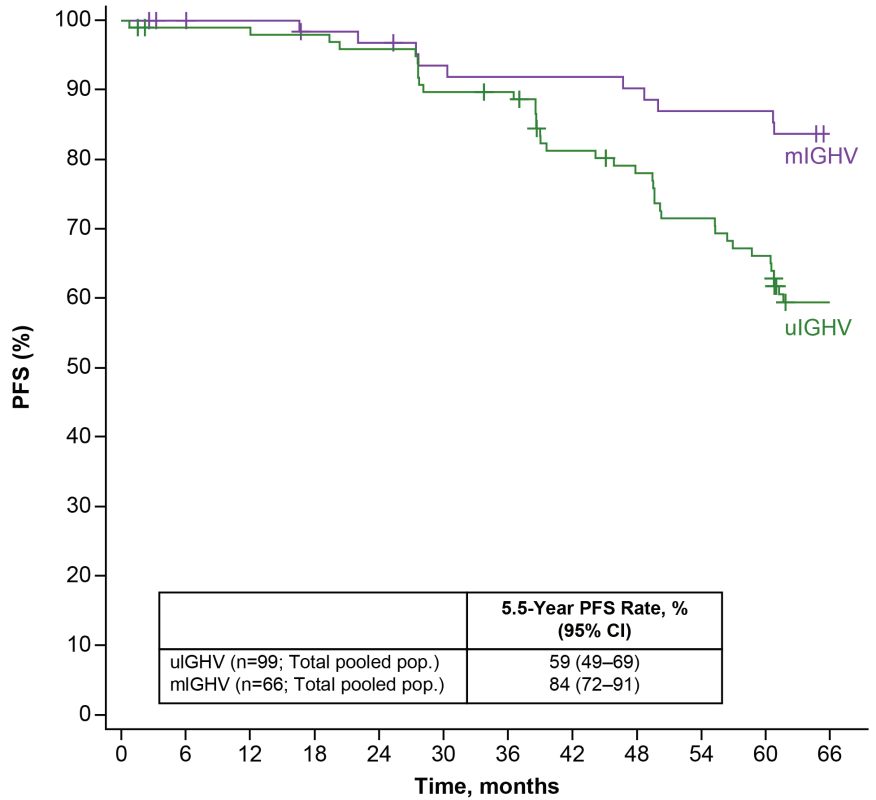
	5.5-Year PFS Rate, % (95% CI)
With del(17p)/*TP53* (n=29; Total pooled pop.)	36 (17–55)
Without del(17p)/*TP53* (n=169 Total pooled pop.)	70 (62–76)

Patients at risk

With del(17p)/*TP53*	29	28	28	23	23	21	21	16	16	11	10	7
Without del(17p)/*TP53*	169	164	163	160	157	148	146	136	131	123	118	103

FD Cohort*	5.5-Year PFS Rate, % (95% CI)
With del(17p)/*TP53* (n=27; FD cohort only)	30 (12–49)
Without del(17p)/*TP53* (n=129; FD cohort only)	66 (57–74)

PFS by IGHV Status in Patients Without del(17p)/mutated *TP53*



	5.5-Year PFS Rate, % (95% CI)
uIGHV (n=99; Total pooled pop.)	59 (49–69)
mIGHV (n=66; Total pooled pop.)	84 (72–91)

Patients at risk

mIGHV	66	64	63	61	60	57	56	56	55	53	53	49
uIGHV	99	96	96	95	93	87	86	76	72	66	61	50

FD Cohort*	5.5-Year PFS Rate, % (95% CI)
uIGHV (n=71; FD cohort only)	53 (40–64)
mIGHV (n=55; FD cohort only)	80 (66–89)

