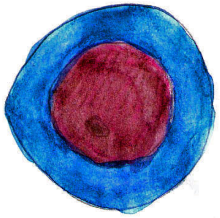
CLL

Michael Hallek
Universität zu Köln



DEUTSCHE STUDIENGRUPPE

CECAD COLOGNE Excellent in Aging Research – Exzellent in Alternsforschung

CIO Center for Integrated Oncology Aachen Bonn Cologne Duesseldorf

Disclosure

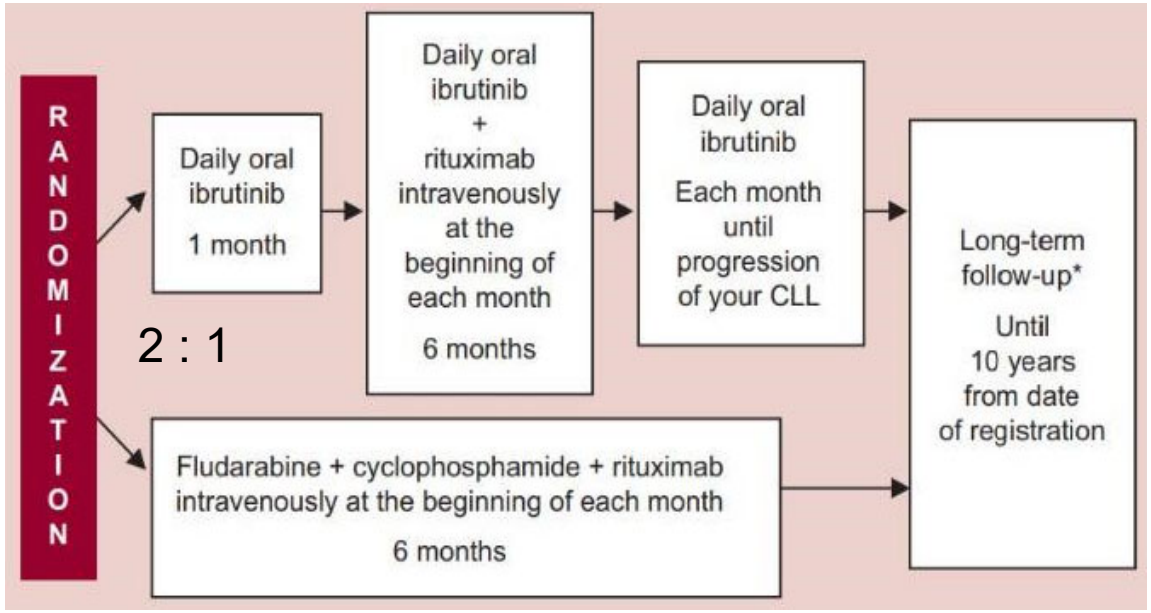
- Research support: Roche, Gilead, Mundipharma, Janssen, Celgene, Pharmacyclics, Abbvie

- Honoraria (speaker's bureau and/or advisory board): Roche, Gilead, Mundipharma, Janssen, Celgene, Pharmacyclics, Abbvie

E1912 STUDIE UPDATE: ERSTLINIE BEI FITTEN PATIENTEN – OHNE *TP53* VERÄNDERUNG

519 Patienten:

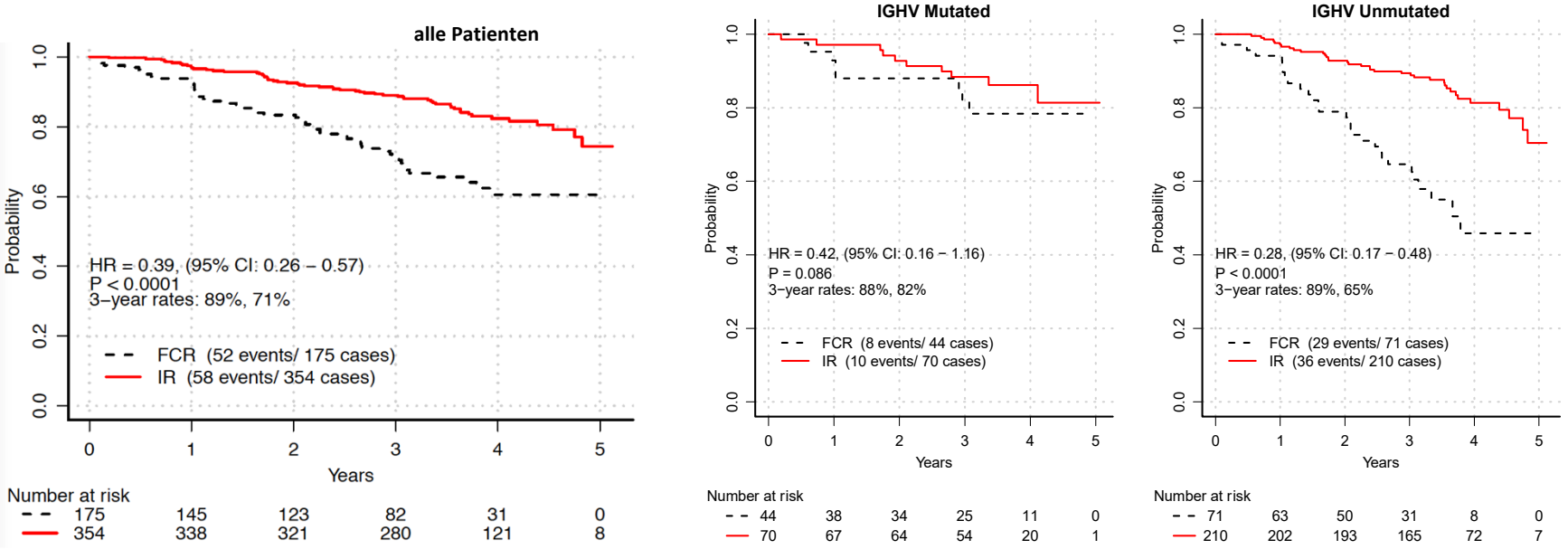
- **unbehandelt**
- **≤ 70 Jahre**
- **behandlungsbedürftig**
- **fit für FCR-Therapie**
- **keine del(17p) (FISH)**
- **keine Grad 3/4 Herzinsuffizienz**
- **Kein Warfarin/ andere Vitamin K-Antagonisten**



