CLINICAL STUDY RESULTS

A Study on the Effects and Safety of Tazemetostat in Men with Advanced Prostate Cancer That Does Not Respond to Sex-Hormone Lowering Treatments

Tazemetostat showed no benefit when added to the standard treatments for men with advanced prostate cancer. As a result, the sponsor stopped this study early. No new safety concerns were found during the study.

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 effects and safety of tazemetostat in men with metastatic castration-resistant prostate cancer (mCRPC).

'Metastatic' means cancer has spread beyond the prostate gland. 'Castration-resistant' means that the cancer keeps growing despite treatment that lowers the levels of male sex hormones (androgens)—responsible for the growth of prostate cancer.

Men with mCRPC usually have symptoms such as pain while urinating, bone pain, tiredness, and weight loss.

Currently, the treatments for mCRPC include androgen-lowering medicines, such as **enzalutamide** and **abiraterone** (along with **prednisone**), which improve survival. However, this effect does not last for long.

Tazemetostat is being tested as a treatment for mCRPC. It is approved in the USA and in parts of Asia to treat certain blood cancers and soft tissue cancers. It works by blocking a protein that is responsible for the growth of cancer.

The aims of this study were to:

- Assess the safety of tazemetostat with enzalutamide and of tazemetostat with abiraterone and prednisone.
- Find a suitable dose of tazemetostat to be used in the next part of the treatment in this study.
- Assess the effect of tazemetostat with enzalutamide compared with enzalutamide alone.

The study took place between November 2019 and November 2024 at 21 study sites in Belgium, Spain, and the United States.

The study was stopped early by the sponsor as the initial analysis of results showed that the main goal of the study was not achieved.

Who took part in this study?

102

MEN

51 to 91

YEARS of AGE

To take part in the study, participants had to:

- be 18 years or older
- be physically active with no major disability
- have mCRPC, confirmed by lab tests
- not have received any chemotherapy for their mCRPC
- have a life expectancy of more than 3 months

Participants could not take part in the study if:

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

What treatments were used in this study?

Study Treatment	Standard Treatment
Tazemetostat was given as tablets at a dose of 400 mg, 600 mg, 800 mg, 1200 mg, or 1600 mg twice daily.	Enzalutamide was given as capsules at a dose of 160 mg once daily. OR Abiraterone was given as tablets at a dose of 1000 mg once daily along with Prednisone given as tablets at a dose of 5 mg twice daily.

Standard treatment is an approved medical treatment that is normally given to people with mCRPC.

This study had 3 stages: screening, treatment and follow-up.

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 given in 2 parts.

In **Part 1**, 21 participants were divided into 2 groups:

- **Group 1:** 7 participants were given tazemetostat at increasing doses (from 400 mg to 800 mg twice a day) with abiraterone/prednisone.
- **Group 2:** 14 participants were given tazemetostat at increasing doses (from 400 mg to 1600 mg twice a day) with enzalutamide.

Participants were given increasing doses of tazemetostat, as long as it was safe, to find a suitable dose for the next part of the treatment. **A dose of tazemetostat of 1200 mg twice daily was chosen to be given with enzalutamide.** The dose was chosen based on the drug's safety, effects, and how the drug moved through the body. Participants were to continue treatment until they had an unacceptable medical problem.

In **Part 2**, 81 participants were assigned to 1 of 2 treatment groups using a computer system. This process is called randomisation. It means that each participant could be assigned to any group, and it helps to make sure that the participants were divided into groups in a balanced and fair way.

- 41 participants received tazemetostat with enzalutamide
- 40 participants received only enzalutamide

This study was "open-label". This means that the researchers and the participants knew which treatment was given to each participant.

In January 2024, an early analysis showed that the study was not meeting its main goal. Therefore, the study was stopped by the sponsor.

Follow-up:

Researchers monitored the health of the participants through a visit to the study site 1 month after the last dose of treatment and then every 3 months. The participants were followed up until either 18 months had passed, their cancer worsened, they began a new anti-cancer treatment, left the study, were lost to follow-up, or passed away.

What were the results of the study?

The researchers found 1200 mg of tazemetostat twice daily to be a suitable dose for Part 2. In Part 2, tazemetostat with enzalutamide showed a similar benefit compared with enzalutamide alone.

What was the suitable dose of tazemetostat found during Part 1 to use in Part 2 of the treatment?

