New Drugs in Hematology, Bologna, 18-20 May 2026

Session X: CLL

First line – Treat until Progression

(With continuous BTKi)

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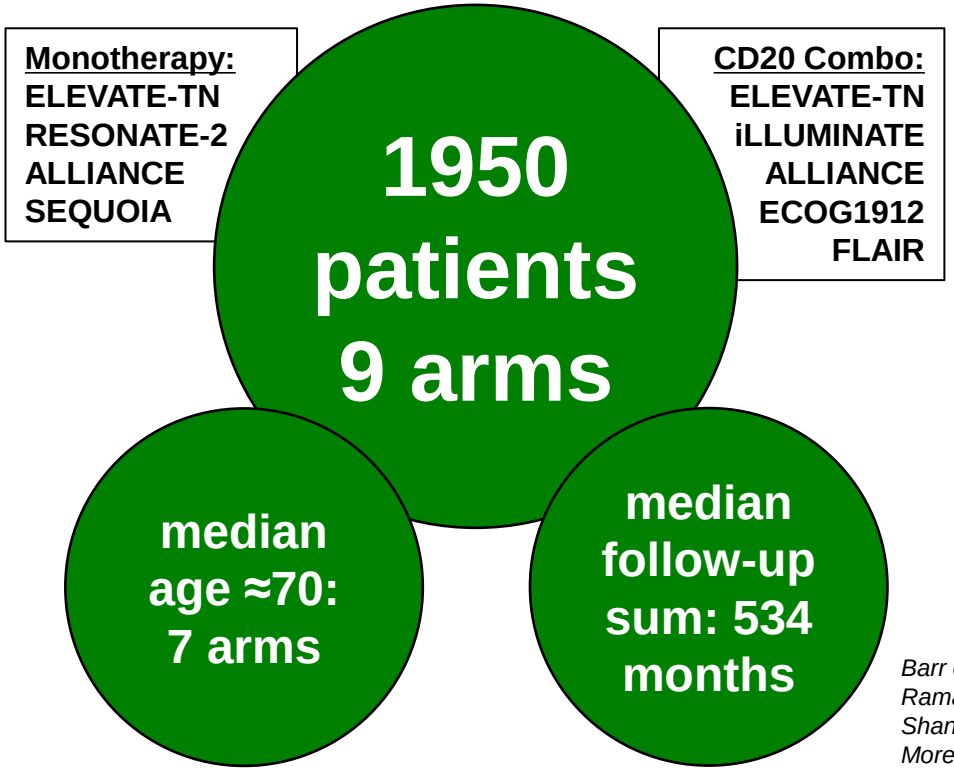
Disclosures – Stephan Stilgenbauer

- Advisory board honoraria
- Speaker honoraria
- Research support
- Travel support

- AbbVie
- Amgen
- AstraZeneca
- BeOne Medicines
- BMS
- Galapagos
- Gilead
- GSK
- Hoffmann-La Roche
- Johnson & Johnson
- Lilly
- MSD
- Novartis
- Nurix
- Sunesis

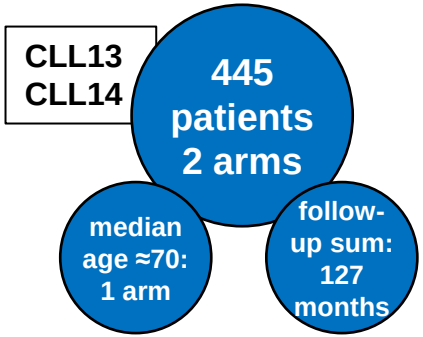
Evidence Base from Phase 3 Trials: Targeted Front-line Therapy Options

Continuous BTKi:
Acalabrutinib, Ibrutinib, Zanubrutinib

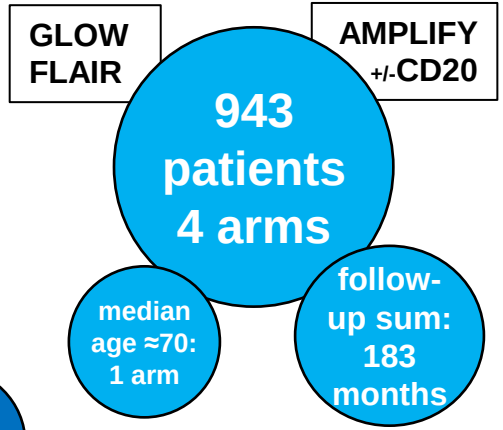


Short-term BCL2 targeting:

Obinutuzumab + Venetoclax



Ibrutinib / Acalabrutinib + Venetoclax



Barr et al. Blood Adv 2022; Woyach et al. Blood 2024; Moreno et al. Haematologica 2022; Ramakrishnan et al. ASH 2023; Sharman et al. ASH 2023; Hillmen Lancet Onc 2023; Shanafelt et al. Blood 2022; Al-Sawaf et al. Blood 2024; Fürstenau et al. Lancet Onc 2024; Moreno et al. ASH 2023; Munir et al. NEJM 2023; Brown et al. NEJM 2025

Safety: Grade 3 – 5 Adverse Events over Time

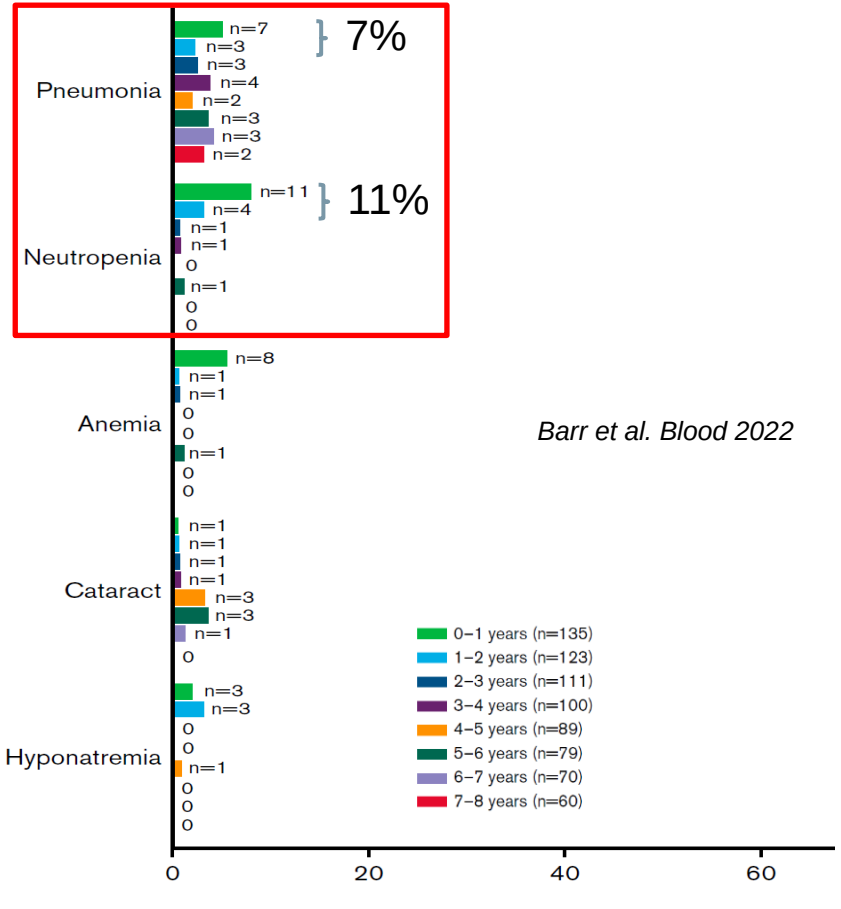
Al-Sawaf et al. Blood 2024

Obinutuzumab+Venetoclax (CLL14, 2 years)

	During Treatment	After Treatment
Neutropenia	51.9%	3.8%
Thrombocytopenia	14.2%	0.5%
Anemia	7.5%	1.9%
Febrile neutropenia	4.2%	0.9%
Leukopenia	2.4%	0.0%
Pneunomia	3.8%	3.3%
Infusion-related reaction	9.0%	0.0%
Tumor lysis syndrome	1.4%	0.0%

Grade 3	Grade 4	Grade 5
Prolonged (e.g., not rapidly responsive to symptomatic medication and/or brief interruption of infusion); recurrence of symptoms following initial improvement; hospitalization indicated for clinical sequelae	Life-threatening consequences; urgent intervention indicated	Death

Ibrutinib (RESONATE-2)



Barr et al. Blood 2022

Safety: Summary of Product Characteristics (FDA): Contraindications, Warnings and Precautions, Adverse Reactions

https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/125486s029lbl.pdf
https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/208573s013lbl.pdf
https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/217003s000lbl.pdf

Obinutuzumab

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use GAZYVA safely and effectively. See full prescribing information for GAZYVA.

GAZYVA® (obinutuzumab) injection, for intravenous use
Initial U.S. Approval: 2013

WARNING: HEPATITIS B VIRUS REACTIVATION and PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY
See full prescribing information for complete boxed warning.