Shanafelt T. et al., Abstract 33

E1912-STUDIE: ERSTLINIE BEI FITTEN PATIENTEN

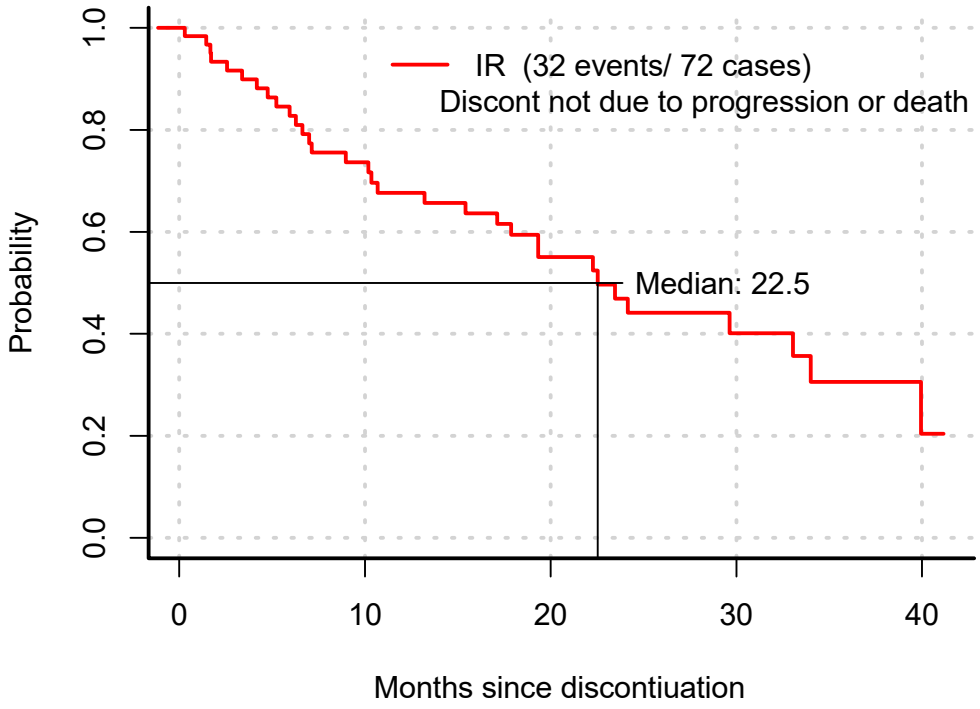
PFS nach 45 Monaten Beobachtung



Shanafelt T. et al., Abstract 33

E1912-STUDIE: ERSTLINIE BEI FITTEN PATIENTEN

PFS für Patienten, die Ibrutinib aufgrund von NW beendeten (20% der Patienten)



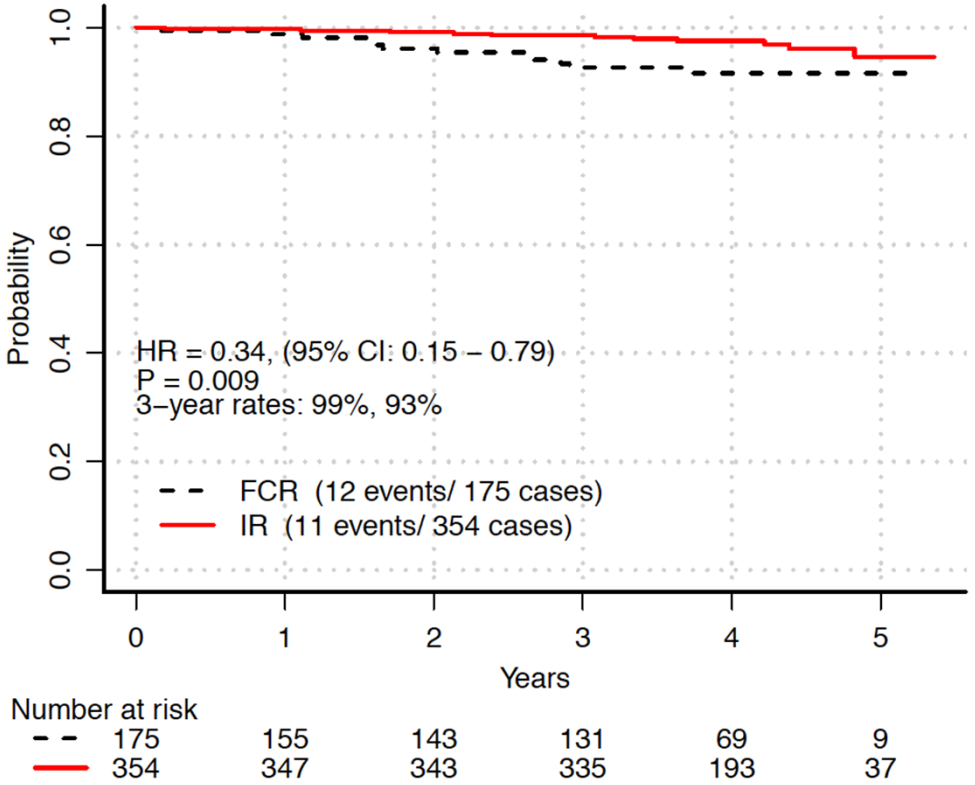
N=72

Median time of therapy 15.1 months

Shanafelt T. et al., Abstract 33

E1912-STUDIE:

