

EVOLVING CLL TREATMENT PARADIGMS

Exploring Chemo-Free Regimens With a Fixed Treatment Duration

You are cordially invited to attend a clinical presentation about VENCLEXTA's chemo-free, fixed duration regimens for previously untreated and relapsed/refractory CLL.

Monday, November 8, 2021, at 6:30 PM EST

Virtual Program

Once registered, you'll be emailed a link to access the virtual event

RSVP

RSVP to this program by Wednesday, 11/3/2021

You can RSVP Chad Smith at (423) 292-5772 or smith.james_chadsm@gene.com at genentechrspv.com by entering code CM41741.



Vincent Herrin, MD

Professor of Medicine
University of Mississippi Medical Center
Flowood, MS

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

VEN+R Demonstrated Durable PFS Without Long-term Treatment^{1*}

MURANO was a randomized (1:1), multicenter, open-label, actively controlled phase 3 trial that evaluated the efficacy and safety of VEN+R vs BR in 389 patients with CLL who had received at least 1 prior therapy. The primary endpoint was IRC-assessed PFS.

In MURANO, the VEN+R regimen was designed to be completed after 24 months (twenty-four 28-day treatment cycles after the 5-week VENCLEXTA dose ramp-up): rituximab was administered at 375 mg/m² on Day 1, Cycle 1 and 500 mg/m² on Day 1, Cycles 2-6; VENCLEXTA was taken 400 mg/day orally from Cycle 1, Day 1 of rituximab through Cycle 24. In the BR arm of MURANO, patients received bendamustine 70 mg/m² intravenously on Days 1 and 2 for a total of 6 Cycles; rituximab was administered intravenously at 375 mg/m² on Day 1, Cycle 1, and at 500 mg/m² on Day 1, Cycles 2-6.

IRC-assessed PFS (primary endpoint)¹

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 to 37.4+ months)

- There were 35 events in the VEN+R arm (26 progressions and 9 deaths occurring without progression) compared with 106 events in the BR arm (91 progressions and 15 deaths occurring without progression)
- The median PFS was not reached with VEN+R vs 18.1 months (95% CI: 15.8-22.3) with BR

*VEN+R is designed to be completed 24 months from Cycle 1, Day 1 of rituximab, in the absence of disease progression or unacceptable toxicity. ¹Clinical cutoff date of May 8, 2020. ²Calculation based on reverse Kaplan-Meier method (where patients who were censored in the OS analysis were treated as events and all deaths were censored).

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 treated with VENCLEXTA. Assess all patients for risk and provide appropriate prophylaxis for TLS, including hydration and anti-hyperuricemics. Monitor blood chemistries and manage abnormalities promptly. Employ more intensive measures (IV hydration, frequent monitoring, hospitalization) as overall risk increases. Interrupt dosing if needed; when restarting VENCLEXTA follow dose modification guidance in the Prescribing Information.
- Concomitant use of VENCLEXTA with P-gp inhibitors or strong or moderate CYP3A

VEN+R=VENCLEXTA + rituximab; PFS=progression-free survival; BR=bendamustine + rituximab; IRC=independent review committee; HR=hazard ratio; CI=confidence interval; INV=investigator; IV=intravenous; P-gp=P-glycoprotein; OS=overall survival.

Please note that this is a promotional educational program; CME credit will not be available.

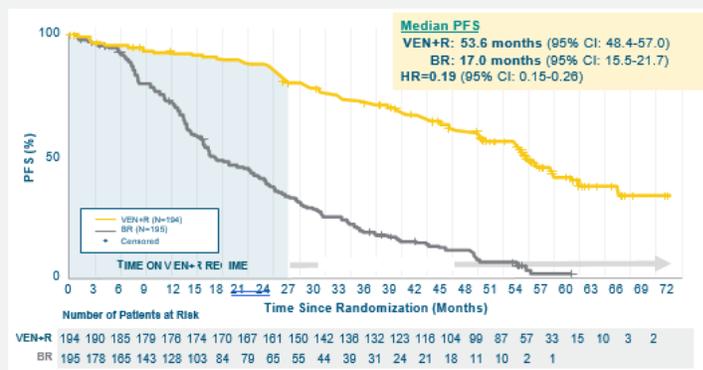
Minnesota, New Jersey, Vermont, and Federal Entities have restrictions on receiving in-kind benefits (eg, meals, valet parking) at company-sponsored programs. You are accountable for understanding such restrictions and complying with them. If you are licensed in or affiliated with any of these states or federal agencies, Genentech policies may restrict you from consuming any portion of the Genentech-sponsored meal at this program or from receiving any other in-kind benefit from Genentech (eg, valet parking) in connection with the program.

When you RSVP please indicate whether you will accept or opt out of Genentech's in-kind benefits (eg, meals, valet parking) at the program. If you choose to opt out you may either pay for the meal and parking on your own, or not consume anything at the program. For all program attendees who receive Genentech's in-kind benefits at this program, Genentech will report the attendee's name and the value received as required by federal and state disclosure laws (for more information on the federal law, please visit sunshine.gene.com).

