Leucemia linfatica cronica

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Disclosures of FR MAURO

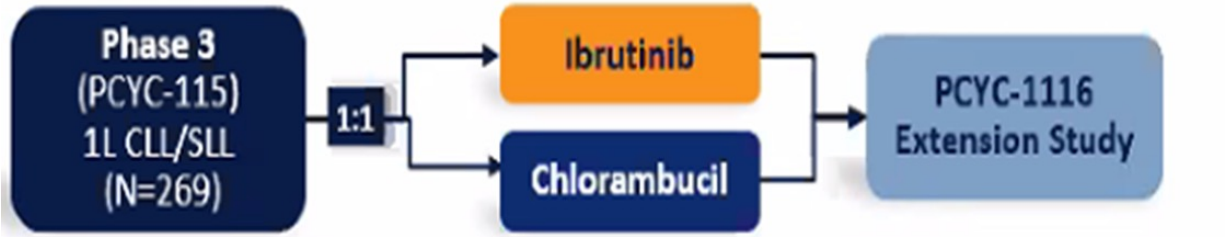
	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Janssen					x	x	
AstraZeneca					x	x	
Abbvie	x				x	x	
Beigene						x	
Takeda	x				x	x	

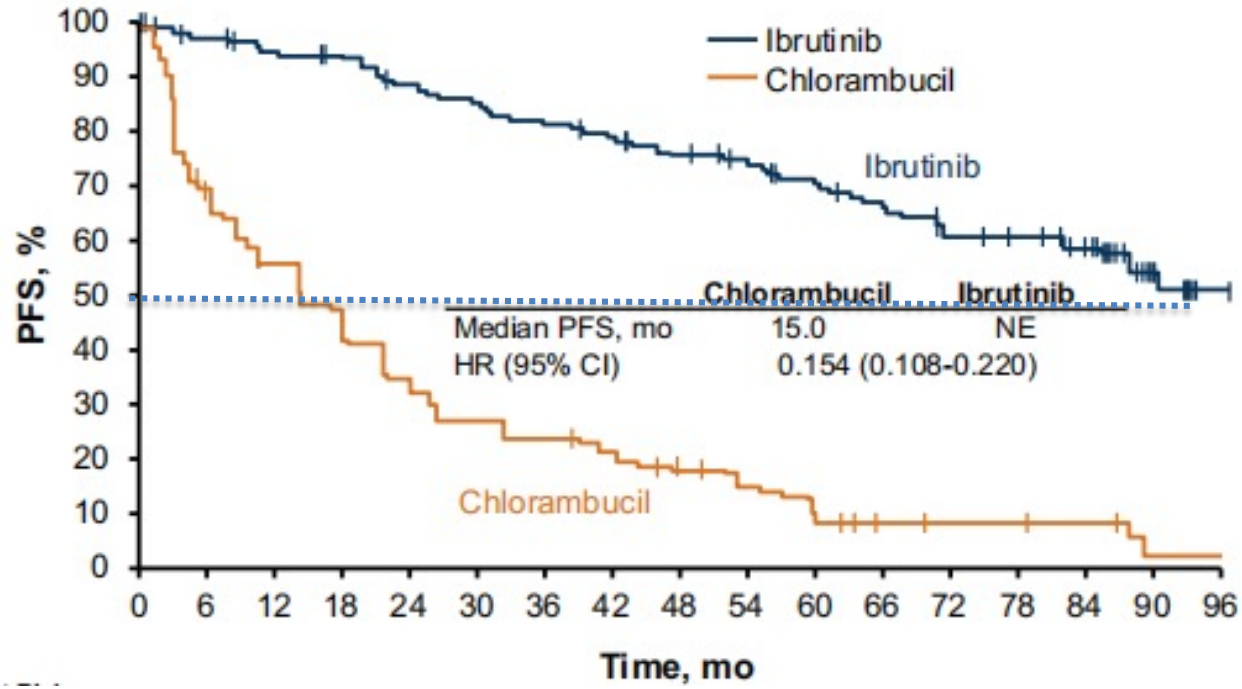
Chronic Lymphocytic Leukemia

HOT NEWS

Ibrutinib	Resonate-2 ECOG E1912
Acalabrutinib	ASCEND ELEVATE TN ELEVATE R/R
Zanubrutinib	SEQUOIA coohort 1- arm B SEQUOIA coohort 2- arm C ALPINE
Pirtobrutinib	BRUIN trial
Venetoclax-obinuruzumab	CLL14
Venetoclax-ibrutinib	CAPTIVATE GLOW CLL13 (Gaia) FLAIR

RESONATE-2: 1L IBRUTINIB-8-YEAR FU





7 year-PFS:

Ibrutinib: 59%
Chlorambucil: 9%

Barr et al. *Blood Adv.* 2022

HOT NEWS IN HEMATOLOGY
Sindromi linfoproliferative ed oltre...

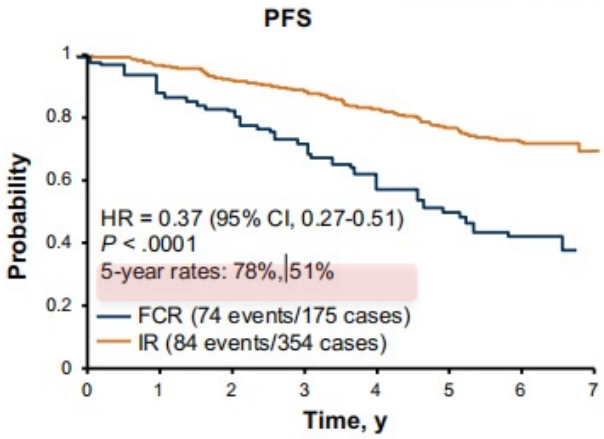
ECOG E1912 TRIAL- IR VS. FCR: >5 YR-FU

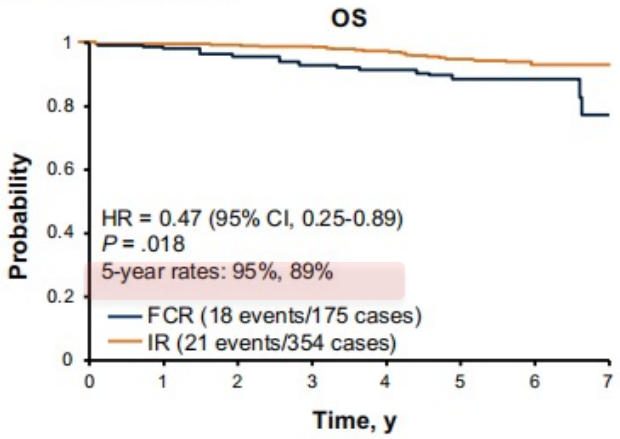
- Phase 3, randomized, open-label trial
- Treatment-naive CLL (N=529)
- ≤70 years of age
- ECOG PS 0-2
- CrCl >40 mL/min
- FCR eligible
- No del(17p) by FISH

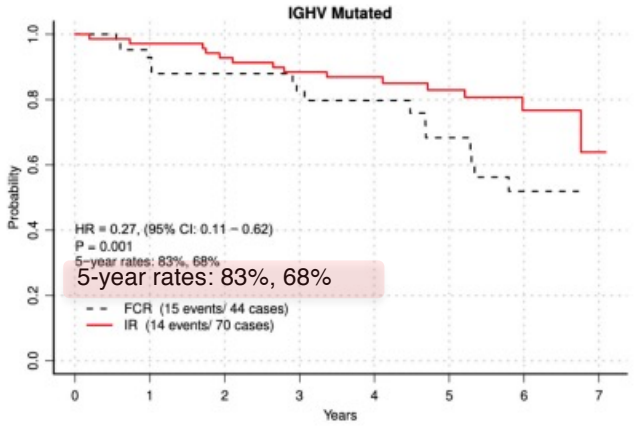
RANDOMIZED 2:1

- Ibrutinib + rituximab (n=354) → Ibrutinib maintenance until PD
- Fludarabine + cyclophosphamide + rituximab (n=175)

Median Follow-Up of 5.8 years[1]





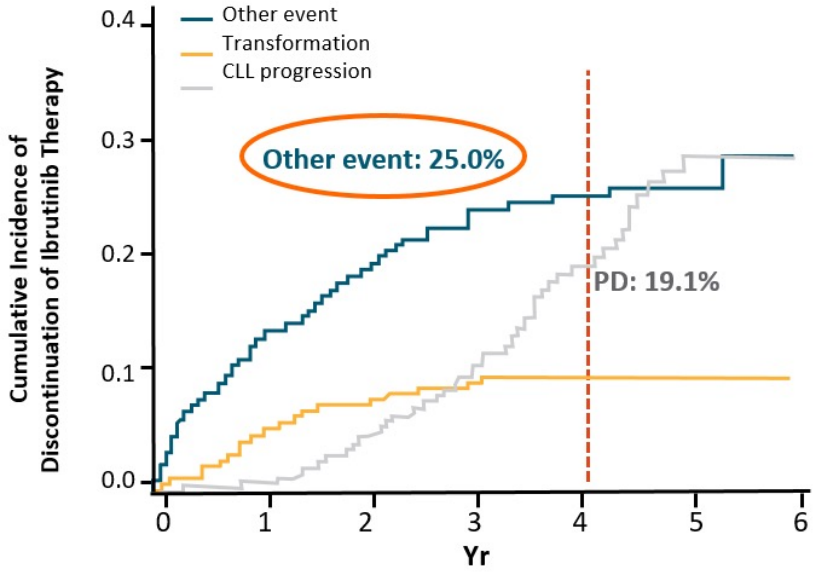


Patients on the IR arm also had superior PFS in both *IGHV* unmutated (HR = 0.27, $P < .001$) and *IGHV* mutated subgroups