- **Hepatitis B Virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure, and death. (5.1)**
- **Progressive Multifocal Leukoencephalopathy (PML) resulting in death. (5.2)**

RECENT MAJOR CHANGES

Dosage and Administration, Recommended Dosage for Follicular Lymphoma (2.3)	2/2022
Dosage Modifications for Adverse Reactions (2.5)	2/2022
Dosage and Administration, Preparation and Administration (2.6)	2/2022

INDICATIONS AND USAGE

GAZYVA is a CD20-directed cytolytic antibody indicated:

- in combination with chlorambucil, for the treatment of patients with previously untreated chronic lymphocytic leukemia. (1, 14)
- in combination with bendamustine followed by GAZYVA monotherapy, for the treatment of patients with follicular lymphoma who relapsed after, or are refractory to, a rituximab-containing regimen. (1, 14)
- in combination with chemotherapy followed by GAZYVA monotherapy in patients achieving at least a partial remission, for the treatment of adult patients with previously untreated stage II bulky, III or IV follicular lymphoma. (1, 14)

DOSAGE AND ADMINISTRATION

- Premedicate for infusion-related reactions and tumor lysis syndrome. (2.1, 5.3, 5.4)
- Administer only as intravenous infusion. Do not administer as an intravenous push or bolus. (2.1)
- The recommended dosage for chronic lymphocytic leukemia is 100 mg on day 1 and 900 mg on day 2 of Cycle 1, 1,000 mg on day 8 and 15 of Cycle 1, and 1,000 mg on day 1 of Cycles 2-6. (2.2)
- The recommended dosage for follicular lymphoma is 1,000 mg on day 1, 8 and 15 of Cycle 1, 1,000 mg on day 1 of Cycles 2-6 or Cycles 2-8, and then 1,000 mg every 2 months for up to 2 years. (2.3)

DOSAGE FORMS AND STRENGTHS

Injection: 1,000 mg/40 mL (25 mg/mL) single-dose vial. (3)

CONTRAINDICATIONS

GAZYVA is contraindicated in patients with known hypersensitivity reactions (e.g., anaphylaxis) to obinutuzumab or any of the excipients, including serum sickness with prior GAZYVA use. (4)

WARNINGS AND PRECAUTIONS

- Infusion-Related Reactions: Premedicate patients with glucocorticoid, acetaminophen, and anti-histamine. Monitor patients closely during infusions. Interrupt, reduce rate, or discontinue for infusion-related reactions based on severity. (2.1, 5.3)
- Hypersensitivity Reactions Including Serum Sickness: Discontinue GAZYVA permanently. (5.4)
- Tumor Lysis Syndrome: Premedicate with anti-hyperuricemics and adequate hydration, especially for patients with high tumor burden, high circulating lymphocyte count or renal impairment. Correct electrolyte abnormalities, provide supportive care, and monitor renal function and fluid balance. (5.5)
- Infections: Do not administer GAZYVA to patients with an active infection. Patients with a history of recurring or chronic infections may be at increased risk of infection. (5.6)
- Neutropenia: In patients with Grade 3 to 4 neutropenia, monitor laboratory tests until resolution and for infection. Consider dose delays and infection prophylaxis, as appropriate. (5.7)
- Thrombocytopenia: Monitor platelet counts and for bleeding. Transfusion may be necessary. (5.8)
- Immunization: Avoid administration of live virus vaccines during GAZYVA treatment and until B-cell recovery. (5.9)
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and use effective contraception. (5.10)

ADVERSE REACTIONS

The most common adverse reactions (incidence ≥ 20% and ≥ 2% greater in the GAZYVA treated arm) were:

- Previously untreated CLL: infusion-related reactions and neutropenia. (6)
- Relapsed or refractory NHL: infusion-related reactions, fatigue, neutropenia, cough, upper respiratory tract infections, and musculoskeletal pain. (6)
- Previously untreated NHL: infusion-related reactions, neutropenia, upper respiratory tract infections, cough, constipation, and diarrhea. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Genentech at 1-888-835-2555 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

- Lactation: Advise not to breastfeed. (8.1)

See 17 for PATIENT COUNSELING INFORMATION.

Venetoclax

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use VENCLEXTA safely and effectively. See full prescribing information for VENCLEXTA.

