

NEW EVIDENCE IN FIRST-LINE AML AND EXPLORING OUTCOMES WITH FIXED-DURATION TREATMENT IN CLL

Pivotal Clinical Trial Data That Support Treatment Decisions and Patient Care

Take this opportunity to learn directly from experts in AML and CLL.

Register using the links below

Tuesday, November 10, 2020

5:00 PM ET | 4:00 PM CT | 3:00 PM MT | 2:00 PM PT

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Tuesday, November 10, 2020

8:00 PM ET | 7:00 PM CT | 6:00 PM MT | 5:00 PM PT

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DURING THIS INTERACTIVE PROGRAM WE WILL:

- Recognize VENCLEXTA as a BCL-2 inhibitor for 1L AML, and 1L and R/R CLL
- Review the phase 3 efficacy and safety outcomes of VENCLEXTA + azacitidine from the pivotal VIALE-A study for patients with 1L AML, ineligible for intensive induction chemotherapy due to age or comorbidities
- Explore the efficacy and safety outcomes of VENCLEXTA's chemo-free, fixed duration CLL regimens

Indications

VENCLEXTA is indicated:

- For the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).
- In combination with azacitidine, or decitabine, or low-dose cytarabine for the treatment of newly-diagnosed acute myeloid leukemia (AML) in adults:
 - 75 years or older, or
 - who have comorbidities that preclude the use of intensive induction chemotherapy.

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. Assess patients for risk and provide 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 P-gp inhibitors or strong or moderate CYP3A inhibitors increases venetoclax exposure, which may increase the risk of TLS at initiation and during ramp-up phase, and requires VENCLEXTA dose adjustment.
- Grade 3 or 4 neutropenia occurred in patients treated with VENCLEXTA. Monitor blood counts and for signs of infection; manage as medically appropriate.
- In patients with AML, baseline neutrophil counts worsened in 95% to 100% of patients treated with VENCLEXTA in combination with azacitidine or decitabine or low-dose cytarabine. Neutropenia can recur with subsequent cycles.
- 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.

BCL-2=B-cell lymphoma; 1L=first-line; R/R=relapsed/refractory; CME=continuing medical education.

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Please see additional Important Safety Information on back.

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

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 **VENCLEXTA**[®]
venetoclax tablets 10mg, 50mg, 100mg

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 dosing ramp-up schedule 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.
- In patients with AML who followed the current 3-day ramp-up dosing schedule and the TLS prophylaxis and monitoring measures, the rate of TLS was 1.1% in patients who received VENCLEXTA in combination with azacitidine. In patients with AML who followed a 4-day ramp-up dosing schedule and the TLS prophylaxis and monitoring measures, the rate of TLS was 5.6% and included deaths and renal failure in patients who received VENCLEXTA in combination with low-dose cytarabine.
- VENCLEXTA can cause rapid reduction in tumor and thus 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.
- Assess patients for risk and provide 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 P-gp inhibitors or strong or moderate CYP3A inhibitors increases venetoclax exposure, which may increase the risk of TLS at initiation and during 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 treated with VENCLEXTA in combination and monotherapy studies. Febrile neutropenia occurred in 4% to 6% of patients.
- In patients with AML, baseline neutrophil counts worsened in 95% to 100% of patients treated with VENCLEXTA in combination with azacitidine or decitabine or low-dose cytarabine. Neutropenia can recur with subsequent cycles.
- Monitor complete blood counts throughout the treatment period. For severe neutropenia, interrupt dosing or reduce duration based on remission status and occurrence. 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.

• In patients with AML receiving combination therapy with azacitidine, the most frequent serious adverse reactions ($\geq 5\%$) were febrile neutropenia (30%), pneumonia (22%), sepsis (excluding fungal; 19%), and hemorrhage (6%). The most common adverse reactions ($\geq 30\%$) of any grade were neutrophils decreased (98%), platelets decreased (94%), lymphocytes decreased (91%), hemoglobin decreased (61%), nausea (44%), diarrhea (43%), febrile neutropenia (42%), musculoskeletal pain (36%), pneumonia (33%), fatigue (31%), and vomiting (30%). Fatal adverse reactions occurred in 23% of patients who received VENCLEXTA in combination with azacitidine, with the most frequent ($\geq 2\%$) being pneumonia (4%), sepsis (excluding fungal; 3%), and hemorrhage (2%).

• In patients with AML receiving combination therapy with decitabine, the most frequent serious adverse reactions ($\geq 10\%$) were sepsis (excluding fungal; 46%), febrile neutropenia (38%), and pneumonia (31%). The most common adverse reactions ($\geq 30\%$) of any grade were febrile neutropenia (69%), fatigue (62%), constipation (62%), musculoskeletal pain (54%), dizziness (54%), nausea (54%), abdominal pain (46%), diarrhea (46%), pneumonia (46%), sepsis (excluding fungal; 46%), cough (38%), pyrexia (31%), hypotension (31%), oropharyngeal pain (31%), edema (31%), and vomiting (31%). One (8%) fatal adverse reaction of bacteremia occurred within 30 days of starting treatment.

• In patients with AML receiving combination therapy with low-dose cytarabine, the most frequent serious adverse reactions ($\geq 10\%$) were pneumonia (17%), febrile neutropenia (16%), and sepsis (excluding fungal; 12%). The most common adverse reactions ($\geq 30\%$) of any grade were platelets decreased (97%), neutrophils decreased (95%), lymphocytes decreased (92%), hemoglobin decreased (63%), nausea (42%), and febrile neutropenia (32%). Fatal adverse reactions occurred in 23% of patients who received VENCLEXTA in combination with LDAC, with the most frequent ($\geq 5\%$) being pneumonia (6%) and sepsis (excluding fungal; 7%).

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.
- 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) more frequently in patients receiving warfarin.

Lactation

- Advise nursing 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.

1. VENCLEXTA Prescribing Information.