Shanafelt TD, et al. Blood 2022

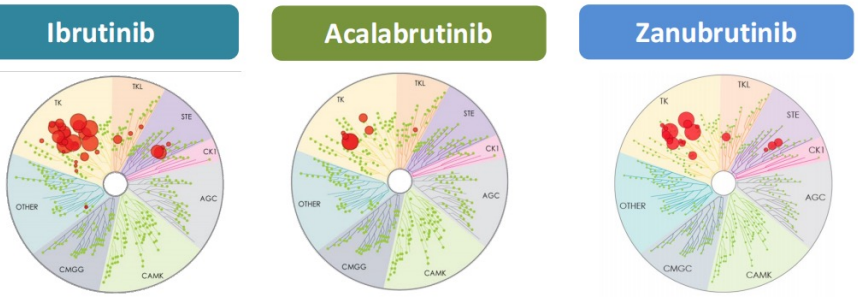
SECOND GENERATION BTK INHIBITORS:EFFECTIVE WITH MORE FAVORABLE TOXICITY PROFILE

Ibrutinib: treatment discontinuations



Woyach et al. *J Clin Oncol*. 2017

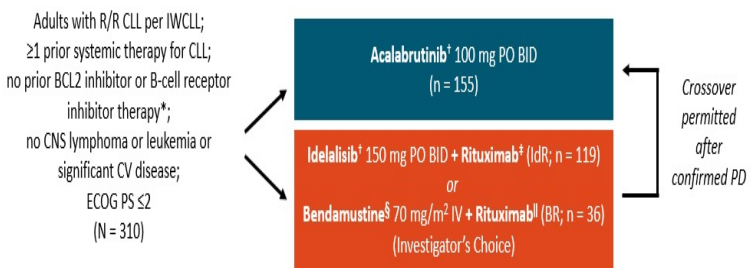
Second generation BTK inhibitors



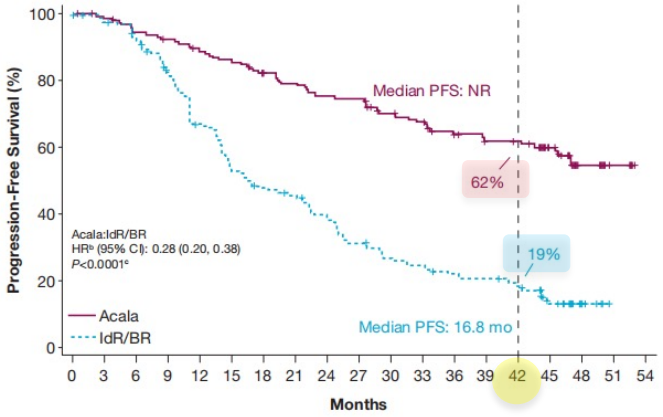
IC_{50}/EC_{50} (nM)

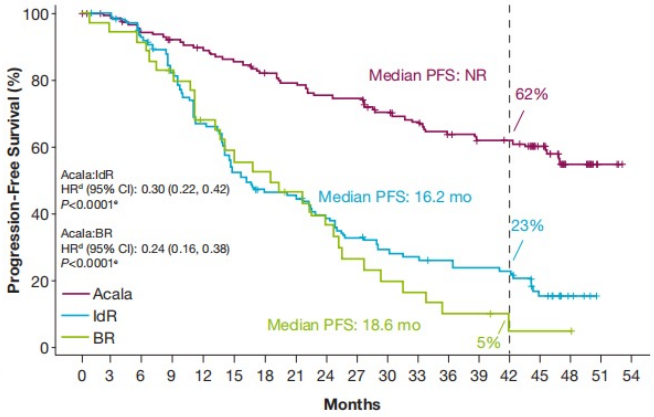
Kinase	Ibrutinib	Acalabrutinib	Zanubrutinib
BTK	1.5	5.1	0.5
TEC	10	126	44
ITK	4.9	> 1000	50
BMX	0.8	46	1.4
EGFR	5.3	> 1000	21
ERBB4	3.4	16	6.9
JAK3	32	> 1000	1377
BLK	0.1	> 1000	2.5

ASCEND TRIAL: ACALABRUTINIB IN R/R PATIENTS WITH CLL: 4 YEAR UPDATED RESULTS

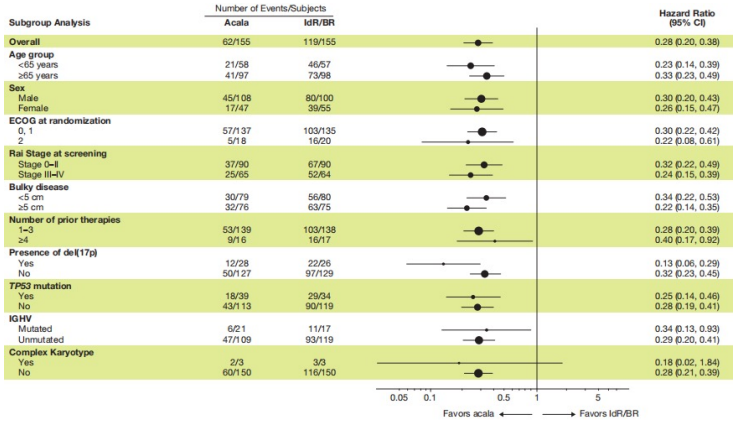


Investigator-Assessed PFS



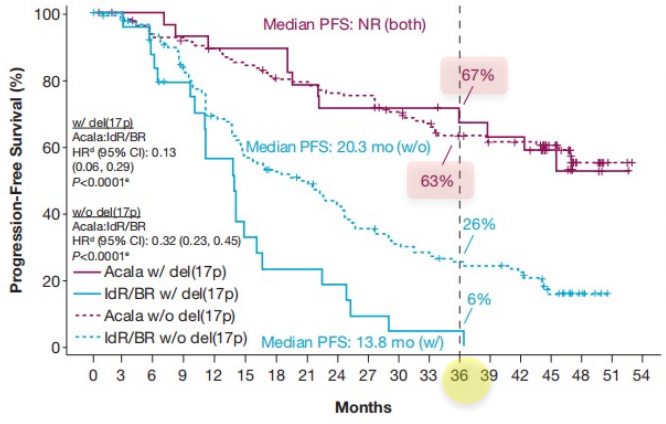


Investigator-Assessed PFS in Patient Subgroups (Acala vs IdR/BR)

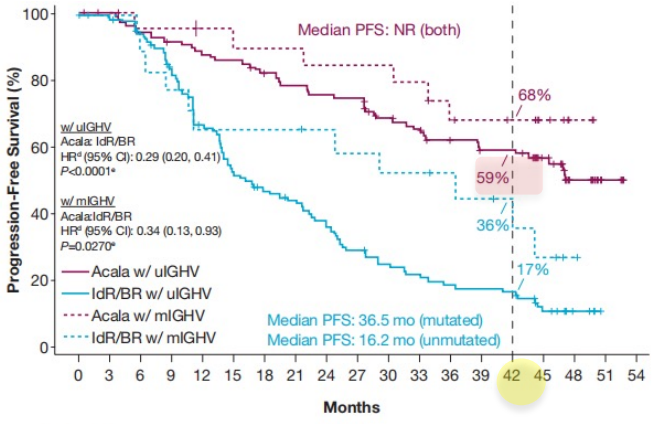


Subgroup Analysis	Number of Events/Subjects Acala	IdR/BR	Hazard Ratio (95% CI)
Overall	62/155	119/155	0.28 (0.20, 0.38)
Age group			
<65 years	21/58	46/57	0.23 (0.14, 0.39)
≥65 years	41/97	73/98	0.33 (0.23, 0.49)
Sex			
Male	45/108	80/100	0.30 (0.20, 0.43)
Female	17/47	39/55	0.26 (0.15, 0.47)
ECOG at randomization			
0, 1	57/137	103/135	0.30 (0.22, 0.42)
2	5/18	16/20	0.22 (0.08, 0.61)
Rai Stage at screening			
Stage 0–II	37/90	67/90	0.32 (0.22, 0.49)
Stage III–IV	25/65	52/64	0.24 (0.15, 0.39)
Bulky disease			
<5 cm	30/79	56/80	0.34 (0.22, 0.53)
≥5 cm	32/76	63/75	0.22 (0.14, 0.35)
Number of prior therapies			
1–3	53/139	103/138	0.28 (0.20, 0.39)
≥4	9/16	16/17	0.40 (0.17, 0.92)
Presence of del(17p)			
Yes	12/28	22/26	0.13 (0.06, 0.29)
No	50/127	97/129	0.32 (0.23, 0.45)
***TP53* mutation**			
Yes	18/39	29/34	0.25 (0.14, 0.46)
No	43/113	90/119	0.28 (0.19, 0.41)
IGHV			
Mutated	6/21	11/17	0.34 (0.13, 0.93)
Unmutated	47/109	93/119	0.29 (0.20, 0.41)
Complex Karyotype			
Yes	2/3	3/3	0.18 (0.02, 1.84)
No	60/150	116/150	0.28 (0.21, 0.39)

Investigator-Assessed PFS by del(17p)

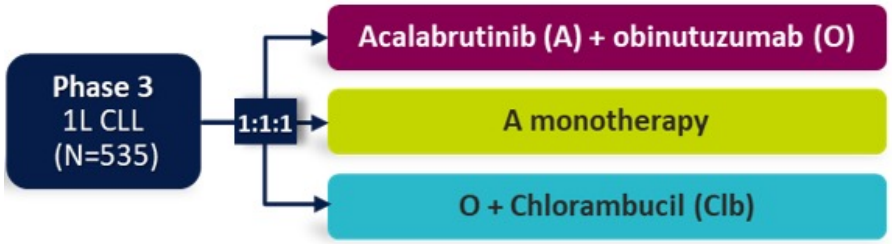


Investigator-Assessed PFS by IGHV



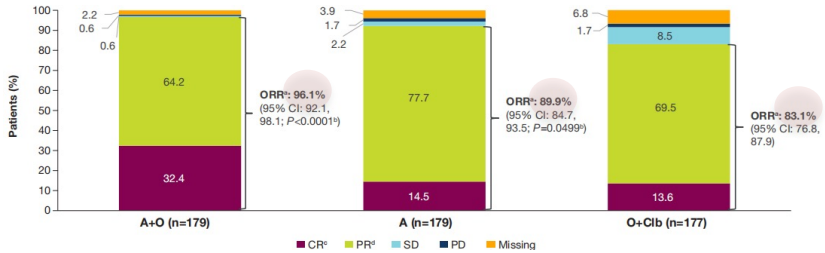
Jurczak et al. ASCO 2022

ELEVATE TN trial: in TN Patients With CLL: 5-year updated results

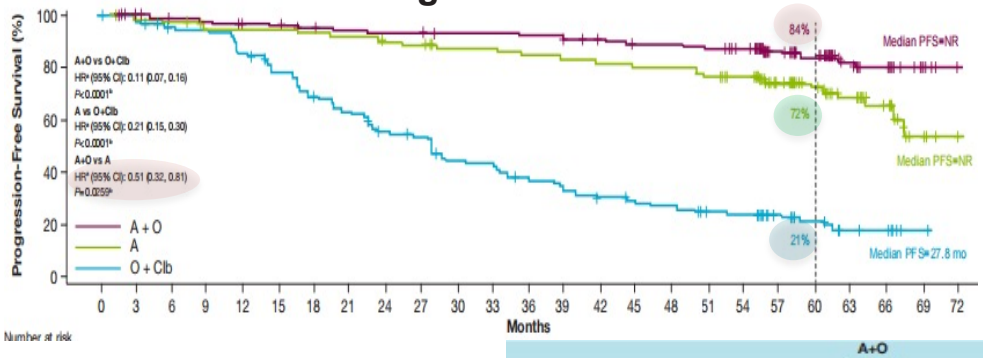


CR increase

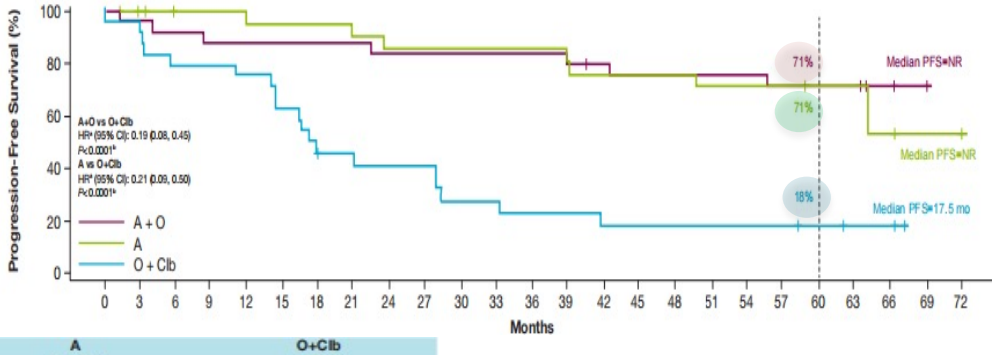
A+O: 24.0%7 , 30.7%8 , and 32.4%
A: 7.8%7 , 11.2%8 , and 14.5%



