POWERED BY V

REMISSION

DEEP RESPONSE* AND LONGER PFS WITH FIXED TREATMENT DURATION[1,2]

1L CLL

VEN+O
Fixed treatment duration regimen of 1 year[1,3†]

INV-assessed PFS[§]: Reduced risk of progression or death vs O+Clb (HR=0.35; 95% CI: 0.23–0.53 [*P*<0.0001]). Median follow-up of 28 months. Median PFS not reached in either arm at the primary analysis.

INV-assessed complete remission (CR/CRi): 50% CR+CRi in VEN+O vs 23% in O+Clb (*P*<0.0001) (as a component of ORR of 85% [95% CI: 79.2–89.2] in VEN+O vs 71% [95% CI: 64.8–77.2] in O+Clb [*P*<0.0007]).

MRD negativity at EoT (PB): 76% (95% CI: 69–81) with VEN+O vs 35% (95% CI: 29–42) with O+Clb (ITT population) (*P*<0.0001).

2L+ CLL

VEN+R
Fixed treatment duration regimen of 2 years[2,3‡]

INV-assessed PFS[§]: Reduced risk of progression or death vs BR (HR=0.17; 95% CI: 0.11–0.25 [*P*<0.0001]). Median follow-up of 23.8 months. Median PFS not reached with VEN+R vs 17 months (15.5–21.6) with BR at primary analysis.

INV-assessed complete remission (CR/CRi)[‖]: 27% in VEN+R vs 8% in BR (as a component of ORR of 93% [95% CI: 88.8–96.4] in VEN+R vs 68% [95% CI: 60.6–74.2] in BR); 3% nPR in VEN+R vs 6% in BR; 63% PR in VEN+R vs 53% PR in BR.

MRD negativity at EoCT (PB)[‖]: 62% with VEN+R vs 13% with BR.

INDICATION[3]:
Chronic Lymphocytic Leukemia

VENCLEXTA is indicated, in combination with rituximab or as monotherapy, for the treatment of patients with chronic lymphocytic leukemia (CLL) who have received at least one prior therapy.

VENCLEXTA is indicated, in combination with obinutuzumab, for the treatment of patients with previously untreated CLL.

For full indications, please refer to VENCLEXTA Singapore Full Prescribing Information.

*Deep response as measured by CR or MRD negativity.
Both VEN+O and VEN+R only included six treatment cycles with obinutuzumab and rituximab, respectively followed by VEN monotherapy for the remainder of the treatment cycles:
†Treatment complete after twelve 28-day cycles. ‡Treatment complete after 5-week ramp-up period and twenty-four 28-day cycles.
§Primary endpoint. ‖Results are descriptive only.

PFS=progression-free survival; CLL=chronic lymphocytic leukaemia; 1L=first line; VEN+O=VENCLEXTA + obinutuzumab; INV=investigator; CI=confidence interval; O+Clb=obinutuzumab + chlorambucil; HR=hazard ratio; CR=complete remission; CRi=complete remission with incomplete bone marrow recovery; ORR=overall response rate (CR+CRi+nPR+PR); PR=partial remission; MRD=minimal residual disease; EoT=end of treatment; PB=peripheral blood; ITT=intent to treat; 2L+=second line + later lines of therapy; VEN+R=VENCLEXTA + rituximab; BR=bendamustine + rituximab; nPR=nodular partial remission; EoCT=end of combination treatment.

abbvie

VENCLEXTA™
venetoclax tablets

VENCLEXTA REGIMENS ARE THE ONLY CHEMO-FREE, FIXED-DURATION REGIMENS THAT CAN BE COMPLETED IN 1 OR 2 YEARS[1,2]

TARGET STOP DATE

VENCLEXTA-based regimens give patients a target treatment-completion date

TIME OFF TREATMENT

Patients have the possibility of a treatment-free period after completing their regimen

LIMITED TREATMENT EXPOSURE

No additional drug exposure or potentially associated adverse events after treatment is completed

FIXED COST

VENCLEXTA offers an option with a defined treatment timetable, which may reduce financial burden

References:

1. Fischer K, Al-Sawaf O, Bahlo J, et al. Venetoclax and obinutuzumab in patients with CLL and coexisting conditions. N Engl J Med. 2019;380(23):2225-2236.

2. 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.

3. VENCLEXTA™ Singapore Product Information: 28 January 2022

For Healthcare Professionals Only. Full prescribing information available upon request.
Adverse event should be reported to AbbVie Pharmacovigilance team at drugsafety.pv@abbvie.com

abbvie

ABBVIE PTE LTD.
9 North Buona Vista Drive #19-01
The Metropolis Tower One Singapore 138588
Tel +65-6715 8100 Fax +65-6715 8101

VENCLEXTA™
venetoclax tablets

SG-VEN-220003 15 June 2022

ABBREVIATED PRESCRIBING INFORMATION

VENCLEXTA™

Active Ingredient: Tablets: Venetoclax 10mg, 50mg, 100mg

Indications:

Chronic Lymphocytic Leukemia VENCLEXTA is indicated, in combination with rituximab or as monotherapy, for the treatment of patients with chronic lymphocytic leukemia (CLL) who have received at least one prior therapy. VENCLEXTA is indicated, in combination with obinutuzumab, for the treatment of patients with previously untreated CLL.

