Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

15-ICML

15th International Conference on Malignant Lymphoma
Palazzo dei Congressi, Lugano, Switzerland, June 18-22, 2019

18.–22. Juni 2019

KML-Experten berichten vom 15-ICML 2019 in Lugano

Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT 15-ICML 18.–22. Juni 2019

Prof. Dr. med. Michael Hallek

Chronische lymphatische Leukämie (CLL)

Direktor der Klinik I für Innere Medizin der Uniklinik Köln |
Leiter Deutsche CLL Studiengruppe (DCLLSG) |
Vorstandsvorsitzender Kompetenznetz Maligne Lymphome e.V.

Kapitel 1

CLL 12-Studie

Watch & Wait oder *Ibrutinib* bei Patienten im frühen Statium ohne Symptome?

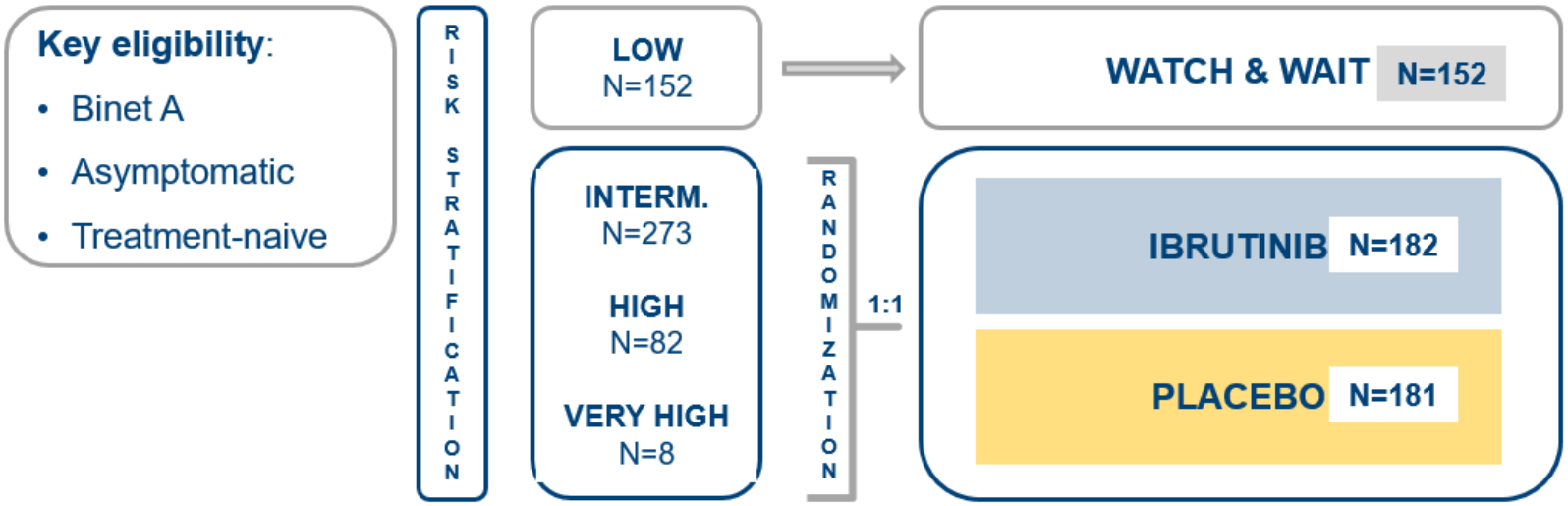
IBRUTINIB VERSUS PLACEBO IN PATIENTS WITH ASYMPTOMATIC, TREATMENT-NAÏVE EARLY STAGE CLL: PRIMARY ENDPOINT RESULTS OF THE PHASE 3 DOUBLE-BLIND RANDOMIZED CLL12 TRIAL

Presenter: P. Langerbeins, DCLLSG, Köln

P. Langerbeins, J. Bahlo, C. Rhein, H. Gerwin, P. Cramer, M. Fürstenau, O. Al-Sawaf, J. von Tresckow, A.M. Fink, K. Kreuzer, U. Vehling-Kaiser, E. Tausch, L. Müller, M. Eckart, R. Schlag, W. Freier, T. Gaska, C. Balser, M. Reiser, M. Stauch, C. Wendtner, K. Fischer, S. Stilgenbauer, B. Eichhorst, M. Hallek

STUDY DESIGN

DEUTSCHE STUDIENGRUPPE CLL



Phase 3, placebo-controlled, double-blind, multicenter trial

Primary endpoint EFS: time from randomization until symptomtatic PD, new treatment, death

Secondary endpoints: survival, PFS, TFS, TTNT, ORR, safety

π_2 : median EFS from 24 to 48 months with ibrutinib (superiority test)

ADVERSE EVENTS

DEUTSCHE STUDIENGRUPPE CLL

	Ibrutinib n=185	Placebo n=178
Any grade AEs (%)	152 (82.2)	151 (84.8)
AEs ≥ grade 3 (%)	80 (43.2)	69 (38.8)
AEs leading to interruption (%)	77 (41.6)	38 (21.3)
Arrhythmias	18	0
Bleeding	8	1
Diarrhea	4	3
Neoplasia	4	3
Infection	3	4
Myocardial infarction	1	6
other	39	21

* Death of unknown cause (n=4), infection (n=2), second cancer (n=2), cardiac failure (n=1)

ADVERSE EVENTS OF CLINICAL INTEREST

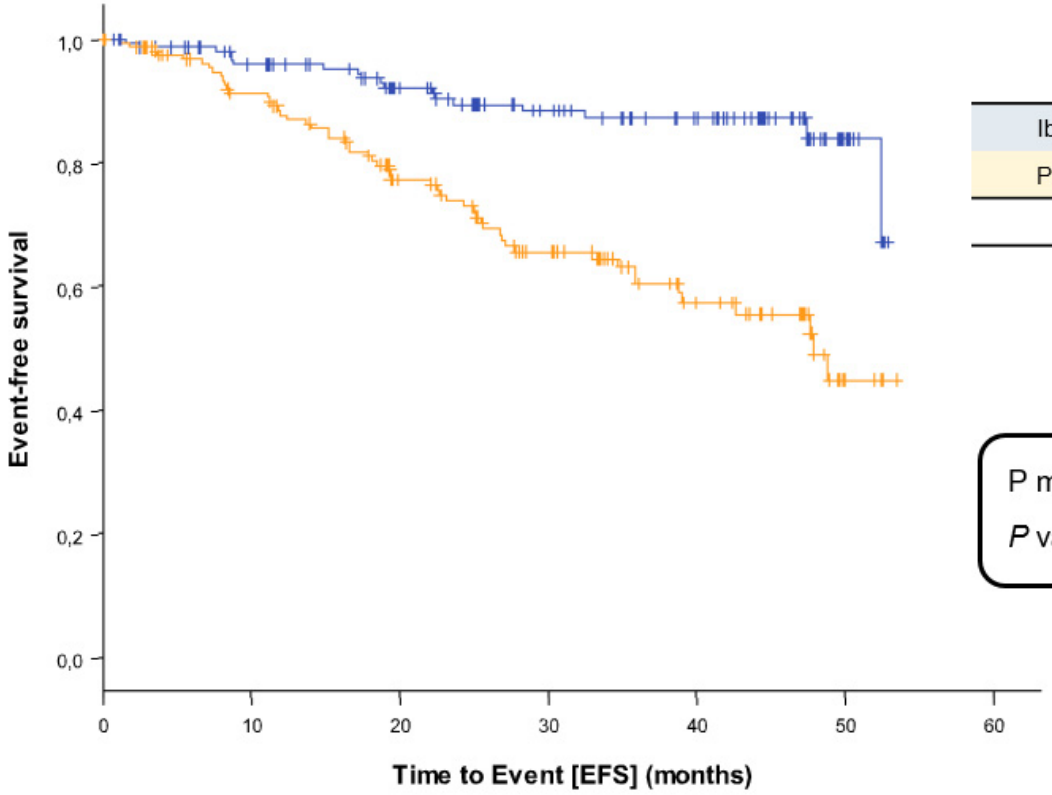
DEUTSCHE STUDIENGRUPPE CLL

	Ibrutinib n=185	Placebo n=178	*P*-value
AE of clinical interest (%)	106 (57.3)	71 (39.9)	0.001
Diarrhea - CTC ≥ 3	**58 (31.4)** 2 (1.1)	**44 (24.7)** 5 (2.8)	n.s.
Bleeding - CTC ≥ 3	**51 (27.6)** 6 (3.2)	**17 (9.6)** 2 (1.2)	0.000
Atrial fibrillation - CTC ≥ 3	**33 (17.8)** 11 (6.5)	**13 (7.3)** 3 (1.7)	0.003
Hypertensive disorders - CTC ≥ 3	**18 (9.7)** 3 (1.6)	**7 (3.9)** 3 (1.7)	0.04

PRIMARY EFS ENDPOINT ANALYSIS

Time to symptomatic progression, CLL treatment and/or death

DEUTSCHE STUDIENGRUPPE CLL



	total	events	N	%
Ibrutinib	182	18	164	90.1
Placebo	181	55	126	69.9
	363	73	290	79.9

P median$_{EFS}$ 47.8 vs. NR

P value <0.0001; HR 0.248

CONCLUSIONS

The primary endpoint analysis of the CLL12 study confirms that…

… ibrutinib improves EFS in asymptomatic, early stage patients with risk of progression.

… there were no differences in adverse events when compared to placebo.

... atrial fibrillation, bleeding and hypertensive disorders affected signifcant more ibrutinib-treated patients and were the main reason for treatment discontinuation

Unless there is no survival benefit the goldstandard for early stage patients remains watch & wait.