Investigator-assessed PFS



Investigator-assessed PFS: del(17p)/ mut*TP53*



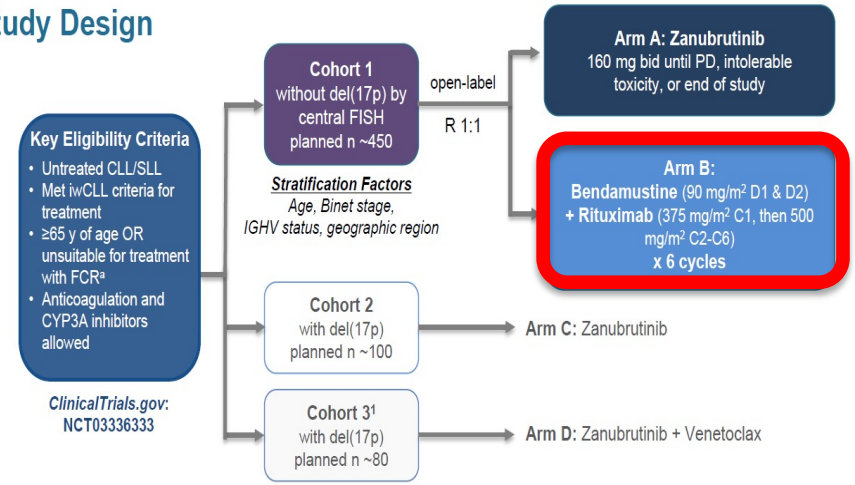
Adverse events of clinical interest

	A+O (n=178)		A (n=179)		O+Clb (n=169)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Cardiac events	43 (24.2)	17 (9.6)	39 (21.8)	18 (10.1)	13 (7.7)	3 (1.8)
Atrial fibrillation	11 (6.2)	2 (1.1)	13 (7.3)	2 (1.1)	1 (0.6)	0
Bleeding	88 (49.4)	8 (4.5)	78 (43.6)	6 (3.4)	20 (11.8)	0
Major bleeding*	12 (6.7)	8 (4.5)	8 (4.5)	6 (3.4)	2 (1.2)	0
Hypertension	17 (9.6)	8 (4.5)	16 (8.9)	7 (3.9)	6 (3.6)	5 (3.0)
Infections	140 (78.7)	50 (28.1)	135 (75.4)	35 (19.6)	75 (44.4)	14 (8.3)
SPMs	31 (17.4)	14 (7.9)	27 (15.1)	7 (3.9)	7 (4.1)	3 (1.8)
SPMs excluding non-melanoma skin	17 (9.6)	12 (6.7)	13 (7.3)	5 (2.8)	3 (1.8)	2 (1.2)

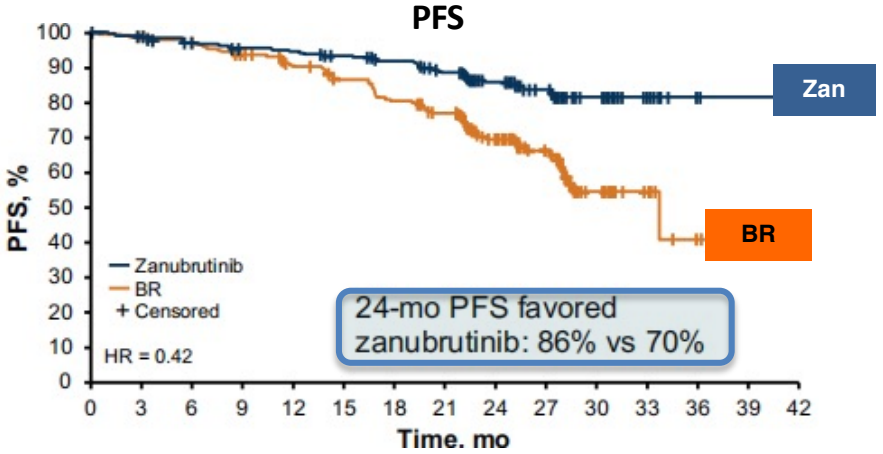
Sharman et al., ASCO 2022

SEQUOIA TRIAL: 1L Zanubrutinib vs BR (Cohort 1-Arm B)

Study Design

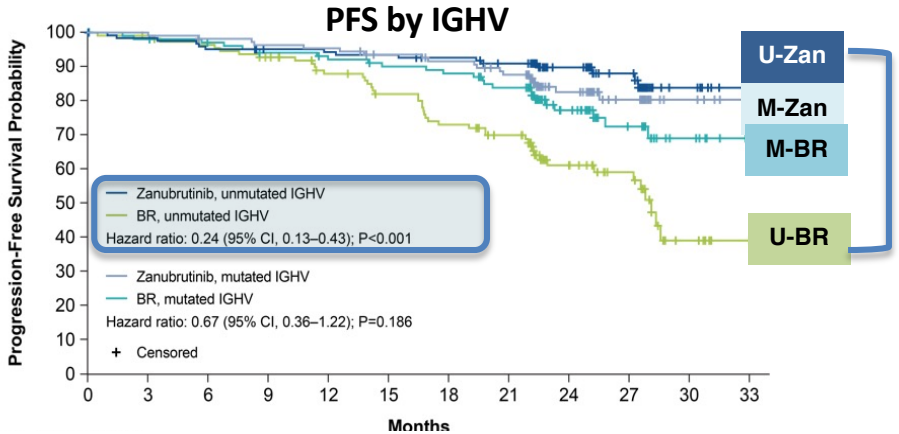


Median follow-up: 26.2 months



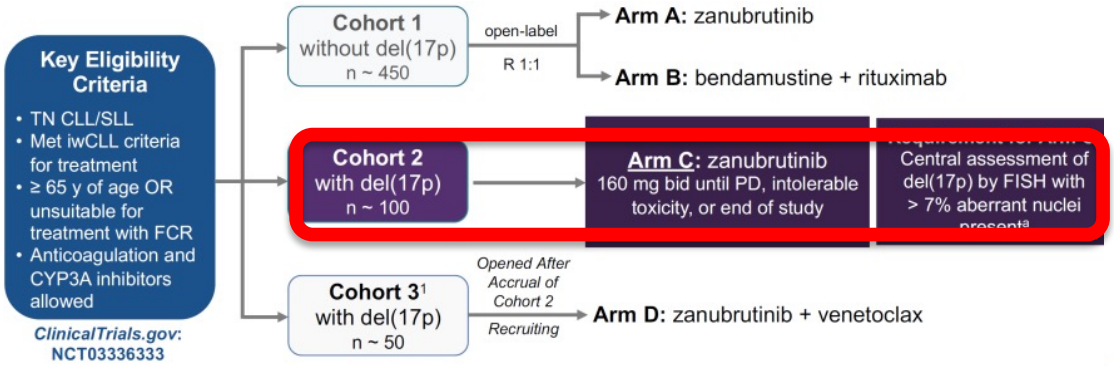
Common Adverse Events (≥12% of Patients in Any Arm)

AE, n (%)	Arm A Zanubrutinib (n=240[a]) Any Grade	Arm A Zanubrutinib (n=240[a]) Grade ≥3	Arm B Bendamustine + Rituxim (n=227[a]) Any Grade	Arm B Bendamustine + Rituxim (n=227[a]) Grade ≥
Contusion	46 (19.2)	0 (0.0)	8 (3.5)	0 (0.0
Upper respiratory tract infection	41 (17.1)	2 (0.8)	27 (11.9)	2 (0.9
Neutropenia[b]	37 (15.4)	27 (11.3)	129 (56.8)	116 (51
Diarrhea	33 (13.8)	0 (0.0)	30 (13.2)	4 (1.8
Arthralgia	32 (13.3)	2 (0.8)	20 (8.8)	1 (0.4
Fatigue	28 (11.7)	3 (1.3)	36 (15.9)	2 (0.9
Rash	26 (10.8)	0 (0.0)	44 (19.4)	6 (2.6
Constipation	24 (10.0)	1 (0.4)	43 (18.9)	0 (0.0
Nausea	24 (10.0)	0 (0.0)	74 (32.6)	3 (1.3
Pyrexia	17 (7.1)	0 (0.0)	60 (26.4)	8 (3.5
Vomiting	17 (7.1)	0 (0.0)	33 (14.5)	3 (1.3
Anemia	11 (4.6)	1 (0.4)	43 (18.9)	4 (1.8
Thrombocytopenia	9 (3.8)	4 (1.7)	31 (13.7)	16 (7.0
Infusion-related reaction[c]	1 (0.4)	0 (0.0)	43 (18.9)	6 (2.6

