VENCLEXTA + GAZYVA® (obinutuzumab) delivers the

STRENGTH TO STOP

AFTER 12 MONTHS OF CHEMO-FREE TREATMENT IN 1L CLL[1]

- The VEN+G regimen is designed to be completed after 12 months (twelve 28-day treatment cycles): GAZYVA is administered in Cycles 1–6 and VENCLEXTA is taken orally 400 mg/day from Cycle 3, Day 1, after the first cycle of GAZYVA and the 5-week VENCLEXTA dose ramp-up
- In a randomized clinical trial of 432 patients with previously untreated CLL (216 patients in each treatment arm), VEN+G significantly reduced the risk of death or progression by 67% vs GAZYVA + chlorambucil (HR=0.33; 95% CI: 0.22–0.51 [*P*<0.0001]). After a median follow-up of 28 months (range: 0.1–36 months), median PFS was not reached in either arm

1L=first line; CLL=chronic lymphocytic leukemia; VEN+G=VENCLEXTA + GAZYVA; HR=hazard ratio; CI=confidence interval; PFS=progression-free survival.

Indication

- VENCLEXTA is indicated for the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).

Select Important Safety Information

- Concomitant use of VENCLEXTA with *strong* CYP3A inhibitors at initiation and during ramp-up is contraindicated in patients with CLL/SLL due to the potential for increased risk of tumor lysis syndrome (TLS).
- Tumor lysis syndrome, including fatal events and renal failure requiring dialysis, has occurred in patients with high tumor burden when treated with VENCLEXTA. Patients should be assessed for TLS risk, including evaluation of tumor burden and comorbidities, and should receive appropriate prophylaxis for TLS, including hydration and anti-hyperuricemics. Reduced renal function further increases the risk. Monitor blood chemistries and manage abnormalities promptly. Employ more intensive measures (IV hydration, frequent monitoring, hospitalization) as overall risk increases.
- Concomitant use of VENCLEXTA with strong or moderate CYP3A inhibitors or P-gp inhibitors may increase the risk of TLS at initiation and during the ramp-up phase, and requires dose adjustment due to increases in VENCLEXTA exposure.
- Grade 3 or 4 neutropenia occurred in patients treated with VENCLEXTA. Monitor blood counts and for signs of infection; manage as medically appropriate.
- Fatal and serious infections such as pneumonia and sepsis have occurred in patients with VENCLEXTA. Monitor patients closely for signs and symptoms of infection and treat promptly. Withhold VENCLEXTA for Grade 3 and higher infection.
- Do not administer live attenuated vaccines prior to, during, or after treatment until B-cell recovery occurs.
- VENCLEXTA may cause embryo-fetal harm. Advise females of reproductive potential to avoid pregnancy during treatment.

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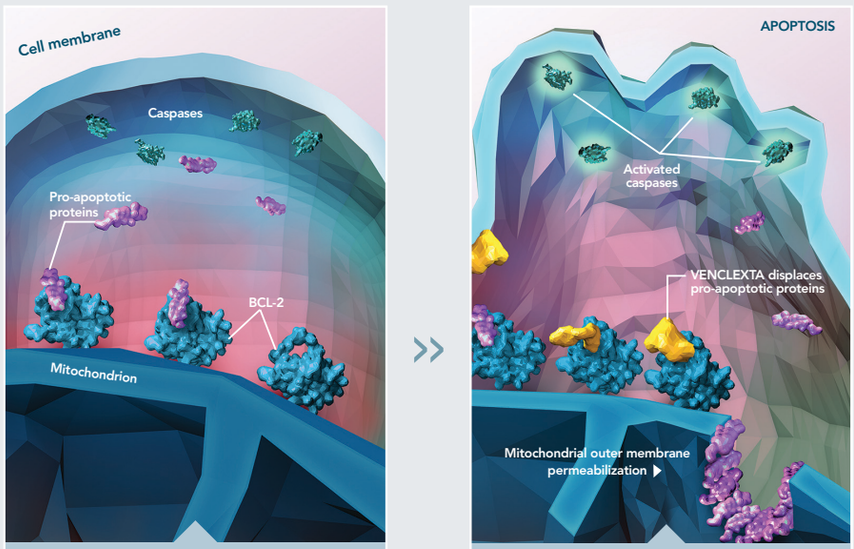
VENCLEXTA combination regimens for CLL work through 2 distinct cytotoxic mechanisms of action[1–3]

MOA

VENCLEXTA is a first-in-class treatment that targets BCL-2 to help restore the process of apoptosis[1,4]

- The ability to evade apoptosis is an important hallmark of cancer. Overexpression of BCL-2 has been demonstrated in CLL cells and has been associated with resistance to chemotherapy



Overexpressed BCL-2 allows hematologic cancer cells to evade apoptosis by sequestering pro-apoptotic proteins.[1]

VENCLEXTA selectively binds to BCL-2, displacing pro-apoptotic proteins and triggering events that lead to apoptosis.[1]

Based on preclinical studies.

GAZYVA® (obinutuzumab) and rituximab are monoclonal antibodies that target the CD20 antigen expressed on the surface of pre-B and mature B lymphocytes[2,3]

- Upon binding to CD20, the antibodies mediate B-cell lysis
- Possible mechanisms of cell lysis include complement-dependent cytotoxicity (CDC) and antibody-dependent cell-mediated cytotoxicity (ADCC)

MOA=mechanism of action; BCL-2=B-cell lymphoma 2.

Important Safety Information

Contraindication

- Concomitant use of VENCLEXTA with *strong* CYP3A inhibitors at initiation and during ramp-up phase is contraindicated in patients with CLL/SLL due to the potential for increased risk of tumor lysis syndrome (TLS).

Tumor Lysis Syndrome

- Tumor lysis syndrome, including fatal events and renal failure requiring dialysis, has occurred in patients with high tumor burden when treated with VENCLEXTA.
- In patients with CLL who followed the current (5 week) dose ramp-up and the TLS prophylaxis and monitoring measures, the rate of TLS was 2% in the VENCLEXTA CLL monotherapy studies. The rate of TLS remained consistent with VENCLEXTA in combination with obinutuzumab or rituximab. With a 2- to 3-week dose ramp-up and higher starting dose in patients with CLL/SLL, the TLS rate was 13% and included deaths and renal failure.

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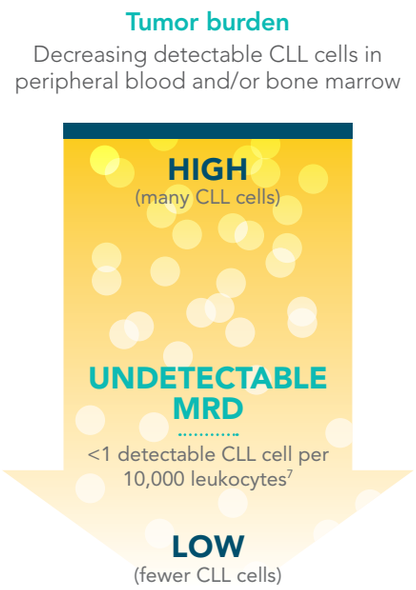
Minimal residual disease (MRD) assessment is emerging as an important measurement of disease in patients with CLL[5,6]

MRD

Achieving undetectable MRD in CLL means a patient has no detectable cancer cells, at a threshold of <1 detectable CLL cell per 10,000 leukocytes[7]



- MRD can be measured in the bone marrow and/or peripheral blood[7]
- MRD status at the end of treatment can be used to help assess the response to therapy[6,7]
- MRD negativity may also be referred to as "undetectable minimal residual disease"[6]
- While undetectable MRD and response rates are both measures of disease, it is possible for a patient with a PR to be MRD negative, and for a patient with a CR to be MRD positive[8]
- FDA considers MRD as not yet an established surrogate for clinical outcomes in patients with CLL[9]
- The FDA MRD guidance indicates that the therapeutic paradigm with small molecule inhibitors of the B-cell receptor signaling pathway and other novel products is rapidly evolving in this area[9]

Updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and iwCLL guidelines, as well as recent guidance from the FDA, indicate that undetectable MRD is emerging as an important measurement of disease.[5,6,9]

PR=partial remission; CR=complete remission; FDA=US Food and Drug Administration; iwCLL=International Workshop on Chronic Lymphocytic Leukemia.

Important Safety Information

Tumor Lysis Syndrome (cont'd)

- VENCLEXTA poses a risk for TLS at initiation and during the ramp-up phase. Changes in blood chemistries consistent with TLS that require prompt management can occur as early as 6 to 8 hours following the first dose of VENCLEXTA and at each dose increase.
- Patients should be assessed for TLS risk, including evaluation of tumor burden and comorbidities, and should receive appropriate prophylaxis for TLS, including hydration and anti-hyperuricemics. Reduced renal function further increases the risk. Monitor blood chemistries and manage abnormalities promptly. Interrupt dosing if needed. Employ more intensive measures (IV hydration, frequent monitoring, hospitalization) as overall risk increases.
- Concomitant use of VENCLEXTA with strong or moderate CYP3A inhibitors or P-gp inhibitors may increase the risk of TLS at initiation and during the ramp-up phase, and requires dose adjustment due to increases in VENCLEXTA exposure.

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History of treatment options in 1L CLL[10]

1L CLL

FIXED-DURATION CHEMOIMMUNOTHERAPY

TREAT-TO-PROGRESSION TARGETED ORAL-BASED THERAPY

FIXED-DURATION CHEMO-FREE THERAPY

VEN+G is the only chemo-free regimen for 1L CLL with a fixed treatment duration of 12 months.[1]

Important Safety Information

Neutropenia

- In patients with CLL, Grade 3 or 4 neutropenia developed in 63% to 64% of patients and Grade 4 neutropenia developed in 31% to 33% of patients treated with VENCLEXTA in combination and monotherapy studies. Febrile neutropenia occurred in 4% to 6% of patients treated with VENCLEXTA in combination and monotherapy studies.
- Monitor complete blood counts throughout the treatment period. Interrupt dosing or reduce dose for severe neutropenia. Consider supportive measures including antimicrobials for signs of infection and use of growth factors (e.g., G-CSF).

Infections

- Fatal and serious infections such as pneumonia and sepsis have occurred in patients treated with VENCLEXTA. Monitor patients closely for signs and symptoms of infection and treat promptly. Withhold VENCLEXTA for Grade 3 and higher infection.

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How can fixed duration treatment benefit your CLL patients?

Break free from chemotherapy and continuous oral treatment in CLL with VENCLEXTA, the only chemo-free regimen with a fixed treatment duration of 12 months in 1L CLL with VEN+G and 24 months* in R/R CLL with VEN+R[1]

TREATMENT-FREE PERIOD

Fixed duration offers patients[1]:

- A return to life without a daily reminder of their treatment and disease
- A defined end to treatment that encourages compliance and optimizes clinical outcomes[11,12]

LIMITED TREATMENT EXPOSURE

No additional VENCLEXTA regimen exposure after completing treatment[1]

FIXED TREATMENT, FIXED COST

No additional VENCLEXTA regimen patient out-of-pocket costs after completing treatment per the recommended dosing[1†]

*From Cycle 1, Day 1 of rituximab after the 5-week VENCLEXTA dose ramp-up.

†Drug cost refers to the Wholesale Acquisition Cost. Coverage and patient out-of-pocket costs for VEN+G and VEN+R vary by health plan. Patients may still incur out-of-pocket costs for other treatments or tests as directed by their healthcare providers.

R/R=relapsed/refractory; VEN+R=VENCLEXTA + rituximab.

Important Safety Information

Immunization

- Do not administer live attenuated vaccines prior to, during, or after treatment with VENCLEXTA until B-cell recovery occurs. Advise patients that vaccinations may be less effective.

Embryo-Fetal Toxicity

- VENCLEXTA may cause embryo-fetal harm when administered to a pregnant woman. Advise females of reproductive potential to avoid pregnancy during treatment.

Increased Mortality in Patients with Multiple Myeloma when VENCLEXTA is Added to Bortezomib and Dexamethasone

- In a randomized trial (BELLINI; NCT02755597) in patients with relapsed or refractory multiple myeloma, the addition of VENCLEXTA to bortezomib plus dexamethasone, a use for which VENCLEXTA is not indicated, resulted in increased mortality. Treatment of patients with multiple myeloma with VENCLEXTA in combination with bortezomib plus dexamethasone is not recommended outside of controlled clinical trials.

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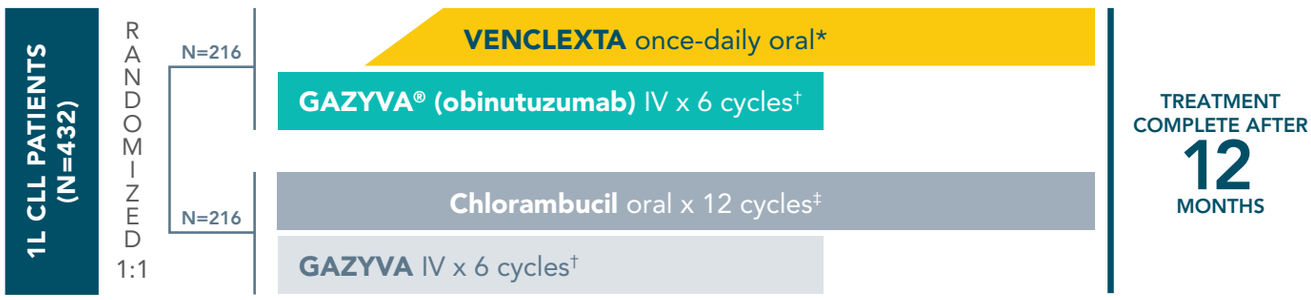
Designed for patients to complete treatment in 12 months[1]

1L CLL

The CLL14 trial evaluated PFS with VEN+G, a fixed-duration treatment regimen

- CLL14 was a multicenter, open-label, actively controlled phase 3 trial (randomized 1:1)



Graphic not to scale.