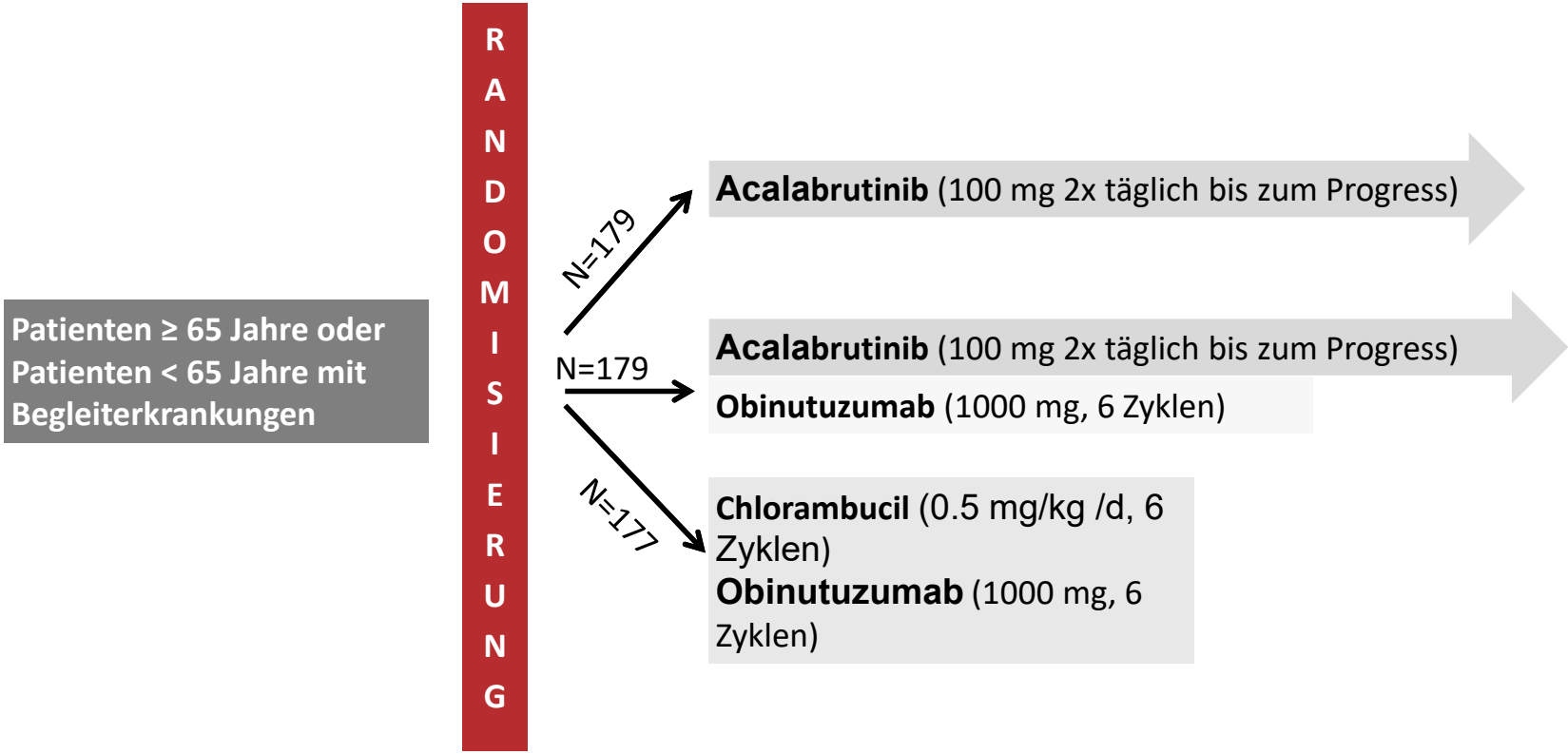
Update Überleben



Shanafelt T. et al., Abstract 33

ELEVATE-STUDIE: ERSTLINIE UNFITTE PATIENTEN

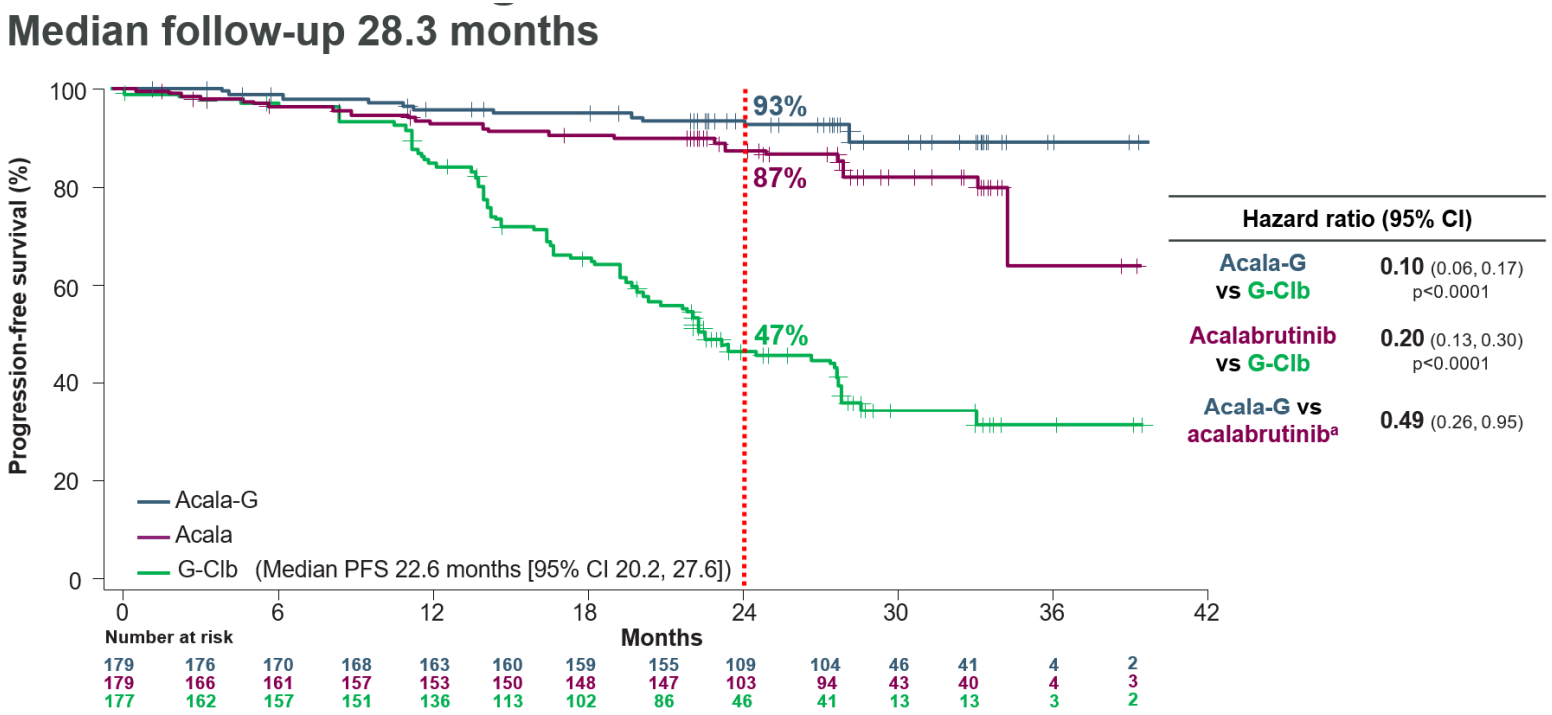
BTK Inhibitor Acalabrutinib



Sharman J. et al., Abstract 31

ELEVATE-STUDIE: ERSTLINIE UNFITTE PATIENTEN

PFS



Kaplan-Meier estimates performed by IRC and all analyses for the intention-to-treat population. No. of events: Acala-G, 14 (7.8%); Acala, 26 (14.5%); G-Clb, 93 (52.5%)
[a]*Post hoc* analysis.
Richter's transformation occurred in: Acala-G n=1, Acala n=5, G-Clb n=1