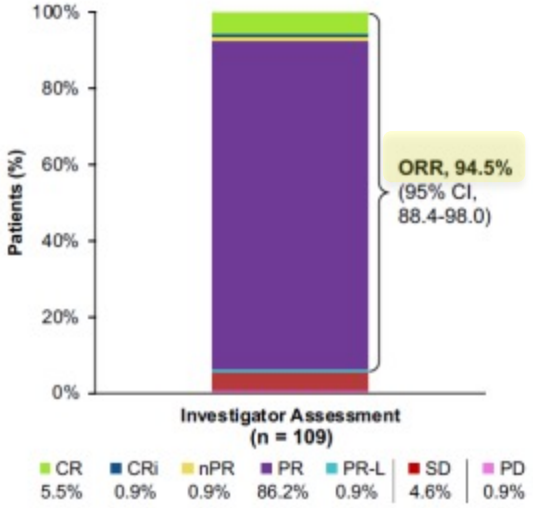


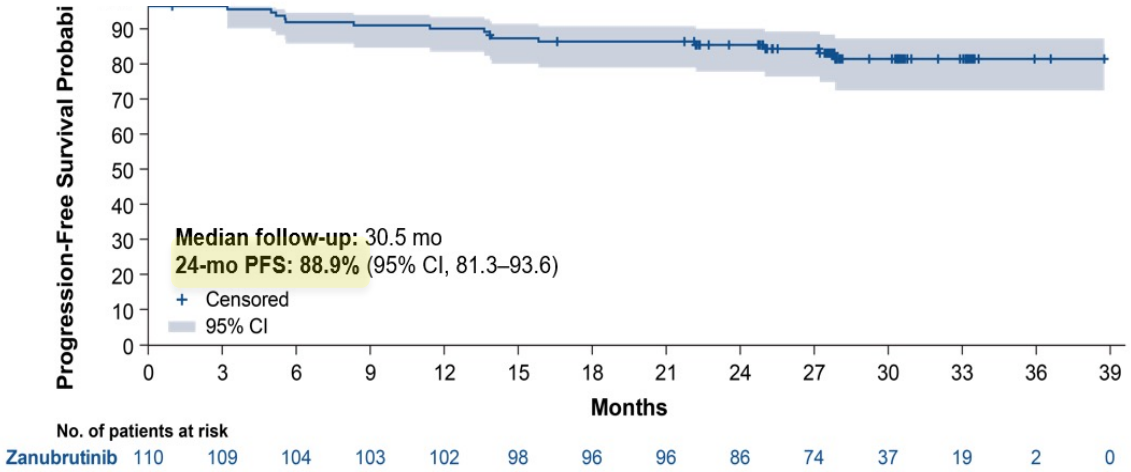
Tam et al., ASH 2021

SEQUOIA TRIAL: 1L Zanubrutinib in patients with del (17p)



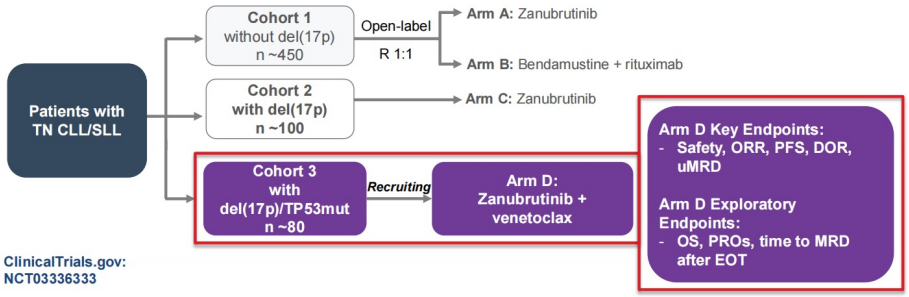
109 TN patients with del(17p) CLL or SLL

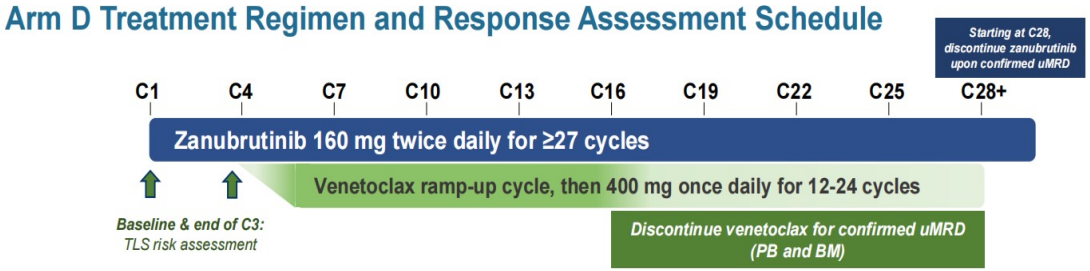




Tam et al.ASH *2021*

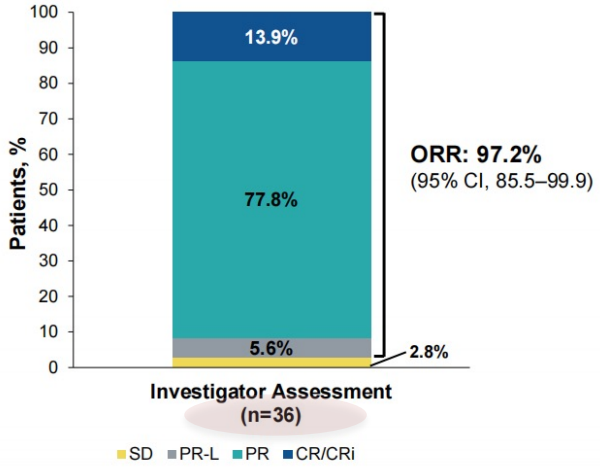
SEQUOIA TRIAL: 1L Zanubrutinib+ Venetoclax in patients with del (17p)

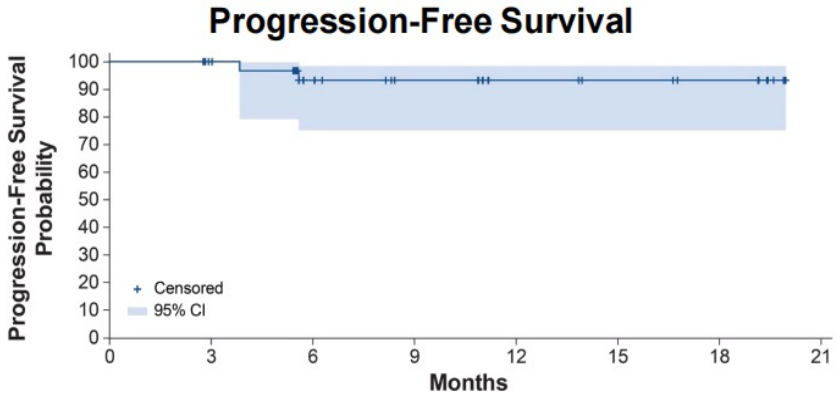




Median Follow-Up: 12.0 Months

	n=49
Disease characteristics	
del(17p) by central lab FISH, n (%)	
Positive	46 (93.9)
Negative (eligible by local lab TP53 mutation)	3 (6.1)
del(17p) percent of abnormal nuclei, median	77.5
del(13q), n (%)	25 (51.0)
del(11q), n (%)	1 (2.0)
Trisomy 12, n (%)	11 (22.4)
Retrospective TP53 mutation,[a] n/N (%)	34/37 (91.9)
IGHV mutational status, n (%)	
Unmutated	43 (87.8)
Mutated	6 (12.2)
Complex karyotype,[b] n/N (%)	
Non-complex (0–2 abnormalities)	4/24 (16.7)
Complex (3 or more abnormalities)	20/24 (83.3)
Complex (5 or more abnormalities)	17/24 (70.8)





Tedeschi et al., ASH 2021

ALPINE TRIAL: Ibrutinib vs Zanubrutinib in Patients With R/R CLL

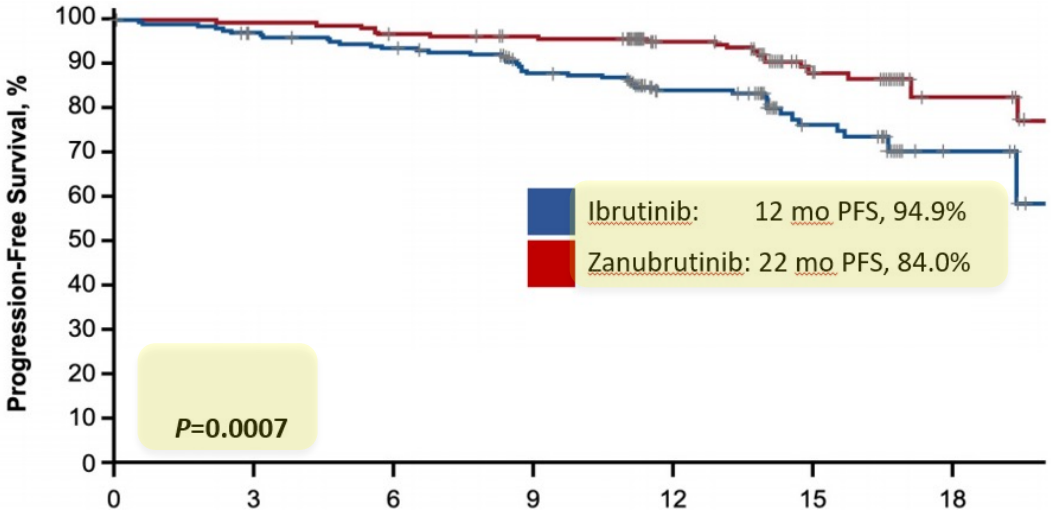
Ongoing randomized, multicenter phase III trial

Patients with CLL requiring treatment
R/R to ≥ 1 previous treatment
ECOG PS 0-2
Adequate organ function
No clinically significant cardiac disease
(planned N = 400)

Ibrutinib 420 mg PO QD

Zanubrutinib 160 mg PO BID

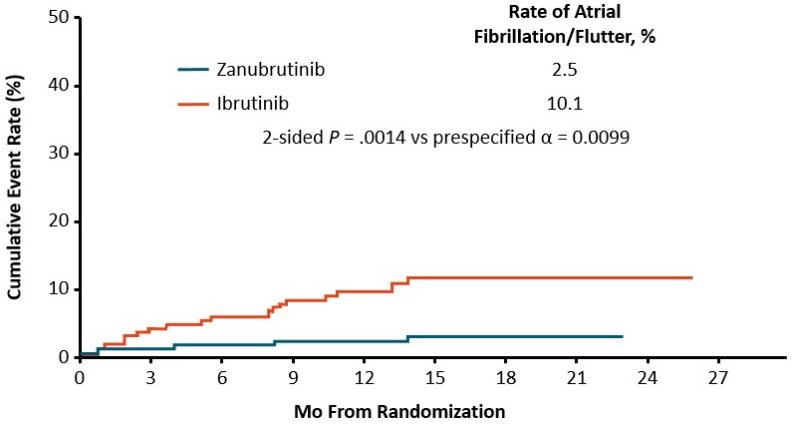
Until PD or unacceptable AE



Response

	Zanubrutinib (n=207), n (%)	Ibrutinib (n=208), n (%)
Primary endpoint: ORR (PR+CR)	162 (**78.3**) 95% CI: 72.0, 83.7	130 (**62.5**) 95% CI: 55.5, 69.1
	Superiority 2-sided *P*=0.0006 compared with pre-specified alpha of 0.0099	

