CLINICAL STUDY RESULTS

A study to learn about the safety and effects of tazemetostat in combination with doxorubicin in people with advanced soft tissue cancer

Overall, the results suggest that tazemetostat in combination with doxorubicin was safe and well-tolerated with no new safety concerns in treating participants with advanced soft tissue cancer.

The results shown in this summary represent one clinical study. Other clinical studies may produce different results.

This lay summary was created by Ipsen with the assistance of a third-party writing service provider

What was the study about?

The purpose of this study was to learn about the safety and effects of tazemetostat in combination with doxorubicin as an initial treatment for people with advanced soft tissue cancer, also called advanced epithelioid sarcoma.

Soft tissue cancer is a cancer that starts from soft tissues such as muscles, tendons (which hold muscles and bones together), and tissues under the skin. Advanced cancer means that the cancer has spread to nearby or distant parts of the body. Symptoms may include a painless lump under the skin, in muscles, or in tendons, usually in the arms or legs. It may later cause swelling, pain, fatigue, and weight loss.

Currently, one of the standard treatments used for advanced soft tissue cancer is doxorubicin as an initial treatment.

Tazemetostat is a drug approved in the United States to treat certain types of cancer. It works by blocking a protein called EZH2, which helps cancer cells grow. By stopping EZH2, tazemetostat may slow down or stop cancer growth in soft tissues.

In this study, tazemetostat in combination with doxorubicin was tested as an initial treatment for advanced soft tissue cancer for the first time.

The treatment in this study was to be done in 2 phases, Phase 1b and Phase 3.

The aims of this study were:

- Phase 1b: to learn how safe and well-tolerated tazemetostat in combination with doxorubicin was and select a suitable dose for the planned Phase 3
- Phase 3: to learn for how long the participants who received tazemetostat in combination with doxorubicin lived without their cancer getting worse, compared with those who received placebo* in combination with doxorubicin

The study stopped early, Phase 3 was not conducted.

*A Placebo looks like tazemetostat tablets but does not have medicine in it.

The study took place between December 2019 and June 2025 at 8 study sites in Canada, the United States, and the United Kingdom.

The study was stopped early by the sponsor due to the low number of participants in the study.

Who took part in this study?

25
PARTICIPANTS

9
MEN

16
WOMEN

53 YEARS
AVERAGE AGE

To take part in the study, participants had to:

- be aged between 18 and 65 years to enter the first part of Phase 1b, where different doses were tested,
- be aged 18 years or older to enter other parts of the study,
- be diagnosed with advanced soft tissue cancer that cannot be removed by surgery to enter Phase 1b and had sufficient cancer tissue for testing to enter Phase 3,
- have cancer that could be measured, and
- be fully active, able to move and perform light work, or at least able to take care of themself.

Participants could not take part in the study if:

- they had a health condition or had received treatment that could affect the result of the study.

What treatments were used in this study?

Study Treatment	Standard Treatment	Placebo
Tazemetostat was given as tablets at doses of 400 milligrams (mg), 600 mg, or 800 mg in Phase 1b and was to be given at a dose of 800 mg in Phase 3, twice daily in 21-day cycles.	Doxorubicin was given as a drip through a vein at a dose of 75 mg/m² (75 mg for each square metre area of participants' body) on the first day of each 21-day cycle for 6 cycles in Phase 1b.	Placebo tablets were to be given in the same way and at the same timings as the tazemetostat tablets in Phase 3.

A placebo looks like the study treatment and is given in the same way but does not have any medicine in it. Researchers sometimes use a placebo to understand if the changes seen were due to the study treatment or if they happened by chance.

A standard treatment is an approved medical treatment that is normally given to people with advanced soft tissue cancer.

This study had 3 parts:

Screening: The study doctor checked if participants could take part in this study within 1 month before starting the study treatment.

Treatment: The treatment was planned to be given in 2 phases: Phase 1b and Phase 3.

Phase 1b: This phase was to assess how safe and well-tolerated the study treatment is and find a suitable dose of tazemetostat to be used in Phase 3.

Twenty-five participants received increasing doses of tazemetostat in combination with doxorubicin. The dose was increased gradually in small groups of participants. Four participants received 400 mg, 6 participants received 600 mg, and 15 participants received 800 mg tazemetostat in combination with doxorubicin 75 mg/m^2.

Participants could continue to receive the treatment as long as it was safe.

Phase 1b was "open label". This means that the researchers and the participants knew which treatment was given to each participant.

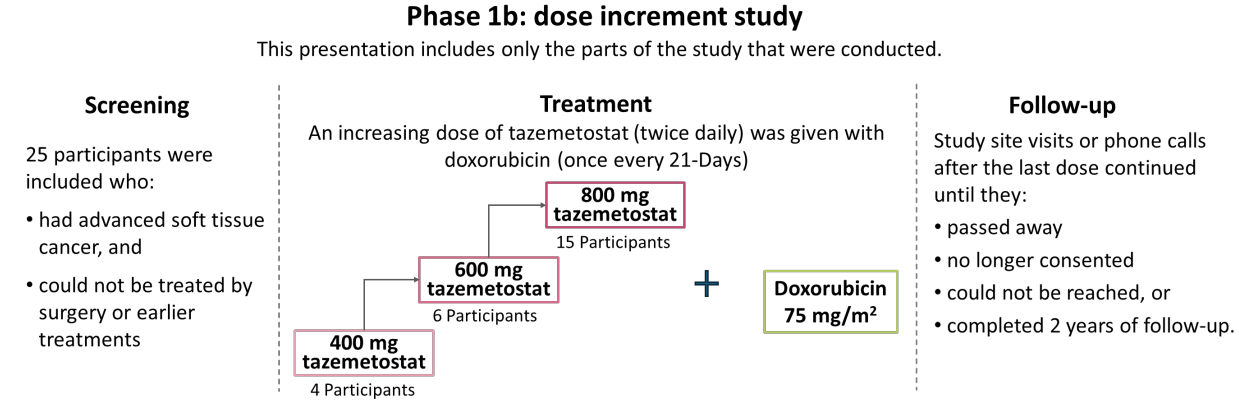
After assessing the results of the dose increment phase, a dose of tazemetostat 800 mg twice daily in combination with doxorubicin was selected as suitable dose for Phase 3.