Acute Myeloid Leukemia VENCLEXTA is indicated, in combination with a hypomethylating agent or in combination with low-dose cytarabine, for the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) who are ineligible for intensive chemotherapy

Dosage and Administration:
Chronic Lymphocytic Leukemia
VENCLEXTA should be dosed on a ramp-up schedule initially to decrease risk of tumor lysis syndrome (TLS), with starting dose 20mg once daily for 7 days (week 1), 50mg once daily for week 2, 100mg once daily for week 3, 200mg once daily for week 4, 400mg once daily for week 5. After the patient has received the daily dose of 400mg for 7 days, the patient may continue taking VENCLEXTA 400mg once daily as monotherapy until disease progression or unacceptable toxicity is observed. If combination therapy for rituximab is indicated, administer rituximab on Day 1 of each 28-day cycle for 6 cycles, with rituximab dosed at 375 mg/m2 intravenously for Cycle 1 and 500 mg/m2 intravenously for Cycles 2-6, after the ramp-up schedule has been completed. Patients should continue VENCLEXTA 400 mg once daily for 24 months from Cycle 1 Day 1 of rituximab. If combination for obinutuzumab is indicated, administer obinutuzumab at 100mg on Cycle 1 Day 1, followed by 900mg which may be administered on Day 1 or Day 2. Administer obinutuzumab at 1000mg on Days 8 and 15 of Cycle 1, and on Day 1 of five subsequent cycles (total of 6 cycles, 28 days each). On Cycle 1 Day 22, start VENCLEXTA according to ramp-up schedule, continuing through Cycle 2 Day 28. Patients should continue VENCLEXTA 400mg once daily from Cycle 3 Day 1 of obinutuzumab to the end of Cycle 12.

Acute Myeloid Leukemia
VENCLEXTA should be dosed on a ramp-up schedule initially to decrease risk of tumor lysis syndrome (TLS), with starting dose of 100mg once daily on day 1, 200mg once daily on day 2, 400mg once daily on day 3. If combination therapy with hypomethylation agents, VENCLEXTA should be given 400mg once daily on day 4 and beyond, If combination therapy with low-dose cytarabine, VENCLEXTA should be given 600mg once daily on day 4 and beyond. Hypomethylating agent or low-dose cytarabine should be initiated on Cycle 1 Day 1. Azacitidine should be administered at 75 mg/m2 either intravenously or subcutaneously on Days 1-7 of each 28-day cycle beginning on Cycle 1 Day 1. Decitabine should be administered at 20 mg/m2 intravenously on Days 1-5 of each 28-day cycle beginning on Cycle 1 Day 1. Cytarabine should be administered at a dose of 20 mg/m2 subcutaneously once daily on Days 1-10 of each 28-day cycle beginning on Cycle 1 Day 1. VENCLEXTA, in combination with a hypomethylating agent or low-dose cytarabine, should be continued until disease progression or unacceptable toxicity is observed.

VENCLEXTA should be swallowed whole with water and a meal at approximately the same time each day.
Assess patient-specific factors for level of risk of TLS and provide prophylactic hydration and anti-hyperuricemics to patients prior to first dose of VENCLEXTA to reduce risk of TLS. Perform tumor burden assessments (including radiographic evaluation), assess blood chemistry in all patients and correct pre-existing abnormalities prior to initiation of treatment with VENCLEXTA. Dosing interruption and/or dose reduction for toxicities may be required. For patients who have had a dosing interruption greater than 1 week during the first 5 weeks of ramp-up phase or greater than 2 weeks after completing the ramp-up phase, reassess for risk of TLS to determine if reinitiation with a reduced dose is necessary. **For risk assessment and prophylaxis of TLS and dose modifications, please refer to the full prescribing information.**

Contraindications:
In patients with CLL, concomitant use of VENCLEXTA with strong CYP3A inhibitors is contraindicated at initiation and during ramp-up phase.

Warning & Precautions:
Tumor Lysis Syndrome (TLS)
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. Changes in electrolytes consistent with TLS that require prompt management can occur as early as 6-8 hours following the first dose of VENCLEXTA and at each dose increase. The risk of TLS is a continuum based on multiple factors, including comorbidities (particularly reduced renal function), tumor burden, and splenomegaly in CLL. All patients should be assessed for risk and should receive appropriate prophylaxis for TLS, including hydration and anti-hyperuricemics. Monitor blood chemistries and manage abnormalities promptly. Employ more intensive measures (intravenous hydration, frequent monitoring, hospitalization) as overall risk increases. Interrupt dosing if needed; when restarting VENCLEXTA, follow dose modification guidance. Concomitant use of VENCLEXTA with strong or moderate CYP3A inhibitors increases venetoclax exposure and may increase the risk for TLS at initiation and during ramp-up phase. Also, inhibitors of P-gp may increase venetoclax exposure.