The meal value reported may vary by program location and be up to \$150 per person (exceptions may apply).

Please see Important Safety Information on back.
Please see accompanying full [Prescribing Information](#).

5-Year Post Hoc Analysis of PFS (INV-Assessed)^{2†}



- After a median follow-up of 59.2 months (range: 0-71.5 months)²
 - There were 101 events in the VEN+R arm (87 progressions and 14 deaths occurring without progression)
 - There were 167 events in the BR arm (148 progressions and 19 deaths occurring without progression)
- The post hoc analysis was not tested for statistical significance
- These data are currently under evaluation by the FDA

inhibitors increases venetoclax exposure, which may increase the risk of TLS at initiation and during the ramp-up phase, and requires VENCLEXTA dose adjustment.

- Grade 3 or 4 neutropenia occurred in patients treated with VENCLEXTA. Monitor complete 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 for signs and symptoms of infection and treat promptly. Withhold VENCLEXTA for Grade 3 and 4 infection until resolution.
- 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 use effective contraception during treatment and for at least 30 days after the last dose.

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 treated with VENCLEXTA.
- VENCLEXTA can cause rapid reduction in tumor and thus poses a risk for TLS at initiation and during the ramp-up phase in all patients, and during reinitiation after dosage interruption in patients with CLL/SLL. 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. TLS, including fatal cases, has been reported after a single 20 mg dose.
- In patients with CLL/SLL 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 trials. 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.
- The risk of TLS is a continuum based on multiple factors, particularly reduced renal function, tumor burden, and type of malignancy. Splenomegaly may also increase the risk of TLS in patients with CLL/SLL.
- Assess all patients for risk and provide appropriate prophylaxis for TLS, including hydration and anti-hyperuricemics. Monitor blood chemistries and manage abnormalities promptly. Employ more intensive measures (IV hydration, frequent monitoring, hospitalization) as overall risk increases. Interrupt dosing if needed; when restarting VENCLEXTA follow dose modification guidance in the Prescribing Information.
- Concomitant use of VENCLEXTA with P-gp inhibitors or strong or moderate CYP3A inhibitors increases venetoclax exposure, which may increase the risk of TLS at initiation and during the ramp-up phase, and requires VENCLEXTA dose adjustment.

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 when treated with VENCLEXTA in combination and monotherapy studies. Febrile neutropenia occurred in 4% to 6% of patients.
- Monitor complete blood counts throughout the treatment period. Interrupt dosing or reduce dose for severe neutropenia. Consider supportive measures including antimicrobials and 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 for signs and symptoms of infection and treat promptly. Withhold VENCLEXTA for Grade 3 and 4 infection until resolution.

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 use effective contraception during treatment and for at least 30 days after the last dose.

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.

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 ($\geq 20\%$) of any grade were neutropenia (60%), diarrhea (28%), and fatigue (21%). 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, most often from infection.
- In patients with CLL receiving combination therapy with rituximab**, the most frequent serious adverse reaction ($\geq 5\%$) was pneumonia (9%). The most common adverse reactions ($\geq 20\%$) of any grade were neutropenia (65%), diarrhea (40%), upper respiratory tract infection (39%), fatigue (22%), and nausea (21%). 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 the last rituximab were reported in 2% (4/194) of patients.
- In patients with CLL/SLL receiving monotherapy**, the most frequent serious adverse reactions ($\geq 5\%$) were pneumonia (9%), febrile neutropenia (5%), and sepsis (5%). The most common adverse reactions ($\geq 20\%$) 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%). Fatal adverse reactions that occurred in the absence of disease progression and within 30 days of venetoclax treatment were reported in 2% of patients in the VENCLEXTA monotherapy studies, most often (2 patients) from septic shock.

Drug Interactions

- Concomitant use with a P-gp inhibitor or a strong or moderate CYP3A inhibitor increases VENCLEXTA exposure, which may increase VENCLEXTA toxicities, including the risk of TLS. Consider alternative medications or adjust VENCLEXTA dosage and monitor more frequently for adverse reactions. Resume the VENCLEXTA dosage that was used prior to concomitant use of a P-gp inhibitor or a strong or moderate CYP3A 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.
- Monitor international normalized ratio (INR) more frequently in patients receiving warfarin.
- 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.

Lactation

- Advise women not to breastfeed during treatment with VENCLEXTA and for 1 week after the last dose.

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, VENCLEXTA may impair male fertility.

Hepatic Impairment

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

Please see accompanying full [Prescribing Information](#).

Reference: 1. VENCLEXTA Prescribing Information. 2. Data on file, AbbVie Inc. ABVRRIT71322.

G-CSF=granulocyte-colony stimulating factor.



abbvie

Genentech
A Member of the Roche Group