Kapitel 2

CLL 14-Studie

Venetoclax + Obinutuzumab: Ergebnisse für ältere Patienten mit Komorbiditäten

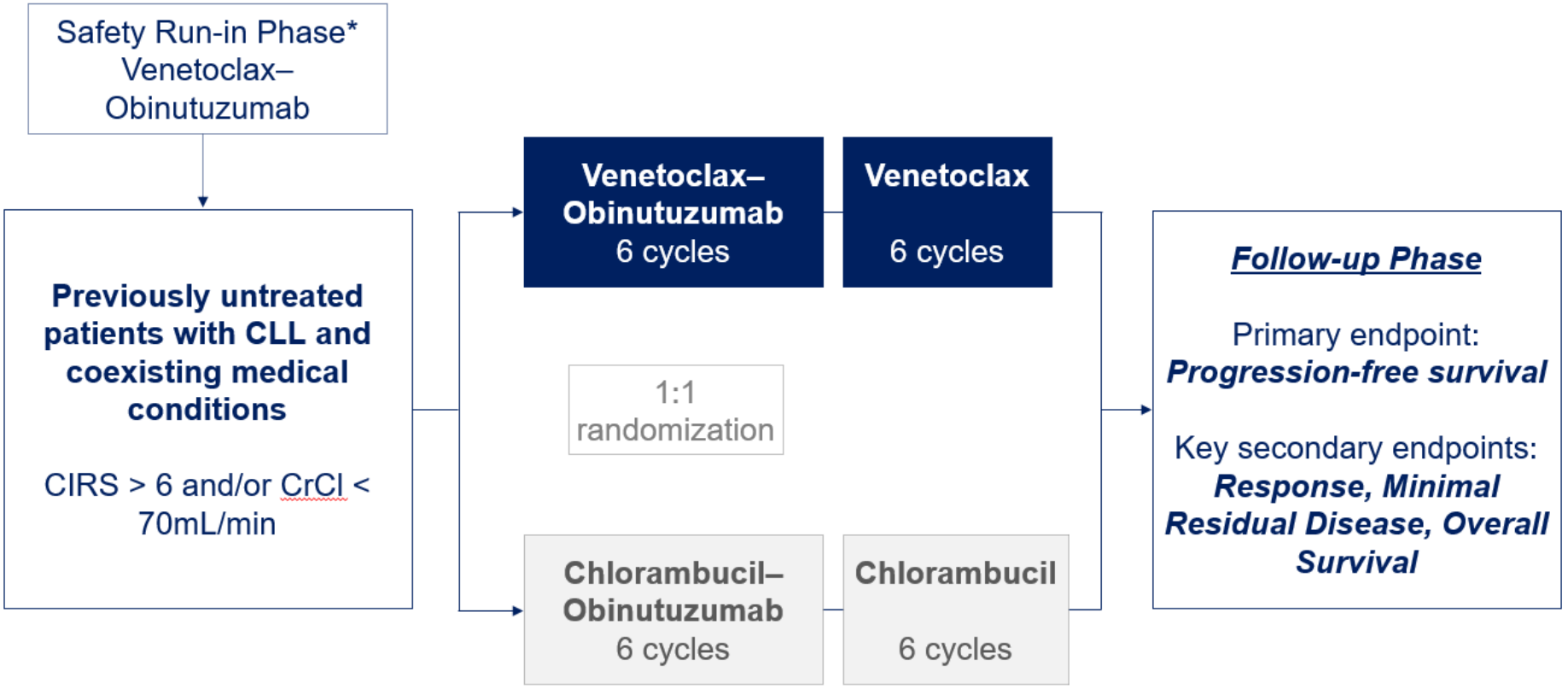
FIXED-DURATION VENETOCLAX PLUS OBINUTUZUMAB IMPROVES PFS AND MINIMAL RESIDUAL DISEASE NEGATIVITY IN PATIENTS WITH PREVIOUSLY UNTREATED CLL AND COMORBIDITIES

Presenter: K. Fischer, DCLLSG, Köln

K. Fischer, M. Porro Lurà, O. Al-Sawaf, J. Bahlo, A. Fink, M. Tandon, M. Dixon, S. Robrecht, S. Warburton, K. Humphrey, O. Samoylova, A.M. Liberati, J. Pinilla-Ibarz, S. Opat, L. Sivcheva, K. Le Dû, L.M. Fogliatto, C. Utoft Niemann, R. Weinkove, S. Robinson, T.J. Kipps, S. Boettcher, E. Tausch, W.L. Schary, B. Eichhorst, C. Wendtner, A.W. Langerak, K. Kreuzer, V. Goede, S. Stilgenbauer, M. Mobasher, M. Ritgen, M. Hallek

Lymphomkompetenz Kompakt: CLL

TRIAL DESIGN



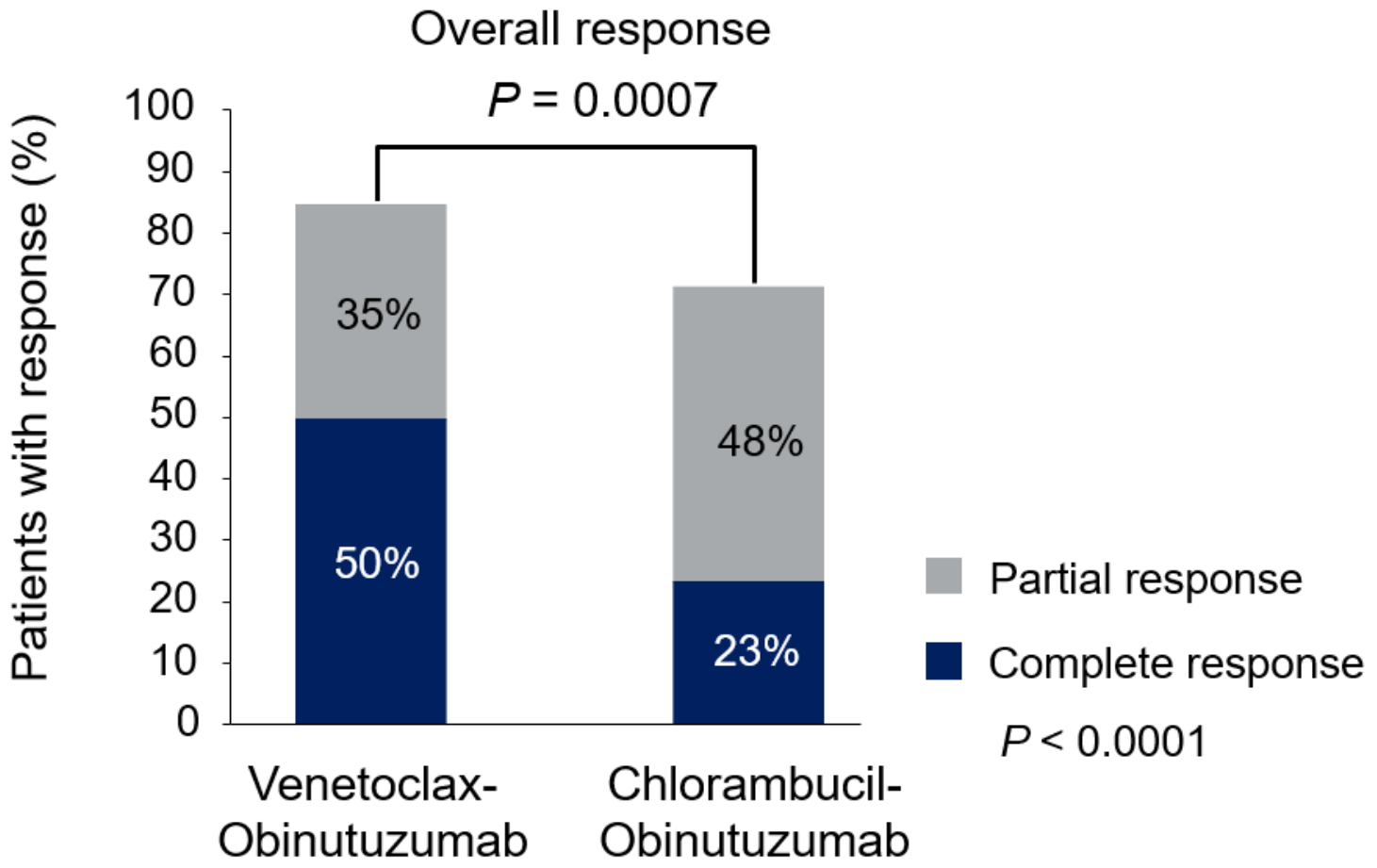
PATIENT CHARACTERISTICS I

	Venetoclax-Obinutuzumab	Chlorambucil-Obinutuzumab
Number of patients, N	216	216
Median age in years	**72**	**71**
Binet stage		
A	21 %	20 %
B	36 %	37 %
C	43 %	43 %
Median total CIRS score	**9**	**8**
Median estimated CreaCl in ml/min	**65.2**	**67.5**
Risk category for TLS		
Low	13 %	12 %
Intermediate	64 %	68 %
High	22 %	20 %

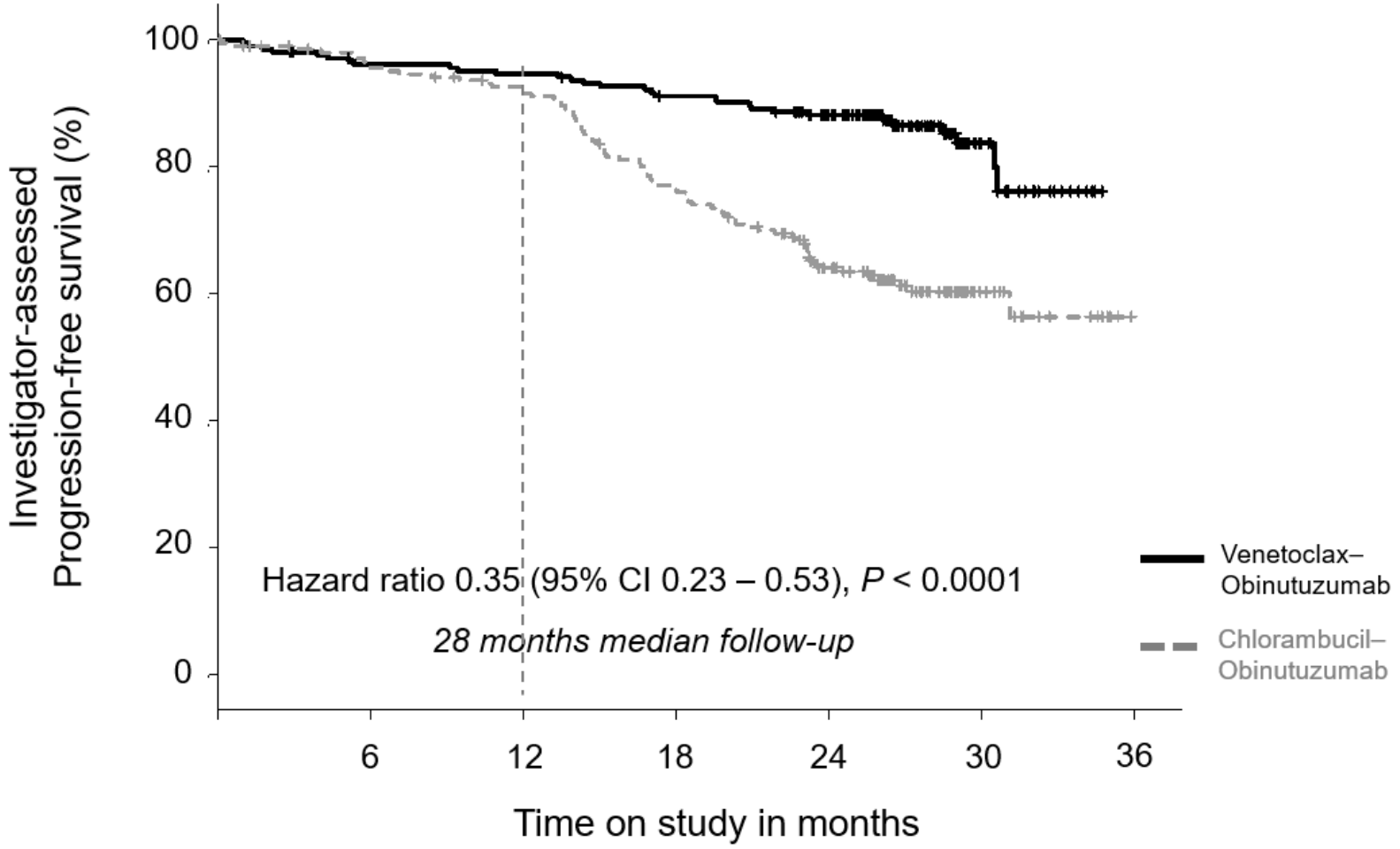
GRADE 3 OR 4 ADVERSE EVENTS

	Venetoclax-Obinutuzumab	Chlorambucil-Obinutuzumab
Number of patients, N	212*	214
Blood and lymphatic system disorders	**60 %**	**55 %**
Neutropenia	53 %	48 %
Thrombocytopenia	14 %	15 %
Anemia	8 %	7 %
Febrile neutropenia	5 %	4 %
Injury, poisoning and procedural comp.	12 %	14 %
Infusion-related reaction	9 %	10 %
Infections and infestations	18 %	15 %
Pneumonia	4 %	4 %
Investigations	15 %	11 %
Neutrophil counts decreased	4 %	5 %
Metabolism and nutrition disorders**	12 %	6 %