98% ALC REDUCTION

After the first treatment cycle of GAZYVA and before the VENCLEXTA dose ramp-up, patients' ALC was reduced by 98%[13§]

- Per the trial protocol, tumor burden was assessed based on ALC and lymph node size. The effect of the first GAZYVA treatment cycle on lymph node size was not evaluated

Select inclusion criteria

- Coexisting medical conditions (total CIRS >6 or CLcr <70 mL/min), age ≥18 years[1]

Select clinical endpoints

- **Primary endpoint:** PFS (IRC-assessed PFS was the basis for FDA approval of VEN+G)
- **Select secondary endpoints:** MRD in bone marrow, CR/CRi (INV-assessed), MRD in peripheral blood, MRD in CR/CRi in bone marrow, MRD in CR/CRi in peripheral blood, ORR (INV-assessed)[1,13]

*VENCLEXTA oral tablets were administered according to the 5-week dose ramp-up schedule: 20 mg daily during Cycle 1, Days 22-28; 50 mg daily during Cycle 2, Days 1-7; 100 mg daily during Cycle 2, Days 8-14; 200 mg daily during Cycle 2, Days 15-21; 400 mg daily during Cycle 2, Days 22-28 and on Days 1-28 of all subsequent cycles until the end of Cycle 12.

†GAZYVA intravenous (IV) infusion was administered at 1000 mg on Day 1 (the first dose could be split as 100 mg and 900 mg on Days 1 and 2), and on Days 8 and 15 of Cycle 1. For all subsequent 28-day cycles, GAZYVA 1000 mg was administered on Day 1 for a total of 6 cycles.

‡Chlorambucil was administered at 0.5 mg/kg orally on Days 1 and 15 of each 28-day cycle for 12 cycles.

§The trial started with an initial cycle of GAZYVA followed by the 5-week VENCLEXTA dose ramp-up, and reduced median lymphocyte count from 55 x 10^9 cells/L at baseline to 1.27 x 10^9 cells/L at Day 15. Median lymphocyte counts are descriptive in nature and not powered for any type of comparison. Changes in TLS risk status based on ALC reduction were at the discretion of the trial investigators.

ALC=absolute lymphocyte count; CIRS=Cumulative Illness Rating Scale; CLcr=creatinine clearance; IRC=independent review committee; CRi=complete remission with incomplete bone marrow recovery; INV=investigator; ORR=overall response rate; TLS=tumor lysis syndrome.

Important Safety Information

Adverse Reactions

- **In patients with CLL receiving combination therapy with obinutuzumab,** serious adverse reactions were most often due to febrile neutropenia and pneumonia (5% each). The most common adverse reactions (≥20%) of any grade were neutropenia (60%), diarrhea (28%), and fatigue (21%).
- **In patients with CLL receiving combination therapy with rituximab,** the most frequent serious adverse reaction (≥5%) was pneumonia (9%). The most common adverse reactions (≥20%) of any grade were neutropenia (65%), diarrhea (40%), upper respiratory tract infection (39%), fatigue (22%), cough (22%), and nausea (21%).
- **In patients with CLL/SLL receiving monotherapy,** the most frequent serious adverse reactions (≥5%) were pneumonia (9%), febrile neutropenia (5%), and sepsis (5%). The most common adverse reactions (≥20%) of any grade were neutropenia (50%), diarrhea (43%), nausea (42%), upper respiratory tract infection (36%), anemia (33%), fatigue (32%), thrombocytopenia (29%), musculoskeletal pain (29%), edema (22%), and cough (22%).

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VEN+G was studied in patients whose age and disease characteristics were representative of the broad CLL patient population[13–15]

1L CLL

Baseline demographics and disease characteristics[1,13]*		
Characteristic	**VEN+G (N=216)**	**GClb (N=216)**
Age, years; median (range)	72 (43–89)	71 (41–89)
Age ≥70, %	62	59
Male, %	68	66
Binet stage, %		
Binet stage A	21	20
Binet stage B	36	37
Binet stage C	43	43
Median CIRS score (range)	9 (0–23)	8 (1–28)
CLcr <70 mL/min, %	60	55
CLL subsets, %		
17p deletion	9	7
TP53 mutation	9	6
11q deletion	18	20
IgVH unmutated	56	57
IgVH mutated	35	38
High TLS risk category, %†	22	20
Lymph nodes ≥10 cm	5	5
Lymph nodes ≥5 cm and ALC ≥25 x 10^9/L	14	12
Medium TLS risk, %	64	68
Low TLS risk, %	13	12
ECOG performance status, %		
0	41	48
1	46	41
2	13	12
Baseline ALC (g/L); median	56	58

*Patients with missing results not included.
†TLS risk category was chosen based on investigator discretion, lymph node size, and ALC.[1]
GClb=GAZYVA + chlorambucil; *TP53*=tumor protein 53; *IgVH*=immunoglobulin heavy-chain variable gene; ECOG=Eastern Cooperative Oncology Group.

Important Safety Information

Drug Interactions

- Concomitant use with a strong or moderate CYP3A inhibitor or a P-gp inhibitor increases VENCLEXTA exposure, which may increase VENCLEXTA toxicities, including the risk of TLS. Adjust VENCLEXTA dosage and closely monitor patients for signs of VENCLEXTA toxicities. Resume the VENCLEXTA dosage that was used prior to concomitant use of a strong or moderate CYP3A inhibitor or a P-gp inhibitor 2 to 3 days after discontinuation of the inhibitor.
- Patients should avoid grapefruit products, Seville oranges, and starfruit during treatment as they contain inhibitors of CYP3A.
- Avoid concomitant use of strong or moderate CYP3A inducers.

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VEN+G demonstrated durable PFS after stopping treatment at 12 months[1]

1L CLL

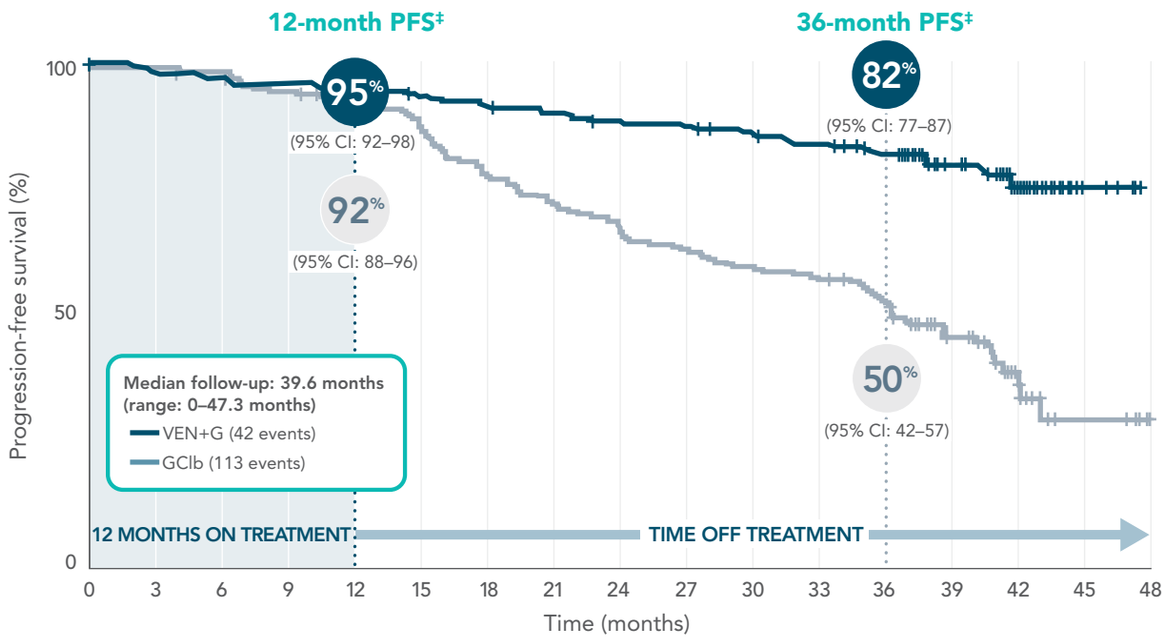
IRC-assessed PFS (primary endpoint)

67%

reduction in risk of progression or death vs GClb (HR=0.33; 95% CI: 0.22–0.51 [*P*<0.0001])

- After a median follow-up of 28 months (range: 0.1–36 months), there were 29 events (14 progression and 15 death events) in the VEN+G arm compared with 79 in the GClb arm (71 progression and 8 death events).* Median PFS was not reached in either arm

36-month post hoc analysis of INV-assessed PFS[16†]



Number of patients at risk

VEN+G	216	200	195	195	192	188	183	179	176	173	167	162	97	79	23	8
GClb	216	201	194	190	184	166	153	141	129	123	117	113	69	54	11	5

The post hoc analysis was not tested for statistical significance.

- With a median follow-up of 39.6 months (range: 0–47.3 months), median PFS was not reached in the VEN+G arm and was estimated to be 35.6 months (95% CI: 33.7–40.7) in the GClb arm [HR=0.31; 95% CI: 0.22–0.44]
- Of the 42 events in the VEN+G arm, 21 were death and 21 were disease progression. Of the 113 events in the GClb arm, 11 were death and 102 were disease progression[1,16]*
- **Overall survival:** In a post hoc analysis (39.6-month median follow-up), overall survival was not sufficiently mature for evaluation, with 27 events in the VEN+G arm and 27 events in the GClb arm

*Number of events based on earliest event of disease progression or death due to any cause. Events due to progression may include deaths occurring post-progression.

†1-year update from primary analysis, based on data as of clinical data cutoff date of August 23, 2019.

‡The 1-year and 3-year PFS estimates were not prespecified and were not tested for statistical significance.

Important Safety Information

Drug Interactions (cont'd)

- Avoid concomitant use of VENCLEXTA with a P-gp substrate. If concomitant use is unavoidable, separate dosing of the P-gp substrate at least 6 hours before VENCLEXTA.
- Monitor international normalized ratio (INR) closely in patients receiving warfarin.

Lactation

- Advise nursing women to discontinue breastfeeding during treatment with VENCLEXTA.

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Descriptive subgroup analyses were performed to evaluate consistency with the primary PFS endpoint[1,13]

1L CLL

- The subgroup analyses were not powered or tested to demonstrate a statistically significant difference in PFS treatment effect for any subgroup examined
- Subgroups represent a small sample of the ITT population and differences in subgroup demographics or disease characteristics may limit the ability to interpret the data. These data are descriptive and interpretation for statistical certainty is limited

IRC-assessed PFS subgroup analyses[1,13]*					Progression or death events (%)[13]			
Demographic Subgroups	**Hazard Ratio**	**95% CI**	Favors **VEN+G**	Favors **GClb**	**VEN+G** n	**Events (%)**	**GClb** n	**Events (%)**
All patients (ITT population)	0.33	0.22–0.51			216	29 (13)	216	79 (37)
Age								
≥70 years	0.35	0.21–0.60			134	20 (15)	127	47 (37)
Cytogenetic hierarchical type								
17p deletion	0.35	0.13–0.94			17	7 (41)	14	10 (71)
***IgVH* mutational status**								
Mutated	0.57	0.25–1.27			76	9 (12)	83	17 (21)
Unmutated	0.21	0.12–0.37			121	16 (13)	123	57 (46)
***TP53* mutational status**								
Mutated	0.31	0.11–0.88			19	6 (32)	13	10 (77)
Unmutated	0.22	0.12–0.40			152	14 (9)	144	52 (36)
ECOG performance status at baseline								
0	0.38	0.19–0.76			89	11 (12)	103	28 (27)
1	0.25	0.14–0.47			99	14 (14)	87	43 (49)
2	0.36	0.09–1.38			27	3 (11)	25	7 (28)

*HR values were stratified for the ITT population.[1]
All other subgroup HR values were unstratified.
ITT=intent to treat.

Important Safety Information

Females and Males of Reproductive Potential

- Advise females of reproductive potential to use effective contraception during treatment with VENCLEXTA and for at least 30 days after the last dose.
- Based on findings in animals, male fertility may be compromised by treatment with VENCLEXTA.

Hepatic Impairment

- Reduce the dose of VENCLEXTA for patients with severe hepatic impairment (Child-Pugh C); monitor these patients more closely for signs of toxicity. No dose adjustment is recommended for patients with mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment.