Sharman J. et al., Abstract 31

ELEVATE-STUDIE: ERSTLINIE UNFITTE PATIENTEN

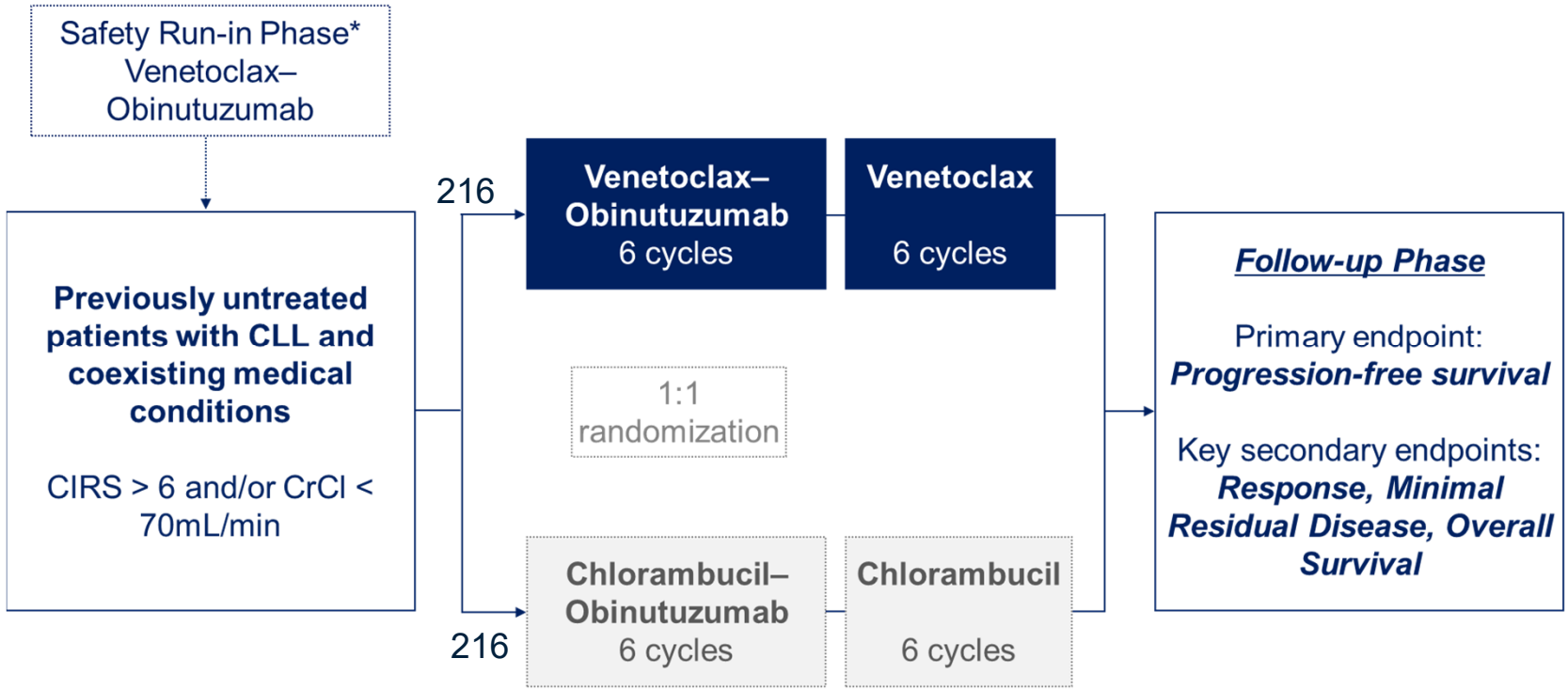
Nebenwirkungen von speziellem Interesse

AEs, n (%)	Acala-G N=178		Acalabrutinib N=179		G-Clb N=169	
	Any	Grade ≥3	Any	Grade ≥3	Any	Grade ≥3
Atrial fibrillation	6 (3.4)	1 (0.6)	7 (3.9)	0	1 (0.6)	0
Hypertension	13 (7.3)	5 (2.8)	8 (4.5)	4 (2.2)	6 (3.6)	5 (3.0)
Bleeding	76 (42.7)	3 (1.7)	70 (39.1)	3 (1.7)	20 (11.8)	0
Major bleeding[a]	5 (2.8)[b]	3 (1.7)	3 (1.7)[c]	3 (1.7)	2 (1.2)[d]	0
Infections	123 (69.1)	37 (20.8)	117 (65.4)	25 (14.0)	74 (43.8)	14 (8.3)
Second primary malignancies, excluding NMSC	10 (5.6)[e]	6 (3.4)	5 (2.8)[f]	2 (1.1)	3 (1.8)[g]	2 (1.2)