Safety Analysis Population	Zanubrutinib (n=204), n (%)		Ibrutinib (n=207), n (%)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Cardiac disorders[a]	28 (13.7)	5 (2.5)	52 (25.1)	14 (6.8)
Atrial fibrillation and flutter (key 2º endpoint)	**5 (2.5)**	**2 (1.0)**	**21 (10.1)**	**4 (1.9)**
Hemorrhage	73 (35.8)	6 (2.9)	75 (36.2)	6 (2.9)
Major hemorrhage[b]	6 (2.9)	6 (2.9)	8 (3.9)	6 (2.9)
Hypertension	34 (16.7)	22 (10.8)	34 (16.4)	22 (10.6)
Infections	122 (59.8)	26 (12.7)	131 (63.3)	37 (17.9)
Neutropenia[c]	58 (28.4)	38 (18.6)	45 (21.7)	31 (15.0)
Thrombocytopenia[c]	19 (9.3)	7 (3.4)	26 (12.6)	7 (3.4)
Secondary primary malignancies	17 (8.3)	10 (4.9)	13 (6.3)	4 (1.9)
Skin cancers	7 (3.4)	3 (1.5)	10 (4.8)	2 (1.0)



Hillmen et al. EHA 2021

ELEVATE R/R: ACALABRUTINIB VS. IBRITINIB IN R/R PATIENTS WITH CLL

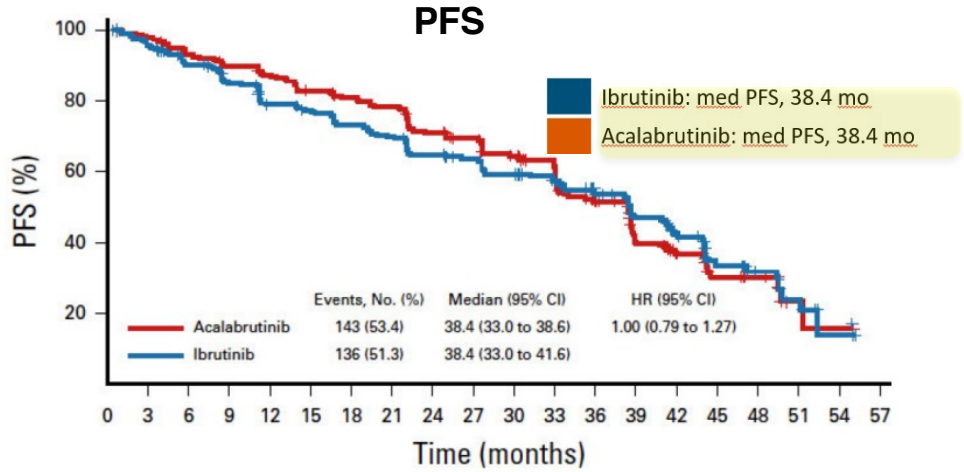
Adults with previously treated CLL requiring therapy (iwCLL 2008 criteria)

Presence of del(17p) or del(11q)
ECOG PS ≤ 2

→ Ibrutinib (n = 268)
→ Acalabrutinib (n = 265)

→ *Until PD or unacceptable AE*

PFS

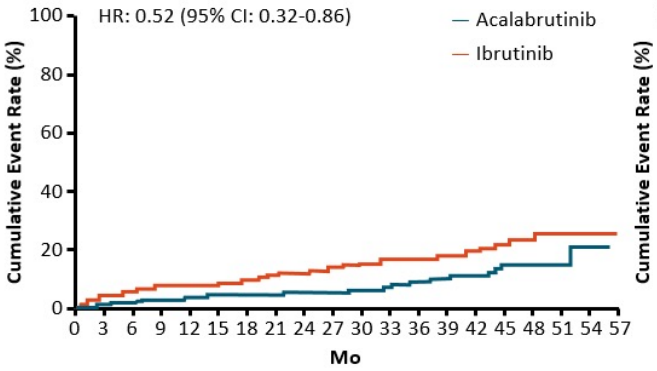


Median follow-up: 41 months

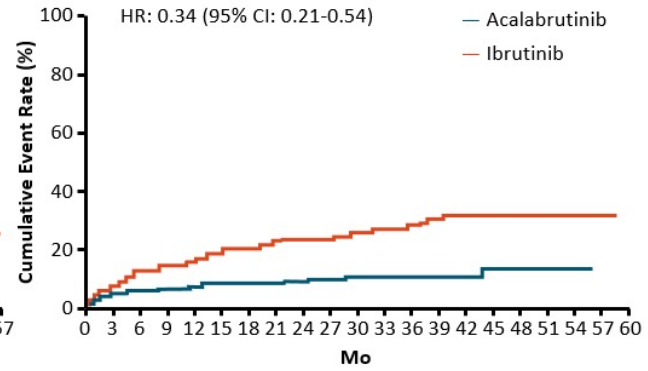
AEs of special interest

Events, n (%)	Any grade		Grade ≥3	
	Acalabrutinib (n=266)	Ibrutinib (n=263)	Acalabrutinib (n=266)	Ibrutinib (n=263)
Cardiac events	64 (24.1)	79 (30.0)	23 (8.6)	25 (9.5)
Atrial fibrillation[a]*	25 (9.4)	42 (16.0)	13 (4.9)	10 (3.8)
Ventricular arrhythmias[b]	0	3 (1.1)	0	1 (0.4)
Bleeding events*	101 (38.0)	135 (51.3)	10 (3.8)	12 (4.6)
Major bleeding events[c]	12 (4.5)	14 (5.3)	10 (3.8)	12 (4.6)
Hypertension[d]*	25 (9.4)	61 (23.2)	11 (4.1)	24 (9.1)
Infections[e]	208 (78.2)	214 (81.4)	82 (30.8)	79 (30.0)
ILD/pneumonitis*	7 (2.6)	17 (6.5)	1 (0.4)	2 (0.8)
SPMs excluding NMSC	24 (9.0)	20 (7.6)	16 (6.0)	14 (5.3)

Atrial Fibrillation



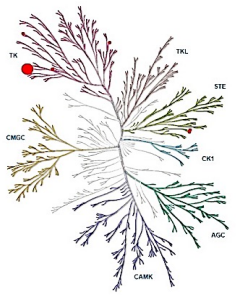
Hypertension



Byrd, et al. JCO 2021

PIRTOBRUTINIB IN R/R PATIENTS WITH CLL PREVIOUSLY TREATED WITH BTKI

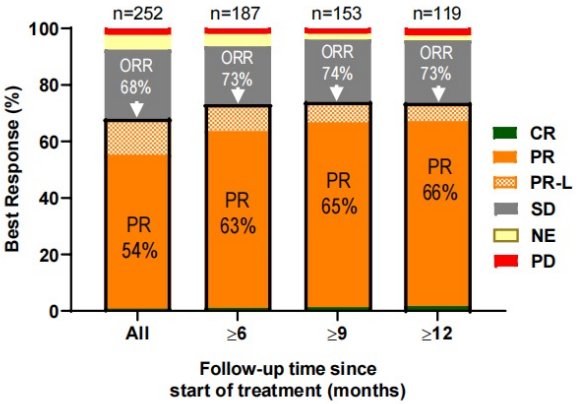
Kinome selectivity[1]
Highly selective for BTK



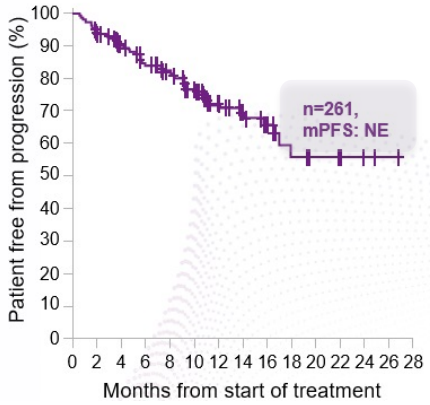
Characteristics	N = 261
Median age, years (range)	69 (36-88)
Female, n (%)	84 (32)
Male, n (%)	177 (68)
ECOG PS[a], n (%)	
0	138 (53)
1	104 (40)
2	19 (7)
Median number of prior lines of systemic therapy (range)	3 (1-11)
Prior therapy, n (%)	
BTK inhibitor	261 (100)
Anti-CD20 antibody	230 (88)
Chemotherapy	207 (79)
BCL2 inhibitor	108 (41)
PI3K inhibitor	51 (20)
CAR-T	15 (6)
Stem cell transplant	6 (2)
Allogeneic stem cell transplant	5 (2)
Autologous stem cell transplant	1 (<1)
Reason discontinued prior BTKi, n (%)	
Progressive disease	196 (75)
Toxicity/Other	65 (25)

Baseline Molecular Characteristics[a]	
Mutation status, n (%)	
BTK C481-mutant	89 (43)
BTK C481-wildtype	118 (57)
PLCG2-mutant	33 (16)
High Risk Molecular Features, n (%)	
17p deletion	51 (28)
TP53 mutation	64 (37)
17p deletion or TP53 mutation	77 (36)
Both 17p deletion and TP53 mutation	38 (27)
IGHV unmutated	168 (84)
11q deletion	45 (25)

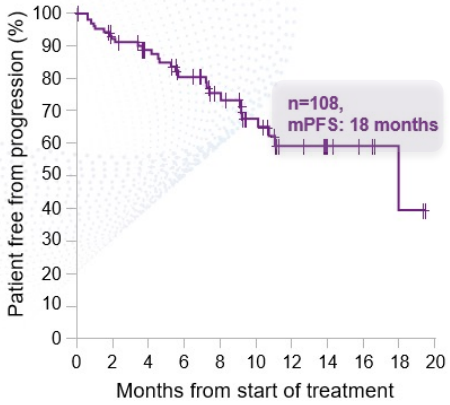
Responses over time



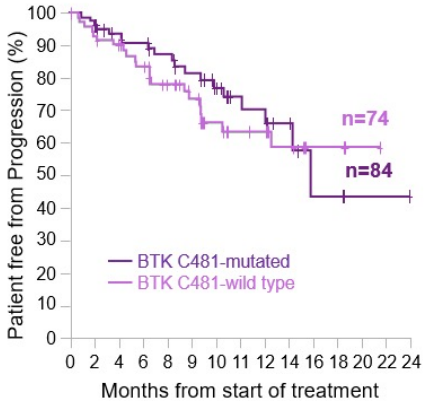
PFS in BTKi pre-treated patients
(median prior lines of therapy: 3)