VENCLEXTA® (venetoclax tablets) for oral use
Initial U.S. Approval: 2016

RECENT MAJOR CHANGES

Indications and Usage, CLL (1.1)	05/2019
Indications and Usage, AML (1.2)	11/2018
Dosage and Administration (2.1, 2.2, 2.3, 2.4)	05/2019
Warnings and Precautions, Neutropenia (5.2)	11/2018
Warnings and Precautions, Infections (5.3)	05/2019

INDICATIONS AND USAGE

VENCLEXTA is a BCL-2 inhibitor indicated:

- For the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL). (1.1)
- In combination with azacitidine or decitabine or low-dose cytarabine for the treatment of newly-diagnosed acute myeloid leukemia (AML) in adults who are age 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy.
  This indication is approved under accelerated approval based on response rates. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. (1.2)

DOSAGE AND ADMINISTRATION

- See Full Prescribing Information for recommended VENCLEXTA starting and ramp-up dosages. (2.1)
- VENCLEXTA tablets should be taken orally once daily with a meal and water. Do not chew, crush, or break tablets. (2.1)
- Perform prophylaxis for tumor lysis syndrome. (2.2)

DOSAGE FORMS AND STRENGTHS

Tablets: 10 mg, 50 mg, 100 mg (3)

CONTRAINDICATIONS

Concomitant use with strong CYP3A inhibitors at initiation and during ramp-up phase in patients with CLL/SLL is contraindicated. (2.4, 4, 7.1)

WARNINGS AND PRECAUTIONS

- Tumor Lysis Syndrome (TLS): Anticipate TLS; assess risk in all patients. Premedicate with anti-hyperuricemics and ensure adequate hydration. Employ more intensive measures (intravenous hydration, frequent monitoring, hospitalization) as overall risk increases. (2.2, 5.1)
- Neutropenia: Monitor blood counts and for signs of infection; manage as medically appropriate. (2.3, 5.2)
- Infections: Monitor for signs and symptoms of infection and treat promptly. Withhold treatment for Grade 3 and higher infection until resolution. (5.3)
- Immunization: Do not administer live attenuated vaccines prior to, during, or after VENCLEXTA treatment. (5.4)
- Embryo-Fetal Toxicity: May cause embryo-fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception during treatment. (5.5)

ADVERSE REACTIONS

In CLL/SLL, the most common adverse reactions (≥20%) for VENCLEXTA when given in combination with obinutuzumab or rituximab or as monotherapy were neutropenia, thrombocytopenia, anemia, diarrhea, nausea, upper respiratory tract infection, cough, musculoskeletal pain, fatigue, and edema (6.1).

In AML, the most common adverse reactions (≥30%) in combination with azacitidine or decitabine or low-dose cytarabine were nausea, diarrhea, thrombocytopenia, constipation, neutropenia, febrile neutropenia, fatigue, vomiting, peripheral edema, pyrexia, pneumonia, dyspnea, hemorrhage, anemia, rash, abdominal pain, sepsis, back pain, myalgia, dizziness, cough, oropharyngeal pain, and hypotension (6.2).

To report SUSPECTED ADVERSE REACTIONS, contact AbbVie Inc. at 1-800-633-9110 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Strong or moderate CYP3A inhibitors or P-gp inhibitors: Adjust dosage of VENCLEXTA. (2.4, 7.1)
- Strong or moderate CYP3A inducers: Avoid co-administration. (7.1)
- P-gp substrates: Take at least 6 hours before VENCLEXTA. (7.2)

USE IN SPECIFIC POPULATIONS

- Lactation: Advise women not to breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 05/2019

Ibrutinib

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use IMBRUVICA safely and effectively. See full prescribing information for IMBRUVICA.

IMBRUVICA® (ibrutinib) capsules, for oral use
IMBRUVICA® (ibrutinib) tablets, for oral use
IMBRUVICA® (ibrutinib) oral suspension
Initial U.S. Approval: 2013

RECENT MAJOR CHANGES

Indications and Usage, cGVHD (1.6)	8/2022
Dosage and Administration (2.1, 2.3, 2.4)	8/2022
Dosage and Administration (2.2)	5/2022
Warnings and Precautions, Cardiac Arrhythmias, Cardiac Failure, and Sudden Death (5.3)	5/2022
Hypertension (5.4)	5/2022

INDICATIONS AND USAGE

IMBRUVICA is a kinase inhibitor indicated for the treatment of:

- Adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy (1.1).
  This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).
- Adult patients with chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma (SLL) (1.2).
- Adult patients with chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma (SLL) with 17p deletion (1.3).
- Adult patients with Waldenström's macroglobulinemia (WM) (1.4).
- Adult patients with marginal zone lymphoma (MZL) who require systemic therapy and have received at least one prior anti-CD20-based therapy (1.5).
  This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).
- Adult and pediatric patients age 1 year and older with chronic graft versus host disease (cGVHD) after failure of one or more lines of systemic therapy (1.6).

DOSAGE AND ADMINISTRATION

- MCL and MZL: 560 mg taken orally once daily (2.1).
- CLL/SLL and WM: 420 mg taken orally once daily (2.1).
- cGVHD:
  - Patients 12 years and older: 420 mg taken orally once daily (2.1).
  - Patients 1 to less than 12 years of age: 240 mg/m² taken orally once daily (up to a dose of 420 mg) (2.1).