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VEN+G demonstrated impressive rates of complete remission and undetectable MRD with 12 months of treatment[1]

1L CLL

Response rates assessed by INV*†

50%
VEN+G
CR/CRi

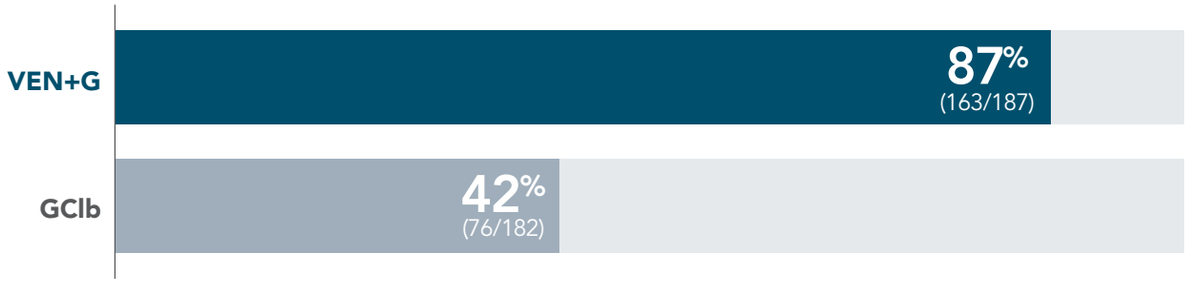
INV-assessed response rates for VEN+G (N=216) vs GClb (N=216), respectively

- **CR+CRi‡:** 50% (n=107) vs 23% (n=50)
  - **CR:** 46% (n=100) vs 22% (n=47)
- **ORR§:** 85% (n=183; 95% CI: 79–89) vs 71% (n=154; 95% CI: 65–77)
- **PR:** 35% (n=76) vs 48% (n=104)

Rates of undetectable MRD in peripheral blood in ITT population (secondary endpoint)

- Undetectable MRD was evaluated using allele-specific oligonucleotide polymerase chain reaction (ASO-PCR) 3 months after treatment ended and was defined as having achieved <1 CLL cell per 10,000 leukocytes
- Undetectable MRD in peripheral blood (ITT population) was 76% (163/216) in VEN+G patients (95% CI: 69–81), compared with 35% (76/216) in GClb patients (95% CI: 29–42)‡
  - In patients with CR, the rate of undetectable MRD in peripheral blood was 87% (87/100) for VEN+G (95% CI: 79–93) and 62% (29/47) for GClb (95% CI: 46–75)‖

Rates of undetectable MRD in peripheral blood in evaluable patients[13]*



- The population with evaluable results (N=369) excludes results missing due to progressive disease (PD), withdrawal (including withdrawal due to toxicity), deaths, MRD status unknown, and other missing samples or assessments. Not prespecified or tested for statistical significance

91% concordance: Of the 134 patients with undetectable MRD in peripheral blood who had matching bone marrow specimens, 122 patients had undetectable MRD in the bone marrow.[1]

- VEN+G undetectable MRD in bone marrow was 57% in the ITT population (n=123/216; 95% CI: 50–64) and 79% in evaluable patients (n=123/156)[13]

*Assessed 3 months after treatment completion.
†Per the 2008 iwCLL guidelines.
‡$P<0.0001$.
§$P=0.0007$.
‖$P=0.0005$.

Important Safety Information

Contraindication

- Concomitant use of VENCLEXTA with *strong* CYP3A inhibitors at initiation and during ramp-up phase is contraindicated in patients with CLL/SLL due to the potential for increased risk of tumor lysis syndrome (TLS).

Tumor Lysis Syndrome

- Tumor lysis syndrome, including fatal events and renal failure requiring dialysis, has occurred in patients with high tumor burden when treated with VENCLEXTA.
- In patients with CLL who followed the current (5 week) dose ramp-up and the TLS prophylaxis and monitoring measures, the rate of TLS was 2% in the VENCLEXTA CLL monotherapy studies. The rate of TLS remained consistent with VENCLEXTA in combination with obinutuzumab or rituximab. With a 2- to 3-week dose ramp-up and higher starting dose in patients with CLL/SLL, the TLS rate was 13% and included deaths and renal failure.

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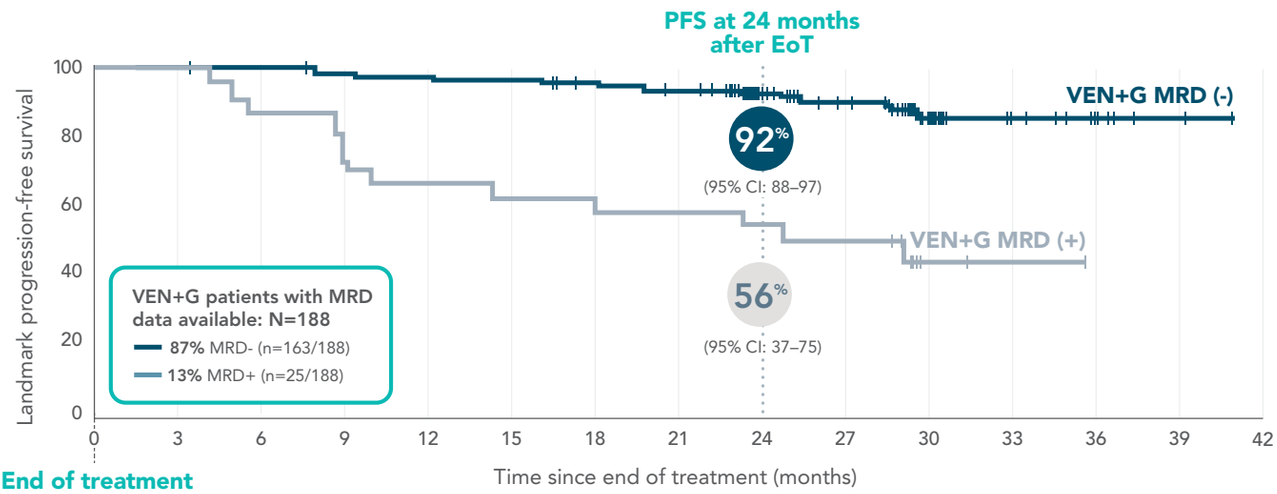
PFS by MRD status

1L CLL

PFS was assessed in evaluable patients who achieved undetectable MRD in peripheral blood 3 months after treatment completion[16]

Post hoc analysis



Number of patients at risk

VEN+G MRD (-)	163	162	161	157	156	155	150	147	91	76	34	16	5	2
VEN+G MRD (+)	25	25	22	18	17	16	15	15	11	10	2	1		

From the 36-month post hoc analysis of INV-assessed PFS (1-year update). The clinical data cutoff date was August 23, 2019. Not tested for statistical significance.

EoT=end of treatment.

Important Safety Information

Tumor Lysis Syndrome (cont'd)

- VENCLEXTA poses a risk for TLS at initiation and during the ramp-up phase. Changes in blood chemistries consistent with TLS that require prompt management can occur as early as 6 to 8 hours following the first dose of VENCLEXTA and at each dose increase.
- Patients should be assessed for TLS risk, including evaluation of tumor burden and comorbidities, and should receive appropriate prophylaxis for TLS, including hydration and anti-hyperuricemics. Reduced renal function further increases the risk. Monitor blood chemistries and manage abnormalities promptly. Interrupt dosing if needed. Employ more intensive measures (IV hydration, frequent monitoring, hospitalization) as overall risk increases.
- Concomitant use of VENCLEXTA with strong or moderate CYP3A inhibitors or P-gp inhibitors may increase the risk of TLS at initiation and during the ramp-up phase, and requires dose adjustment due to increases in VENCLEXTA exposure.

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VEN+G offers a well-studied safety profile with exposure limited to 12 months[1]

1L CLL

VEN+G safety from the CLL14 trial

- In the VEN+G arm, fatal adverse reactions that occurred in the absence of disease progression and with onset within 28 days of the last study treatment were reported in 2% (4/212) of patients in VEN+G compared to 1% (3/214) of patients in the GClb arm[1,13]
- Serious adverse reactions were reported in 49% of patients in the VEN+G arm, most often due to febrile neutropenia and pneumonia (5% each)
- The median duration of exposure to VENCLEXTA was 10.5 months (range: 0–13.5 months). The median number of cycles was 6 for obinutuzumab and 12 for chlorambucil

Rates of discontinuation, dose reduction, and dose interruption

- In the VEN+G arm, adverse reactions led to treatment discontinuation in 16% of patients, dose reduction in 21%, and dose interruption in 74%
- Neutropenia led to dose interruption of VENCLEXTA in 41% of patients, reduction in 13%, and discontinuation in 2%

Common (≥10%) adverse reactions in patients treated with VEN+G

	VEN+G		GClb	
Adverse Reaction by Body System	**Any Grade (%) n=212**	**Grade ≥3 (%) n=212**	**Any Grade (%) n=214**	**Grade ≥3 (%) n=214**
Blood and lymphatic system disorders				
Neutropenia*	60	56	62	52
Anemia*	17	8	20	7
Gastrointestinal disorders				
Diarrhea	28	4	15	1
Nausea	19	0	22	1
Constipation	13	0	9	0
Vomiting	10	1	8	1
General disorders and administration site conditions				
Fatigue*	21	2	23	1
Infections and infestations				
Upper respiratory tract infection*	17	1	17	1

*Includes multiple adverse reaction terms.

For common laboratory abnormalities data, please see Table 10 in the VENCLEXTA full Prescribing Information

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VEN+G offers a well-studied safety profile with exposure limited to 12 months[1]

1L CLL

No clinical TLS was observed in the CLL14 trial[1,13]

0%
CLINICAL TLS

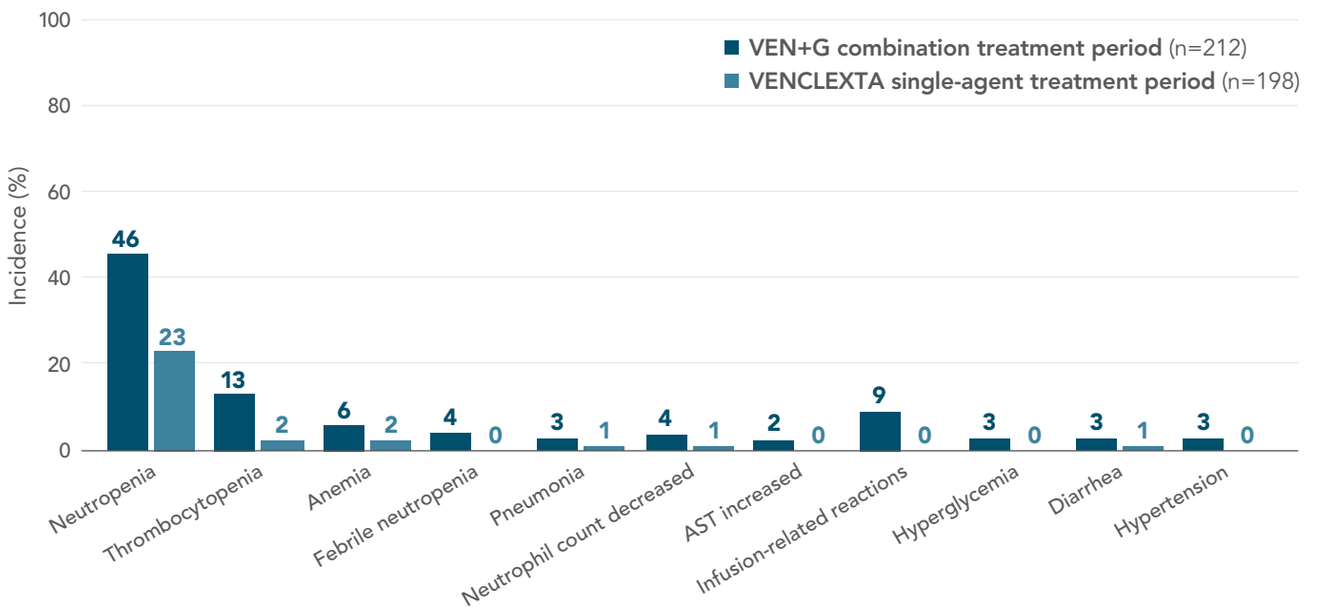
- The dose ramp-up was designed to gradually debulk tumor burden and mitigate TLS risk[1]
- By implementing the TLS prophylaxis and monitoring protocol, 0% incidence of clinical TLS was observed in the 1L CLL trial. Laboratory TLS occurred in 1% (3/212) of patients treated with VEN+G[1,13]
- All 3 TLS events resolved and did not lead to withdrawal from the study. GAZYVA® (obinutuzumab) administration was delayed in 2 cases in response to the TLS events[1]

During treatment with single-agent VENCLEXTA after completion of VEN+G combination treatment[1]:

- The most common all-grade adverse reaction (≥10% of patients) reported was neutropenia (26%)
- The most common grade ≥3 adverse reactions (≥2% of patients) were neutropenia (23%) and anemia (2%)

No additional VEN+G drug exposure after stopping treatment at 12 months[1]

New incidence of Grade 3 and 4 adverse events (AEs) decreased after the combination treatment period[13]*



*Incidence of ≥2% during combination period.
AST=aspartate aminotransferase.

- VEN+G combination-therapy period: includes treatment-emergent adverse events occurring on or before last exposure date of GAZYVA + 29 days
- VENCLEXTA single-agent period: includes treatment-emergent adverse events occurring after start of VENCLEXTA monotherapy period to last exposure date of VENCLEXTA + 29 days
- Multiple occurrences of the same adverse event in an individual during the same treatment period are counted only once for that treatment period

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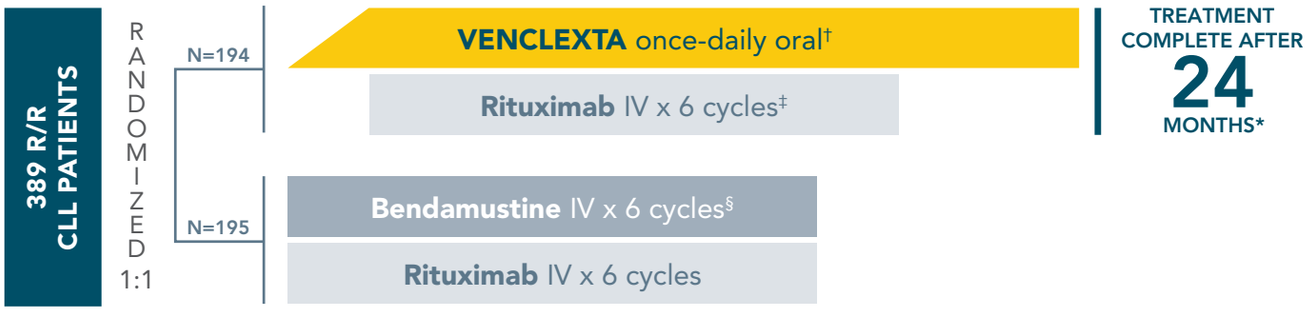
Designed to stop treatment at 24 months[1]*

R/R CLL

The MURANO trial evaluated PFS with VEN+R, a fixed-duration treatment regimen



Graphic not to scale.