Neutropenia
In patients with CLL, grade 3 or 4 neutropenia has occurred in patients treated with VENCLEXTA in combination studies and monotherapy studies. In patients with AML, grade 3 or 4 neutropenia is common before starting treatment. The neutrophil counts can worsen with VENCLEXTA in combination with a hypomethylating agent or low-dose cytarabine. Neutropenia can recur with subsequent cycles of therapy. Monitor complete blood counts throughout the treatment period. Dose interruptions or dose reductions are recommended for severe neutropenia. Consider supportive measures including antimicrobials for any signs of infection and prophylactic use of growth factors (e.g., G-CSF).

Serious Infection
Serious infections, including events of sepsis and events with fatal outcome, have been reported in patients treated with VENCLEXTA. Monitor patients for fever and any symptoms of infection and treat promptly. Interrupt dosing as appropriate.

Immunization
Live vaccines should not be administrated during treatment with VENCLEXTA and thereafter until B-cell recovery.

Pregnancy & Lactation:
Females of reproductive potential should undergo pregnancy testing before initiation of VENCLEXTA and should use effective contraception during treatment and for at least 30 days after the last dose. VENCLEXTA should not be used during pregnancy. Breastfeeding should be discontinued during treatment with VENCLEXTA.

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:
Clinical Trial Experience in CLL
In combination with rituximab: In clinical trials, the most common adverse reactions (≥10%) were neutropenia, anemia, diarrhea, nausea, constipation, fatigue, upper respiratory tract infection. The most common grade 3 or 4 adverse reaction (≥2%) was neutropenia.

In combination with obinutuzumab: In clinical trials, the most common adverse reactions (≥10%) were neutropenia, diarrhea, anemia, nausea, constipation, vomiting. The most common grade 3 or 4 adverse reaction (≥2%) was neutropenia.

Monotherapy: In clinical trials, the most common adverse reactions (≥10%) were neutropenia, anemia, lymphopenia, diarrhea, nausea, vomiting, constipation, fatigue, upper respiratory tract infection, pneumonia, hyperkalemia, hyperphosphatemia and hypocalcemia. The most frequently reported serious adverse reactions (≥2%) unrelated to disease progression were pneumonia and febrile neutropenia.

Clinical Trial Experience in AML
In combination with azacitidine: In clinical trials, serious adverse reactions were reported in 83% of patients, with most frequent (≥5%) being febrile neutropenia, pneumonia, and sepsis.

In combination with decitabine: In clinical trials, the most common adverse reactions (≥30%) of any grade were thrombocytopenia/platelet count decreased, febrile neutropenia, nausea, fatigue, pneumonia, diarrhea, hypokalemia, hypotension, decreased appetite, dizziness, vomiting, neutropenia/neutrophil count decreased, and headache.

In combination with low-dose cytarabine: In clinical trials, serious adverse reactions were reported in 67% of patients, with the most frequent (≥10%) being pneumonia, febrile neutropenia, and sepsis.

Drug Interactions:
Venetoclax is predominantly metabolized by CYP3A4. Concomitant use of VENCLEXTA with strong CYP3A inhibitors is contraindicated at initiation and during ramp-up phase. Avoid concomitant use of moderate CYP3A inhibitors with VENCLEXTA at initiation and during ramp-up phase. If a moderate CYP3A inhibitor must be used, reduce the initiation and ramp-up doses of VENCLEXTA by at least 50%. Monitor patients more closely for signs of VENCLEXTA toxicities. For patients who have completed the ramp-up phase and are on a steady daily dose of VENCLEXTA, reduce the VENCLEXTA dose by at least 50% when used concomitantly with moderate CYP3A inhibitors and by at least 75% when used concomitantly with strong CYP3A inhibitors. Resume the VENCLEXTA dose that was used prior to initiating the CYP3A inhibitor 2 to 3 days after discontinuation of the inhibitor.

Avoid concomitant use of VENCLEXTA with strong CYP3A or moderate CYP3A inducers. However, no dose-adjustment is needed with Azithromycin.

Avoid concomitant use of VENCLEXTA with P-gp inhibitors at initiation and during ramp-up phase; if a P-gp inhibitor must be used, monitor closely for signs of toxicities. Co-administration of narrow therapeutic index P-gp substrates (e.g., digoxin, everolimus, and sirolimus) with VENCLEXTA should be avoided. If a narrow therapeutic index P-gp substrate must be used, it should be taken at least 6 hours before VENCLEXTA. A 50% dose reduction throughout treatment is recommended for patients with severe hepatic impairment; monitor these patients closely for signs of toxicity.

Full prescribing information is available upon request. Please read the full prescribing information before prescribing, available from AbbVie Pte Ltd.
SG_API VENCLEXTA PI Jan 2022.