Kapitel 3

Neue Substanzen

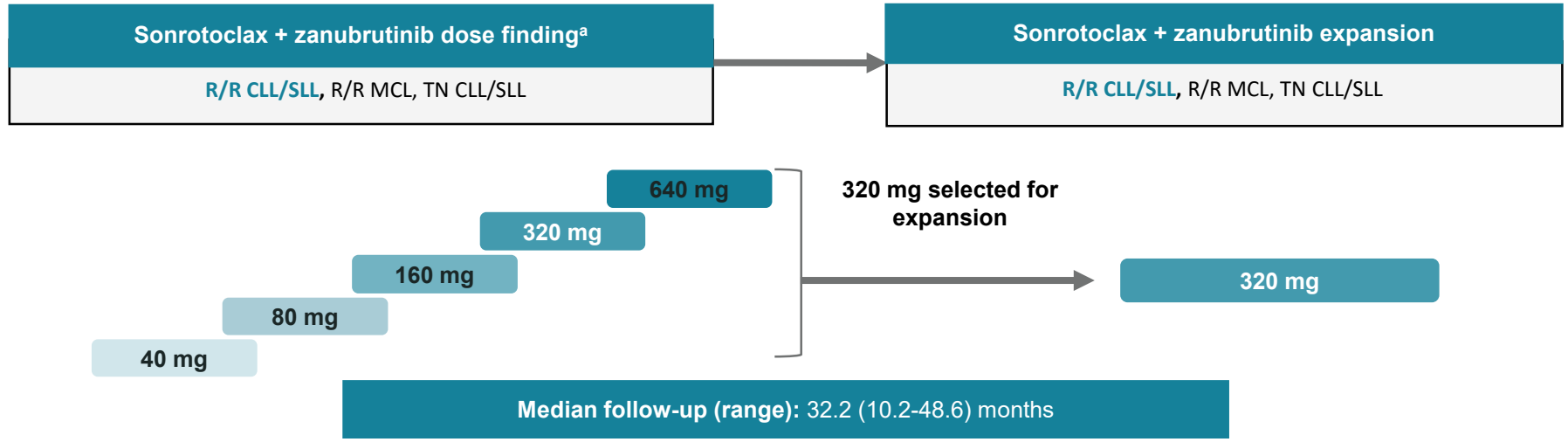
Nächst-Generations-BCL2-Hemmer

S159: Updated Results From the Phase 1 Study of Sonrotoclax (BGB-11417), a Novel BCL2 Inhibitor, in Combination With Zanubrutinib for Relapsed/Refractory CLL/SLL Demonstrate Deep and Durable Responses

Chan Cheah, Nedlands, Australien

Sonrotoclax-Zanubrutinib in rezidivierter CLL

Studiendesign



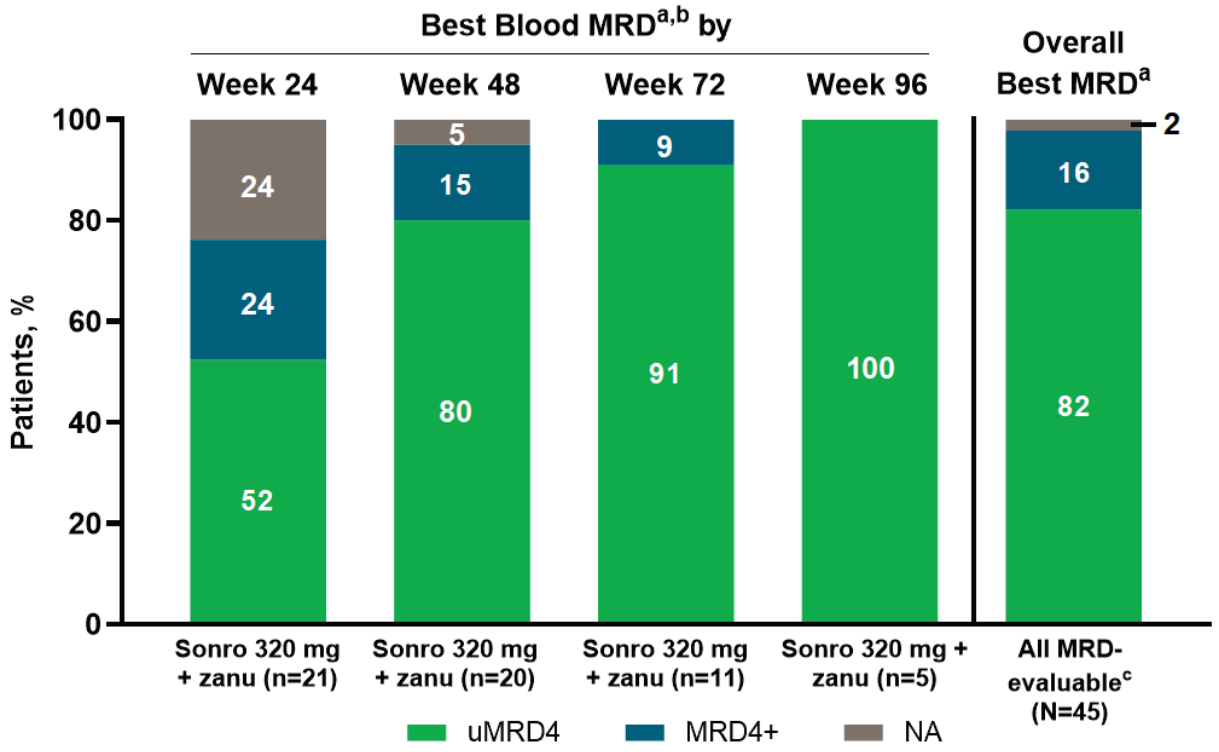
Sonrotoclax-Zanubrutinib in rezidivierter CLL