- MURANO was a phase 3 multicenter, open-label, actively controlled trial (randomized 1:1)
- The 5-week VENCLEXTA dose ramp-up was designed to gradually reduce tumor burden (debulk) and decrease the risk of TLS
- Tumor burden assessments, including radiographic evaluation and blood chemistry assessment, are recommended prior to VENCLEXTA initiation to assess the risk for TLS

Select inclusion criteria

- ≥18 years of age; 1–3 prior lines of therapy, including at least 1 chemo-containing regimen; and prior bendamustine only if duration of response (DoR) ≥24 months[17]

Select clinical endpoints

- **Primary endpoint:** PFS (IRC-assessed PFS was the basis for approval of VEN+R)
- **Select secondary endpoints:** IRC-assessed CR/CRi, IRC-assessed ORR, OS, INV-assessed PFS, undetectable MRD[17,18]
  - Key secondary endpoints were ranked for hierarchical testing as: (1) IRC-assessed CR/CRi rate, (2) IRC-assessed ORR, and (3) OS. Because the study did not reach significance at the first key secondary endpoint (IRC-assessed CR/CRi rate), the remaining key secondary endpoints could not be tested for statistical significance

*From Cycle 1, Day 1 of rituximab, in the absence of disease progression or unacceptable toxicity.

†VENCLEXTA oral tablets were administered according to the 5-week dose ramp-up schedule: 20 mg daily in Week 1, 50 mg daily in Week 2, 100 mg daily in Week 3, 200 mg daily in Week 4, and 400 mg daily from Week 5 through all subsequent weeks for 24 months from Cycle 1, Day 1 of rituximab.

‡Rituximab was administered after the initial VENCLEXTA dose ramp-up and was infused on Day 1 of each 28-day cycle for 6 cycles, with a dose of 375 mg/m^2 for Cycle 1 and 500 mg/m^2 for Cycles 2-6.

§Patients randomized to bendamustine + rituximab received bendamustine at 70 mg/m^2 on Days 1 and 2 for 6 cycles (28-day cycle) and rituximab at the above-described dose and schedule.

OS=overall survival.

Important Safety Information

Neutropenia

- In patients with CLL, Grade 3 or 4 neutropenia developed in 63% to 64% of patients and Grade 4 neutropenia developed in 31% to 33% of patients treated with VENCLEXTA in combination and monotherapy studies. Febrile neutropenia occurred in 4% to 6% of patients treated with VENCLEXTA in combination and monotherapy studies.
- Monitor complete blood counts throughout the treatment period. Interrupt dosing or reduce dose for severe neutropenia. Consider supportive measures including antimicrobials for signs of infection and use of growth factors (e.g., G-CSF).

Infections

- Fatal and serious infections such as pneumonia and sepsis have occurred in patients treated with VENCLEXTA. Monitor patients closely for signs and symptoms of infection and treat promptly. Withhold VENCLEXTA for Grade 3 and higher infection.

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Baseline patient characteristics were generally well balanced between study arms[18,19]

R/R CLL

MURANO demographics and baseline characteristics*		
Characteristic	**VEN+R** (n=194)	**BR** (n=195)
Age, years; median (range)	65 (28–83)	66 (22–85)
Male, %	70	77
ECOG performance status, %		
0	57	56
1	42	43
2	1	1
Tumor burden, %		
Absolute lymphocyte count ≥25 x 10^9/L	67	69
1 or more nodes ≥5 cm	46	48
Fludarabine refractory, %	14	16
CLL subsets, %		
17p deletion	27	27
11q deletion	35	38
TP53 mutation	25	28
IgVH unmutated	68	68
Time since diagnosis, years; median (range)	6.44 (0.5–28.4)	7.11 (0.3–29.5)

*Patients with missing results not included.

The majority of patients in the study had 1 prior therapy. Chemotherapy with or without anti-CD20 was the most common prior therapy[1,18–20]

MURANO prior therapies		
Number of prior lines of therapy, %	**VEN+R** (n=194)	**BR** (n=195)
Median number (range)	1 (1–5)	
1	57	60
2	30	22
≥3	13	18
Previous CLL regimens		
Median number (range)	1 (1–5)	
Prior alkylating agents, %	95	93
Prior purine analogs, %	81	81
Prior CD20 antibodies, %	76	79
Prior B-cell receptor pathway inhibitors, %	2	3
Prior FCR, %	54	55
Prior BR, %	2	3

BR=bendamustine + rituximab; FCR=fludarabine, cyclophosphamide, rituximab.

Important Safety Information

Immunization

- Do not administer live attenuated vaccines prior to, during, or after treatment with VENCLEXTA until B-cell recovery occurs. Advise patients that vaccinations may be less effective.

Embryo-Fetal Toxicity

- VENCLEXTA may cause embryo-fetal harm when administered to a pregnant woman. Advise females of reproductive potential to avoid pregnancy during treatment.

Increased Mortality in Patients with Multiple Myeloma when VENCLEXTA is Added to Bortezomib and Dexamethasone

- In a randomized trial (BELLINI; NCT02755597) in patients with relapsed or refractory multiple myeloma, the addition of VENCLEXTA to bortezomib plus dexamethasone, a use for which VENCLEXTA is not indicated, resulted in increased mortality. Treatment of patients with multiple myeloma with VENCLEXTA in combination with bortezomib plus dexamethasone is not recommended outside of controlled clinical trials.

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VEN+R demonstrated durable PFS after stopping treatment at 24 months[1]

R/R CLL

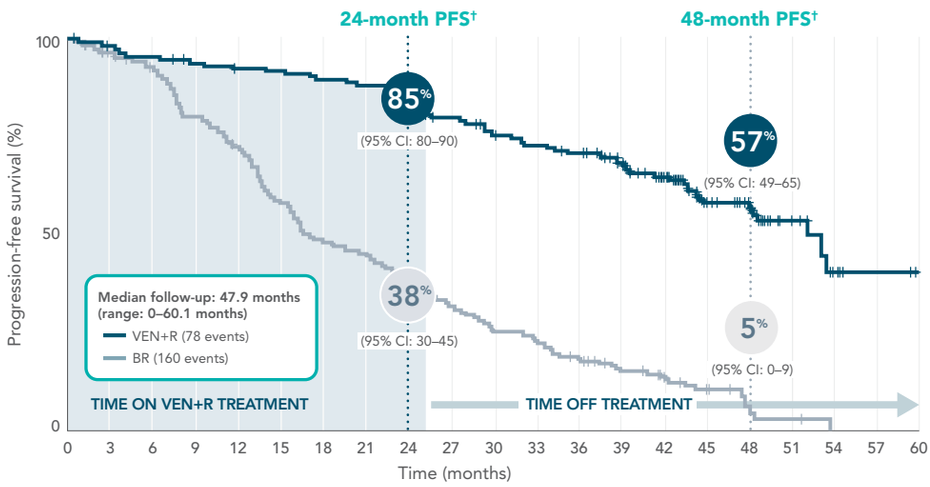
IRC-assessed PFS (primary endpoint)

81%

reduction in risk of progression or death vs BR (HR=0.19; 95% CI: 0.13–0.28 [*P*<0.0001])

- After a median follow-up of 23.4 months (range: 0–37.4+ months):
  - There were 35 events in the VEN+R arm (26 progression and 9 death events) compared with 106 events in the BR arm (91 progression and 15 death events)
  - The median PFS was not reached (NR) with VEN+R vs 18.1 months (95% CI: 15.8–22.3) with BR

48-month post hoc analysis of PFS (INV-assessed)[21]*



Number of patients at risk

VEN+R	194	190	185	179	176	174	170	167	161	150	141	134	130	118	101	55	40	14	7	2
BR	195	178	165	143	129	104	85	80	66	56	45	40	32	23	14	9	3	2		

The post hoc analysis was not tested for statistical significance.

- Median PFS was estimated to be 52.3 months‡ (95% CI: 47.9–NE) with VEN+R and was 17.1 months (95% CI: 15.7–22.1) for BR [HR=0.19; 95% CI: 0.14–0.25]
- Of the 78 events in the VEN+R arm, 14 were death and 64 were disease progression. Of the 160 events in the BR arm, 18 were death and 142 were disease progression
- Landmark PFS at 18 months post-treatment for patients who completed VEN+R (n=130) was 76% (95% CI: 67–84). Median time off treatment was 22.2 months (95% CI: 19.8–22.7)§

The National Comprehensive Cancer Network® (NCCN®) recommends venetoclax (VENCLEXTA®) in combination with rituximab as a Category 1 preferred regimen‖ for the treatment of R/R CLL/SLL patients with or without 17p deletion.[6]

*2-year data update, based on data as of clinical data cutoff date of May 8, 2019.
†2-year and 4-year PFS estimates were not prespecified and were not tested for statistical significance.
‡Median PFS for VEN+R exceeds median follow-up.
§54 patients completed the 18-month post-treatment follow-up visit (not prespecified and not powered to demonstrate statistically significant differences).
‖See NCCN Guidelines® for the NCCN definitions of Categories of Preference and Categories of Evidence and Consensus.
NE=not estimable; SLL=small lymphocytic lymphoma.

Important Safety Information

Adverse Reactions

- **In patients with CLL receiving combination therapy with obinutuzumab,** serious adverse reactions were most often due to febrile neutropenia and pneumonia (5% each). The most common adverse reactions (≥20%) of any grade were neutropenia (60%), diarrhea (28%), and fatigue (21%).
- **In patients with CLL receiving combination therapy with rituximab,** the most frequent serious adverse reaction (≥5%) was pneumonia (9%). The most common adverse reactions (≥20%) of any grade were neutropenia (65%), diarrhea (40%), upper respiratory tract infection (39%), fatigue (22%), cough (22%), and nausea (21%).
- **In patients with CLL/SLL receiving monotherapy,** the most frequent serious adverse reactions (≥5%) were pneumonia (9%), febrile neutropenia (5%), and sepsis (5%). The most common adverse reactions (≥20%) of any grade were neutropenia (50%), diarrhea (43%), nausea (42%), upper respiratory tract infection (36%), anemia (33%), fatigue (32%), thrombocytopenia (29%), musculoskeletal pain (29%), edema (22%), and cough (22%).

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Treatment after VEN+R and 4-year overall survival

R/R CLL

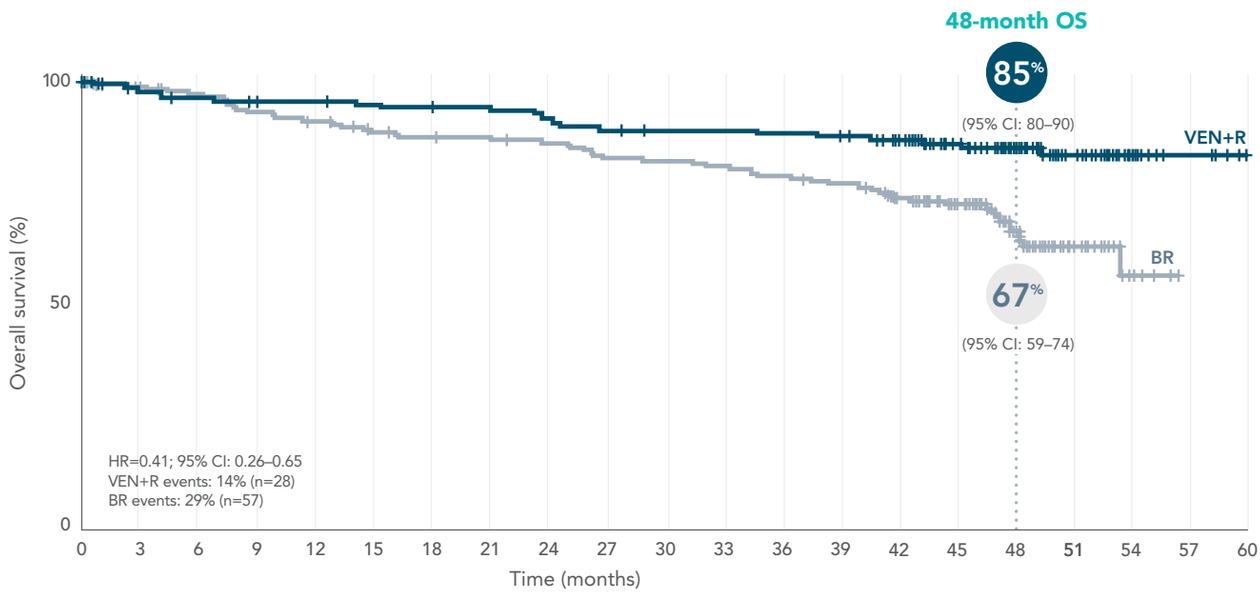
Treatment after VEN+R:

In a follow-up analysis of the VEN+R patient cohort, 42 (22%) of 194 patients received subsequent therapy with modalities that included: BTK inhibitor (n=12), BCL-2 inhibitor (n=14), PI3K inhibitor (n=1), CIT (n=14), and other (n=1).[22,23]

- Among the 12 patients treated with a BTK inhibitor, 10 patients achieved a response and 2 patients were not evaluable

BTK=Bruton's tyrosine kinase; PI3K=phosphoinositide 3-kinase; CIT=chemoimmunotherapy.

