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## Looking Out for Neutropenia in Chronic Lymphocytic Leukemia

### Announcer:

Welcome to ReachMD. The following program, "Looking Out for Neutropenia in Chronic Lymphocytic Leukemia" is developed and sponsored by AbbVie. This activity is intended for United States and Puerto Rico health care professionals only.

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### Dr. Nodzon:

I am Dr. Lisa Nodzon, an advanced oncology certified nurse practitioner in the Department of Malignant Hematology at Moffitt Cancer Center in Tampa, Florida.

In this video I will be discussing neutropenia in relation to CLL treatment with venetoclax.

Since leukemia is a disease of the bone marrow, neutropenia should always be on the treater's mind regardless of what treatment is being used. Both the disease itself and treatments for it can cause neutropenia. That said, neutropenia was the most common adverse event seen in both the first-line CLL14 venetoclax trial and in the MURANO relapsed/refractory CLL trial.

Let's review some of the data. Rates of adverse reactions of any grade neutropenia ranged from 60 to 65 percent in the CLL14 and MURANO trials, while adverse reaction rates of Grade 3 or higher neutropenia occurred in 56 to 62 percent of patients. Febrile neutropenia occurred in 4 to 6 percent of patients.

When we look at the typical time horizon for neutropenic events, we tend to see them pop up earlier in treatment and then become less frequent as treatment continues, and particularly once response is achieved. Because of this, I'm always ready to address it early and treat it as I would with any other patient in our cancer center who develops neutropenia.

From my experience, one of the biggest questions we always get that's often overlooked is if growth factor (or G-CSF) was allowed during clinical trials, and the answer is yes. G-CSF is definitely something to be considered and should be utilized when clinically indicated. In our practice we utilize growth factor as clinically needed to maintain neutrophil counts.

So, how do we as clinicians provide best Monitoring Practices, while balancing the risks?

We want to monitor complete blood counts throughout the treatment period, and interrupt the dosing for severe neutropenia as follows. When we see the first occurrence of Grade 3 neutropenia with infection or fever, or Grade 4 hematologic toxicities (except lymphopenia), we need to interrupt venetoclax. In order to reduce risk of infection, G-CSF may be administered if indicated. Once the toxicity has resolved to grade 1 or baseline level, venetoclax therapy may be resumed at the same dose. We also must use clinical judgement in dosing as some of our patients with initiating of venetoclax have cytopenias due to marrow infiltration or prior therapy.

Now, when there is a second or subsequent occurrence, we need to again interrupt venetoclax, but also follow dose reduction guidelines when resuming treatment after resolution. A larger dose reduction may occur per physician discretion. And, always consider supportive measures including antimicrobials for any signs of infection and use of growth factors.

Thanks for your time today. Please stay tuned for important safety information

### Announcer:

#### Indication

- Venetoclax is a BCL-2 inhibitor indicated for the treatment of adult patients with chronic lymphocytic leukemia (or CLL) or small lymphocytic lymphoma (or SLL).

#### Contraindications

- **Strong CYP3A Inhibitors:** Concomitant use with strong CYP3A inhibitors at initiation and during ramp-up phase in patients with CLL and SLL is contraindicated.

#### Warnings and Precautions

- **TLS:** Tumor lysis syndrome (or TLS), including fatal events and renal failure requiring dialysis, has occurred in patients treated with venetoclax. Anticipate TLS; assess risk in all patients. Premedicate with anti-hyperuricemics and ensure adequate hydration. Employ more intensive measures (intravenous hydration, frequent monitoring, and hospitalization) as overall risk increases.
- **Neutropenia:** Monitor blood counts. Interrupt dosing and resume at same or reduced dose. Consider supportive care measures.
- **Infections:** Fatal and serious infections such as pneumonia and sepsis have occurred in patients treated with venetoclax. Monitor patients for signs and symptoms of infection and treat promptly. Withhold venetoclax for Grade 3 and 4 infection until resolution and resume at same or reduced dose.
- **Immunization:** Do not administer live attenuated vaccines prior to, during, or after venetoclax treatment until b-cell recovery.
- **Embryo-Fetal Toxicity:** May cause embryo-fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception.
- **Increased mortality in patients with multiple myeloma (or MM) when venetoclax is added to bortezomib and dexamethasone.** In a randomized trial in patients with relapsed or refractory MM, the addition of venetoclax to bortezomib plus dexamethasone, a use for which venetoclax is not indicated, resulted in increased mortality. Treatment of patients with MM with venetoclax in combination with bortezomib plus dexamethasone is not recommended outside of controlled clinical trials.

#### Adverse Reactions

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

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