PFS in BTKi and BCL-2i pre-treated patients
(median prior lines of therapy: 5)



PFS by *BTK C481* mutation status* in patients with PD on a prior BTKi



Safety Profile

	Treatment-emergent AEs, (≥15%), %				
Adverse Event	Grade 1	Grade 2	Grade 3	Grade 4	Any Grade
Fatigue	13%	8%	1%	-	23%
Diarrhea	15%	4%	<1%	<1%	19%
Neutropenia[a]	1%	2%	8%	6%	18%
Contusion	15%	2%	-	-	17%
AEs of special interest[b]					
Bruising[c]	20%	2%	-	-	22%
Rash[d]	9%	2%	<1%	-	11%
Arthralgia	8%	3%	<1%	-	11%
Hemorrhage[e]	5%	2%	1%[g]	-	8%
Hypertension	1%	4%	2%	-	7%
Atrial fibrillation/flutter[f]	-	1%	<1%	<1%	2%[h]

Mato et al., EHA 2022

HOT NEWS IN HEMATOLOGY
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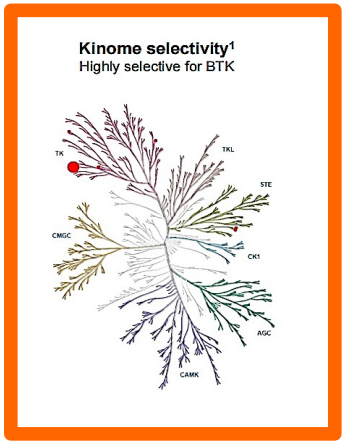
ed oltre...

PIRTOBRUTINIB IN R/R PATIENTS WITH CLL PREVIOUSLY TREATED WITH BTKI



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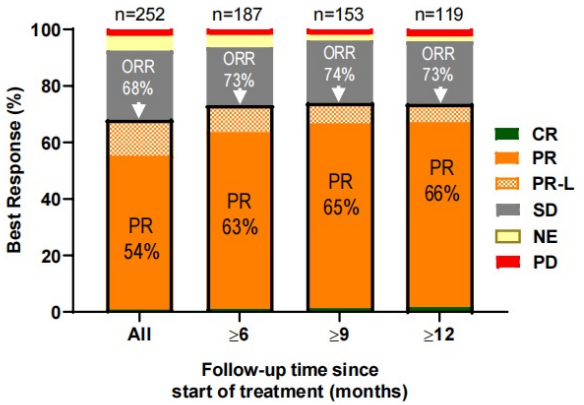
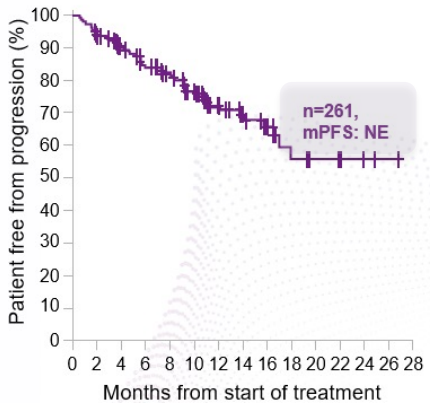
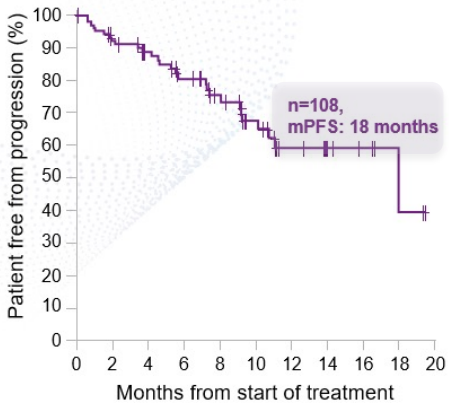


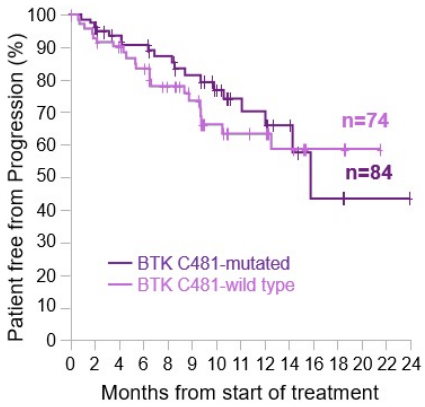
PFS in BTKi pre-treated patients
(median prior lines of therapy: 3)



PFS in BTKi and BCL-2i pre-treated patients
(median prior lines of therapy: 5)



PFS by *BTK C481* mutation status* in patients with PD on a prior BTKi



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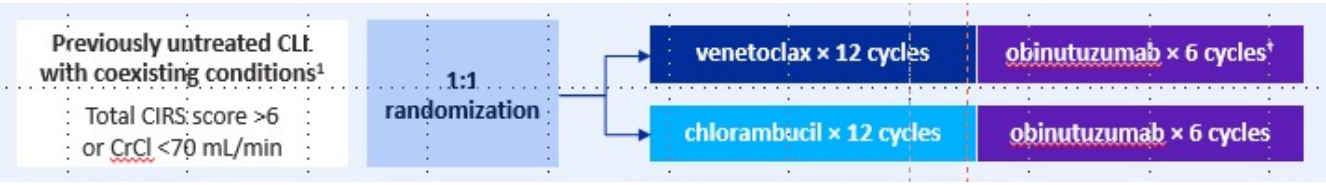
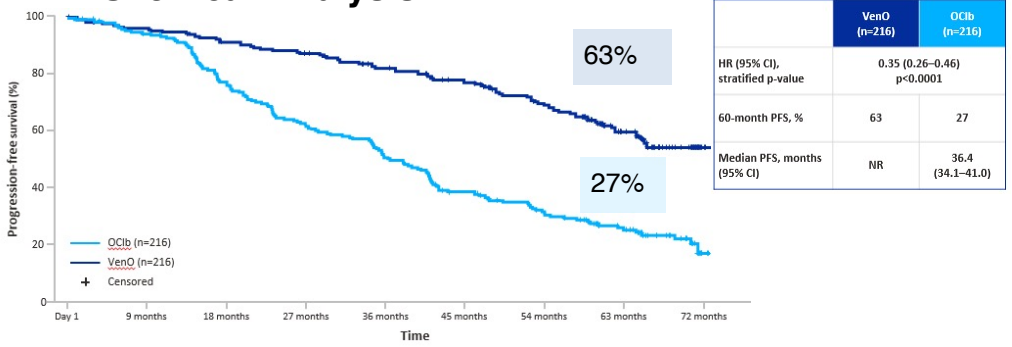
Atrial fibrillation/flutter[f]	-	1%	<1%	<1%	2%[h]

Mato et al., EHA 2022

VENETOCLAX+OBINUTUZUMAB IN TN PATIENTS WITH CLL (CLL14 TRIAL): 5-YEAR FU

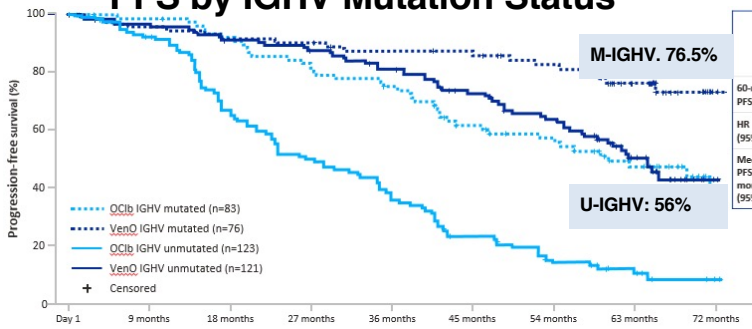


PFS: 5-Year Analysis



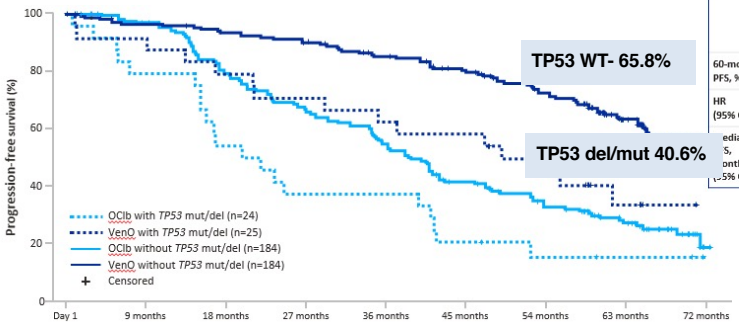
	VenO (n=216)	OClb (n=216)
HR (95% CI), stratified p-value	0.35 (0.26–0.46) p<0.0001	
60-month PFS, %	63	27
Median PFS, months (95% CI)	NR	36.4 (34.1–41.0)

PFS by IGHV Mutation Status



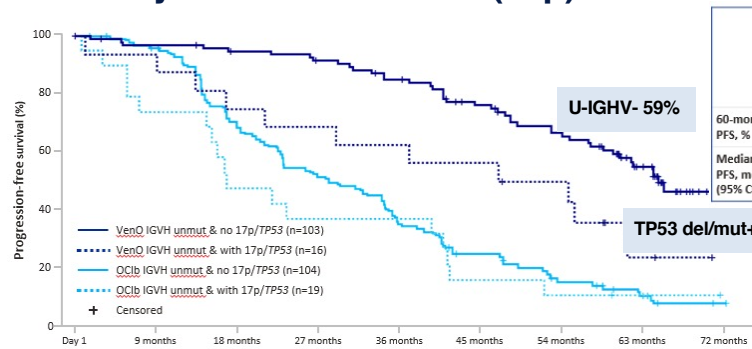
	VenO IGHV mutated (n=76)	OClb IGHV mutated (n=83)	VenO IGHV unmutated (n=121)	OClb IGHV unmutated (n=123)
60-month PFS, %	76.5	49.7	55.8	12.5
HR (95% CI)	0.41 (0.23-0.73)		HR 0.25 (0.17-0.36)	
Median PFS, months (95% CI)	NE (NE–NE)	59.9 (46.0-NE)	64.2 (57.0–NE)	26.9

PFS *TP53* Mutation Status



	VenO TP53 mut/del (n=25)	OClb TP53 mut/del (n=24)	VenO no TP53 mut/del (n=184)	OClb no TP53 mut/del (n=184)
60-month PFS, %	40.6	15.6	65.8	49.0
HR (95% CI)	0.36 (0.14-0.88)		HR 0.33 (0.24-0.45)	
Median PFS, months (95% CI)	49.0 (29.0–NE)	20.8 (15.2-40.9)	NR (65.4–NE)	38.9 (34.7-42.0)

PFS by IGHV Unmut ± del(17p)/TP53 mut.