Tablets or capsules should be taken orally with a glass of water. Do not open, break, or chew the capsules. Do not cut, crush, or chew the tablets. See full prescribing information for oral suspension administration instructions (2.1).

DOSAGE FORMS AND STRENGTHS

Capsules: 70 mg and 140 mg (3)
Tablets: 140 mg, 280 mg, 420 mg, and 560 mg (3)
Oral suspension: 70 mg/mL (3)

CONTRAINDICATIONS

None (4)

WARNINGS AND PRECAUTIONS

- Hemorrhage: Monitor for bleeding and manage (5.1).
- Infections: Monitor patients for fever and infections, evaluate promptly, and treat (5.2).
- Cardiac Arrhythmias, Cardiac Failure, and Sudden Death: Monitor for symptoms of arrhythmias and cardiac failure and manage (5.3).
- Hypertension: Monitor blood pressure and treat (5.4).
- Cytopenias: Check complete blood counts monthly (5.5).
- Second Primary Malignancies: Other malignancies have occurred in patients, including skin cancers, and other carcinomas (5.6).
- Tumor Lysis Syndrome (TLS): Assess baseline risk and take precautions. Monitor and treat for TLS (5.7).
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception (5.8, 8.1, 8.3).

ADVERSE REACTIONS

- The most common (≥30%) adverse reactions in patients with B-cell malignancies (MCL, CLL/SLL, WM and MZL) are thrombocytopenia, diarrhea, fatigue, musculoskeletal pain, neutropenia, rash, anemia, and bruising (6).
- The most common (≥20%) adverse reactions in adult or pediatric patients with cGVHD are fatigue, anemia, bruising, diarrhea, thrombocytopenia, musculoskeletal pain, pyrexia, muscle spasms, stomatitis, hemorrhage, nausea, abdominal pain, pneumonia, and headache (6).

To report SUSPECTED ADVERSE REACTIONS, contact Pharmacyclics at 1-877-477-3536 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- CYP3A Inhibitors: Modify IMBRUVICA dose as described (2.3, 7.1).
- CYP3A Inducers: Avoid coadministration with strong CYP3A inducers (7.2).

USE IN SPECIFIC POPULATIONS

- Lactation: Advise not to breastfeed. (8.2)
- Hepatic Impairment: Avoid use of IMBRUVICA in patients with severe hepatic impairment. In patients with mild or moderate impairment, reduce IMBRUVICA dose (2.4, 8.6).

See 17 for PATIENT COUNSELING INFORMATION and FDA approved patient labeling.

Revised: 8/2022

BRUIN CLL-313: Adverse Events of Interest

	Pirtobrutinib (n=140)		BR (n=132)	
	Any Grade n (%)	Grade ≥3 n (%)	Any Grade n (%)	Grade ≥3 n (%)
Infection	80 (57.1)	19 (13.6)	44 (33.3)	11 (8.3)
Infection without COVID-19	72 (51.4)	19 (13.6)	38 (28.8)	9 (6.8)
Bleeding	36 (25.7)	1 (0.7)	2 (1.5)	0 (0)
Hemorrhage	17 (12.1)	1 (0.7)	2 (1.5)	0 (0)
Bruising	16 (11.4)	0 (0)	0 (0)	0 (0)
Petechiae and purpura	8 (5.7)	0 (0)	0 (0)	0 (0)
Neutropenia	21 (15.0)	13 (9.3)	68 (51.5)	60 (45.5)
Anemia	14 (10.0)	6 (4.3)	21 (15.9)	10 (7.6)
Thrombocytopenia	12 (8.6)	4 (2.9)	23 (17.4)	9 (6.8)
Atrial fibrillation and atrial flutter	2 (1.4)	1 (0.7)	2 (1.5)	1 (0.8)
≥75 years old	1 (5.0)	0	1 (4.3)	0
Hypertension	11 (7.9)	4 (2.9)	6 (4.5)	4 (3.0)

Jurczak et al. ASH 2025; Jurczak et al. JCO 2026

Why start with continuous BTK inhibitor? (courtesy A. Tredeschi)

Trials with significant OS improvement over chemoimmunotherapy:

Continuous BTKi: RESONATE-2, ELEVATE-TN, ECOG1912

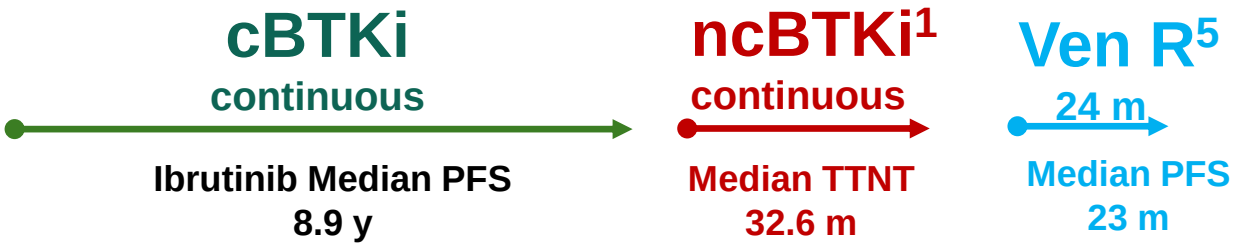
Fixed duration BCL2i: (GLOW)?