RESPONSE TO TREATMENT



PROGRESSION-FREE SURVIVAL

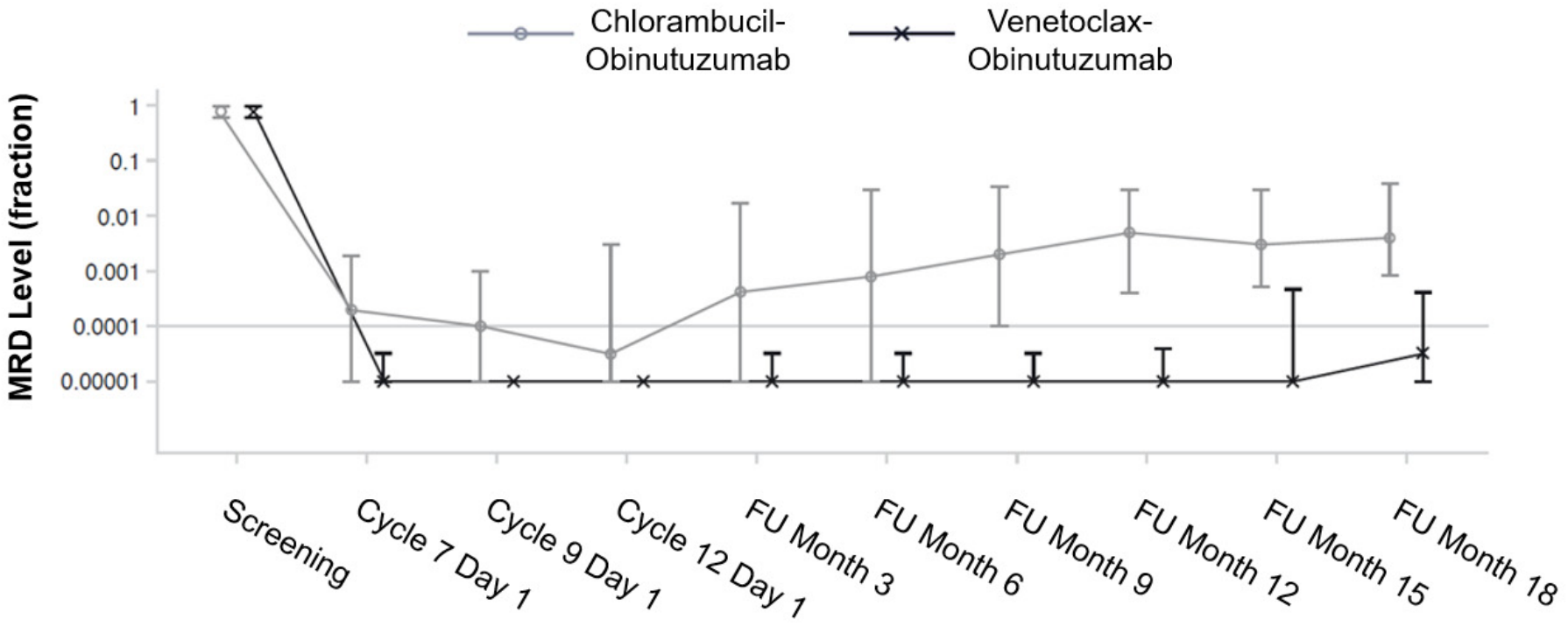


MRD NEGATIVITY BY NGS

	Venetoclax-Obinutuzumab	Chlorambucil-Obinutuzumab
Number of patients, N	216	216
Minimal residual disease level		
$< 10^{-6}$	42 %	7 %
$\geq 10^{-6}$ and $<10^{-5}$	26 %	13 %
$\geq 10^{-5}$ and $<10^{-4}$	11 %	14 %
$\geq 10^{-4}$ and $<10^{-2}$	6 %	23 %
$\geq 10^{-2}$	5 %	29 %
No sample / not evaluable	12 %	14 %

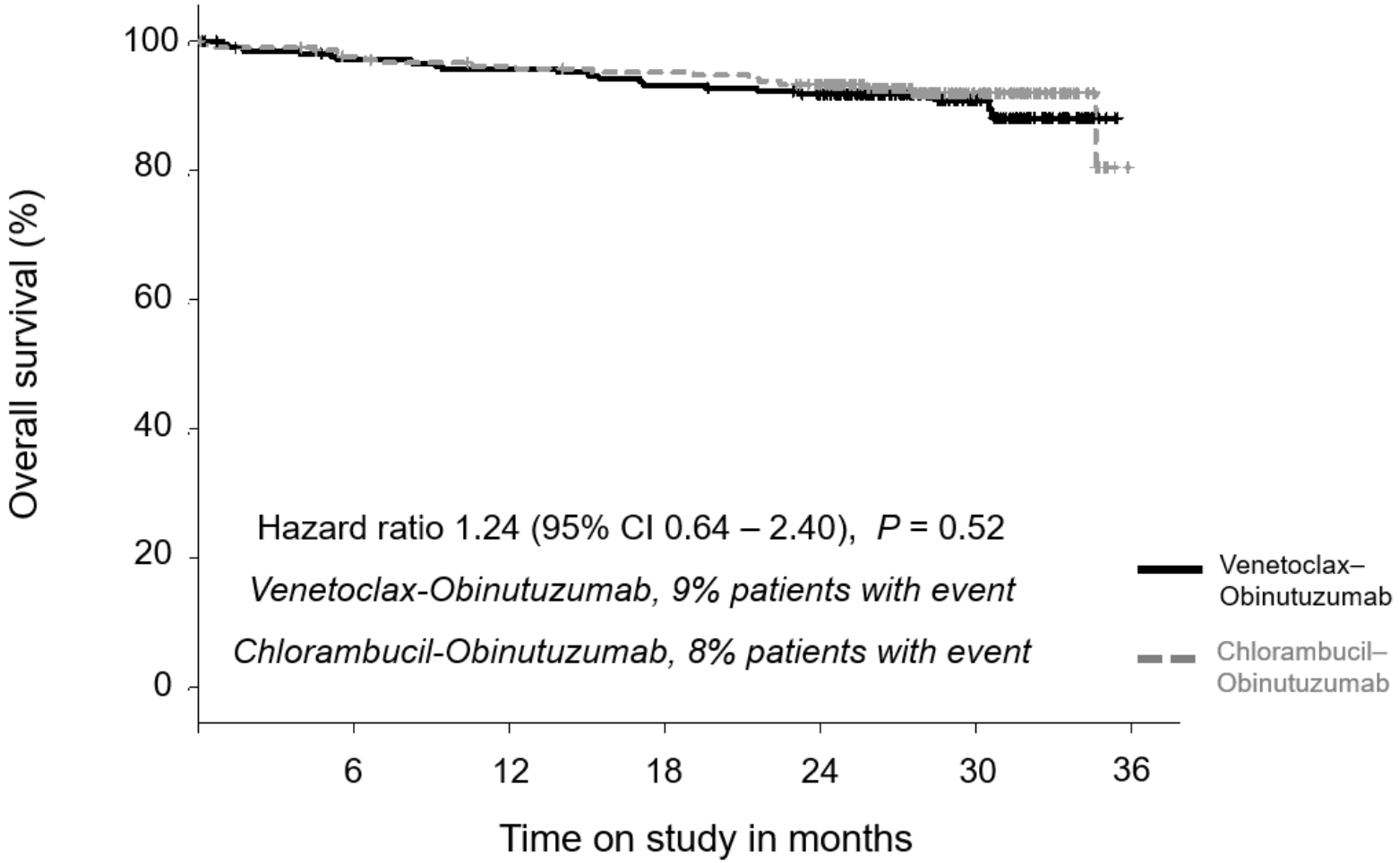
By NGS in peripheral blood 3 months after completion of treatment

MRD LEVELS OVER TIME



Lymphomkompetenz Kompakt: CLL

OVERALL SURVIVAL



CONCLUSION
A FIXED-DURATION, TARGETED THERAPY COMBINING VENETOCLAX AND OBINUTUZUMAB …

… can be applied safely to elderly CLL patients with relevant comorbidity:

… provides a superior outcome compared to chlorambucil and obinutuzumab regarding:

- PFS.
- Overall response rate.
- Complete response rate.
- MRD negative responses.
- In all relevant subgroups including IGVH unmutated, del(17p) or TP53 mutated patients.

… achieves the highest rate of MRD negative responses so far observed in a randomized prospective study.

Kapitel 3

CLL 14-Studie

Welche genetische Subgruppen profitieren besonders?