Fourteen participants were planned to be treated with the selected dose to further learn about the study treatment. However, before they were included, the study was stopped.

Phase 3: This phase was planned to learn how effective the selected dose of study treatment was compared with the standard treatment. However, Phase 3 was not conducted as the study was stopped early due to the low number of participants.

Follow-up: The researchers monitored the health of the study participants every 3 months through a visit to the study site or a phone call until either they passed away, no longer gave consent to follow-up, could not be reached, or until a maximum of 2 years after the last study treatment dose.

Each participant could have been in this study for up to maximum of 2 years.



What did researchers find out in the study?

Tazemetostat in combination with doxorubicin was safe and well-tolerated, with no new medical concerns other than those already known about each treatment individually

Was tazemetostat in combination with doxorubicin safe and well-tolerated in Phase 1b?

This was assessed based on the unacceptable medical concerns that led to stopping or lowering of the dose and the overall health of the participants during the first 21 days of their treatment in Phase 1b.

In Phase 1b, 1 participant each receiving 600 mg and 800 mg of tazemetostat in combination with doxorubicin experienced an unacceptable medical concern of abnormally low number of neutrophils with fever. Neutrophils are a type of white blood cell that helps the body fight infections.

The combination treatment was found to be safe and well-tolerated. The medical concerns seen with tazemetostat in combination with doxorubicin were similar to the medical concerns already known for each treatment when used alone.

What was the suitable dose of tazemetostat in combination with doxorubicin for use in Phase 3?

After assessing the results of the dose increment study in Phase 1b, a dose of tazemetostat 800 mg twice daily in combination with doxorubicin was selected as suitable dose for Phase 3.

In Phase 3, researchers had planned to assess how long the participants who received tazemetostat in combination with doxorubicin lived without their cancer getting worse after treatment, compared with those who received placebo in combination with doxorubicin. However, the study was stopped before the start of Phase 3.

How did the treatment make participants feel?

During the study, participants were asked to report any 'adverse events', that is, if they felt unwell, experienced any kind of medical event, or noticed anything different about their bodies. Researchers recorded all adverse events reported by participants, whatever the cause. For example, if some participants caught COVID-19, this was reported as an adverse event, although it was not related to the study treatment.

If the study doctor thinks an adverse event may be related to the study treatment, it is called a 'side effect'. A side effect is considered 'serious' when it is life-threatening, causes lasting problems, or leads to hospitalisation.

- Forty eight percent (12 out of 25 participants) in this study experienced a serious side effect.
- One participant died during the study due to the side effect of a heart problem known to be associated with doxorubicin.

Overall, 100% (all 25 participants) experienced side effects:

Three participants stopped taking part in the study because of the side effects of blockage in the small intestine, vomiting, and not enough oxygen in the lungs.

The most commonly reported serious side effects that happened in at least 2 participants are shown below, both as a percentage (%) followed by the actual number of participants in the group (e.g. 28% or 7 out of 25).

Side Effects	Tazemetostat in combination with doxorubicin (25 Participants)
Abnormally low number of neutrophils with fever Neutrophils are a type of white blood cell that helps body fight infections	28% (7 out of 25) 
Abnormally low numbers of neutrophils	16% (4 out of 25) 
Low number of red blood cells	8% (2 out of 25) 
Low blood platelet count Platelets are of cells in blood that help stop bleeding	8% (2 out of 25) 

The most commonly reported side effects in at least 5 participants are shown below.

Side Effects	Tazemetostat in combination with doxorubicin (25 Participants)
Abnormally low numbers of neutrophils	76% (19 out of 25) 
Low number of red blood cells	52% (13 out of 25) 
Abnormally low number of neutrophils with fever	28% (7 out of 25) 
Decreased in white blood cell count	24% (6 out of 25) 
Low blood platelet count	20% (5 out of 25) 
Decrease in neutrophil count	20% (5 out of 25) 

More information

To learn more about this study, please visit:

- ClinicalTrials.gov and search for study NCT04204941 or
- Clinicaltrialsregister.eu/ctr-search/search and search for study 2019-003648-55

For more information about current treatments available, please speak to your healthcare provider. If you have any questions about this study, please contact the sponsor, Ipsen at:

clinical.trials@ipsen.com

Future research

There are future studies planned with tazemetostat for advanced epithelioid sarcoma.

Study identification and other information

FULL STUDY TITLE: A Phase 1b/3 Global, Randomized, Double-blind, Placebo-Controlled Trial of Tazemetostat in Combination with Doxorubicin as Frontline Therapy for Advanced Epithelioid Sarcoma

STUDY NUMBERS: Europe: 2019-003648-55 | United States: NCT04204941 |

PROTOCOL: EZH-301

OTHER INFORMATION: Phase Ib studies can take several months, and Phase III studies can take several years to complete. Analysis of the study results will show how safe and/or effective a study treatment was during the study.

We thank all the volunteers who took part in this study. Without their support, advances in treatments for medical conditions would not be possible.

We would also like to thank the people who took the time to review this document to make it easier for a general audience to read.