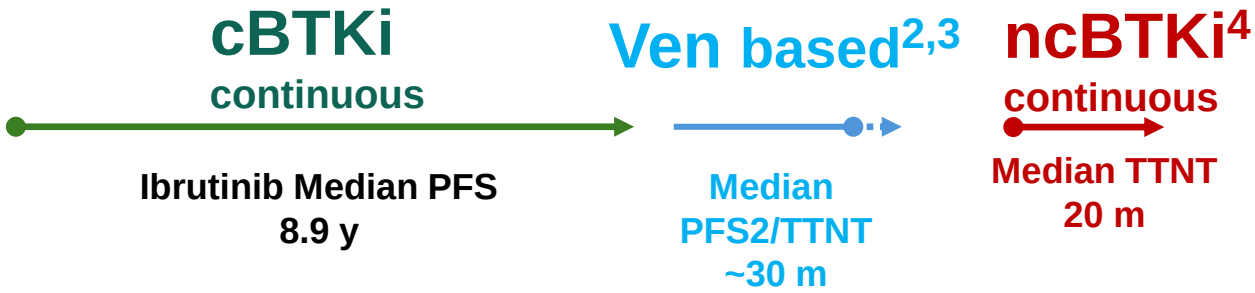
Efficacy irrespective of risk factors (IGHV, 17p deletion, *TP53* mutation)

Burger et al, EHA 2025

Shanafelt et al, Blood Advances 2025

Why start with continuous BTK inhibitor? (courtesy A. Tredeschi): Well-established 2nd and 3rd Line Teament Options





1 Eyre T et al, ASH 2025
2 Hampel PH et al, ASH 2024 ;
3 Ghosh et al, AmJ Hematol 2025
4 Sharman J et al, JCO 2025
5 Thompso et al, ASH 2024

CLL17: STUDY DESIGN

Patients with previously untreated CLL

1:1:1 randomization
Stratification according to fitness, del17p/*TP53*, IGHV

Ibrutinib 420 mg po daily until PD

Venetoclax 400 mg po daily (c1 d22 – c12)
Obinutuzumab 1000 mg iv (c1 d1(2)/8/15, c 2-6 d1)

Venetoclax 400 mg po daily (c4 d1 – c15)
Ibrutinib 420 mg po daily (c1 d1 – c15)

976 patients screened, in 174 sites, across 13 countries.

Patient enrollment from February 2021 to November 2022.

Median observation time: 34.2 months (IQR 30.3-39.3)

Al-Sawaf et al. ASH 2025; *Al-Sawaf et al. NEJM 2026*

CLL17: PATIENT CHARACTERISTICS

		VO	VI	I
	N	**303**	**305**	**301**
Demographics	Male (%)	216 (71.3)	204 (66.9)	196 (65.1)
	Median age (range)	66 (40-90)	66 (37-83)	65 (34-85)
	Age >65 (%)	155 (51.2)	158 (51.8)	146 (48.5)
	Median CIRS (range)	3 (0-17)	3 (0-18)	3 (1-15)
	GFR <70 (%)	101 (33.6)	109 (35.7)	95 (31.7)
	Unfit* (%)	134 (44.5)	136 (44.6)	130 (43.2)
Risk factors	High TLS risk (by ALC and LN)	76 (25.7)	70 (23.0)	67 (22.6)
	Unmutated IGHV status	171 (56.4)	172 (56.4)	171 (56.8)
	*TP53*mut/del17p	23 (7.6)	25 (8.2)	21 (7.0)
	High/Very High CLL-IPI	176 (61.5)	172 (59.3%)	172 (59.9%)
	Binet B/C	232 (76.6%)	213 (69.8%)	225 (75.0%)
	CKT ≥ 3	42 (15.8)	53 (20.0)	58 (21.9)