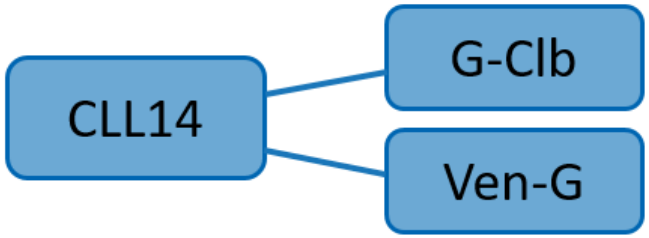
GENETIC MARKERS AND OUTCOME IN THE CLL14 TRIAL OF THE GCLLSG COMPARING FRONT LINE OBINUTUZUMAB PLUS CHLORABMUCIL OR VENETOCLAX IN PATIENTS WITH COMORBIDITY - Best abstract submitted by a young investigator / travel grant recipient

Presenter: E. Tausch, Uniklinikum Ulm

E. Tausch, J. Bahlo, S. Robrecht, C. Schneider, J. Bloehdorn, S. Schrell, C. Galler, O. Al-Sawaf, A. Fink, B. Eichhorst, K. Kreuzer, M. Tandon, K. Humphrey, Y. Jiang, W. Schary, M. Porro Lurà, H. Döhner, K. Fischer, M. Hallek, S. Stilgenbauer

CLL14: G-Clb vs. Ven-G in untreated patients with CLL and relevant comorbidities

Population:

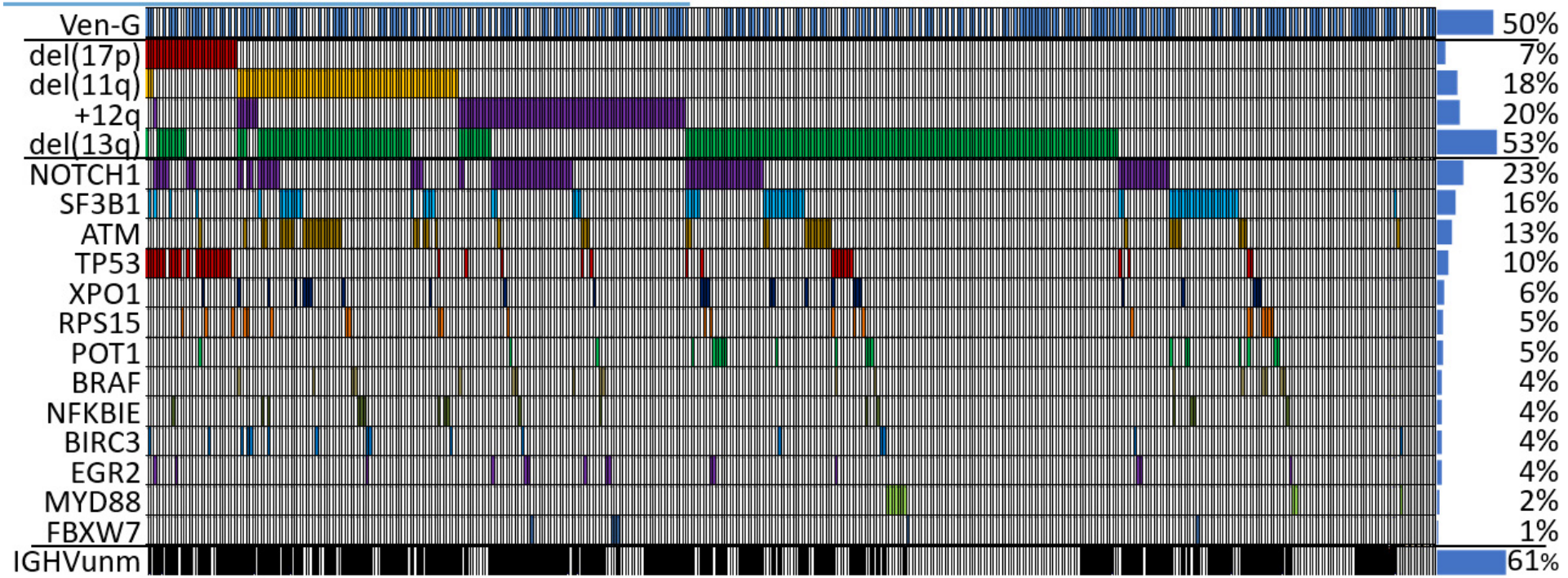


- International phase III trial (196 centers, 21 countries)
- Untreated CLL n=432 with "active disease"
- Median Age 72 years, CIRS score 8, Creat Clear 66.4m
- Randomized into 6 cyles Obinutuzumab +
  - 12 cycles Chlorambucil (G-Clb)
  - 12 cycles Venetoclax (Ven-G)

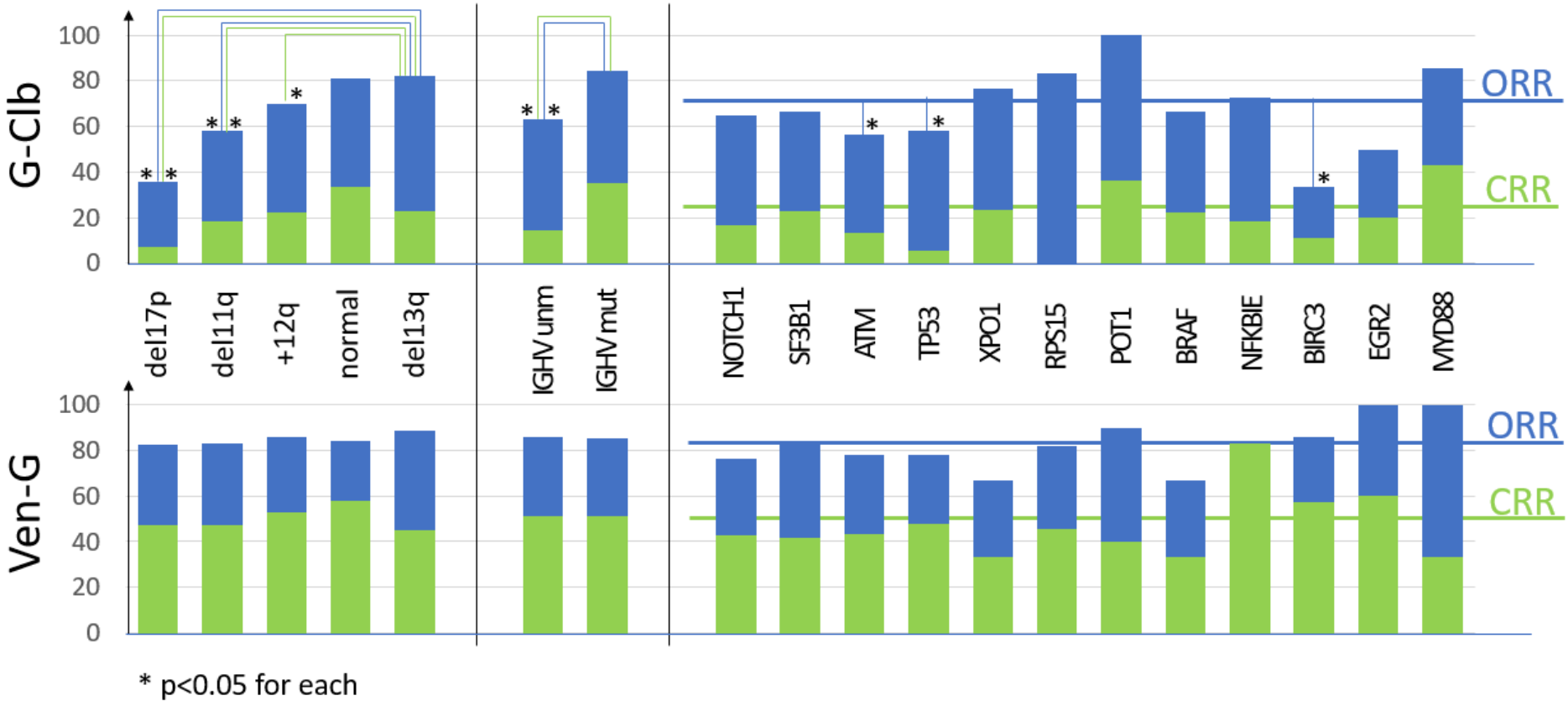
Methods

Cytogenetics via FISH: 418/432 patients (97%)
IGHV (threshold <98% homology): 408/432 patients (94%)
Custom Targeted NGS panel for mutations: 421/432 patients (97%)
TP53, NOTCH1, SF3B1, ATM, MYD88, FBXW7, POT1, BIRC3, XPO1, NFKBIE, EGR2, RPS15.

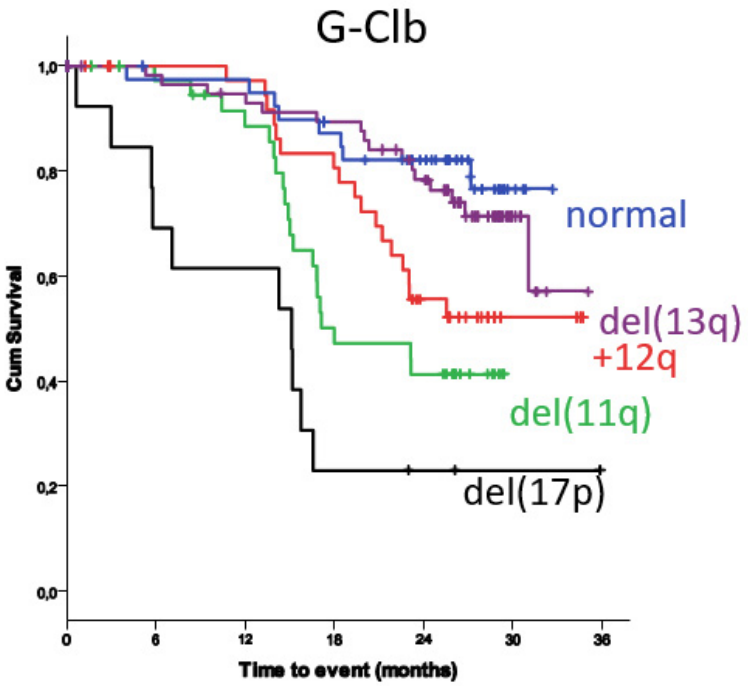
Incidence of aberrations, mutations and IGHV status

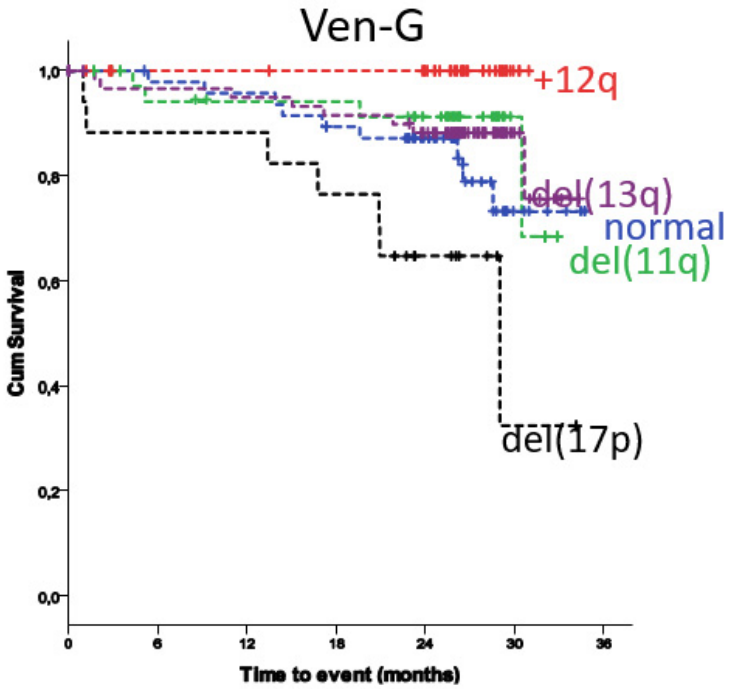


Complete and overall response with G-Clb/Ven-G:



