

Tazemetostat and Secondary Malignancies



WHAT YOU NEED TO KNOW

Tazemetostat is an investigational drug under evaluation in clinical trials. It is a pill that selectively inhibits EZH2 and has shown anti-cancer activity and generally good tolerability in early clinical development. The full safety profile of tazemetostat has not been established and all drugs present some level of risk.

Investigational means that the drug is currently being tested for the treatment of cancer and is not approved by the Food and Drug Administration (FDA). In early clinical trials, certain side effects associated with tazemetostat were identified. As a prospective trial participant, this pamphlet is designed to walk you through those side effects including risk factors, what to look for, and what action to take if you experience any events, signs, or symptoms.

Side effects of special interest are events of medical or scientific concern for a drug, for which monitoring and rapid communication can be appropriate. Side effects related to tazemetostat are second malignancies.

SECONDARY MALIGNANCIES

- Secondary malignancies are new, different cancers that may develop in some cancer patients, sometimes years after an initial treatment
- The risk of the occurrence of these two types of secondary malignancies have been identified as side effects of special interest in tazemetostat clinical trials

T-Cell Lymphoblastic Lymphoma (T-LBL)/T-cell Acute Lymphoblastic Lymphoma (T-ALL)

- These types of lymphomas usually occur in patients with an active thymus such as pediatric and adolescent patients with high exposure of tazemetostat
- 1 T-LBL event has been reported in a pediatric patient out of >750 adult and pediatric patients treated on a tazemetostat clinical trial. This occurred on a high dose over 1 year of treatment
- Over 700 adults have been treated with tazemetostat with no observed cases of T-LBL/ALL

Myelodysplastic Syndromes (MDS)/Acute Myeloid Leukemia (AML)/Myeloproliferative Neoplasms (MPN)

- MDS, AML, and MPN are conditions that interfere with normal blood production
- 2 MDS and 1 MPN cases have been reported in adult NHL patients on tazemetostat clinical trials. These cases were confounded by prior cancer treatments
- The link to tazemetostat is unclear based on confounding factors, such as prior treatment history or the presence of the disease before starting tazemetostat
- Additional safety monitoring and mitigation steps have been added to all tazemetostat clinical trials to reduce the risk of MDS, AML, and MPN

RISK FACTORS FOR SECONDARY MALIGNANCIES

- Previous chemotherapy or radiation treatment for other cancers (especially women treated for breast cancer, patients treated for other blood or bone marrow conditions, patients treated for head and neck cancers, gastrointestinal cancers, lung cancer, and possibly men treated for prostate cancer)
- Environmental risk factors
- Familial cancer syndromes or gene changes that are inherited

RISK FACTORS FOR T-LBL/T-ALL

HTLV-I virus

Trisomy 21, Down syndrome, changes in certain genes

Ionizing radiation during childhood

Environmental exposures

RISK FACTORS FOR MDS/AML/MPN

Cytogenetic abnormalities known to be associated with MDS

Certain genetic conditions such as: Down syndrome, Fanconi anemia, dyskeratosis congenita, MonoMAC syndrome, Bloom syndrome, Shwachman syndrome, Diamond-Blackfan syndrome

Thrombocytopenia, neutropenia, anemia, other blood cancers

History of myeloid malignancies, including MDS

Environmental exposures

SIGNS AND SYMPTOMS

Epizyme has added additional blood tests and imaging to prevent, if possible, or detect early occurrence of secondary malignancies.* Additionally, there are many signs and symptoms to monitor:

- Flu-like symptoms (fever, loss of appetite, shortness of breath, tiredness or fatigue)
- Rapid heartbeat
- Pale complexion
- Prolonged bleeding and easy bruising
- Frequent infections
- Swollen gums
- Weight loss
- Discomfort in bones or joints
- Enlarged spleen
- Enlarged liver
- Headaches
- Blurred vision
- Night sweats
- Raised blood pressure

*For more information and detail, please refer to your informed consent form.

What to do if you experience an event, sign, or symptom

If you experience any of the noted signs or symptoms or have additional questions, please contact your physician right away:

If you need additional information, please email us at **clinicaltrials@epizyme.com** or call us at **855-500-1011** (U.S. toll-free).

References

1. American Cancer Society. What are second cancers? <https://www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/second-cancers-in-adults/intro.html>. Accessed September 18, 2018.
2. Cortelazzo S, et al. *Crit Rev Oncol Hematol*. 2017;113:304-317.
3. AA-MDS International Foundation. Acute Myeloid Leukemia (AML). <https://www.aamds.org/diseases/related/acute-myeloid-leukemia-aml>. Accessed September 18, 2018.
4. Leukaemia Foundation. Myeloproliferative neoplasms (MPN). <https://www.leukaemia.org.au/disease-information/myeloproliferative-disorders/>. Accessed September 18, 2018.
5. Cancer.Net website. What is a second cancer. <https://www.cancer.net/survivorship/what-second-cancer>. Accessed September 18, 2018.