* Defined by cumulative illness rating scale >6 and/or GFR <70 ml/min

Al-Sawaf et al. ASH 2025; *Al-Sawaf et al. NEJM 2026*

CLL17: ADVERSE EVENTS

Selected adverse events of interest, all CTC grades

	VO	VI	I
Safety population – No. (%)	**295**	**303**	**298**
Blood and lymphatic system disorders	174 (59.0)	130 (42.9)	85 (28.5)
Febrile neutropenia	14 (4.7)	7 (2.3)	0 (0)
Neutropenia	155 (52.5)	110 (36.3)	49 (16.4)
Cardiac disorders	41 (13.9)	72 (23.8)	103 (34.6)
Atrial fibrillation	11 (3.7)	38 (12.5)	50 (16.8)
Gastrointestinal disorders	176 (59.7)	225 (74.3)	189 (63.4)
Diarrhea	80 (27.1)	143 (47.2)	104 (34.9)
Infections and infestations	225 (76.3)	243 (80.2)	238 (79.9)
COVID-19	113 (38.3)	128 (42.2)	117 (39.3)
Pneumonia	41 (13.9)	28 (9.2)	40 (13.4)
Metabolism and nutrition disorders	90 (30.5)	75 (24.8)	72 (24.2)
Tumor lysis syndrome	12 (4.1)	4 (1.3)	1 (0.3)
Neoplasms benign, malignant and unspecified	35 (11.9)	35 (11.6)	55 (18.5)
Richter Transformation	4 (1.4)	1 (0.3)	4 (1.3)
Vascular disorders	60 (20.3)	102 (33.7)	124 (41.6)
Hypertension	34 (11.5)	51 (16.8)	72 (24.2)

Al-Sawaf et al. ASH 2025; *Al-Sawaf et al. NEJM 2026*

CLL17: ADVERSE EVENTS

Selected adverse events of interest

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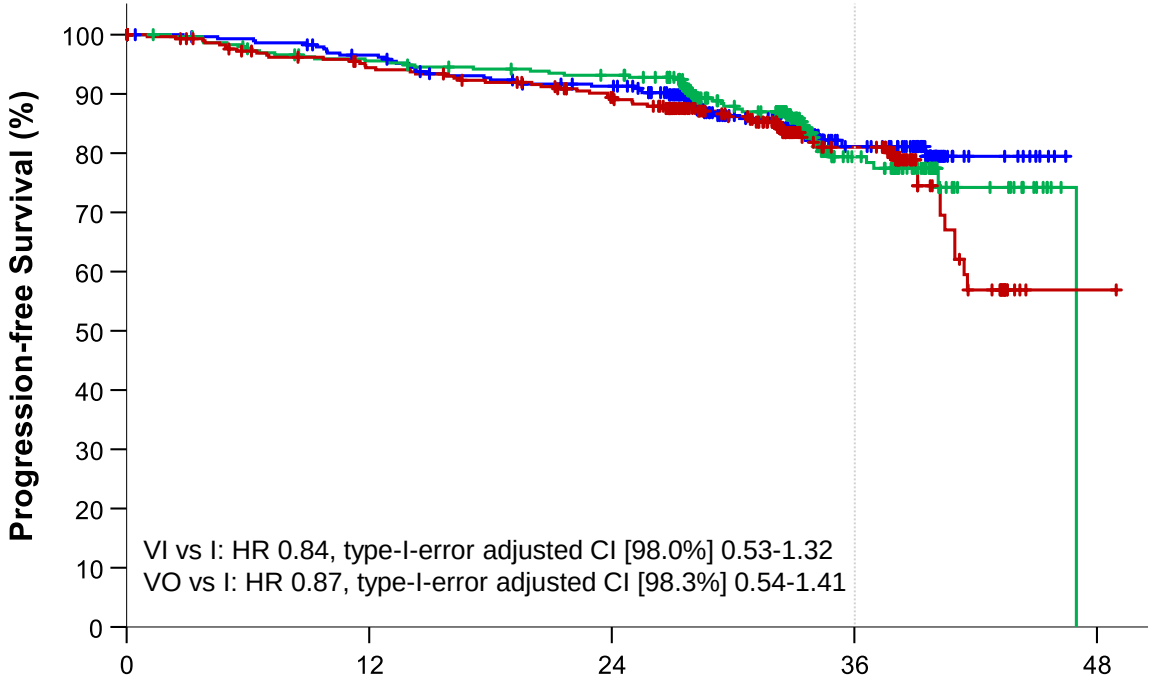
COVID-19	113 (38.3)	128 (42.2)	117 (39.3)
Pneumonia	41 (13.9)	28 (9.2)	40 (13.4)
Grade 3-5 Infections	**VO**	**VI**	**I**
	295	**303**	**298**
Infections and infestations	103 (34.9)	76 (25.1)	74 (24.8)
COVID-19	47 (15.9)	26 (8.6)	20 (6.7)
Pneumonia	29 (9.8)	22 (7.3)	22 (7.4)