Genomic aberrations and PFS





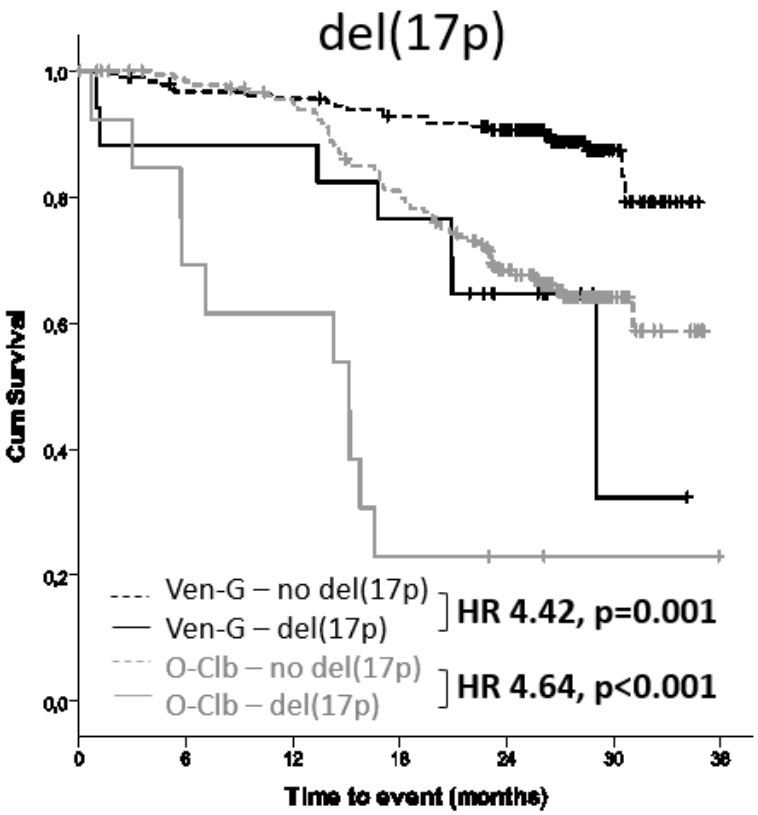
del(17p) vs. del(13q): HR 7.41 (3.36-16.32) p<0.001

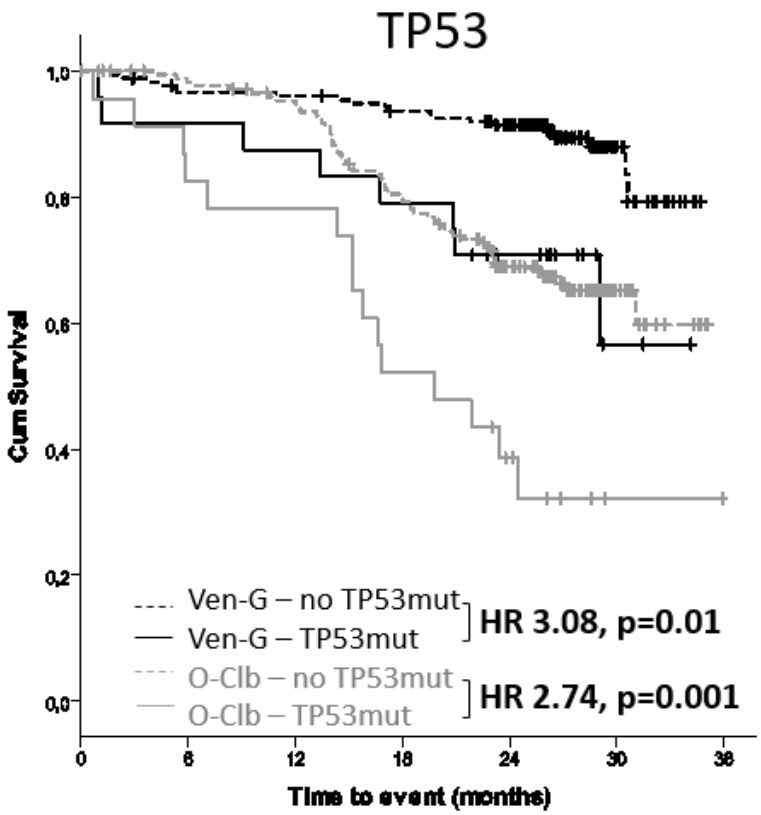
del(11q) vs. del(13q): HR 3.44 (1.80-6.60) p<0.001

+12q vs. del(13q): HR 2.22 (1.13-4.35) p=0.02

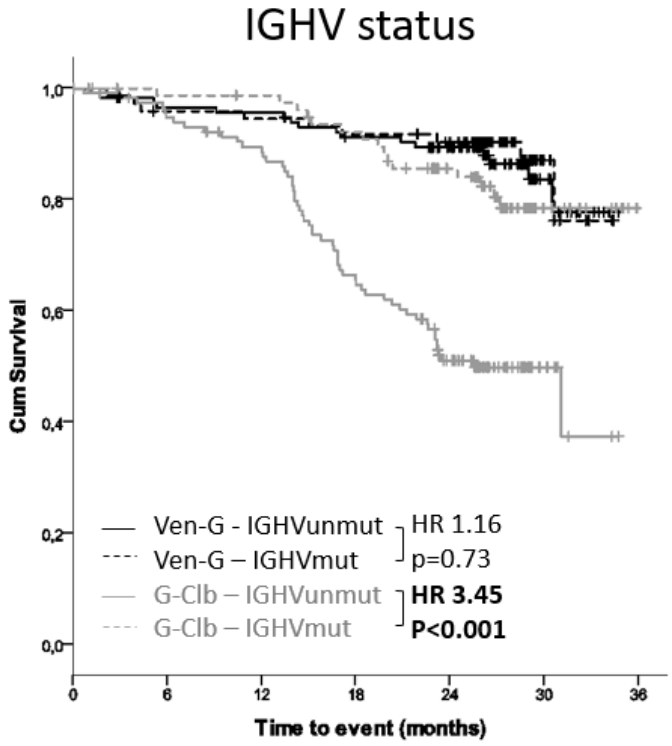
del(17p) vs. del(13q): HR 4.19 (1.55-11.33) p=0.005

del(17p) / *TP53* mutation and PFS





IGHV as a predictive factor: Ven-G is particularly effective in unmutated IGHV



Multivariable analysis testing for treatment interaction: IGHV as a predictive factor

	HR	95% CI	P value
IGHV unmut vs. mut	3.475	1.963-6.154	<0.001
Ven-G vs. G-Clb	0.64	0.280-1.462	0.289
IGHV * treatment interaction	0.333	0.123-0.903	**0.031**

Genetic markers and impact on overall survival

Univariate analysis for G-Clb

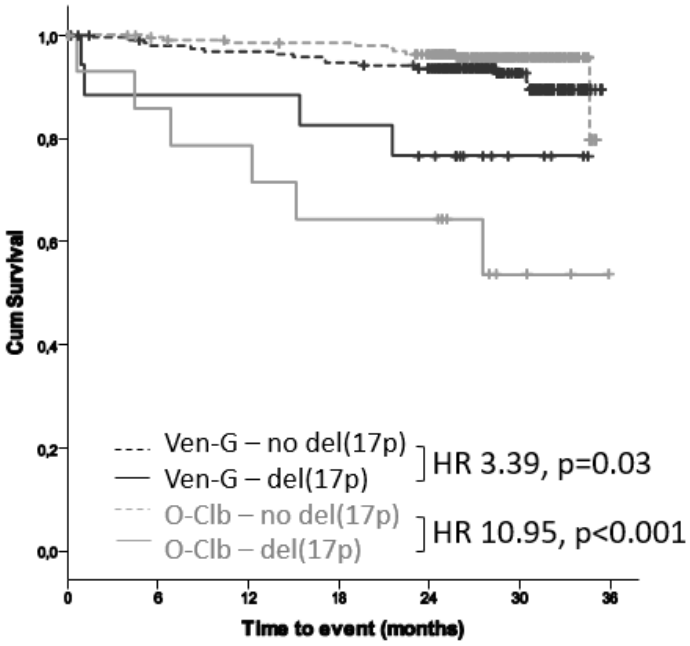
	HR	95%CI	p
del(17p)	10.95	3.85-31.14	<0.001
BRAF	6.61	1.84-23.74	0.004
TP53	5.48	1.87-16.07	0.002
IGHVunm	5.38	1.19-24.40	0.03

Univariate analysis for Ven-G

	HR	95%CI	p
del(17p)	3.391	1.124-10.23	0.03

24 of 37 deaths were fatal adverse events

del(17p)



Summary

Ven-G is superior to G-Clb regarding CRR/ORR and PFS for all major genetic subgroups.

del(17p) and *TP53*^{mut} remains adverse prognostic factors for PFS with Ven-G treatment.

Venetoclax is particularly effective in IGHV unmutated patients.

Kapitel 3

CLL 14-Studie

Vorteile für Patienten mit komplexem Karyotyp (CKT)?

HIGH EFFICACY OF VENETOCLAX PLUS OBINUTUZUMAB IN PATIENTS WITH COMPLEX KARYOTYPE (CKT) AND CHRONIC LYMPHOCYTIC LEUKEMIA (CLL): A PROSPECTIVE ANALYSIS FROM THE CLL14 TRIAL

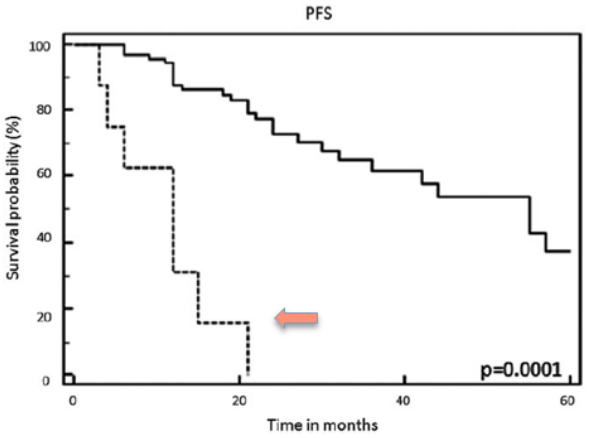
Presenter: O. Al Sawaf, DCLLSG, Köln

O. Al-Sawaf, E. Lilienweiss, J. Bahlo, S. Robrecht, A. Fink, M. Patz, M. Tandon, K. Humphrey, Y. Jiang, W. Schary, M. Porro Lurà, M. Ritgen, E. Tausch, S. Stilgenbauer, B. Eichhorst, K. Fischer, M. Hallek, K. Kreuzer