Sharman J. et al., Abstract 31

CLL14 STUDIE: ERSTLINIE UNFITTE PATIENTEN

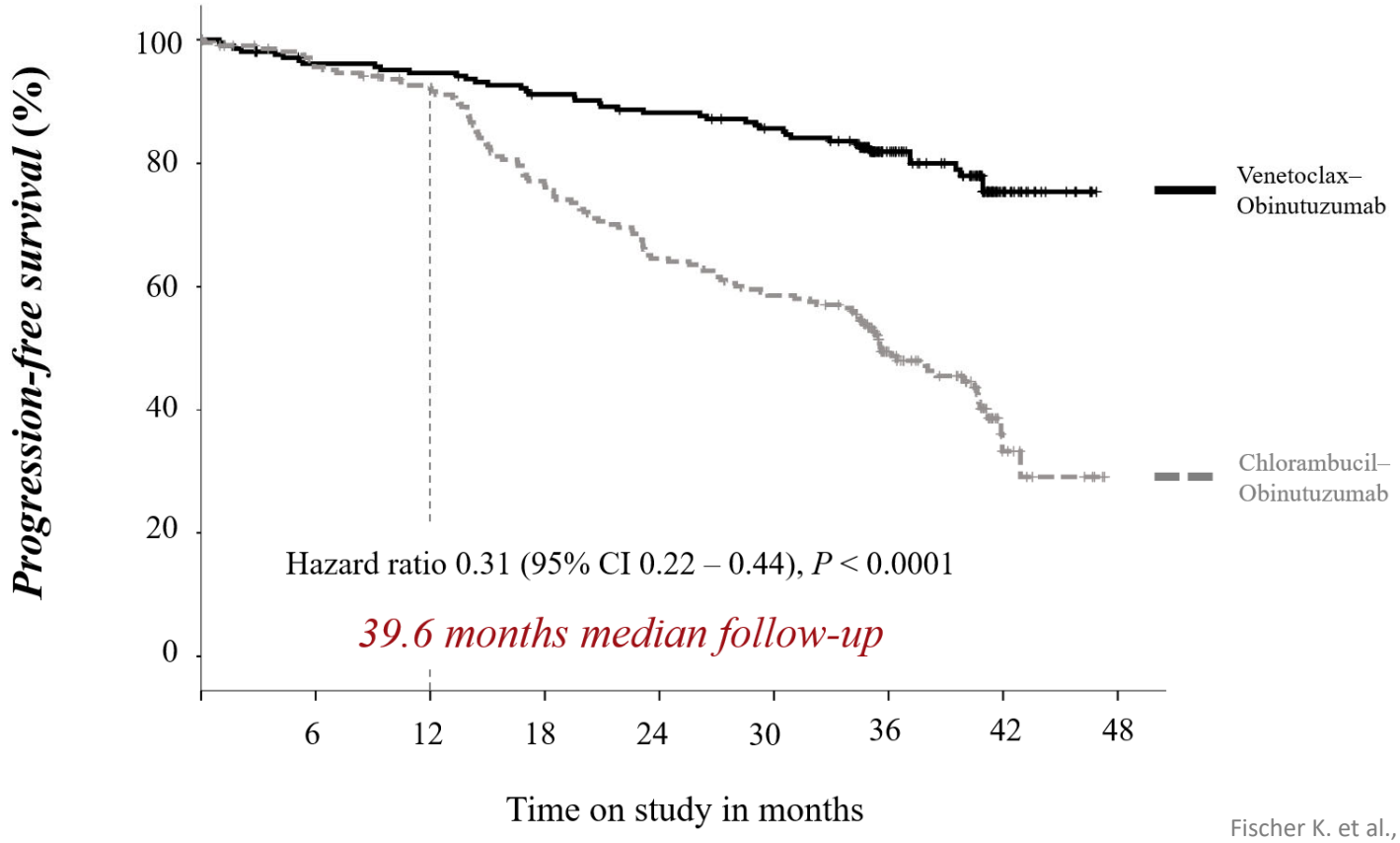
Design



Fischer K. et al., Abstract 36

CLL14 STUDIE: ERSTLINIE UNFITTE PATIENTEN

Update PFS

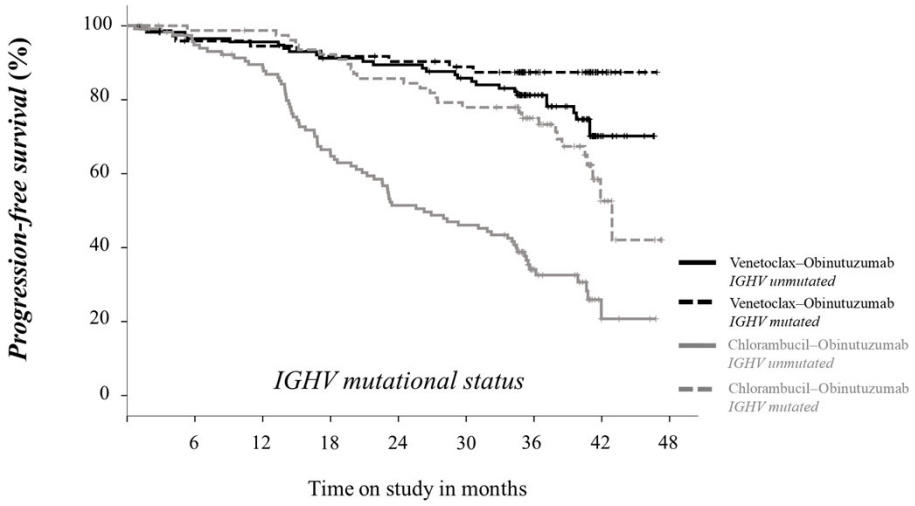


Fischer K. et al., Abstract 36

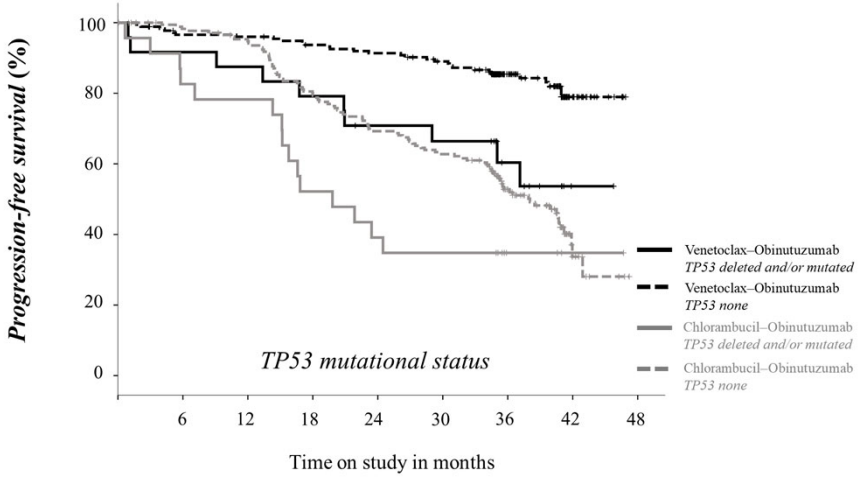
CLL14 STUDIE: ERSTLINIE UNFITTE PATIENTEN

PFS für Subgruppen

Nach IGHV Status



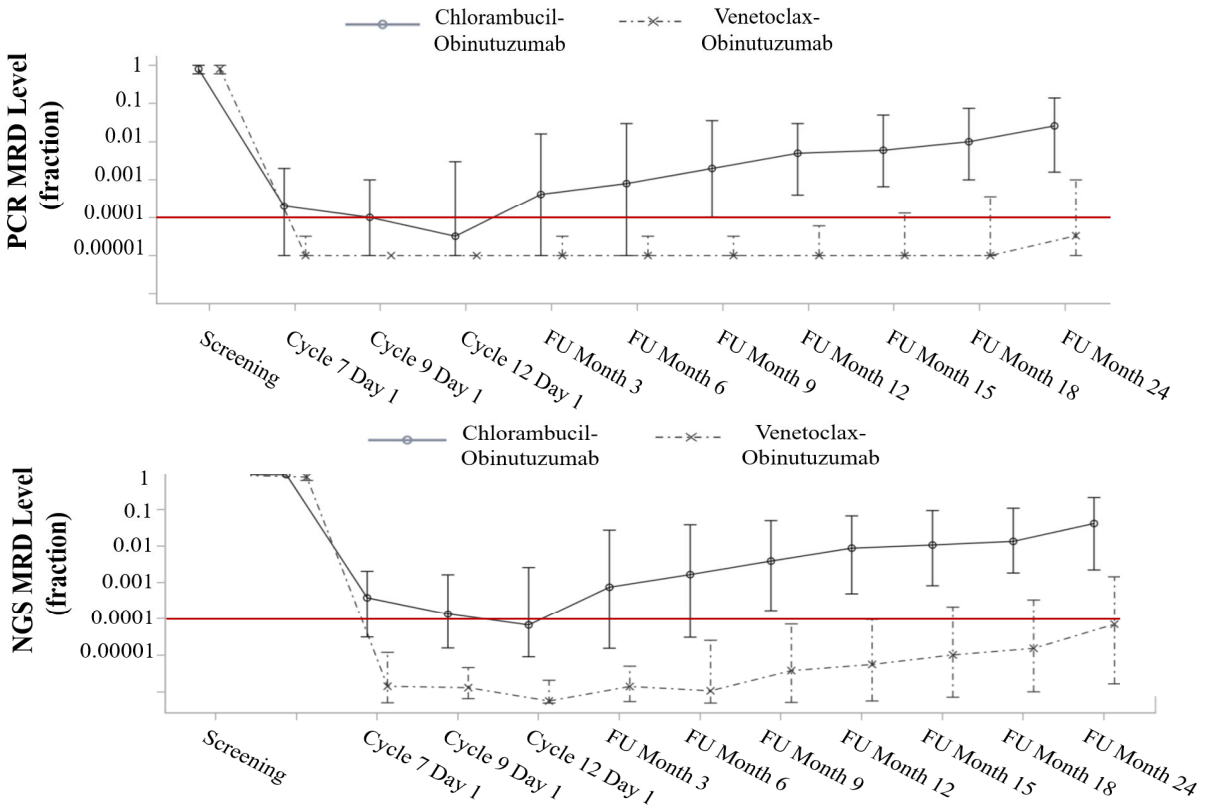
Nach *TP53* Status



Fischer K. et al., Abstract 36

CLL14 STUDIE: ERSTLINIE UNFITTE PATIENTEN

MRD PCR vs NGS



Fischer K. et al., Abstract 36

COMPARISON OF MRD RESULTS OF 4 RECENT TRIALS

First Author	Journal, Year	Name of Trial	Therapeutic intervention		PB MRD 10^{-4} ITT based		Time point
Fischer	NEJM 2019	CLL14	Venetoclax + Obinutuzumab	1L	165/216	76 %	@ 15 months
Cramer	Lancet Oncol 2018	CLL2-BAG	(Benda)→ Venetoclax + Obinutuzumab	1L	31/34	91%	@ 15 months
				RR	24/29	83%	@ 15 months
Jain	NEJM 2019	MDACC	Ibrutinib + Venetoclax	1L	20/80*	25%	@12 months
Hillmen	JCO 2019	CLARITY	Ibrutinib + Venetoclax	RR	28/53	53%	@14 months

*bone marrow

EMA/210087/2020
EMEA/H/C/004106

Venclyxto (*venetoclax*)

An overview of Venclyxto and why it is authorised in the EU

What is Venclyxto and what is it used for?