CLL17: PROGRESSION-FREE SURVIVAL



Patients at risk

VO	303	278	256	77	0
VI	305	278	267	82	0
I	301	267	243	94	1

3-year PFS

I 81.0%

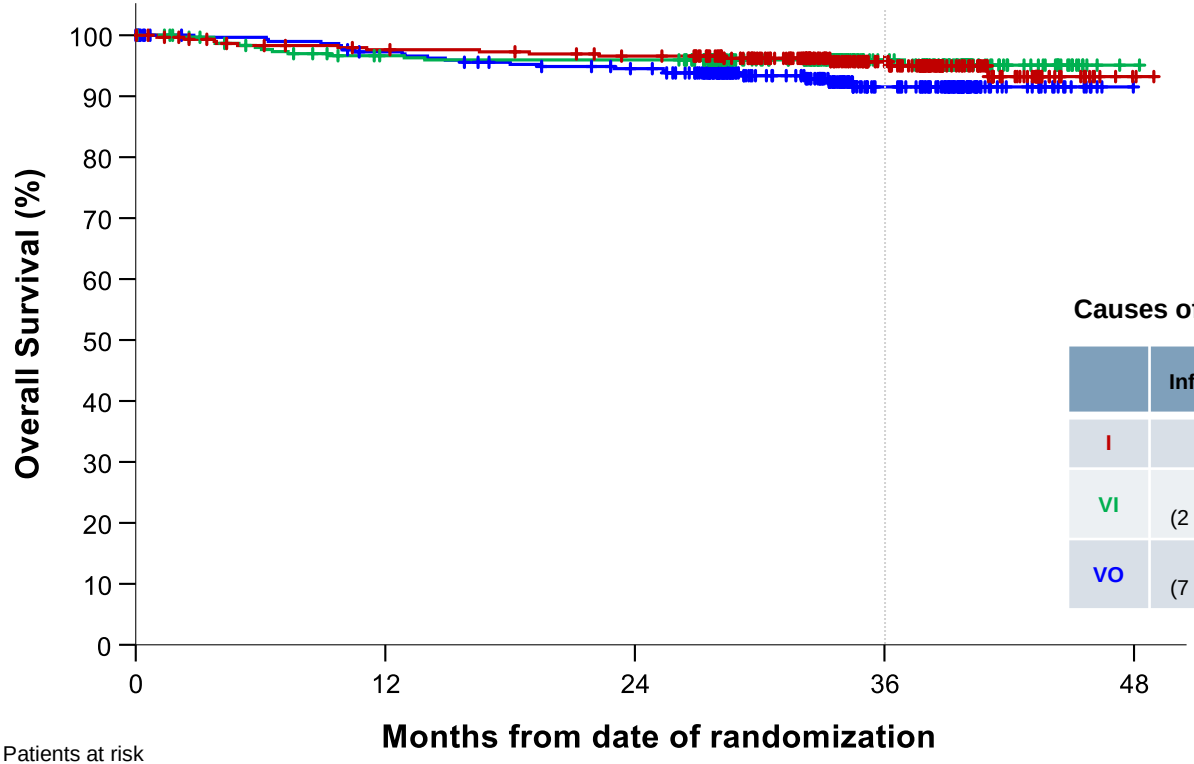
VI 79.4 %

VO 81.1%

	PD	Death
I	46	11
VI	37	13
VO	25	21

Al-Sawaf et al. ASH 2025; *Al-Sawaf et al. NEJM 2026*

CLL17: OVERALL SURVIVAL



3-year OS

I 95.7%

VI 96.0%

VO 91.5%

Causes of death

	Infection	Cardio-vascular	PD/RT	SPM	Other	Total
I	3	5	0	2	4	14
VI	7 (2 Covid)	3	0	2	1	13
VO	12 (7 Covid)	5	1	4	0	22

VI vs I: HR 0.96, 95% CI 0.45-2.05

VO vs I: HR 1.67, 95% CI 0.86-3.28

Al-Sawaf et al. ASH 2025; *Al-Sawaf et al. NEJM 2026*

Continuous BTK Inhibitors are preferred Front-Line CLL Treatment

Efficacy:

Outstanding PFS and proven OS benefit (vs. FCR!)

Availability of confirmed salvage options after (rare!) failure (switch to ncBTKi, R-Venetoclax, or BTKd)

Superior in unmutated IGHV, and 17p-/*TP53*^{mut} (OS!)

Tolerability:

Well tolerated, and 2nd / 3rd generation BTKi available with further improvement

No cumbersome TLS prophylaxis & management, no hospital stays and therefore convenient therapy initiation

No need for CD20 antibody (obinutuzumab) addition with complications of IRR, PML, COVID, deaths (!) etc.