48-month post hoc analysis of overall survival[21]



Number of patients at risk

VEN+R	194	190	185	183	182	179	178	176	173	168	166	165	164	163	154	110	84	34	15	6	1
BR	195	181	175	167	162	155	152	150	147	141	140	138	134	130	116	94	58	29	7		

The post hoc analysis was not tested for statistical significance.

- At the time of analysis, the overall survival data were immature. Median overall survival had not been reached in either arm. The rates of death per arm and hazard ratio were unstable and do not reflect the actual overall survival benefit
- The rates of death were 14% (n=28) in the VEN+R arm and 29% (n=57) in the BR arm

Important Safety Information

Drug Interactions

- Concomitant use with a strong or moderate CYP3A inhibitor or a P-gp inhibitor increases VENCLEXTA exposure, which may increase VENCLEXTA toxicities, including the risk of TLS. Adjust VENCLEXTA dosage and closely monitor patients for signs of VENCLEXTA toxicities. Resume the VENCLEXTA dosage that was used prior to concomitant use of a strong or moderate CYP3A inhibitor or a P-gp inhibitor 2 to 3 days after discontinuation of the inhibitor.
- Patients should avoid grapefruit products, Seville oranges, and starfruit during treatment as they contain inhibitors of CYP3A.
- Avoid concomitant use of strong or moderate CYP3A inducers.

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VEN+R demonstrated impressive response rates and undetectable MRD with 24 months* of treatment[1]

R/R CLL

IRC-assessed overall response rate

92%
VEN+R ORR

IRC-assessed response rates for VEN+R (N=194) vs BR (N=195), respectively

- **ORR:** 92% (n=179; 95% CI: 88–96) vs 72% (n=141; 95% CI: 65–78)
- **CR+CRi:** 8% (n=16) vs 4% (n=7)
- **PR:** 82% (n=160) vs 68% (n=133)
- **nPR:** 2% (n=3) vs 1% (n=1)

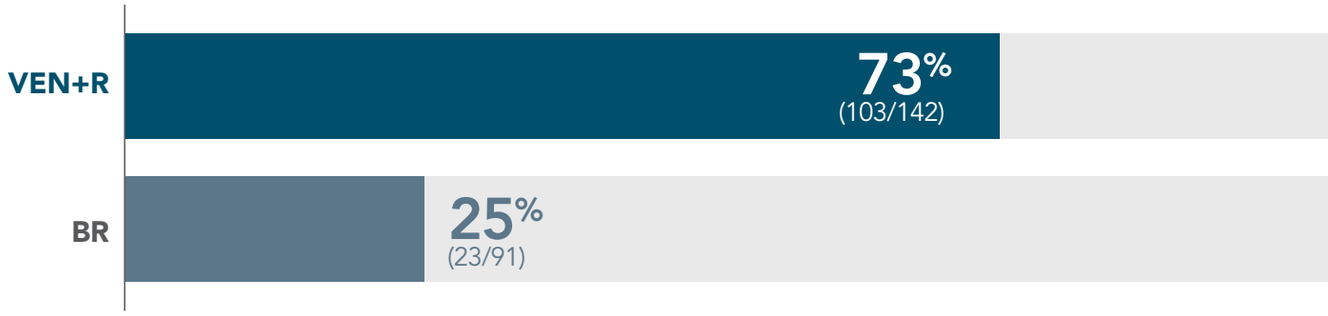
- Response rates were assessed per 2008 iwCLL NCI-WG guidelines
- INV-assessed ORR in VEN+R was 93% (n=181; 95% CI: 89–96) compared with 68% (n=132; 95% CI: 61–74) in BR[19]
- INV-assessed CR/CRi for VEN+R was 27% (n=52) compared with 8% in the BR arm (n=16)[19]
- INV-assessed vs IRC-assessed CR/CRi discordance was primarily due to interpretation of residual adenopathy on CT scans; specifically, 33 out of 51 total discordant patients had lesions ≤3 cm across both arms, despite bone marrow clearance[17,18]

IRC-assessed ORR, PR, and nPR, as well as INV-assessed ORR, CR/CRi, and MRD, were not tested for statistical significance. The differences observed for the IRC-assessed CR+CRi rates in the VEN+R and BR treatment arms were not statistically significant.[19]

Rates of undetectable MRD in peripheral blood in ITT population (secondary endpoint)

- Undetectable MRD was evaluated using allele-specific oligonucleotide polymerase chain reaction (ASO-PCR) and was defined as having achieved <1 CLL cell per 10,000 leukocytes[21,23]
- Undetectable MRD was assessed in peripheral blood 3 months after the last dose of rituximab in the ITT population that achieved PR or better: 53% (103/194) for VEN+R vs 12% (23/195) for BR
  - In patients with CR/CRi, the rate of undetectable MRD in peripheral blood was 3% (6/194) for VEN+R and 2% (3/195) for BR

Rates of undetectable MRD in peripheral blood in evaluable patients[21†‡]



- The population with evaluable results (N=233) excludes results missing due to progressive disease (PD), withdrawal (including withdrawal due to toxicity), deaths, MRD status unknown, and other missing samples or assessments. Not prespecified or tested for statistical significance

*From Cycle 1, Day 1 of rituximab.
†Assessed 3 months after combination treatment.
‡The number of patients is based on the EoCT MRD status from the 2017 CSR, where one patient wasn't categorized as negative due to missing EoCT response visit.
nPR=nodular partial remission; NCI-WG=National Cancer Institute–sponsored Working Group; CT=computed tomography; EoCT=end of combination treatment; CSR=clinical study report.

Important Safety Information

Drug Interactions (cont'd)

- Avoid concomitant use of VENCLEXTA with a P-gp substrate. If concomitant use is unavoidable, separate dosing of the P-gp substrate at least 6 hours before VENCLEXTA.
- Monitor international normalized ratio (INR) closely in patients receiving warfarin.

Lactation

- Advise nursing women to discontinue breastfeeding during treatment with VENCLEXTA.

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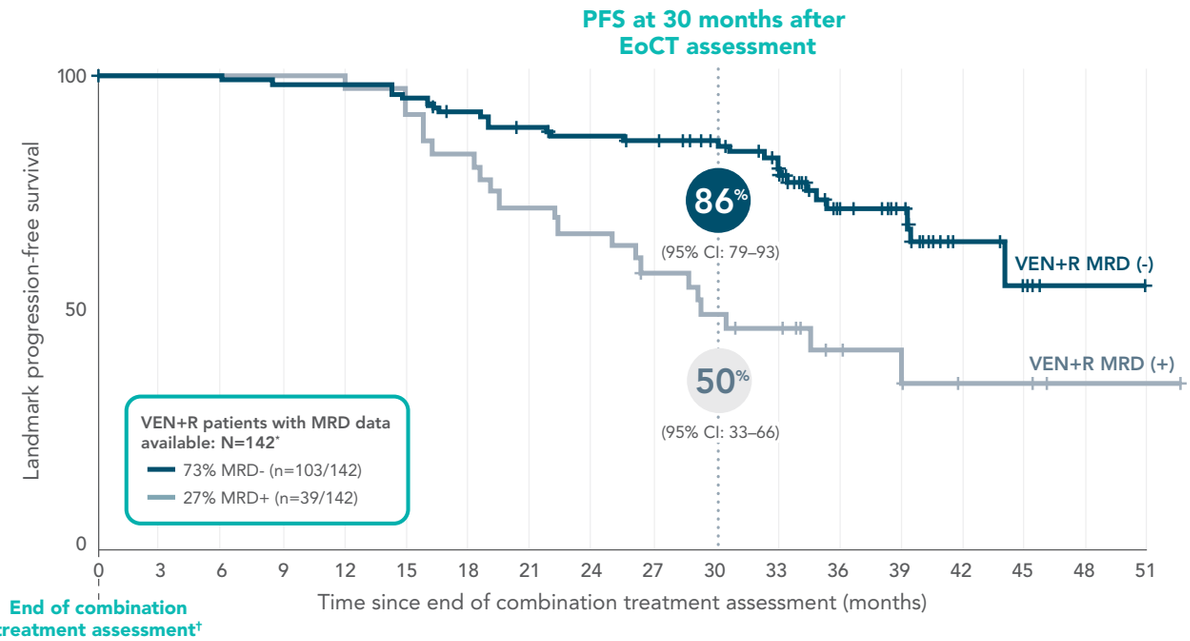
PFS by MRD status

R/R CLL

PFS was assessed in evaluable patients who achieved undetectable MRD in peripheral blood 3 months after the end of combination treatment[1,21]

Post hoc analysis



Number of patients at risk

VEN+R MRD (-)	103	103	103	101	101	98	92	88	85	83	76	68	36	22	8	6	1	
VEN+R MRD (+)	39	36	36	36	36	35	30	26	24	20	17	15	8	6	3	3	1	1

From the 48-month post hoc analysis of INV-assessed PFS (2-year update). The clinical data cutoff date was May 8, 2019. Not tested for statistical significance.

*The number of patients is based on the EoCT MRD status from the 2017 CSR, where one patient wasn't categorized as negative due to missing EoCT response visit.

†The end of combination treatment assessment occurs 3 months after the end of combination treatment.[1]

EoCT=end of combination treatment; CSR=clinical study report.

Important Safety Information

Females and Males of Reproductive Potential

- Advise females of reproductive potential to use effective contraception during treatment with VENCLEXTA and for at least 30 days after the last dose.
- Based on findings in animals, male fertility may be compromised by treatment with VENCLEXTA.

Hepatic Impairment

- Reduce the dose of VENCLEXTA for patients with severe hepatic impairment (Child-Pugh C); monitor these patients more closely for signs of toxicity. No dose adjustment is recommended for patients with mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment.

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VEN+R offers a well-studied safety profile with exposure limited to 24 months[1]*

R/R CLL

At the time of data analysis, the median duration of exposure was 22 months in the VEN+R arm compared with 6 months in the BR arm

- In the VEN+R arm, fatal adverse reactions that occurred in the absence of disease progression and within 30 days of the last VENCLEXTA treatment and/or 90 days of last rituximab treatment were reported in 2% (4/194) of patients. Serious adverse reactions were reported in 46% of patients in the VEN+R arm, with the most frequent (≥5%) being pneumonia (9%)
- 93% (173/187) of patients in the VEN+R arm and 68% (127/188) of patients in the BR arm completed 6 combination treatment cycles[19]
  - 7 patients in each arm did not receive combination therapy: In the VEN+R arm, 7 patients did not receive rituximab, and in the BR arm, 7 patients did not receive either bendamustine or rituximab[17]
  - Patients needed to receive at least 90% of the target dose to be counted as receiving a full cycle[19]
- The MURANO trial was not designed to demonstrate a statistically significant difference in adverse reaction rates for VEN+R compared with BR, for any specific adverse reaction or laboratory abnormality

Rates of discontinuation, dose reduction, and dose interruption

- Discontinuation due to any adverse reactions occurred in 16% of patients on VEN+R and in 10% of patients on BR
- Dose reduction due to adverse reactions occurred in 15% of patients in each arm. Dose interruption due to adverse reactions occurred in 71% of patients on VEN+R and in 40% of patients on BR
- Neutropenia led to dose interruption of VENCLEXTA in 46% of patients and discontinuation in 3%, and thrombocytopenia led to discontinuation in 3% of patients

Common (≥10%) adverse reactions reported with ≥5% higher all-grade or ≥2% higher grade ≥3 incidence in patients treated with VEN+R compared with BR

	VEN+R		BR	
Adverse Reaction by Body System	**Any Grade (%) n=194**	**Grade ≥3 (%) n=194**	**Any Grade (%) n=188**	**Grade ≥3 (%) n=188**
Blood and lymphatic system disorders				
Neutropenia†	65	62	50	44
Gastrointestinal disorders				
Diarrhea	40	3	17	1
Infections and infestations				
Upper respiratory tract infection†	39	2	23	2
Lower respiratory tract infection†	18	2	10	2
Musculoskeletal and connective tissue disorders				
Musculoskeletal pain†	19	1	13	0
Metabolism and nutrition disorders				
Tumor lysis syndrome	3	3	1	1

*24 months from Cycle 1, Day 1 of rituximab.

†Includes multiple adverse reaction terms.