	VenO IGHV unmutated & TP53 mut/del (n=16)	VenO IGHV unmutated no TP53 mut/del (n=103)	VenO (n=216)
60-month PFS, %	35.7	59.4	63
Median PFS, months (95% CI)	50.9 (21.1–61.4)	64.8 (59.8–NE)	NR

Al-Sawaf EHA 2022

THE CLL13-GAIA TRIAL IN TN PATIENTS WITH CLL

Fit patients with CLL N=926

Select inclusion criteria:
CIRS ≤6 & normal CrCl*
Excludes:
del(17p)/*TP53*^{mut}

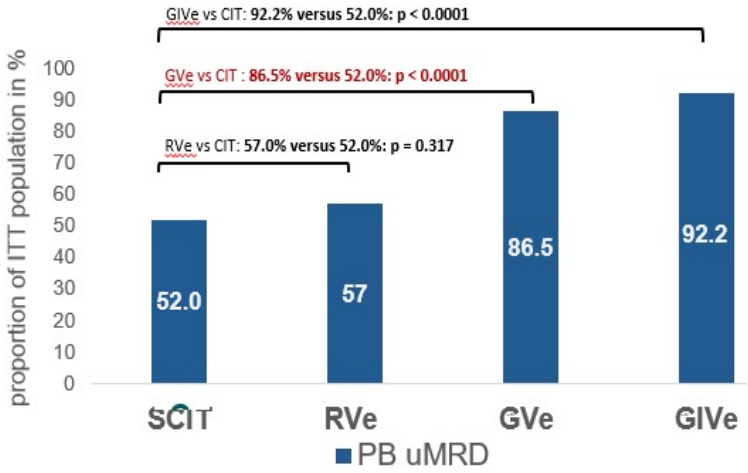
Stratification factors:
- Age
- Binet stage
- Country

1:1:1:1 randomization

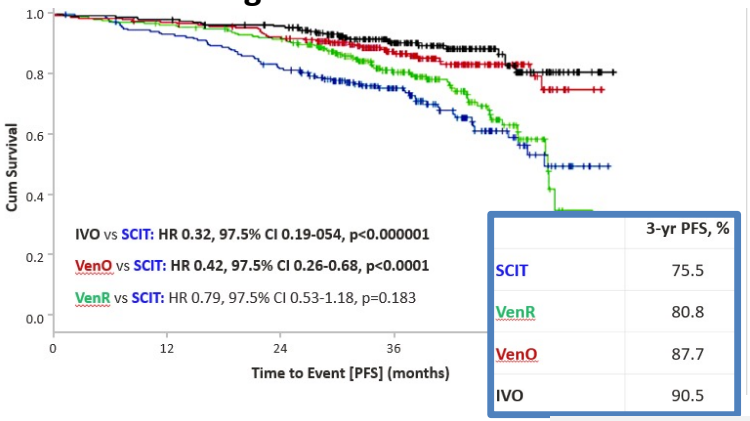
n=229	CIT: FCR ≤65 yrs (n=150); BR >65 yrs (n=79) × 6 cycles	CIT
n=237	Venetoclax 400 mg PO QD (ramp-up) × 12 cycles + Rituximab 375 (500) mg/m² IV × 6 cycles	R Ve
n=229	Venetoclax 400 mg PO QD (ramp-up) × 12 cycles + Obinutuzumab 1,000 mg IV × 6 cycles	G Ve
n=231	Venetoclax 400 mg PO QD (ramp-up) × 12 cycles + Ibrutinib 420 mg PO QD x 12 cycles up to cycle 36 if no uMRD + Obinutuzumab 1,000 mg IV × 6 cycles	G I Ve

Co-Primary Endpoints
- uMRD (<10-4) in PB at month 15 (VenO vs CIT)
- PFS (IVO vs CIT)

Key Secondary Endpoints
- MRD in PB at month 15 (all other comparisons)
- MRD in BM at final restaging
- PFS (all other comparisons)
- ORR
- CR/CRi rate
- OS

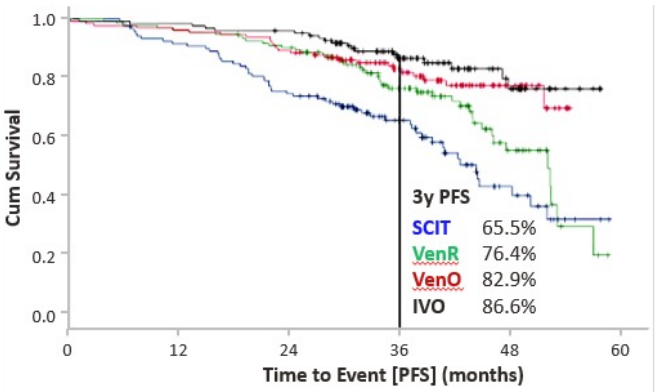


PFS according to treatment arm

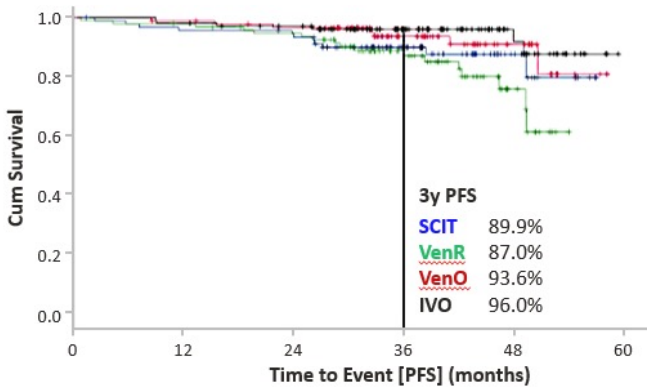


	3-yr PFS, %
SCIT	75.5
VenR	80.8
VenO	87.7
IVO	90.5

Unmutated IGHV



Mutated IGHV



SCIT — VenR — VenO — IVO

Eichhorst B, *et al.* EHA2022

GLOW TRIAL: 1L Ibrutinib+Venetoclax vs Chlorambucil+Obinutuzumab

Stratified by IGHV status, del(11q) presence

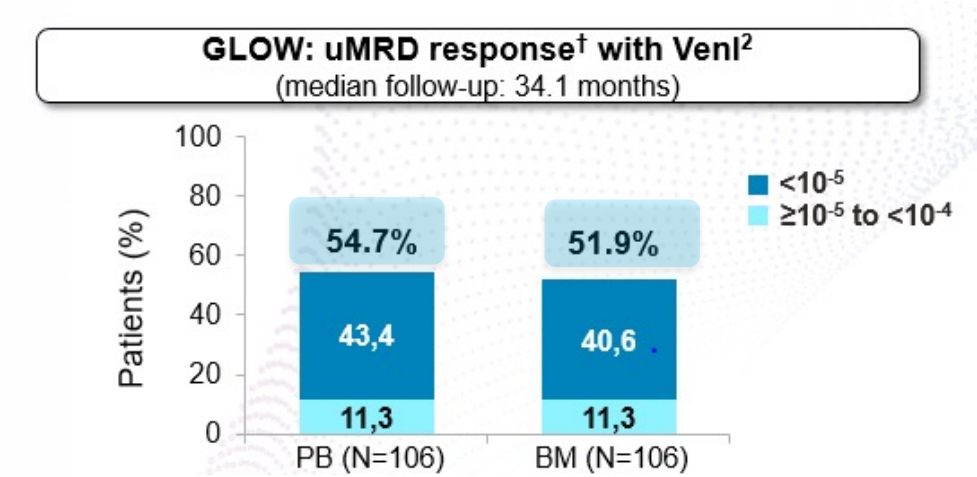
Patients with previously untreated CLL; aged ≥65 yr or <65 yr with CIRS >6 or CrCl <70 mL/min; no del(17p) or known *TP53* mutation; ECOG PS 0-2 (N = 211)

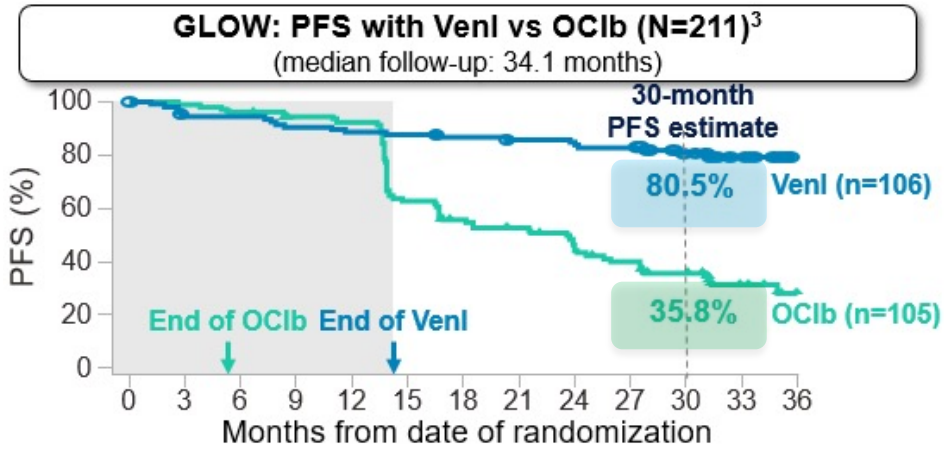
→ **Ibrutinib** 420 mg PO QD x 3 cycles followed by **Ibrutinib** + **Venetoclax*** 12 cycles (n = 106)

→ **Chlorambucil** 0.5 mg/kg on D1, 15 x 6 cycles + **Obinutuzumab** 1000 mg on D1-2, 8, 15 of cycle 1 and D1 of cycles 2-6 (n = 105)

*Ramp-up from 20 to 400 mg over 5 wks starting in cycle 4.