Patientencharakteristika

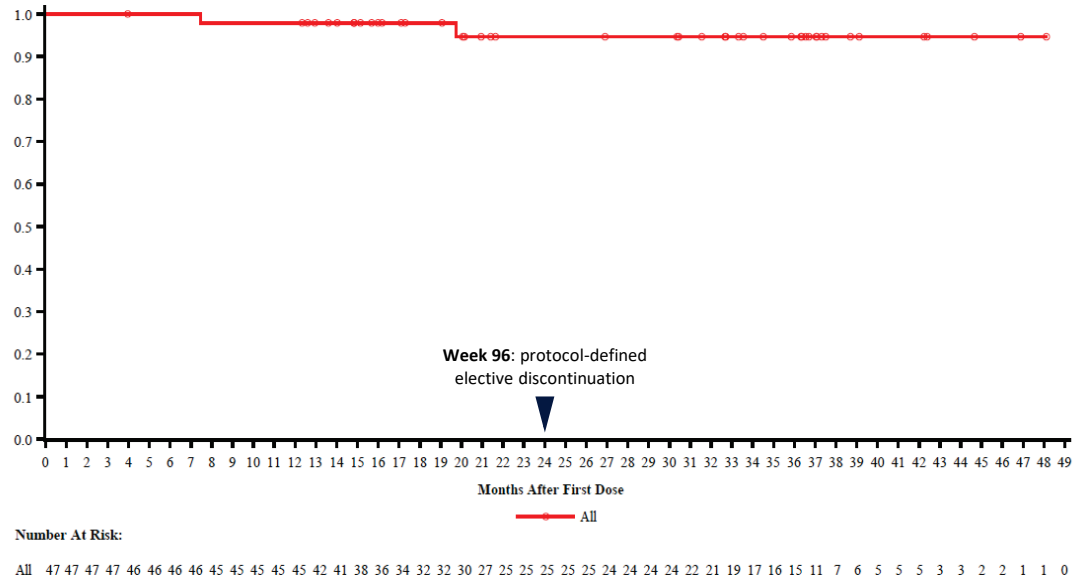
Characteristic	Sonro 40 mg + zanu (n=4)	Sonro 80 mg + zanu (n=9)	Sonro 160 mg + zanu (n=6)	Sonro 320 mg + zanu (n=22)	Sonro 640 mg + zanu (n=6)	All (N=47)
Study follow-up, median (range), months	46.8 (10.2-48.6)	40.6 (22.9-47.3)	42.0 (41.1-43.6)	19.6 (13.2-39.7)	30.9 (23.8-35.5)	32.2 (10.2-48.6)
Age, median (range), years	60.0 (50-71)	62.0 (55-75)	61.5 (41-76)	67.0 (36-76)	59.5 (53-69)	65.0 (36-76)
Male, n (%)	4 (100)	8 (89)	3 (50)	18 (82)	2 (33)	35 (74)
ECOG PS						
0	4 (100)	5 (56)	4 (67)	11 (50)	4 (67)	28 (60)
1	0	3 (33)	2 (33)	10 (45)	2 (33)	17 (36)
del(17p), n/tested (%)	3/4 (75)	4/8 (50)	1/6 (17)	3/18 (17)	0	11/42 (26)
del(17p) and/or *TP53* mutation[a], n/tested (%)	**3/4 (75)**	**5/8 (63)**	**1/6 (17)**	**7/19 (37)**	**0**	**16/42 (38)**
Unmutated IGHV, n/tested (%)	**2/4 (50)**	**8/9 (89)**	**3/6 (50)**	**14/17 (82)**	**3/5 (60)**	**30/41 (73)**
Prior therapy						
No. of lines of prior therapy, median (range)	1.5 (1-2)	1.0 (1-2)	1.0 (1-2)	1.0 (1-3)	1.0 (1-1)	1.0 (1-3)
Prior BTK inhibitor, n (%)[b]	1 (25)	1 (11)	1 (17)	3 (14)	1 (17)	7 (15)
Prior BTK inhibitor duration, median (range), months	86.6 (86.6-86.6)	1.6 (1.6-1.6)	18.5 (18.5-18.5)	38.1 (34.2-49.1)	24.0 (24.0-24.0)	34.2 (1.6-86.6)