For common laboratory abnormalities data, please see Table 12 in the VENCLEXTA full Prescribing Information

Select important adverse reactions[17]

Adverse Reaction	VEN+R (n=194)	BR (n=188)
Grade 3 or 4 febrile neutropenia	4	10
Grade 3 or 4 infections and infestations	18	22

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VEN+R offers a well-studied safety profile with exposure limited to 24 months[1]*

R/R CLL

No clinical TLS was observed in MURANO after implementing TLS monitoring and prophylaxis[1]

0%
CLINICAL TLS

- The dose ramp-up was designed to gradually debulk tumor burden and mitigate TLS risk
- After the study protocol was amended to implement TLS prophylaxis and monitoring, 0% incidence of clinical TLS was observed in the R/R CLL trial. Incidence of TLS occurred in 3% (6/194) of patients treated with VEN+R overall
- All TLS events occurred during the ramp-up period and were resolved within 2 days. All 6 patients completed the ramp-up and reached the recommended daily dose of 400 mg of VENCLEXTA

Other adverse reactions (all grades) reported in ≥10% of patients in the VEN+R arm in MURANO, and other important adverse reactions

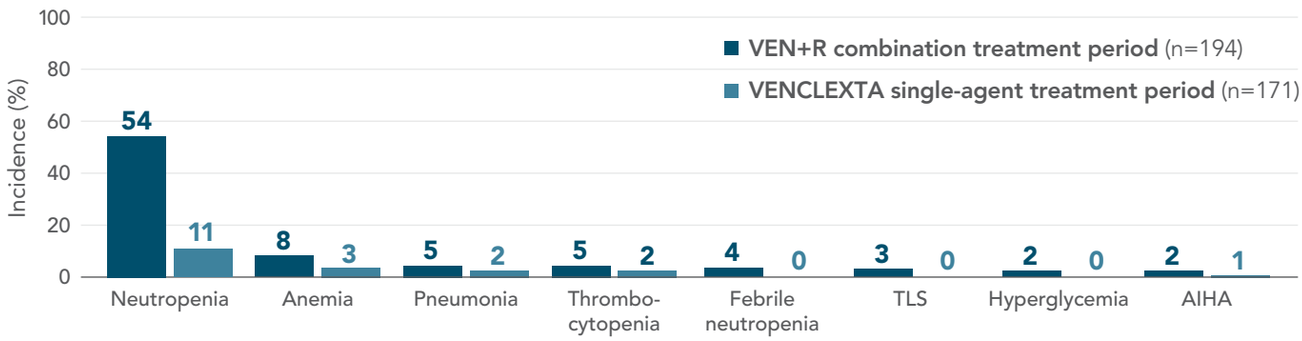
- Fatigue (22%), cough (22%), nausea (21%), anemia (16%), pyrexia (15%), thrombocytopenia (15%), constipation (14%), abdominal pain (13%), rash (13%), headache (11%), insomnia (11%), mucositis (10%), pneumonia (10%), vomiting (8%), febrile neutropenia (4%), sepsis (1%)

Adverse reactions during treatment with single-agent VENCLEXTA after completion of VEN+R combination treatment

- The most common all-grade adverse reactions (≥10% of patients) reported were upper respiratory tract infection (21%), diarrhea (19%), neutropenia (16%), and lower respiratory tract infections (11%)
- The most common Grade 3 or 4 adverse reactions (≥2% of patients) were neutropenia (12%) and anemia (3%)

No additional VEN+R drug exposure after 24 months†

New incidence of Grade ≥3 AEs decreased after combination treatment period[19,20‡]



*24 months from Cycle 1, Day 1 of rituximab.
†From Cycle 1, Day 1 of rituximab.
‡Incidence of ≥2% during combination period.
AIHA=autoimmune hemolytic anemia.

- VEN+R combination-therapy period: includes treatment-emergent AEs with an onset date from initiation of the VENCLEXTA dose ramp-up to within 90 days after last rituximab dose[19]
- VENCLEXTA single-agent period: includes patients who had at least 1 VENCLEXTA dose more than 90 days after last rituximab dose and treatment-emergent AEs with an onset date more than 90 days after last rituximab dose[19]
- Multiple occurrences of the same AE in an individual during the same treatment period are counted only once for that treatment period[19]

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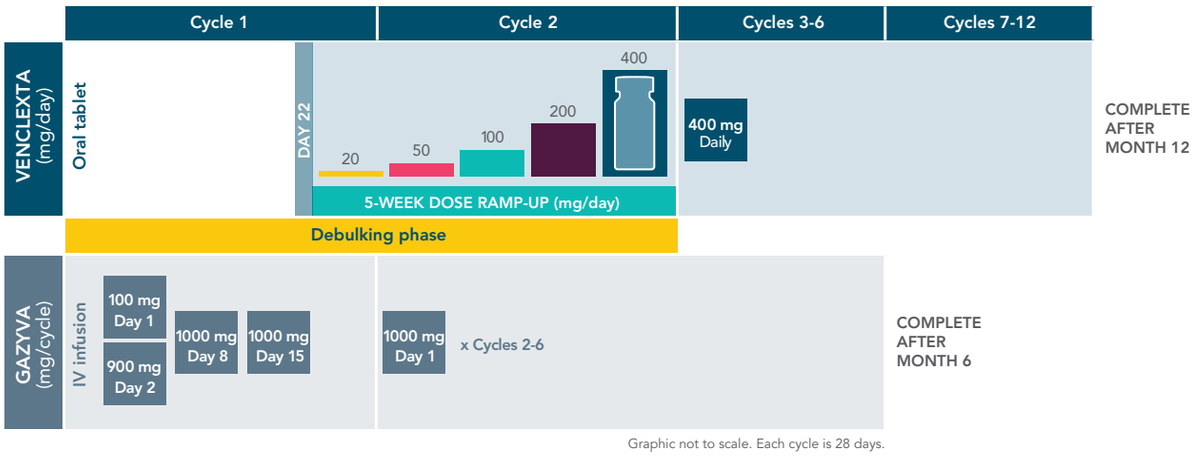
The only chemo-free regimen designed to stop treatment at 12 months in 1L CLL[1]...

1L CLL

VEN+G dosing



Graphic not to scale. Each cycle is 28 days.

98% ALC REDUCTION

After the first treatment cycle of GAZYVA® (obinutuzumab) and before the VENCLEXTA dose ramp-up, patients' ALC was reduced by 98%[13*†‡]

*Reduced by a median count of 55 x 10^9 cells/L at baseline to a median count of 1.27 x 10^9 cells/L at Day 15.

†Median lymphocyte counts are descriptive in nature and not powered for any type of comparison. Changes in TLS risk status based on ALC reduction were at the discretion of the trial investigators.

‡Per the trial protocol, tumor burden was assessed based on ALC and lymph node size. The effect of the first GAZYVA treatment cycle on lymph node size was not evaluated.

Dose information

VENCLEXTA[1]

- Tumor burden assessments, including radiographic evaluation and blood chemistry assessment, are recommended prior to VENCLEXTA initiation to assess the risk for TLS
- On Cycle 1, Day 22, start VENCLEXTA according to the 5-week ramp-up schedule
- After completing the ramp-up schedule on Cycle 2, Day 28, patients should continue VENCLEXTA 400 mg once daily from Cycle 3, Day 1 until the last day of Cycle 12
- The CLL/SLL Starting Pack provides color-coded weekly wallet blister packs for the first 4 weeks, according to the ramp-up schedule
- The recommended daily dose of 400 mg is supplied as 100-mg tablets
- For information regarding the risk assessment and prophylaxis for TLS and VENCLEXTA dose modifications for toxicities, please see pages 24-25 and 26-27, or sections 2.2 and 2.3 of the VENCLEXTA full Prescribing Information

GAZYVA

- Refer to the GAZYVA Prescribing Information for recommended dosing information

Important Safety Information

Contraindication

- Concomitant use of VENCLEXTA with *strong* CYP3A inhibitors at initiation and during ramp-up phase is contraindicated in patients with CLL/SLL due to the potential for increased risk of tumor lysis syndrome (TLS).

Tumor Lysis Syndrome

- Tumor lysis syndrome, including fatal events and renal failure requiring dialysis, has occurred in patients with high tumor burden when treated with VENCLEXTA.
- In patients with CLL who followed the current (5 week) dose ramp-up and the TLS prophylaxis and monitoring measures, the rate of TLS was 2% in the VENCLEXTA CLL monotherapy studies. The rate of TLS remained consistent with VENCLEXTA in combination with obinutuzumab or rituximab. With a 2- to 3-week dose ramp-up and higher starting dose in patients with CLL/SLL, the TLS rate was 13% and included deaths and renal failure.

Please see additional Important Safety Information throughout the piece.
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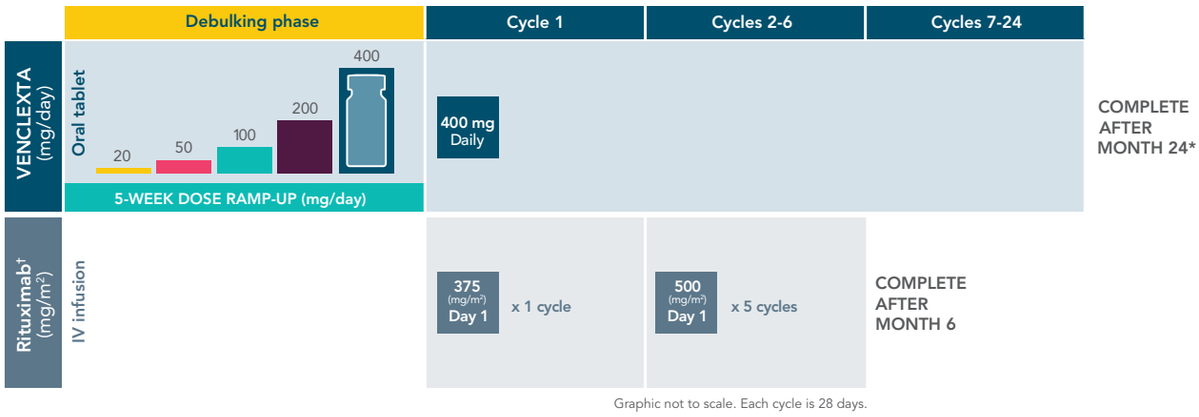
...and 24 months* in R/R CLL[1]

R/R CLL

VEN+R dosing



Graphic not to scale. Each cycle is 28 days.

- To gradually reduce tumor burden (debulk) and decrease the risk of TLS, start with the 5-week VENCLEXTA dose ramp-up

*24 months from Cycle 1, Day 1 of rituximab.
†Start rituximab after patient has received the 400-mg dose of VENCLEXTA for 7 days.

Dose information

VENCLEXTA

- The VENCLEXTA starting dose is 20 mg once daily for 7 days, ramping up weekly to 50 mg,100 mg, 200 mg, and finally 400 mg once daily
- After ramp-up, VENCLEXTA should be taken at the recommended daily dose for 24 months
- The CLL/SLL Starting Pack provides color-coded weekly wallet blister packs for the first 4 weeks, according to the ramp-up schedule
- The recommended daily dose of 400 mg is supplied as 100-mg tablets
- For information regarding the risk assessment and prophylaxis for tumor lysis syndrome and VENCLEXTA dose modifications for toxicities, please see pages 24-25 and 26-27, or sections 2.2 and 2.3 of the VENCLEXTA full Prescribing Information

RITUXIMAB

- Refer to the rituximab Prescribing Information for recommended dosing information

Important Safety Information

Tumor Lysis Syndrome (cont'd)

- VENCLEXTA poses a risk for TLS at initiation and during the ramp-up phase. Changes in blood chemistries consistent with TLS that require prompt management can occur as early as 6 to 8 hours following the first dose of VENCLEXTA and at each dose increase.
- Patients should be assessed for TLS risk, including evaluation of tumor burden and comorbidities, and should receive appropriate prophylaxis for TLS, including hydration and anti-hyperuricemics. Reduced renal function further increases the risk. Monitor blood chemistries and manage abnormalities promptly. Interrupt dosing if needed. Employ more intensive measures (IV hydration, frequent monitoring, hospitalization) as overall risk increases.
- Concomitant use of VENCLEXTA with strong or moderate CYP3A inhibitors or P-gp inhibitors may increase the risk of TLS at initiation and during the ramp-up phase, and requires dose adjustment due to increases in VENCLEXTA exposure.

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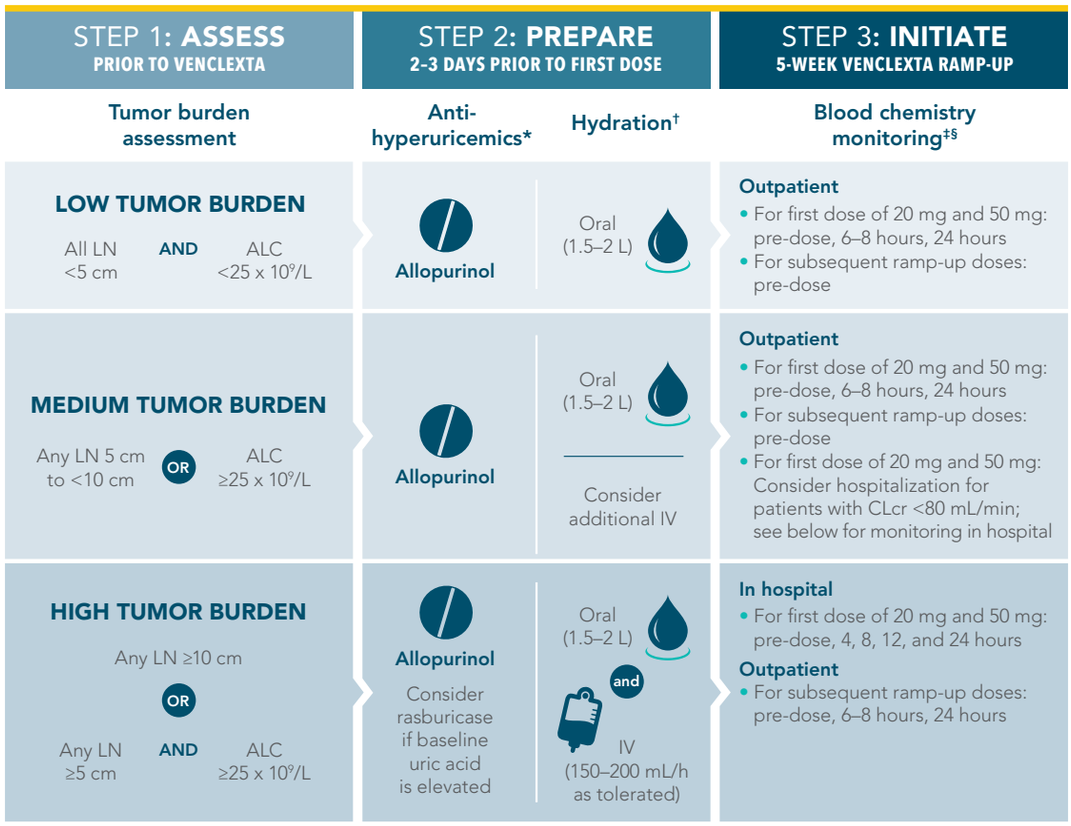
Prior to initiating VENCLEXTA

Risk assessment, prophylaxis, and monitoring measures for TLS[1]

- The risk of TLS is a continuum based on multiple factors, including tumor burden and comorbidities. Reduced renal function (CLcr <80 mL/min) further increases the risk
- Changes in blood chemistries consistent with TLS that require prompt management can occur as early as 6 to 8 hours following the first dose and each dose increase



The risk of TLS may decrease as tumor burden decreases.