Venclyxto is a cancer medicine used to treat adults with a blood cancer known as chronic lymphocytic leukaemia (CLL). It is used either in combination with other cancer medicines or on its own.

Venclyxto can be used with obinutuzumab in patients who have not previously been treated for CLL or with rituximab in patients who have received at least one previous treatment. Obinutuzumab and rituximab are immunotherapy medicines (medicines that act through the body's defence system).

It can also be used on its own in:

- patients with particular genetic changes (17p deletion or TP53 mutation) who cannot be treated with medicines known as B-cell receptor pathway inhibitors (ibrutinib and idelalisib) or if these medicines have stopped working.
- patients who do not have these genetic changes, after treatments with chemotherapy combined with immunotherapy as well as a B-cell receptor pathway inhibitor have both not worked.

Venclyxto contains the active substance venetoclax.

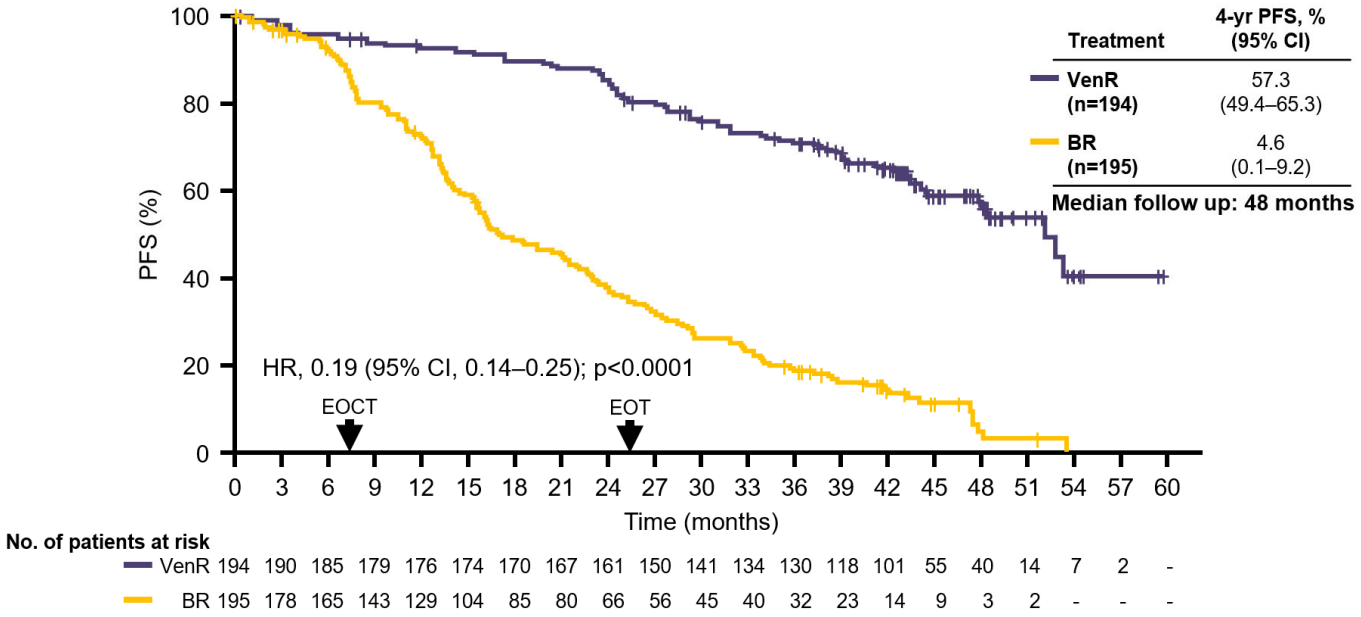
CLL first line treatment (updated April 2020)

Stage	del(17p) or p53mut	Fitness	IGVH	Therapy
Binet A-B, Rai 0-II, inactive disease	Irrelevant	Irrelevant	Irrelevant	None
Active disease or Binet C or Rai III-IV	Yes	Irrelevant	Irrelevant	Ibrutinib/Acalabrutinib or Venetoclax + Obinutuzumab or Idelalisib + Rituximab (if contraindications for ibrutinib)*
	No	Go go	M	FCR (BR above 65 years) or ibrutinib or Venetoclax + Obinutuzumab*
			U	Ibrutinib or FCR (BR above 65 years) or Venetoclax + Obinutuzumab*
		Slow go	M	Venetoclax + Obinutuzumab or Chlorambucil + Obinutuzumab or Ibrutinib/Acalabrutinib*
			U	Venetoclax + Obinutuzumab or Ibrutinib/Acalabrutinib or Chlorambucil + Obinutuzumab*

* Consider and discuss with patient: long-term vs fixed (6-12 m) duration therapy, lack of convincing evidence of overall survival differences, specific side effects of each therapeutic option (myelosuppression, infections, secondary malignancies for CIT; cardiac toxicity, bleeding and autoimmune disease for Ibru; TLS and infections for Ven-Obi; autoimmune disease (diarrhea) and opportunistic infections for Idelalisib).