Characteristic, %	Ibr + Ven	Clb + O	RR
Age, ≥65 yr	52.2	17.0	3.07
Rai stage III-IV	50.9	15.1	3.37
IGHV unmutated	58.2	14.8	3.93
del11q	60.0	11.1	5.40

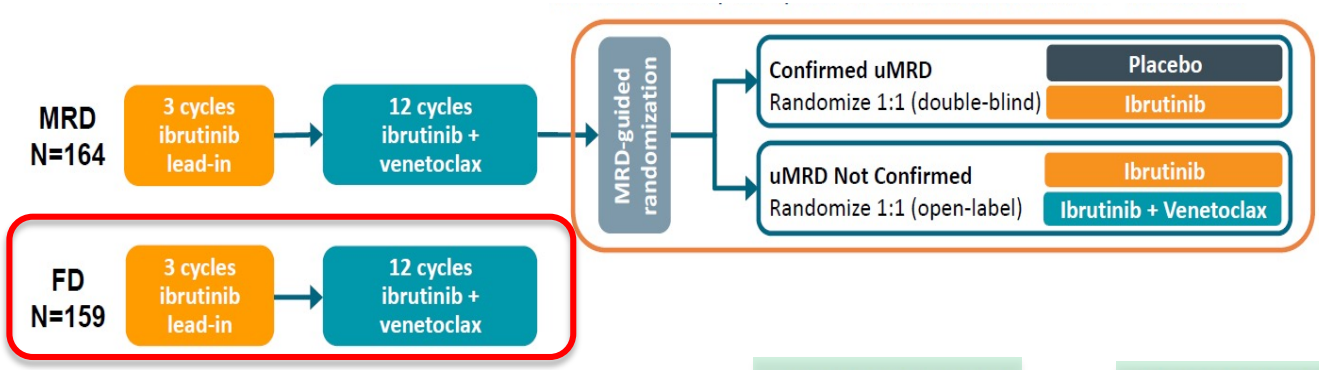




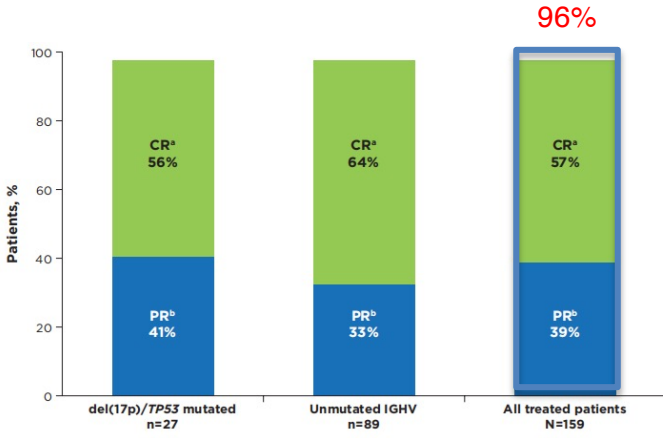
Deep responses observed in both BM and PB in patients with uIGHV

Munir. ASH 2021

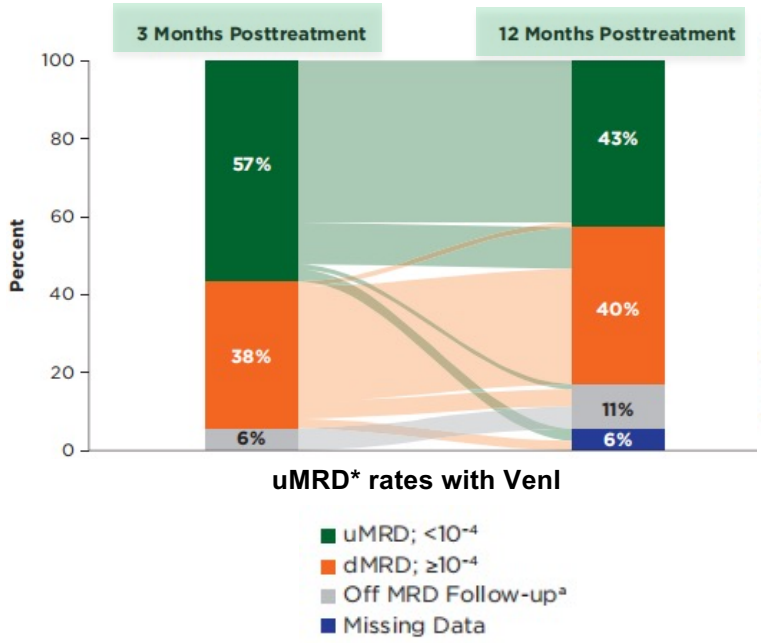
CAPTIVATE TRIAL: **1L** ibrutinib plus venetoclax- FD cohort, 3-year FU



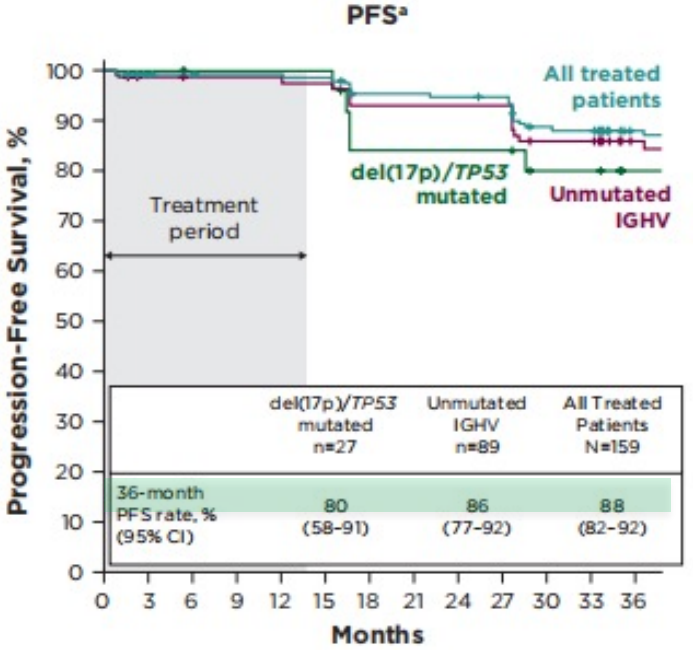
Characteristic	All Treated Patients (n = 159)
Median age, yr (range)	60 (33-71)
High-risk features, n (%)	
▪ Unmutated *IGHV*	89 (56)
▪ del(17p)/*TP53* mutation	27 (17)
▪ del(17p)	20 (13)
▪ del(11q)*	28 (18)
▪ Complex karyotype†	31 (19)



Response rates with Ven I



uMRD* rates with VenI



Ghia. et al., ASCO 2021; Moreno et al., EHA 2022

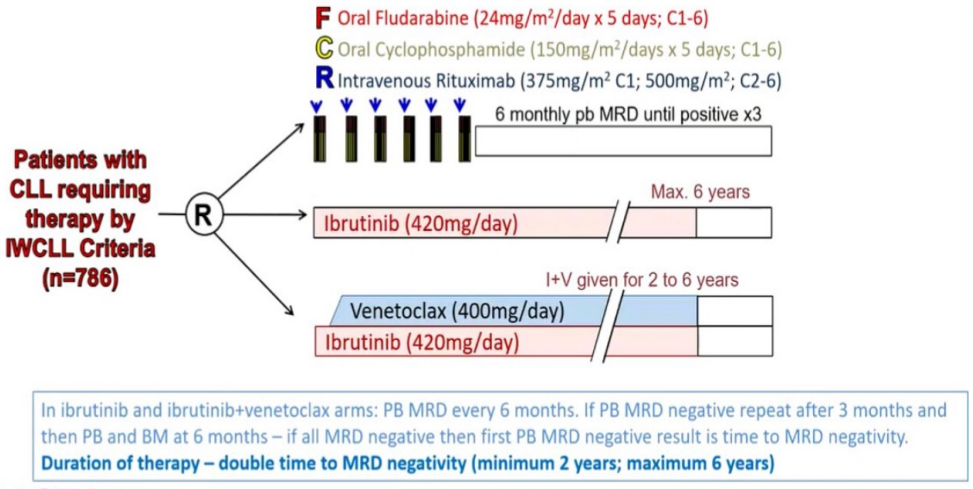
1L IBRUTINIB+ VENETOCLAX: INTERIM ANALYSIS OF THE PHASE III NCRI FLAIR TRIAL

FLAIR randomized trial **ibrutinib vs. ibrutinib+venetoclax**

- Pts <75 yrs or with <20% 17p
- **Duration of therapy defined by MRD** with treatment
- for up to 6 years, the earliest therapy could stop was 2 years

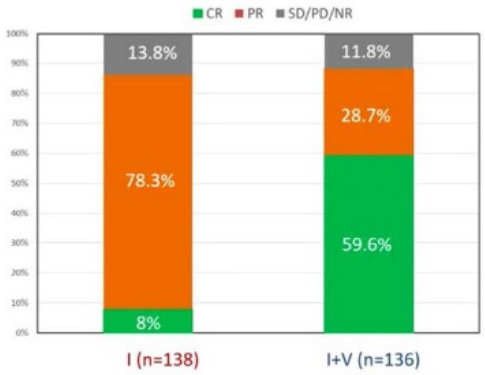
MRD assessed centrally by FC in PB and BM

Interim analysis in the first 274 pts
(I [n=138] and I+V [n=136]) reaching 2 yrs post-randomisation.



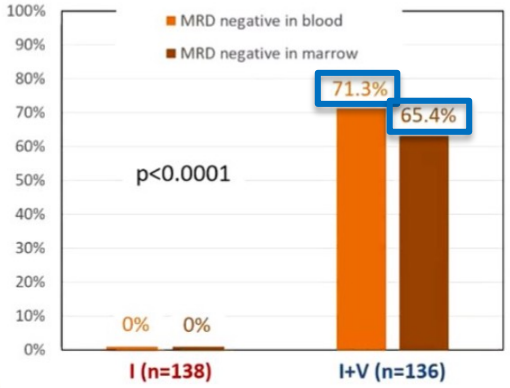
In ibrutinib and ibrutinib+venetoclax arms: PB MRD every 6 months. If PB MRD negative repeat after 3 months and then PB and BM at 6 months – if all MRD negative then first PB MRD negative result is time to MRD negativity.
Duration of therapy – double time to MRD negativity (minimum 2 years; maximum 6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

iwCLL Response at 9 months



	I (n=138)	I+V (n=136)
ORR	119 (86.2%)	120 (88.2%)
CR	11 (8.0%)	81 (59.6%)

Primary endpoint: uMRD at 2 years



N (%), Exact 95% CI	I (n=138)	I+V (n=136)
MRD Negative in the marrow	0 [0%, 2.64%]	89 (65.4%) [56.81%, 73.38%]
MRD Negative in the blood	0 [0%, 2.64%]	97 (71.3%) [62.95%, 78.75%]

- MRD assessed by 8-colour flow cytometry
- MRD negative defined by IWCLL criteria of <1 CLL cell in 10,000 leucocytes

Hillmen et al., EHA 2022

CLL: HOT NEWS- SUMMARY

- Long term responses with BTKi
- Second-generation and investigational BTKis offer higher selectivity with the improved safety profile and outcomes
- Pirtobrutinib improved outcomes and efficacy in patients with BTKi-resistant CLL
- Venetoclax and BTKi combinations produce deep responses further improves PFS outcomes

Grazie