*Start allopurinol or xanthine oxidase inhibitor 2–3 days prior to initiation of VENCLEXTA.

†1.5–2 L of water (6–8 glasses) should be consumed every day starting 2 days before the first dose and throughout the ramp-up phase, especially the first day of each dose increase. Administer intravenous hydration for any patient who cannot tolerate oral hydration.

‡Review in real time.

§For patients at risk of TLS, monitor blood chemistries at 6–8 hours and at 24 hours at each subsequent ramp-up dose.

LN=lymph node.

Blood chemistry monitoring: potassium, calcium, creatinine, phosphorus, uric acid (review in real time)

Important Safety Information

Neutropenia

- In patients with CLL, Grade 3 or 4 neutropenia developed in 63% to 64% of patients and Grade 4 neutropenia developed in 31% to 33% of patients treated with VENCLEXTA in combination and monotherapy studies. Febrile neutropenia occurred in 4% to 6% of patients treated with VENCLEXTA in combination and monotherapy studies.
- Monitor complete blood counts throughout the treatment period. Interrupt dosing or reduce dose for severe neutropenia. Consider supportive measures including antimicrobials for signs of infection and use of growth factors (e.g., G-CSF).

Infections

- Fatal and serious infections such as pneumonia and sepsis have occurred in patients treated with VENCLEXTA. Monitor patients closely for signs and symptoms of infection and treat promptly. Withhold VENCLEXTA for Grade 3 and higher infection.

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Instructions for taking VENCLEXTA[1]

Advise patients to take VENCLEXTA exactly as prescribed and **not to change their dose or to stop taking VENCLEXTA** unless they are told to do so by their doctor.

VENCLEXTA tablets should be swallowed whole and **not chewed, crushed, or broken**.

Advise patients of the importance of **keeping scheduled appointments** for blood work or other laboratory tests.

Patients should **avoid grapefruit products, Seville oranges, and starfruit** during treatment with VENCLEXTA.

Patients should take VENCLEXTA **once daily with a meal and water** at approximately the same time each day.

Advise patients to **keep VENCLEXTA in the original packaging during the first 4 weeks of treatment** and not to transfer the tablets to a different container.

Advise patients to be adequately hydrated every day when taking VENCLEXTA to reduce the risk of TLS. 1.5–2 L of water **(6–8 glasses, or 56 ounces)** should be consumed every day starting 2 days before the first dose and throughout the ramp-up phase, especially the first day of each dose increase.

If a patient misses a dose <u>within 8 hours</u> of the time it is usually taken:

The patient should take the missed dose right away and take the next dose as usual.

If a patient misses a dose by <u>more than 8 hours</u>:

The patient should not take the missed dose and should take the next dose at the usual time.

If a <u>patient vomits</u> following dosing:

No additional dose should be taken that day. The next dose should be taken at the usual time the following day.

Important Safety Information

Immunization

- Do not administer live attenuated vaccines prior to, during, or after treatment with VENCLEXTA until B-cell recovery occurs. Advise patients that vaccinations may be less effective.

Embryo-Fetal Toxicity

- VENCLEXTA may cause embryo-fetal harm when administered to a pregnant woman. Advise females of reproductive potential to avoid pregnancy during treatment.

Increased Mortality in Patients with Multiple Myeloma when VENCLEXTA is Added to Bortezomib and Dexamethasone

- In a randomized trial (BELLINI; NCT02755597) in patients with relapsed or refractory multiple myeloma, the addition of VENCLEXTA to bortezomib plus dexamethasone, a use for which VENCLEXTA is not indicated, resulted in increased mortality. Treatment of patients with multiple myeloma with VENCLEXTA in combination with bortezomib plus dexamethasone is not recommended outside of controlled clinical trials.

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Dose modifications or interruptions can help manage potential adverse reactions[1]

Interrupt dosing or reduce dose for toxicities

- For patients who have had a dosing interruption greater than 1 week during the first 5 weeks of the ramp-up phase or greater than 2 weeks after completing the ramp-up phase, reassess the risk of TLS to determine if reinitiation with a reduced dose is necessary (eg, all or some levels of the ramp-up schedule)

Recommended VENCLEXTA dose modifications for toxicities*	
TLS	
Any occurrence: Blood chemistry changes or symptoms suggestive of TLS	Withhold the next day's dose. If resolved within 24–48 hours of last dose, resume at the same dose.
	For any blood chemistry changes requiring more than 48 hours to resolve, resume at a reduced dose. See dose-reduction guidelines in chart on facing page.
	For any events of clinical TLS,† resume at a reduced dose following resolution. See dose-reduction guidelines in chart on facing page.
Nonhematologic toxicities	
1st occurrence: Grade 3 or 4 nonhematologic toxicities	Interrupt VENCLEXTA. Once the toxicity has resolved to Grade 1 or baseline level, VENCLEXTA therapy may be resumed at the same dose. No dose modification is required.
2nd and subsequent occurrences: Grade 3 or 4 nonhematologic toxicities	Interrupt VENCLEXTA. Follow dose-reduction guidelines in chart on facing page when resuming VENCLEXTA treatment after resolution. A larger dose reduction may occur at the discretion of the physician.
Hematologic toxicities	
1st occurrence: Grade 3 neutropenia with infection or fever, or Grade 4 hematologic toxicities (except lymphopenia)	Interrupt VENCLEXTA. To reduce the infection risks associated with neutropenia, G-CSF may be administered with VENCLEXTA if clinically indicated. Once the toxicity has resolved to Grade 1 or baseline level, VENCLEXTA therapy may be resumed at the same dose.
2nd and subsequent occurrences: Grade 3 neutropenia with infection or fever, or Grade 4 hematologic toxicities (except lymphopenia)	Interrupt VENCLEXTA. Consider using G-CSF as clinically indicated. Follow dose-reduction guidelines in chart on facing page when resuming VENCLEXTA treatment after resolution. A larger dose reduction may occur at the discretion of the physician.

Consider discontinuing VENCLEXTA for patients who require dose reductions to less than 100 mg for more than 2 weeks.

- Monitor complete blood counts throughout the treatment period

*Adverse reactions were graded using NCI CTCAE version 4.0.
†Clinical TLS was defined as laboratory TLS with clinical consequences such as acute renal failure, cardiac arrhythmias, or sudden death and/or seizures.
G-CSF=granulocyte colony-stimulating factor; NCI CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events.

Dose modifications or interruptions can help manage potential adverse reactions[1]

Dose reduction for toxicity during VENCLEXTA treatment	
Dose at interruption, mg	**Restart dose, mg***
400	300
300	200
200	100
100	50
50	20
20	10

*During the ramp-up phase, continue the reduced dose for 1 week before increasing the dose.

Dose modifications for use with CYP3A and P-gp inhibitors

Concomitant use of VENCLEXTA with *strong* CYP3A inhibitors at initiation and during the ramp-up phase is contraindicated due to the potential for increased risk of TLS.

Management of potential VENCLEXTA interactions with CYP3A and P-gp inhibitors		
Coadministered drug	**Initiation and ramp-up phase**	**Steady daily dose† (after ramp-up phase)**
Posaconazole	Contraindicated	Reduce the VENCLEXTA dose to 70 mg
Other strong CYP3A inhibitor	Contraindicated	Reduce the VENCLEXTA dose to 100 mg
Moderate CYP3A inhibitor	Reduce the VENCLEXTA dose by at least 50%	
P-gp inhibitor		

†Consider alternative medications or reduce the VENCLEXTA dose as described in this table.

- Resume the VENCLEXTA dose that was used prior to initiating the CYP3A inhibitor or P-gp inhibitor 2 to 3 days after discontinuation of the inhibitor

Dose modifications for use in severe hepatic impairment

- A 50% dose reduction throughout treatment is recommended for patients with severe hepatic impairment; monitor these patients more closely for signs of toxicity

CYP3A=cytochrome P450 3A; P-gp=P-glycoprotein.

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Supporting people who have been prescribed VENCLEXTA

Patient support services

Serious illnesses come with many challenges. Getting VENCLEXTA shouldn't be one of them.

We believe every person should get the VENCLEXTA they have been prescribed, and we offer programs to make this happen.

If your patients:

Need help understanding their insurance coverage and related financial responsibilities, **VENCLEXTA Access Solutions®** is here to help.

Have insurance and need help paying for their medicine, **Affordability Options** may be available:

- The Genentech BioOncology® Co-pay Assistance Program†
- Referrals to independent co-pay assistance foundations‡

Do not have insurance coverage or have financial concerns and meet certain eligibility criteria, the **Genentech Patient Foundation*** may be able to provide free medicine.

Want information and resources about VENCLEXTA, the **VENCOMPASS Program** supports patients taking VENCLEXTA for an approved use during the ramp-up phase and throughout their therapy.

The Genentech Patient Resource Center can help answer questions and connect you to the right Genentech patient support service. Call (877) GENENTECH (877-436-3683) to get started.

*To be eligible for free Genentech medicine from the Genentech Patient Foundation, insured patients who have coverage for their medicine must have pursued all other forms of financial assistance and meet certain income requirements. Uninsured patients and insured patients without coverage for their medicine must meet different income requirements.

†Eligibility criteria apply. Not valid for patients using federal or state government programs to pay for their medications. Patient must be taking the Genentech medication for an FDA-approved indication. See full terms and conditions at CopayAssistanceNow.com.

‡VENCLEXTA Access Solutions does not influence or control the operations or eligibility criteria of any independent co-pay assistance foundation and cannot guarantee co-pay assistance after a referral from VENCLEXTA Access Solutions. The foundations to which we refer patients are not exhaustive or indicative of VENCLEXTA Access Solutions' endorsement or financial support. There may be other foundations to support the patient's disease state.

No additional patient out-of-pocket costs for VENCLEXTA regimens after treatment is completed per the recommended dosing—12 months in 1L CLL and 24 months§ in R/R CLL.[1‖]

§From Cycle 1, Day 1 of rituximab.

‖Drug cost refers to the Wholesale Acquisition Cost. Coverage and patient out-of-pocket costs for VENCLEXTA-based regimens vary by health plan. Patients may still incur out-of-pocket costs for other treatments or tests as directed by their healthcare providers.

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Supporting people who have been prescribed VENCLEXTA

VENCOMPASS®

Providing support for patients taking VENCLEXTA

This program is intended to support your patients taking VENCLEXTA for an approved use during the ramp-up phase and throughout their therapy. VENCOMPASS is not intended to replace your medical advice. All information to be provided will be based on full Prescribing Information and Medication Guide.

VENCOMPASS Nurses have experience in cancer care and can provide support through

- Hydration, dosing, and weekly laboratory reminders
- Answering product-specific questions
- Directing patients to organizations that can provide additional support

VENCOMPASS Nurses do not provide medical advice and are trained to direct patients to speak with their healthcare professional about any treatment-related questions.

For VENCOMPASS, please visit **www.VENCLEXTA.com**
or call **(844) 9-COMPASS/(844) 926-6727** for more information.