MURANO-STUDIE: REZIDIVTHERAPIE VEN+R VS BR

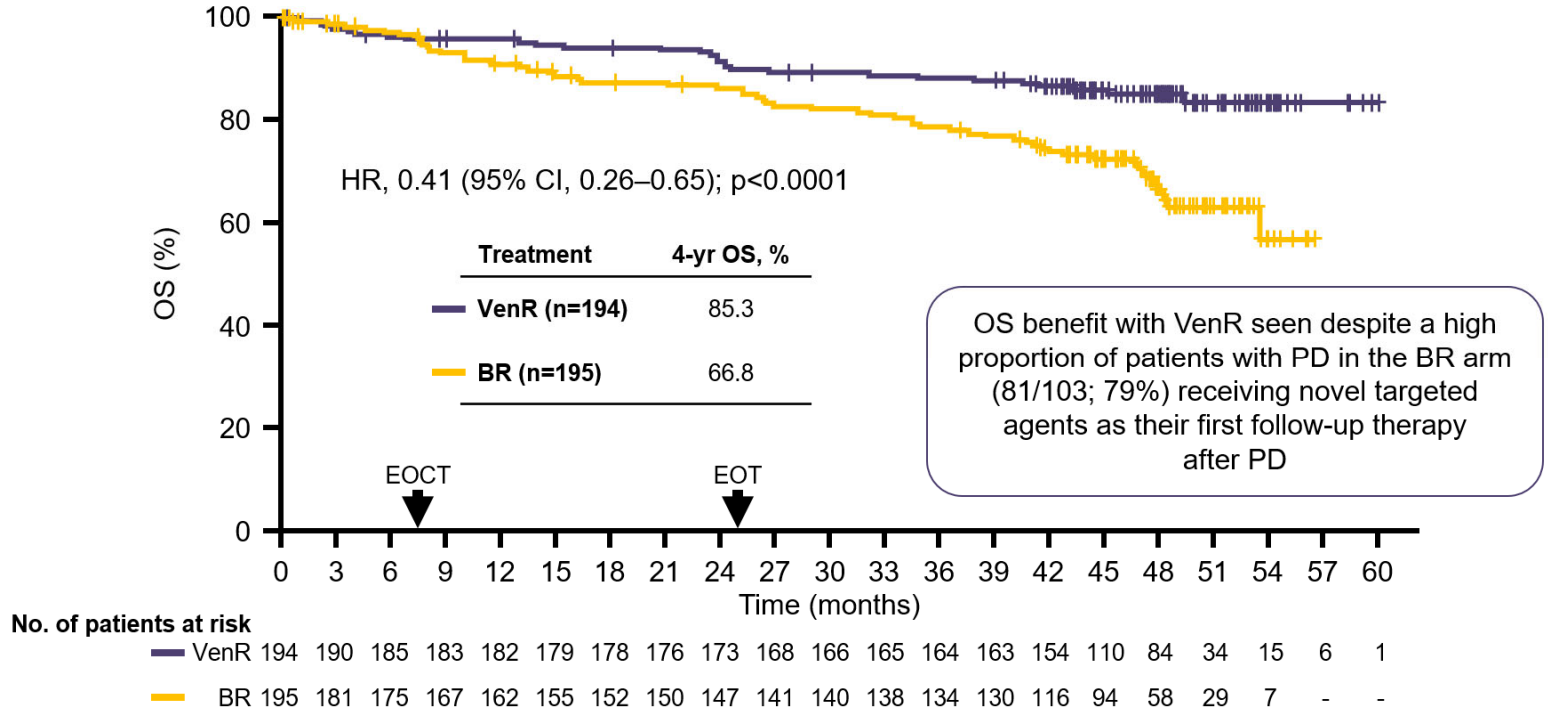
PFS nach 4 Jahren Beobachtung



Seymour J. et al., Abstract 355

MURANO-STUDIE: REZIDIVTHERAPIE VEN+R VS BR

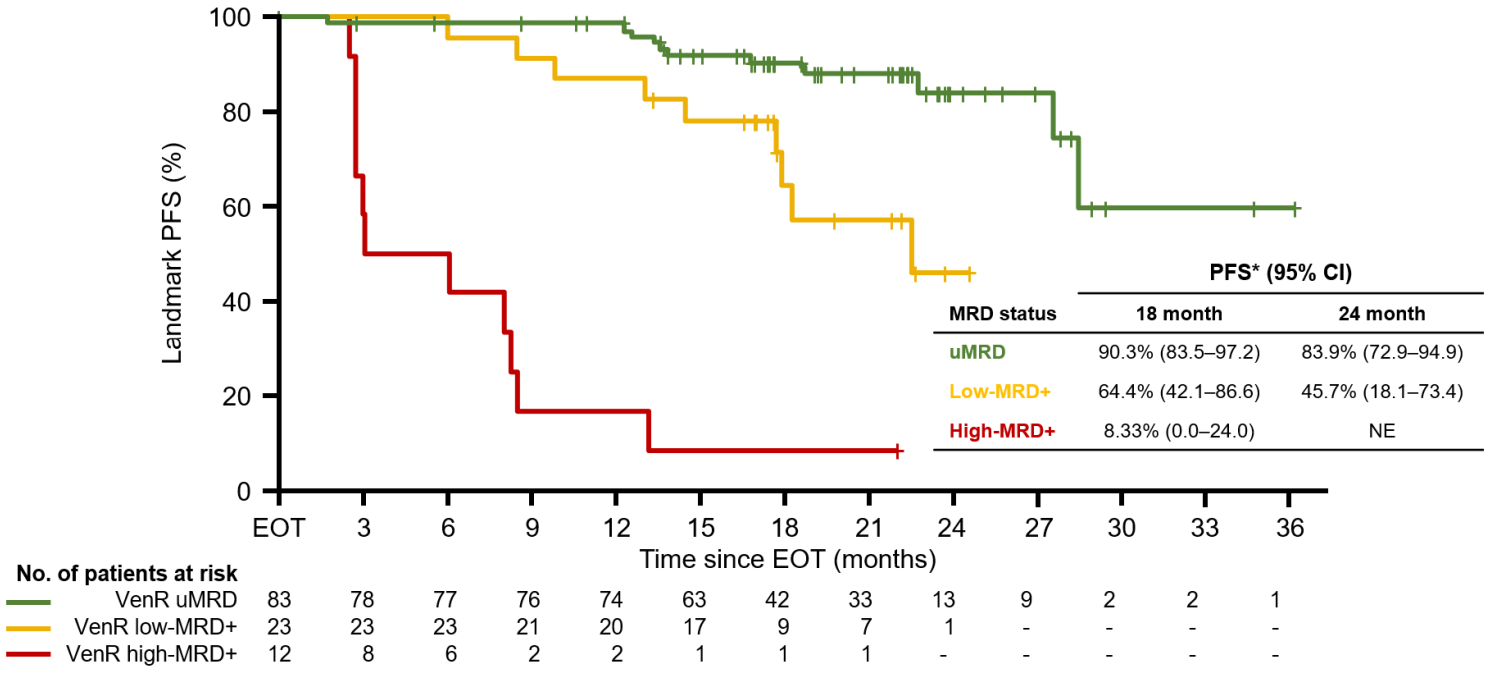
OS nach 4 Jahren Beobachtung



Seymour J. et al., Abstract 355

MURANO-STUDIE: REZIDIVTHERAPIE VEN+R VS BR

PFS nach MRD Status zum Zeitpunkt des Therapieendes



Seymour J. et al., Abstract 355

REGISTER-STUDIE: BTK-INHIBITOR NACH VENETOCLAX

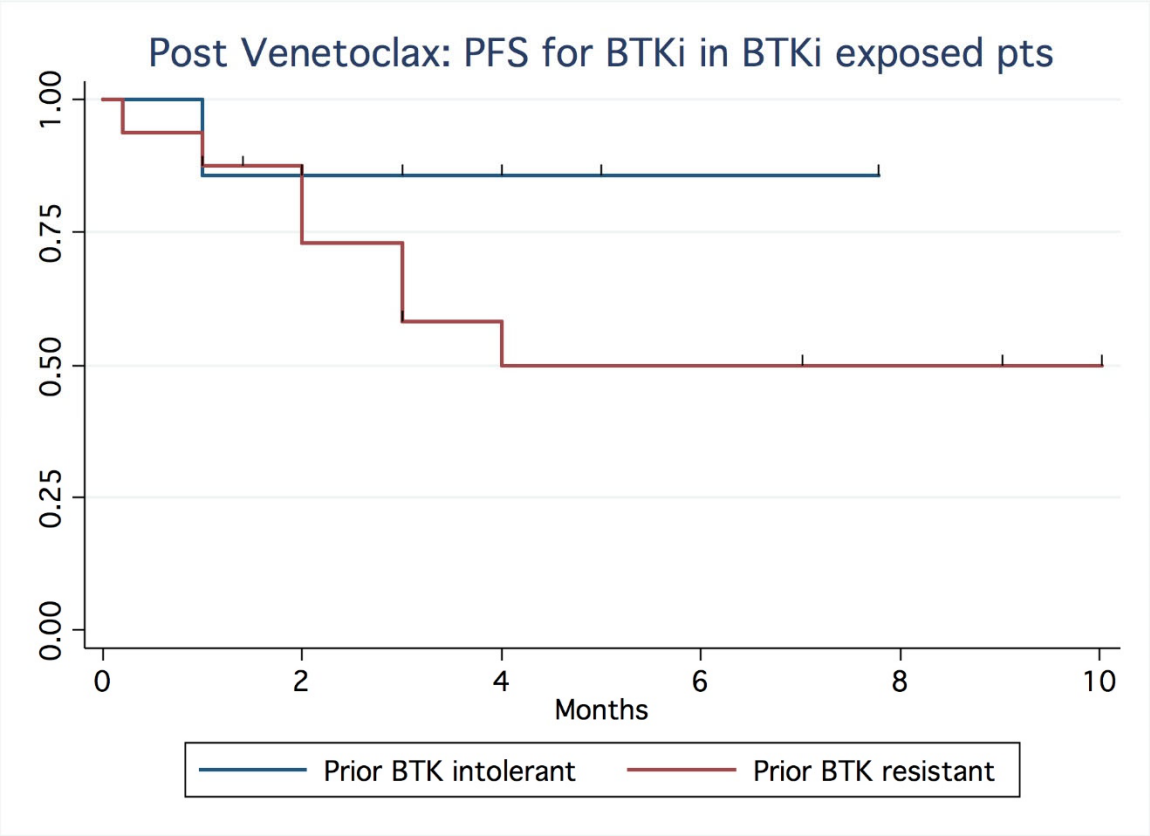
Multizentrische, retrospektive Kohortenstudie an 31 Zentren

326 patients discontinued venetoclax across 31 sites		
Baseline Characteristics	**Results**	**Number with available data**
Age at venetoclax start, median (range)	66 years (38-91)	324
TP53 disruption (del17p or *TP53* mut)	56%	312
Complex karyotype (≥3 abnormalities)	39%	279
NOTCH1 mutated	18%	103
IGHV unmutated	82%	171
Therapy prior to venetoclax		