COMPLEX KARYOTYPE IN CLL

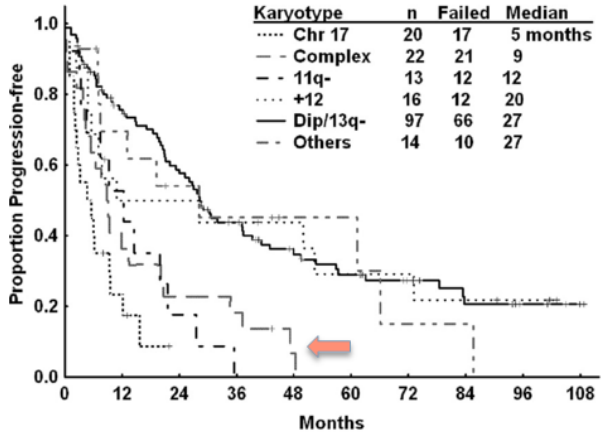
- presence of ≥ 3 chromosomal aberrations
- common in 10-30% of patients with CLL
- Adverse prognostic factor:

FCR in untreated CLL



Le Bris et al, Hematol Oncol, 2016

FCR in r/r CLL

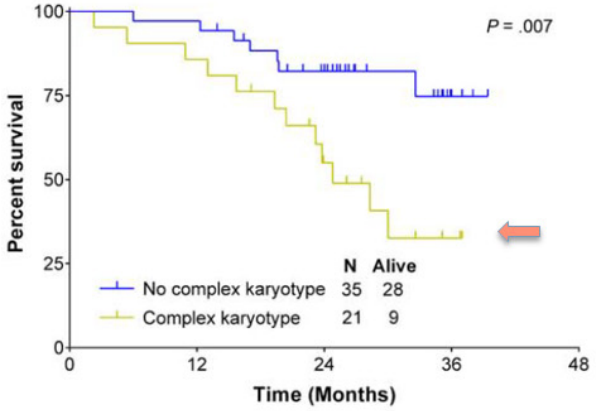


Badoux et al, Blood, 2011

COMPLEX KARYOTYPE IN CLL

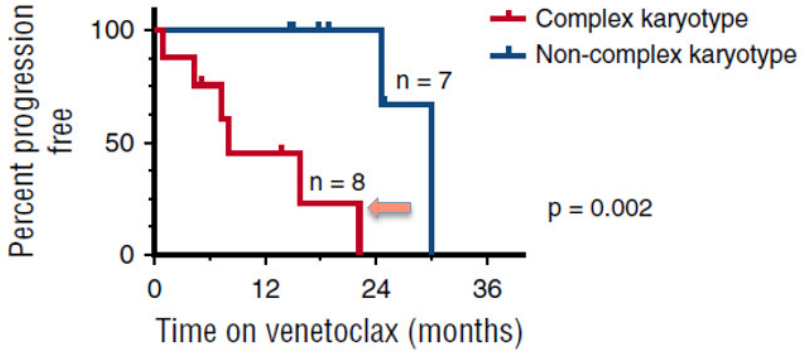
- presence of ≥ 3 chromosomal aberrations
- common in 10-30% of patients with CLL
- Adverse prognostic factor:

Ibrutinib in r/r CLL



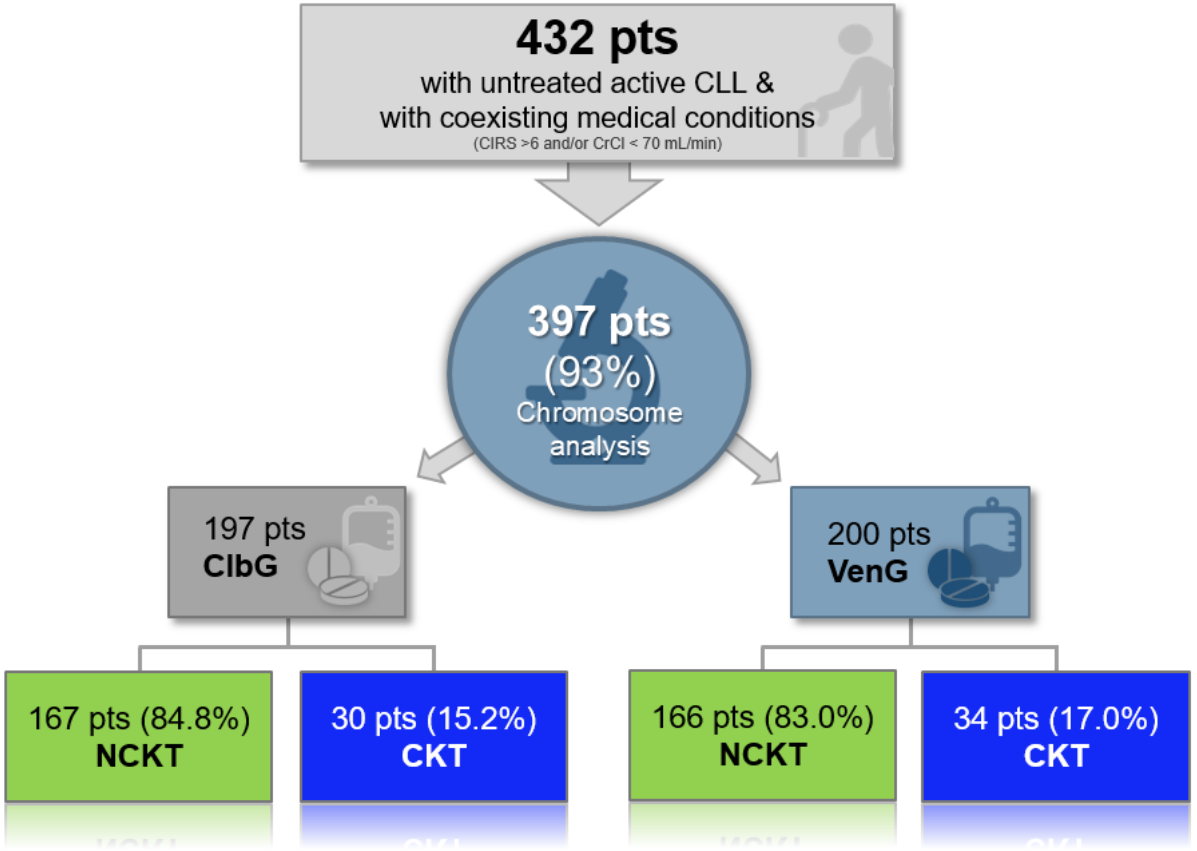
Thompson et al, Cancer, 2015

Venetoclax in r/r CLL



Anderson et al, Blood, 2017

KARYOTYPE ANALYSIS

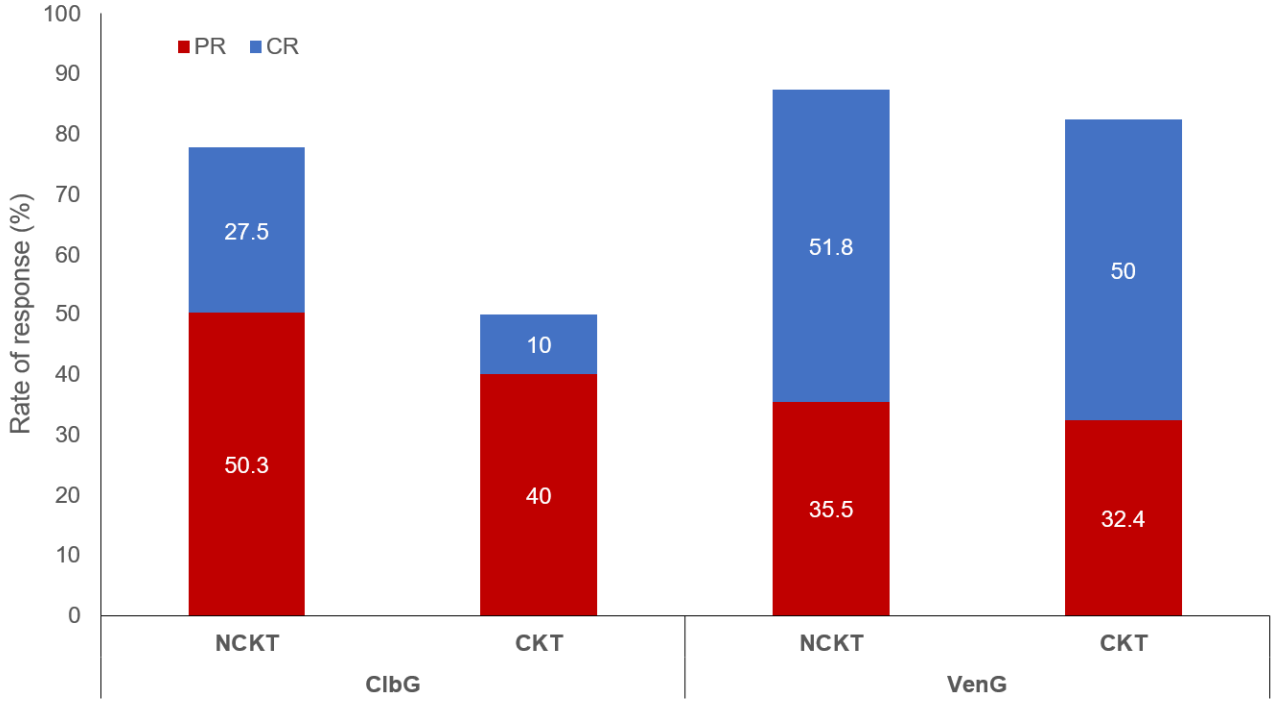


PATIENT CHARACTERISTICS II

DEUTSCHE STUDIENGRUPPE CLL

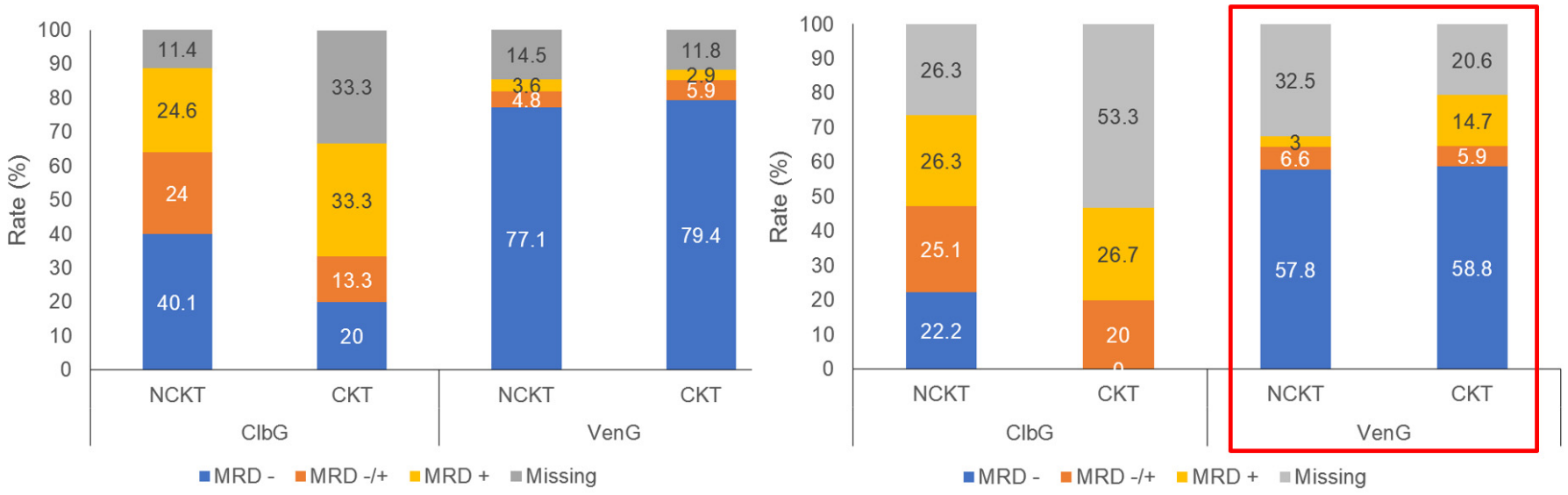
	CLBG		VENG	
	NCKT	CKT	NCKT	CKT
Cytogenetic subgroup – n (%)	**163**	**29**	**163**	**33**
del(17p)	5 (3.1)	8 (27.6)	5 (3.1)	11 (33.3)
del(11q)	27 (16.6)	7 (24.1)	25 (15.3)	8 (24.2)
Trisomy 12	27 (16.6)	9 (31.0)	30 (18.4)	5 (15.2)
Not del(17p)/del(11q)/trisomy 12/del(13q)	37 (22.7)	3 (10.3)	42 (25.8)	3 (9.1)
del(13q) alone	67 (41.1)	2 (6.9)	61 (37.4)	6 (18.2)
IGHV mutational status – n (%)				
Unmutated	95 (58.6)	18 (62.1)	96 (61.5)	20 (66.7)
Mutated	67 (41.4)	11 (37.9)	60 (38.5)	10 (33.3)
***TP53* mutational status – n (%)**				
Unmutated	155 (93.9)	21 (72.4)	151 (92.6)	25 (73.5)
Mutated	10 (6.1)	8 (27.6)	12 (7.4)	9 (26.5)

RESPONSE


100
90
80
70
60
50
40
30
20
10
0
Rate of response (%)
PR
CR
27.5
50.3
10
40
51.8
35.5
50
32.4
NCKT
CKT
NCKT
CKT
ClbG
VenG

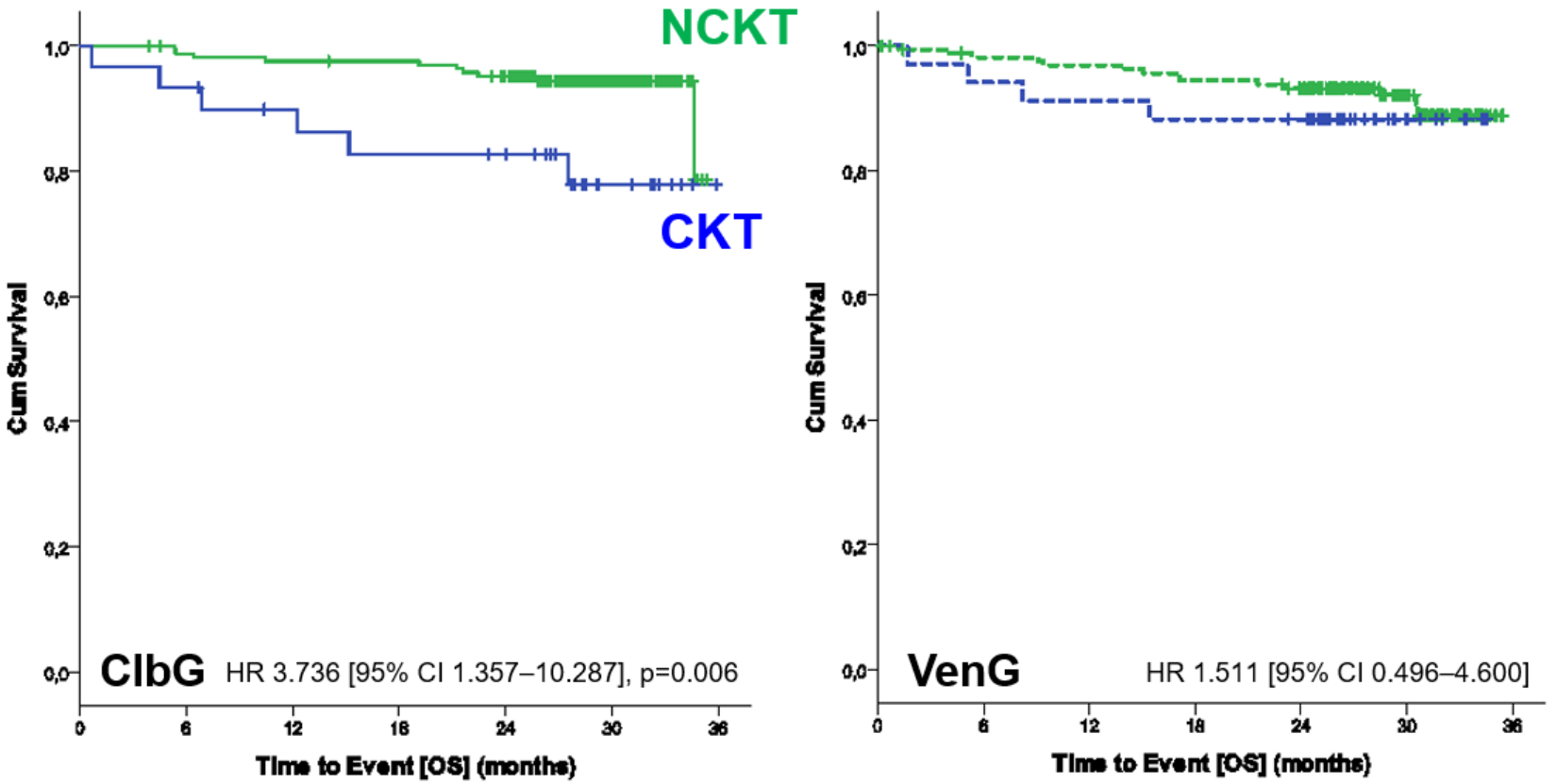
Lymphomkompetenz Kompakt: CLL

MINIMAL RESIDUAL DISEASE



OVERALL SURVIVAL

DEUTSCHE STUDIENGRUPPE CLL



SUMMARY

CKT can be observed in **approx. 15%** of elderly, treatment-naïve pts with CLL

CKT, **irrespective of *TP53* status**, is associated with **shorter PFS and OS** in pts treated with **chemoimmunotherapy**

No difference between NCKT and CKT in **PFS and OS** is observed when **treated with VenG**

Frontline treatment with **VenG is able to overcome** the adverse prognosis associated with CKT

Kapitel 5

CAR-T-Zell-Therapie

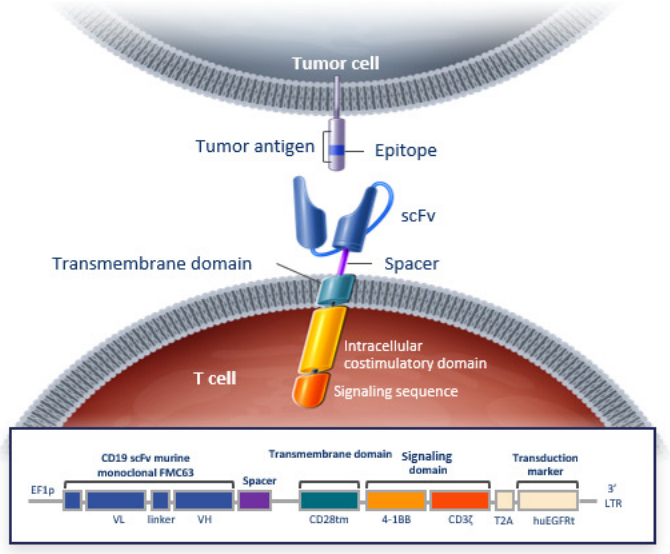
Einsatz auch bei intensiv vorbehandelten CLL-Patienten?

TRANSCEND CLL 004: MINIMAL RESIDUAL DISEASE AFTER LISOCABTAGENE MARALEUCEL IN PATIENTS WITH RELAPSED/REFRACTORY CHRONIC LYMPHOCYTIC LEUKEMIA/SMALL LYMPHOCYTIC LYMPHOMA

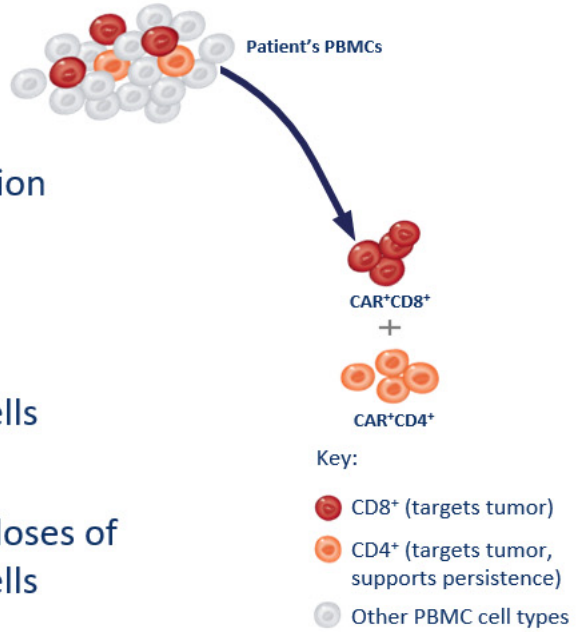
Presenter: Tanya Siddiqi, City of Hope National Medical Center, Duarte, California, USA

T. Siddiqi, K.A. Dorritie, J.D. Soumerai, D.M. Stephens, J.A. Dubovsky, H.H. Gillenwater, L. Gong, J. Thorpe, L. Yang, W.G. Wierda

Lisocabtagene Maraleucel (liso-cel; JCAR017) CD19-Targeted Defined Cell Product



- Immunomagnetic selection
- Lentiviral transduction
- Expansion
- CD4+ and CD8+ CAR T cells formulated separately
- Administered at target doses of CD4+ and CD8+ CAR T cells



CAR, chimeric antigen receptor; CD, cluster of differentiation; huEGFRt, truncated human epidermal growth factor receptor; LTR, long terminal repeat; PBMC, peripheral blood mononuclear cells; scFv, single-chain variable fragment; VH, variable heavy chain; VL, variable light chain.