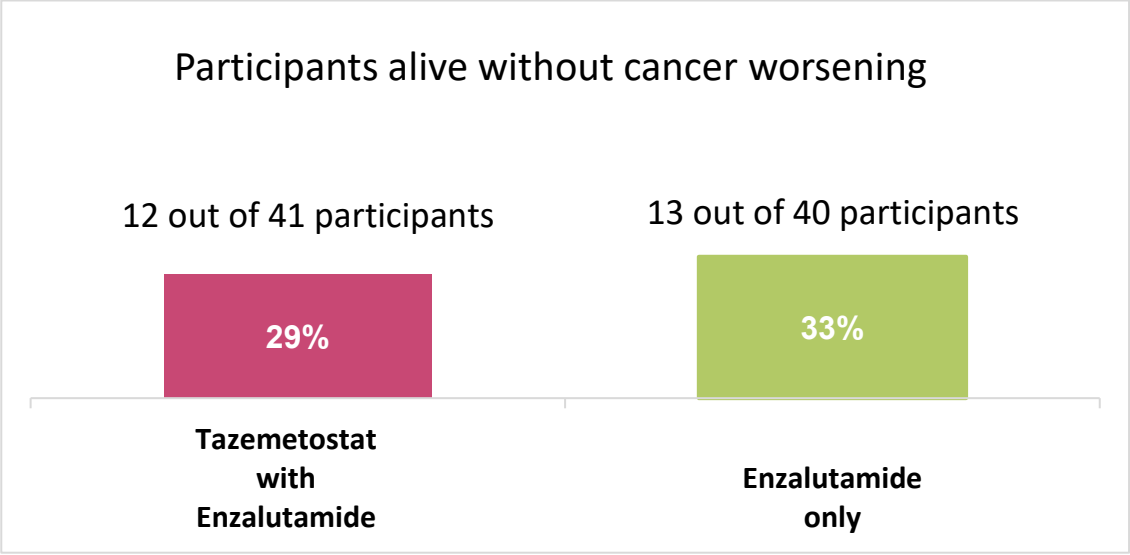
The suitable dose of tazemetostat found during Part 1 to use in Part 2 of the treatment was **1200 mg** twice daily.

How long did the participants taking tazemetostat with enzalutamide live without their cancer getting worse compared with those taking enzalutamide alone?

Researchers wanted to see if adding tazemetostat to enzalutamide could help participants live longer without their cancer getting worse, based on scan results. In an early analysis researchers observed:

29% (12 out of 41) of participants taking tazemetostat with enzalutamide lived without their cancer getting worse compared with 33% (13 out of 40) of participants taking enzalutamide alone.

As **no benefit was seen in adding tazemetostat to enzalutamide**, the study was stopped by the sponsor.



How did the treatment make participants feel?

During the study, participants were asked to report any 'adverse events', for example, 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, some participants caught COVID-19 and 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.

- Adverse events that are life-threatening, cause lasting problems or require an individual to go to the hospital are considered serious.
- 5% (1 out of 21 participants) in Part 1 and 5% (4 out of 81 participants) in Part 2 experienced serious side effects.
- No participants died during the study due to side effects.

Overall, 86% (18 out of 21 participants) in **Part 1** experienced a side effect:

- **86% (12 out of 14 participants)** who received **tazemetostat with enzalutamide**
- **86% (6 out of 7 participants)** who received **tazemetostat with abiraterone and prednisone**

5% (1 out of 21 participants) in **Part 1** stopped taking part in the study because of a side effect.

In **Part 1**, no participants taking **tazemetostat with enzalutamide** experienced serious side effects. 14% (1 out of 7) of participants taking **tazemetostat with abiraterone and prednisone** experienced a serious side effect of type 2 diabetes.

The most commonly reported side effects in **Part 1** seen in at least 3 participants in any group are shown below, both as a percentage (%) followed by the actual number of participants in the group (for example, 43% or 6 out of 14).

Side Effects	Tazemetostat with Enzalutamide (14 Participants)	Tazemetostat with Abiraterone and Prednisone (7 Participants)
Extreme tiredness	43% (6 out of 14) 	43% (3 out of 7) 
Feeling sick to your stomach	29% (4 out of 14) 	14% (1 out of 7) 
Decrease of red blood cells in the blood	29% (4 out of 14) 	0% (0 out of 7) 
Diarrhoea	21% (3 out of 14) 	14% (1 out of 7) 
Loss of appetite	21% (3 out of 14) 	0% (0 out of 7) 

Overall, 80% (65 out of 81 participants) in **Part 2** experienced a side effect:

- **90% (37 out of 41 participants)** who received **tazemetostat with enzalutamide**
- **70% (28 out of 40 participants)** who received **enzalutamide only**

6% (5 out of 81 participants) in **Part 2** stopped taking part in the study because of a side effect.

In **Part 2**, 7% (3 out of 41) of participants taking tazemetostat with enzalutamide, experienced serious side effects of irregular heartbeat, heart failure, and high blood pressure. 3% (1 out of 40) of participants taking enzalutamide alone experienced a serious side effect of extreme tiredness and weakness.

The most commonly reported side effects in **Part 2** seen in at least 10 participants in any group are shown below.

Side Effects	Tazemetostat with Enzalutamide (41 Participants)	Enzalutamide (40 Participants)
Extreme tiredness	59% (24 out of 41) 	25% (10 out of 40) 
Feeling sick to your stomach	44% (18 out of 41) 	15% (6 out of 40) 
Loss of appetite	24% (10 out of 41) 	10% (4 out of 40) 

More information

To learn more about this study, please visit:

- ClinicalTrials.gov and search for study NCT04179864 or
- Clinicaltrialsregister.eu/ctr-search/search and search for study 2019-003649-14.

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

At the time this report was written, no future research was planned on this topic.

Study identification and other information

FULL STUDY TITLE: CELLO-1: A Phase Ib/II Open-Label Study Evaluating Tazemetostat in Combination with Enzalutamide or Abiraterone/Prednisone in Chemotherapy-Naïve Subjects with Metastatic Castration-Resistant Prostate Cancer.

STUDY NUMBERS: Europe: 2019-003649-14| United States: NCT04179864|

PROTOCOL: EZH-1101

OTHER INFORMATION: Phase I or II studies can take several months 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.