References: 1. VENCLEXTA Prescribing Information. **2.** RITUXAN Prescribing Information, March 2020. **3.** GAZYVA Prescribing Information, March 2020. **4.** Souers AJ, Leverson JD, Boghaert ER, et al. ABT-199, a potent and selective BCL-2 inhibitor, achieves antitumor activity while sparing platelets. *Nat Med.* 2013;19(2):202-208. **5.** Hallek M, Cheson BD, Catovsky D, et al. iwCLL guidelines for diagnosis, indications for treatment, response assessment, and supportive management of CLL [published online March 14, 2018]. *Blood.* 2018;131(25):2745-2760. doi:10.1182/blood-2017-09-806398. **6.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. V4.2020. National Comprehensive Cancer Network, Inc. 2019. All rights reserved. Accessed February 24, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. **7.** Owen C, Christofides A, Johnson N, Lawrence T, MacDonald D, Ward C. Use of minimal residual disease assessment in the treatment of chronic lymphocytic leukemia [published online May 16, 2017]. *Leuk Lymphoma.* 2017;58(12):2777-2785. doi:10.1080/10428194.2017.1318439. **8.** Thompson PA, Wierda WG. Eliminating minimal residual disease as a therapeutic end point: working toward cure for patients with CLL. *Blood.* 2016;127(3):279-286. **9.** US Food and Drug Administration. Hematologic malignancies: regulatory considerations for use of minimal residual disease in development of drug and biological products for treatment. Guidance for industry. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/hematologic-malignancies-regulatory-considerations-use-minimal-residual-disease-development-drug-and. January 2020. Accessed February 28, 2020. **10.** Parikh SA. Chronic lymphocytic leukemia treatment algorithm 2018 [published online October 3, 2018]. *Blood Cancer J.* 2018;8(10):93. doi:10.1038/s41408-018-0131-2. **11.** Greer JA, Amoyal N, Nisotel L, et al. A systematic review of adherence to oral antineoplastic therapies [published online February 26, 2016]. *Oncologist.* 2016;21(3):354-376. doi:10.1634/theoncologist.2015-0405. **12.** Ruddy K, Mayer E, Partridge A. Patient adherence and persistence with oral anticancer treatment. *CA Cancer J Clin.* 2009;59(1):56-66. **13.** Data on file, AbbVie Inc. ABVRRTI69608. **14.** Howlader N, Noone AM, Krapcho M, et al, eds. National Cancer Institute Surveillance, Epidemiology, and End Results Program. SEER Cancer Statistics Review, 1975-2010. https://seer.cancer.gov/archive/csr/1975_2010/. Published April 2013. Updated June 14, 2013. Accessed January 2, 2020. **15.** Thurmes P, Call T, Slager S, et al. Comorbid conditions and survival in unselected, newly diagnosed patients with chronic lymphocytic leukemia. *Leuk Lymphoma.* 2008;49(1):49-56. **16.** Data on file, AbbVie Inc. ABVRRTI69785. **17.** Seymour JF, Kipps TJ, Eichhorst B, et al. Venetoclax–rituximab in relapsed or refractory chronic lymphocytic leukemia. *N Engl J Med.* 2018;378(12):1107-1120. **18.** Seymour JF, Kipps TJ, Eichhorst B, et al. Venetoclax–rituximab in relapsed or refractory chronic lymphocytic leukemia. *N Engl J Med.* 2018;378(12) (suppl appendix). **19.** Data on file, AbbVie Inc. ABVRRTI69609. **20.** Seymour JF, Kipps TJ, Eichhorst B, et al. MURANO trial establishes feasibility of time-limited venetoclax–rituximab combination therapy in relapsed/refractory chronic lymphocytic leukemia. Presented at: 60th American Society of Hematology Annual Meeting and Exposition; December 1-4, 2018; San Diego, CA. **21.** Data on file, AbbVie Inc. ABVRRTI70042. **22.** Seymour JF, Kipps TJ, Eichhorst B, et al. Four-year analysis of MURANO study confirms sustained benefit of time-limited venetoclax–rituximab (VenR) in relapsed/refractory (R/R) chronic lymphocytic leukemia (CLL). Presented at: 61st American Society of Hematology Annual Meeting and Exposition; December 7-10, 2019; Orlando, FL. **23.** Kater AP, Seymour JF, Hillmen P, et al. Fixed duration of venetoclax-rituximab in relapsed/refractory chronic lymphocytic leukemia eradicates minimal residual disease and prolongs survival: post-treatment follow-up of the MURANO phase III study [published online December 3, 2018]. *J Clin Oncol.* 2019;37(4):269-277. doi:10.1200/JCO.18.01580.

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STRENGTH TO DELIVER DURABLE EFFICACY

82%
3-YEAR PFS

VEN+G demonstrated durable PFS after stopping treatment at 12 months[1,16]

- Primary analysis showed that after a median follow-up of 28 months, VEN+G reduced the risk of progression or death by 67% vs GClb (HR=0.33; 95% CI: 0.22–0.51 [*P*<0.0001]). Median PFS not reached in either arm[1]
- At 36-month follow-up, the rate of PFS was 82% (95% CI: 77–87) with VEN+G vs 50% (95% CI: 42–57) with GClb[16]*

87%
MRD- IN PB

Undetectable MRD in patients with evaluable data was 87% in peripheral blood (vs 42% in GClb)[1,13†]

- Undetectable MRD in peripheral blood (ITT population) was 76% in VEN+G patients, compared with 35% in GClb patients

CONFIDENTLY START AND STOP TREATMENT

0%
CLINICAL TLS

0% incidence of clinical TLS was observed in the 1L CLL trial by following the TLS prophylaxis and monitoring protocol[13]

- Laboratory TLS occurred in 1% (3/212) of patients treated with VEN+G. All 3 TLS events resolved and did not lead to withdrawal from the study. GAZYVA® (obinutuzumab) administration was delayed in 2 cases in response to the TLS events[1]
- The most frequent serious adverse reaction (≥5%) was febrile neutropenia (5%). The most common adverse reactions (≥20%) of any grade were neutropenia (60%), diarrhea (28%), and fatigue (21%)[1]

No additional VEN+G drug exposure after stopping treatment at 12 months[1]

FIXED TREATMENT, FIXED COST

12
MONTHS

No additional VEN+G regimen patient out-of-pocket costs after completing treatment per the recommended dosing[1‡]

*The 36-month PFS rates were not prespecified and were not tested for statistical significance.
†Undetectable MRD was defined as having achieved <1 CLL cell per 10,000 leukocytes at 3 months after completion of treatment. Excludes results missing due to progressive disease, withdrawal, deaths, and MRD status unknown.
‡Drug cost refers to the Wholesale Acquisition Cost. Coverage and patient out-of-pocket costs for VEN+G vary by health plan. Patients may still incur out-of-pocket costs for other treatments or tests as directed by their healthcare providers.
PB=peripheral blood.

Important Safety Information

Adverse Reactions

- **In patients with CLL receiving combination therapy with obinutuzumab,** serious adverse reactions were most often due to febrile neutropenia and pneumonia (5% each). The most common adverse reactions (≥20%) of any grade were neutropenia (60%), diarrhea (28%), and fatigue (21%).
- **In patients with CLL receiving combination therapy with rituximab,** the most frequent serious adverse reaction (≥5%) was pneumonia (9%). The most common adverse reactions (≥20%) of any grade were neutropenia (65%), diarrhea (40%), upper respiratory tract infection (39%), fatigue (22%), cough (22%), and nausea (21%).
- **In patients with CLL/SLL receiving monotherapy,** the most frequent serious adverse reactions (≥5%) were pneumonia (9%), febrile neutropenia (5%), and sepsis (5%). The most common adverse reactions (≥20%) of any grade were neutropenia (50%), diarrhea (43%), nausea (42%), upper respiratory tract infection (36%), anemia (33%), fatigue (32%), thrombocytopenia (29%), musculoskeletal pain (29%), edema (22%), and cough (22%).

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STRENGTH TO DELIVER DURABLE EFFICACY

57%
4-YEAR PFS

VEN+R demonstrated durable PFS after stopping treatment at 24 months[1,21]

- Primary analysis showed that after a median follow-up of 23.4 months, VEN+R reduced the risk of progression or death by 81% vs BR (HR=0.19; 95% CI: 0.13–0.28 [*P*<0.0001]). Median not reached in VEN+R vs 18.1 months in BR [95% CI: 15.8–22.3][1]
- Four-year PFS rates were 57% (95% CI: 49–65) and 5% (95% CI: 0–9) for VEN+R and BR, respectively[21]*
- In a post hoc analysis with a median follow-up of 22.2 months since VENCLEXTA completion, the 18-month post-treatment PFS for patients who completed 2 years of treatment was 76% (95% CI: 67–84)[21]*

53%
MRD- IN PB

Undetectable MRD in peripheral blood for the ITT population was 53% in VEN+R compared with 12% in BR[1†]

CONFIDENTLY START AND STOP TREATMENT

0%
CLINICAL TLS

0% incidence of clinical TLS was observed after implementation of the current TLS prophylaxis and monitoring protocol[1]

- Incidence of TLS occurred in 3% (6/194) of patients treated with VEN+R overall. All TLS events occurred during the ramp-up period and were resolved within 2 days. All 6 patients completed the ramp-up and reached the recommended daily dose of 400 mg of VENCLEXTA
- The most frequent serious adverse reaction (≥5%) was pneumonia (9%). The most common adverse reactions (≥20%) of any grade were neutropenia (65%), diarrhea (40%), upper respiratory tract infection (39%), fatigue (22%), cough (22%), and nausea (21%)

No additional VEN+R drug exposure after stopping treatment at 24 months[1]

FIXED TREATMENT, FIXED COST

24
MONTHS‡

No additional VEN+R regimen patient out-of-pocket costs after completing treatment per the recommended dosing[1§]

*Four-year PFS and 18-month post-treatment were not prespecified and not tested for statistical significance.
†Undetectable MRD was defined as having achieved <1 CLL cell per 10,000 leukocytes at 3 months after the last dose of rituximab.
‡From Cycle 1, Day 1 of rituximab after the 5-week VENCLEXTA dose ramp-up.
§Drug cost refers to the Wholesale Acquisition Cost. Coverage and patient out-of-pocket costs for VEN+R vary by health plan. Patients may still incur out-of-pocket costs for other treatments or tests as directed by their healthcare providers.

Important Safety Information

Drug Interactions

- Concomitant use with a strong or moderate CYP3A inhibitor or a P-gp inhibitor increases VENCLEXTA exposure, which may increase VENCLEXTA toxicities, including the risk of TLS. Adjust VENCLEXTA dosage and closely monitor patients for signs of VENCLEXTA toxicities. Resume the VENCLEXTA dosage that was used prior to concomitant use of a strong or moderate CYP3A inhibitor or a P-gp inhibitor 2 to 3 days after discontinuation of the inhibitor.
- Patients should avoid grapefruit products, Seville oranges, and starfruit during treatment as they contain inhibitors of CYP3A.
- Avoid concomitant use of strong or moderate CYP3A inducers.

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THE ONLY CHEMO-FREE REGIMENS WITH THE STRENGTH TO STOP

AFTER
12 MONTHS
in 1L CLL WITH VEN+G[1]

AFTER
24 MONTHS
in R/R CLL WITH VEN+R[1]

- The VEN+G regimen is designed to be completed after 12 months (twelve 28-day treatment cycles): GAZYVA® (obinutuzumab) is administered in Cycles 1–6, and VENCLEXTA is taken orally 400 mg/day from Cycle 3, Day 1, after the first cycle of GAZYVA and the 5-week VENCLEXTA dose ramp-up
- The VEN+R regimen is designed to be completed after 24 months (twenty-four 28-day treatment cycles after the 5-week VENCLEXTA dose ramp-up): rituximab is administered at 375 mg/m^2 on Day 1, Cycle 1 and 500 mg/m^2 on Day 1, Cycles 2–6; VENCLEXTA is taken 400 mg/day orally from Cycle 1, Day 1 of rituximab through Cycle 24
- After a median follow-up of 28 months, VEN+G reduced the risk of progression or death by 67% vs GClb (HR=0.33; 95% CI: 0.22–0.51 [*P*<0.0001]). Median PFS not reached in either arm
- After a median follow-up of 23.4 months, VEN+R reduced the risk of progression or death by 81% vs BR (HR=0.19; 95% CI: 0.13–0.28 [*P*<0.0001]). Median not reached in VEN+R vs 18.1 months in BR [95% CI: 15.8–22.3]

Offer your patients a chance to look forward to a treatment-free period.

Indication

- VENCLEXTA is indicated for the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).

Select Important Safety Information

- Concomitant use of VENCLEXTA with *strong* CYP3A inhibitors at initiation and during ramp-up is contraindicated in patients with CLL/SLL due to the potential for increased risk of tumor lysis syndrome (TLS).
- Tumor lysis syndrome, including fatal events and renal failure requiring dialysis, has occurred in patients with high tumor burden when treated with VENCLEXTA. Patients should be assessed for TLS risk, including evaluation of tumor burden and comorbidities, and should receive appropriate prophylaxis for TLS, including hydration and anti-hyperuricemics. Reduced renal function further increases the risk. Monitor blood chemistries and manage abnormalities promptly. Employ more intensive measures (IV hydration, frequent monitoring, hospitalization) as overall risk increases.
- Concomitant use of VENCLEXTA with strong or moderate CYP3A inhibitors or P-gp inhibitors may increase the risk of TLS at initiation and during the ramp-up phase, and requires dose adjustment due to increases in VENCLEXTA exposure.
- Grade 3 or 4 neutropenia occurred in patients treated with VENCLEXTA. Monitor blood counts and for signs of infection; manage as medically appropriate.
- Fatal and serious infections such as pneumonia and sepsis have occurred in patients with VENCLEXTA. Monitor patients closely for signs and symptoms of infection and treat promptly. Withhold VENCLEXTA for Grade 3 and higher infection.
- Do not administer live attenuated vaccines prior to, during, or after treatment until B-cell recovery occurs.
- VENCLEXTA may cause embryo-fetal harm. Advise females of reproductive potential to avoid pregnancy during treatment.

Please see additional Important Safety Information throughout the piece.
Please see accompanying full Prescribing Information or visit www.rxabbvie.com/pdf/venclexta.pdf.

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VENCLEXTA®
venetoclax tablets 10mg, 50mg, 100mg

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