Sonrotoclax-Zanubrutinib in rezidivierter CLL

MRD-Ansprechen



PFS



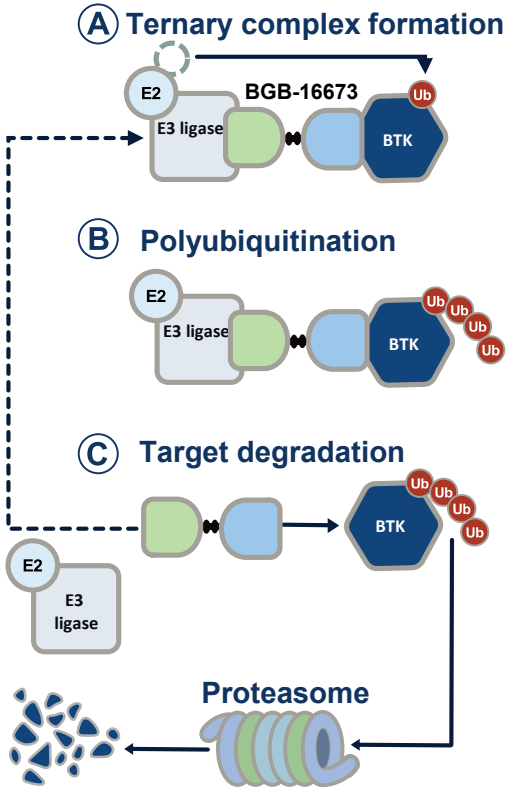
BTK Degrader

S158: Updated Efficacy and Safety of the Bruton Tyrosine Kinase Degrader BGB-16673 in Patients With Relapsed or Refractory CLL/SLL: Results From the Ongoing Phase 1 CaDAnCe-101 Study

Lydia Scarfo, Mailand, Italien

BTK Degrader

Wirkweise



Patientencharacteristika

	Total (N=66)
Age, median (range), years	70 (47-91)
Male, n (%)	45 (68.2)
ECOG PS, n (%)	
0	38 (57.6)
1	27 (40.9)
2	1 (1.5)
CLL/SLL risk characteristics at study entry, n/N with known status (%)	
Binet stage C	29/62 (46.8)
Unmutated IGHV	38/49 (77.6)
del(17p) and/or *TP53* mutation	43/66 (65.2)
Complex karyotype (≥3 abnormalities)	22/44 (50.0)