Lines of therapy, median (range)	3 (0-11)	326
Prior ibrutinib	60%	324
Prior BTKi	61%	324
Prior Idelalisib	19%	324

Mato A. et al., Abstract 355

REGISTER-STUDIE: BTK-INHIBITOR NACH VENETOCLAX

PFS



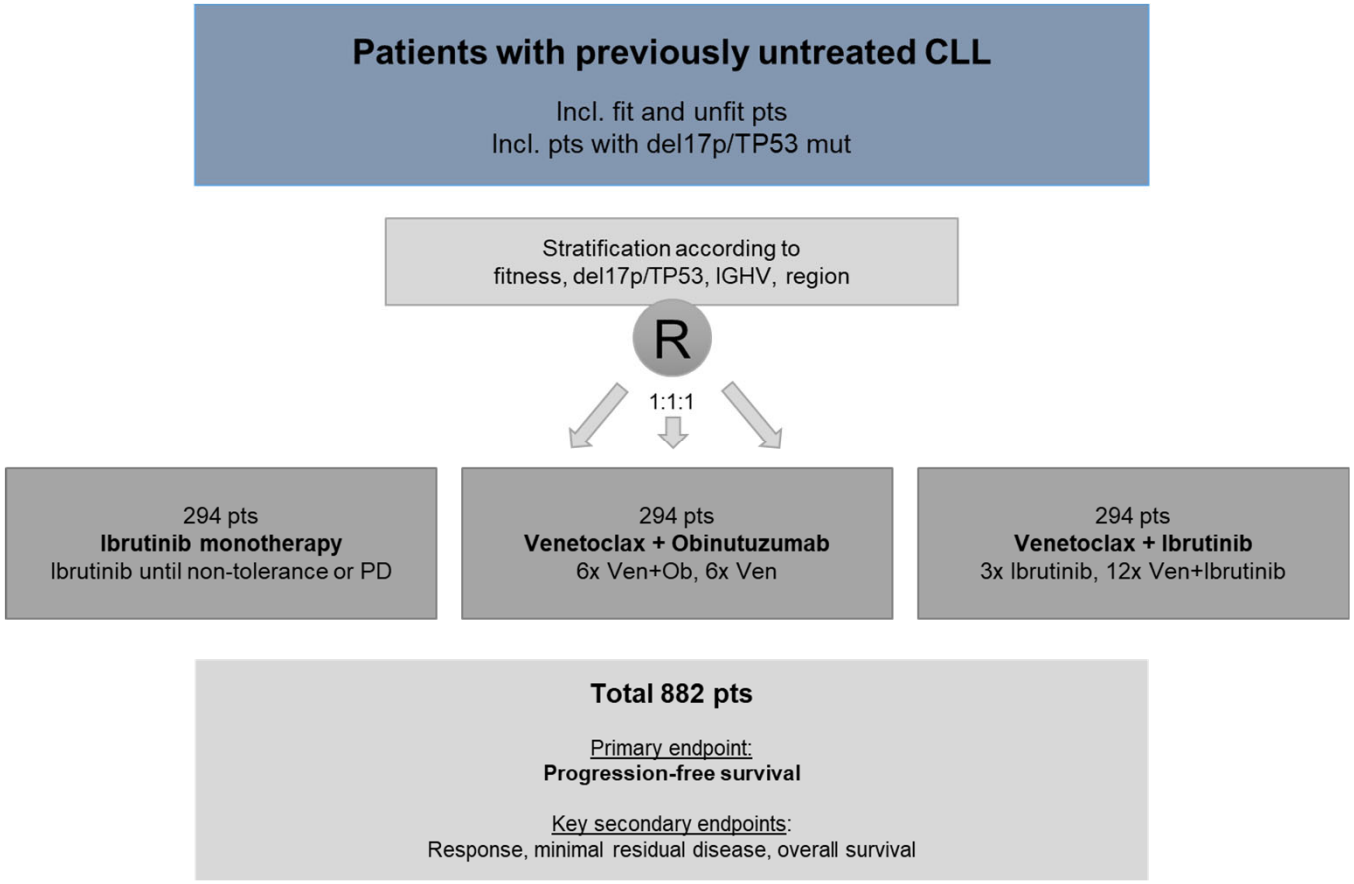
Mato A. et al., Abstract 355

CLL 2L treatment February 2020

Response to 1L Therapy	Fitness	Therapy
Refractory or progress within 3 years	Go go	Change to one of the following options: Ibrutinib, Idelalisib+R, Venetoclax+Rituximab, Chemoimmunotherapy (FCR or BR), Lenalidomide (+R), Alemtuzumab + Dexamethasone. Discuss consolidation with allogeneic SCT.
	Slow go	Change to one of the following options: Ibrutinib, Idelalisib + R, Venetoclax + Rituximab, Alemtuzumab + Dexamethasone, Chemoimmunotherapy (Chlorambucil + Rituximab or Obinutuzumab, BR, FCR-lite), Lenalidomide (+R), high-dose rituximab.
Progress after 3 years	All	Repetition of 1L therapy is possible.

STUDY DESIGN

CLL17



DCLLSG-STUDIEN 2020