TRANSCEND CLL 004 Phase 1 Study Design (NCT03331198)

Key Eligibility

- Relapsed/refractory CLL/SLL
- Failed or ineligible for BTKi[a]
- High-risk disease[b]: failed ≥2 prior therapies
- Standard-risk disease: failed ≥3 prior therapies
- ECOG PS 0-1

Dose-Escalation: mTPI-2 Design[c]

28-day DLT period

Primary Objectives

Determine recommended dose

Safety

Exploratory Objectives

Antitumor activity

Pharmacokinetic profile

Dose Level	Dose	Evaluable (N=23)
1	50×10^6 CAR+ T cells	9
2	100×10^6 CAR+ T cells	14

[a]Failure defined as SD or PD as best response, or PD after previous response, or discontinuation due to intolerance (unmanageable toxicity). Ineligibility defined as requirement for full-dose anticoagulation or history of arrhythmia. [b]Complex cytogenetics abnormalities, del(17p), TP53 mutation, or unmutated IGHV. [c]Guo W et al. *Contemp Clin Trials.* 2017;58:23-33.
BTKi, Bruton tyrosine kinase inhibitor; CAR, chimeric antigen receptor; CLL, chronic lymphocytic leukemia; DLT, dose-limiting toxicity; ECOG PS, Eastern Cooperative Oncology Group Performance Status; IGHV, immunoglobulin heavy chain variable region; mTPI, modified toxicity probability interval for dose escalation; PD, progressive disease; SD, stable disease; SLL, small lymphocytic lymphoma.

Baseline Characteristics

Characteristic	All Patients (N=23)	DL1 (n=9)	DL2 (n=14)
Median age, y (range)	66 (49-79)	67 (49-76)	66 (53-79)
Male, n (%)	11 (47.8)	4 (44.4)	7 (50.0)
Bulky disease >5 cm, n (%)[a]	8 (34.8)	3 (33.3)	5 (35.7)
SPD (cm^2), median (range)	24.7 (2-197)	30.0 (2-119)	24.7 (5-197)
LDH (U/L), median (range)	243 (119-634)	227.0 (174-634)	275.0 (119-527)
Received bridging therapy, n (%)	17 (73.9)	5 (55.6)	12 (85.7)
Stage, n (%)			
Rai stage III/IV	15 (65.2)	6 (66.7)	9 (64.3)
Binet stage C	16 (69.6)	7 (77.8)	9 (64.3)
High-risk features (any), n (%)	19 (82.6)	6 (66.7)	13 (92.9)
Del (17p)	8 (34.8)	3 (33.3)	5 (35.7)
TP53 mutation	14 (60.9)	4 (44.4)	10 (71.4)
Complex karyotype[b]	11 (47.8)	5 (55.6)	6 (42.9)
Prior lines of therapy, median (range)	5 (2-11)	5.0 (3-8)	5.0 (2-11)
Prior ibrutinib, n (%)	23 (100)	9 (100)	14 (100)
Ibrutinib relapse/refractory, n (%)	21 (91.3)	9 (100)	12 (85.7)
Ibrutinib progression and prior venetoclax,[c] n (%)	13 (56.5)	5 (55.6)	8 (57.1)

[a]Bulky disease defined as at least one lesion longest diameter >5 cm. [b]At least 3 chromosomal aberrations.[c]12 patients progressed on venetoclax; one patient had best response of SD after 3 months of treatment.
DL, dose level; LDH, lactate dehydrogenase; SD, stable disease; SPD, sum of the product of diameters.

TEAEs of Special Interest

	All Patients (N=23)	DL1 (n=9)	DL2 (n=14)
CRS—any grade, n (%)	17 (73.9)	7 (77.8)	10 (71.4)
Median time to first onset, day (range)	4 (1-10)	6 (1-9)	3.5 (1-10)
Median duration, day (range)	5 (2-30)	5 (3-30)	5.5 (2-27)
Grade 3, n (%)	2 (8.7)	0	2 (14.3)
NE[a]—any grade, n (%)	9 (39.1)	2 (22.2)	7 (50.0)
Median time to first onset, day (range)	4.0 (2-21)	16 (11-21)	4 (2-11)
Median duration, day (range)	21.0 (6-169)	8.5 (6-11)	38 (9-169)
Grade ≥3,[b] n (%)	5 (21.7)	2 (22.2)	3 (21.4)
Any, n (%)			
CRS or NE[a]	18 (78.3)	7 (77.8)	11 (78.6)
CRS and NE[a]	8 (34.8)	2 (22.2)	6 (42.9)
Tocilizumab and/or steroid use	17 (73.9)	5 (55.6)	12 (85.7)
Tumor lysis syndrome—any grade, n (%)	4 (17.4)	1 (11.1)	3 (21.4)
Grade ≥3, n (%)	4 (17.4)	1 (11.1)	3 (21.4)
Cardiac events, n (%)	1 (4.3)	1 (11.1)	0

- **No grade 5 TEAEs of special interest occurred**

[a]NE are treatment-related events defined by the investigator. [b]NE are not mutually exclusive; encephalopathy n=3; aphasia n=1; confusional state n=1; muscular weakness n=1; somnolence n=1.
CRS, cytokine release syndrome; DL, dose level; NE, neurological events; TEAE, treatment-emergent adverse event.

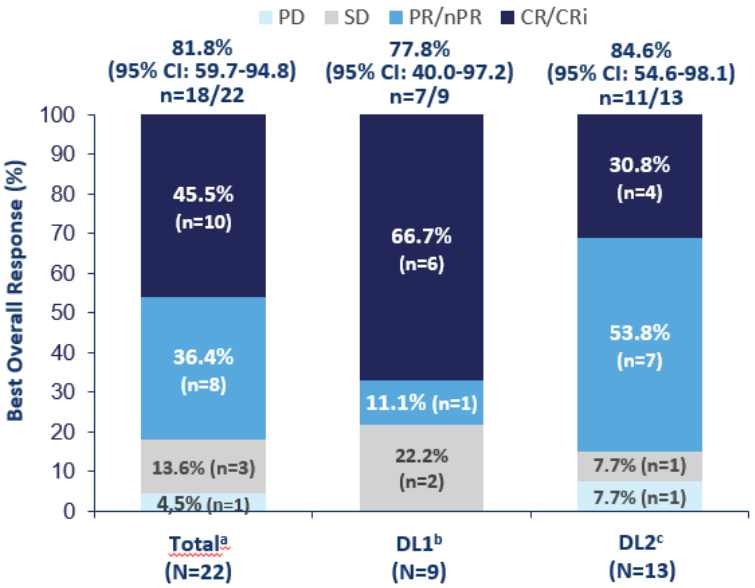
Serious TEAEs Reported in >1 Patient

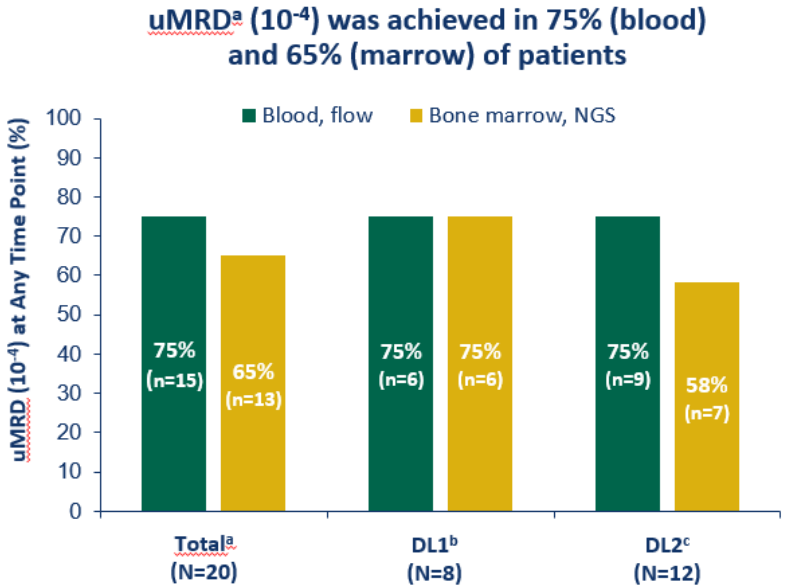
	All Patients (N=23)	DL1 (n=9)	DL2 (n=14)
Serious TEAEs of any grade, n (%)	**13 (56.5)**	**4 (44.4)**	**9 (64.3)**
Cytokine release syndrome	6 (26.1)	1 (11.1)	5 (35.7)
Pyrexia	4 (17.4)	3 (33.3)	1 (7.1)
Encephalopathy	3 (13.0)	1 (11.1)	2 (14.3)
Febrile neutropenia	3 (13.0)	0	3 (21.4)
Pneumonia	3 (13.0)	2 (22.2)	1 (7.1)
Acute kidney injury	2 (8.7)	2 (22.2)	0
Aphasia	2 (8.7)	1 (11.1)	1 (7.1)
Lung infection	2 (8.7)	1 (11.1)	1 (7.1)
Tumor lysis syndrome	2 (8.7)	0	2 (14.3)

- **There were 6 on-study deaths**
  - **Disease progression, n=4**
  - **Grade 5 respiratory failure (DL1), n=1 (unrelated to liso-cel treatment)**
  - **Unknown reason, n=1**

DL, dose level; TEAE, treatment-emergent adverse event.

Best Overall Response and Undetectable MRD





Median study follow-up, 9 months | Minimum follow-up, 1 month

[a]Evaluable for response defined as having a pretreatment assessment and at least one postbaseline assessment; evaluable for MRD was defined as patients with detectable MRD at baseline. One patient was not evaluable for response. [b]50×10^6 CAR T+ cells. [c]100×10^6 CAR T+ cells.
CAR, chimeric antigen receptor; CI, confidence interval; CR, complete response; CRi, complete response with incomplete blood count recovery; DL, dose level; MRD, minimal residual disease; NGS, next-generation sequencing; nPR, nodular partial response; PD, progressive disease; PR, partial response; SD, stable disease; uMRD, undetectable minimal residual disease.

Conclusions

Liso-cel demonstrated manageable toxicity and promising clinical activity in a heavily pretreated patient population with high-risk CLL, all of whom had received prior ibrutinib, with over half also having received prior venetoclax

- Adverse events were manageable at both dose levels
  - Low rates of grade 3 CRS (8.7%) and grade 3 or 4 NE (21.7%)
- At a median follow up of 9 months, liso-cel treatment resulted in a high proportion of durable responses, including complete responses, with a high best ORR of 82% and CR/CRi rate of 46%

Clinical responses are rapid, improve over time, are deep and durable

- The majority of responses (68%) and uMRD (60%) were achieved by Day 30
- 27% of patients showed deepening responses over time
- Durable objective responses (67%) and uMRD (64%) are maintained at 6 months post-dose
- 83% (5/6) of patients with CR at 6 months remain in CR, including 3 patients who maintain CR beyond 12 months

These findings justify the conduct of the phase 2 portion of the study, which is currently enrolling at dose level 2 (100×10^6 CAR+ T cells)

- The phase 1 portion continues to enroll a separate cohort of patients treated with liso-cel in combination with ibrutinib

CAR, chimeric antigen receptor; CLL, chronic lymphocytic leukemia; CR, complete response; CRi, complete response with incomplete blood count recovery; CRS, cytokine release syndrome; MRD, minimal residual disease; NE, neurological events; ORR, overall response rate; uMRD4, undetectable minimal residual disease sensitivity 10^{-4}.

Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT 15-ICML 18.–22. Juni 2019

Die Kurzpräsentationen sind online unter

www.lymphome.de/15-icml

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Klinik I für Innere Medizin • Uniklinik Köln

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