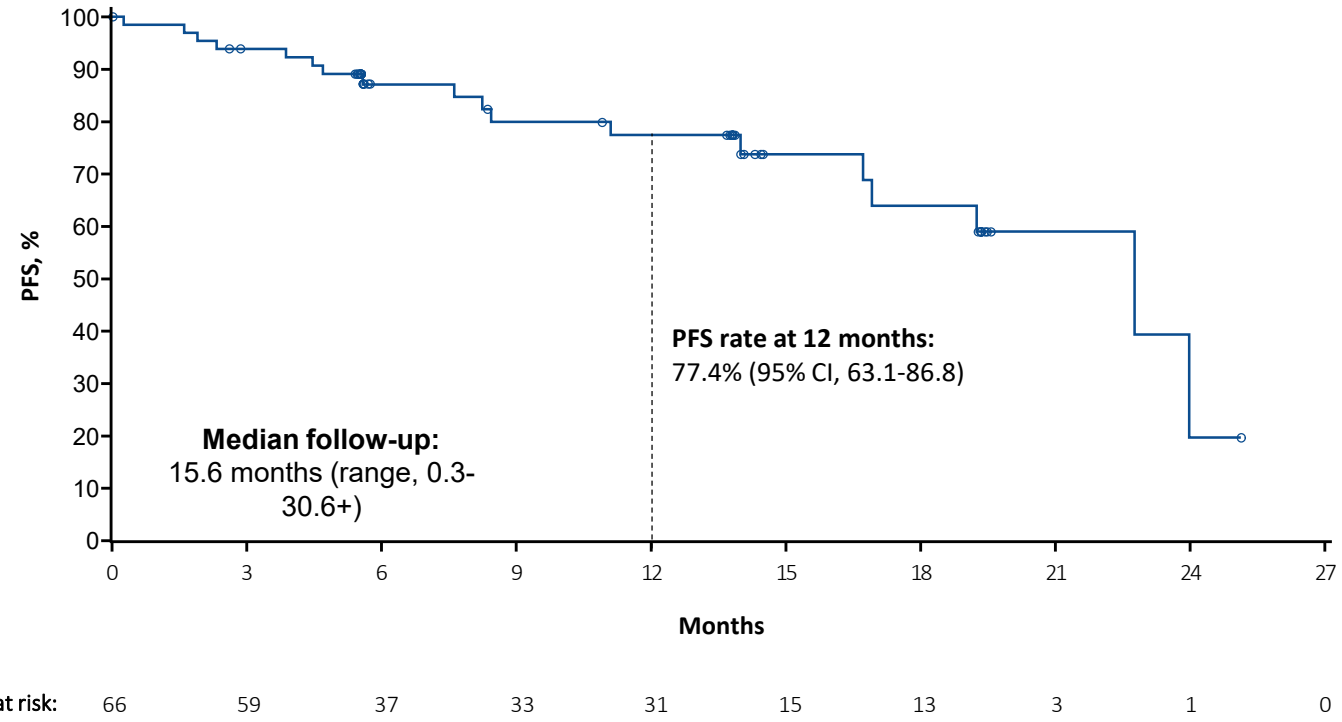
	Total (N=66)
Mutation status, n/N (%)	
BTK mutation present	24/63 (38.1)
PLCG2 mutation present	10/63 (15.9)
BTK and *PLCG2* mutation present	5/63 (7.9)
No. of prior lines of therapy, median (range)	4 (2-10)
Prior therapy, n (%)	
Chemotherapy	47 (71.2)
cBTK inhibitor	62 (93.9)
ncBTK inhibitor	14 (21.2)
BCL2 inhibitor	54 (81.8)
cBTK + BCL2 inhibitors	42 (63.6)
cBTK + ncBTK + BCL2 inhibitors	12 (18.2)
Discontinued prior BTK inhibitor due to PD, n/N (%)[a]	55/62 (88.7)

BTK Degrader

Ansprechraten

Subgroup	ORR, n/N with known status (%)
Double exposure (previously received cBTKi + BCL2i)	38/42 (90.5)
Triple exposure (previously received cBTKi + ncBTKi + BCL2i)	9/12 (75.0)
del(17p) and/or *TP53* mutation	35/43 (81.4)
Complex karyotype (≥3 abnormalities)	16/22 (72.7)
***BTK* mutations**	18/24 (75.0)
***PLCG2* mutations**	9/10 (90.0)

PFS



Zusammenfassung | Take-Home-Messages

- MRD-gesteuerte Therapie möglicherweise mit Survival-Vorteil - hier allerdings Unklarheiten bezgl. Art der MRD-Steuerung und Praxistauglichkeit

- Zeitlich begrenzte Therapien (~1 Jahr) hochwirksam mit langen therapiefreien Intervallen

- Proof-of-concept von 2nd-generation BCL2-Inhibitoren sowie BTK Degrader aus Phase-1/2 Daten - randomisierte Daten ausstehend

Alle Kurzpräsentationen sind online unter

www.lymphome.de/eha2025

Für den Inhalt verantwortlich:

PD Dr. med. Othman Al-Sawaf

Uniklinik Köln

Lymphom Kompetenz KOMPAKT

Kompetenznetz Maligne Lymphome

KML KONGRESSE

Expert:innen berichten zu Lymphomen & Leukämien

EHA 2025

MAILAND, ITALIEN

12. – 15. Juni 2025

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