Plain Language Summary of Publication

Future ONCOLOGY

A plain language summary of results from the GARNET study of dostarlimab in patients with endometrial cancer

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Summary

What is this summary about?
Dostarlimab, also known by the brand name JEMPERLI, is a medicine that can be used to treat certain types of endometrial cancer. GARNET is an ongoing phase 1 clinical study that is testing the safety and side effects of dostarlimab and the best way to administer it to patients. The results presented in this summary are from a time point in the middle of the study

How to say (double click sound icon to play sound)...

- **Dostarlimab:** doh-STAR-luh-mab

What were the results?
The results from the GARNET study published in 2022 showed how well dostarlimab worked for people participating in the study. Dostarlimab was found to reduce the size of tumors in patients with certain types of endometrial cancer. The patients treated with dostarlimab had side effects that could be managed and few severe side effects.

What do the results mean?
The results of the GARNET study led to dostarlimab being approved to treat patients with certain types of endometrial cancer. For patients with advanced-stage endometrial cancer, or endometrial cancer that has come back after chemotherapy (recurrent), there are few treatment options. The results suggest that dostarlimab may provide long-term benefits for these patients.

Who is this article for?

This summary is intended to provide information for patients with advanced or recurrent endometrial cancer and their family members or caregivers. It may also be helpful for patient advocates and health care professionals.

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Where can I find the original article on which this summary is based?

You can read the original article published in *Journal for Immunotherapy of Cancer* for free at:
https://jitc.bmj.com/content/10/1/e003777

Why is this study being done?

- The GARNET study includes people with advanced or recurrent endometrial cancer who are being treated with dostarlimab, a type of immunotherapy.
- The study is looking at how well dostarlimab works at reducing tumor size and if it causes any side effects.

What is endometrial cancer?

Endometrial cancer is a type of cancer that begins in the lining of the uterus (womb).

Endometrial cancer is the most common gynecologic cancer.

In about 1 of 3 cases of endometrial cancer, there is a particular irregularity in the cancer cells' DNA called mismatch repair deficiency (dMMR). DNA repair happens in all human cells, but in dMMR, the process to repair damaged DNA no longer works correctly. Cells without dMMR are referred to as mismatch repair proficient (MMRp).

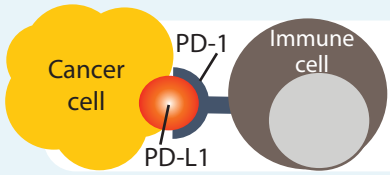
Patients with endometrial cancer have few options if chemotherapy does not fully treat the cancer.

In addition to dMMR, researchers have identified another irregularity in cancer cells called high microsatellite instability (MSI-H). Cells without MSI-H are referred to as microsatellite stable (MSS).

Together, these indicators, called 'biomarkers', are used to classify the type of endometrial cancer as dMMR/MSI-H or MMRp/MSS.

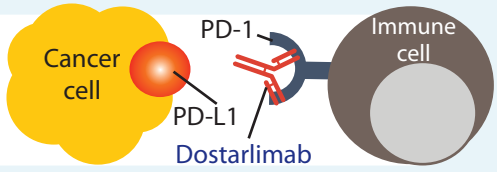
What is immunotherapy?

- Immunotherapy works by helping the patient's immune system find and attack cancer cells, potentially killing the cancer cells that make up the tumor.
- Dostarlimab works by blocking a protein called programmed death 1 (PD-1).



When cancer cells have a protein called programmed death-ligand 1 (PD-L1) on their surface, cells in the immune system (called 'immune cells' here) that have PD-1 will find them, and they connect, like a handshake. This tricks the immune system into not attacking the cancer cells.

Dostarlimab attaches to PD-1 and stops the 'handshake'. This immune cell can now tell other cells in the immune system that there are cancer cells that need to be attacked.



Who took part in the study?

To participate in the GARNET study, patients had to have already been treated with a least 1 regimen of a particular type of treatment called 'platinum-based chemotherapy' and had either not responded to the treatment, or responded but the cancer came back.

Once patients had joined the study, they were tested for dMMR/MSI-H or MMRp/MSS biomarkers to identify the type of endometrial cancer they had.

Testing for dMMR/MSI-H or MMRp/MSS is common when a patient has endometrial cancer.

To test for these biomarkers, tumor samples are taken by an oncologist (a specialist cancer doctor) and sent to a laboratory. This technique helps doctors and researchers understand the type of cancer a patient has.

In total, 290 patients with advanced endometrial cancer were enrolled in the study, 129 patients who had dMMR/MSI-H endometrial cancer (Group 1) and 161 patients who had MMRp/MSS endometrial cancer (Group 2).

How was the study carried out?

The GARNET study is ongoing. The results presented in this summary were from a time point in the middle of the study (interim).

Study start
March 2016 → Interim Results Published 2020 → Interim Results Published 2022 (this summary) → **Estimated Study Completion**
October 2027

Patients were given dostarlimab intravenously over a 30-minute period. The treatment was once every 3 weeks for 4 cycles, then once every 6 weeks over the period of time the patients participated in the study.

The average time that patients were followed over the course of the study was 16.3 months for Group 1 and 11.5 months for Group 2.

Measuring the size of the tumor

- Patients who had tumors that could be measured when they started the study and had been in the study for at least 6 months were included in the analysis.
- This allowed enough time for the tumor to shrink in response to the treatment and to see if the response (shrinkage) would last.

Looking at side effects

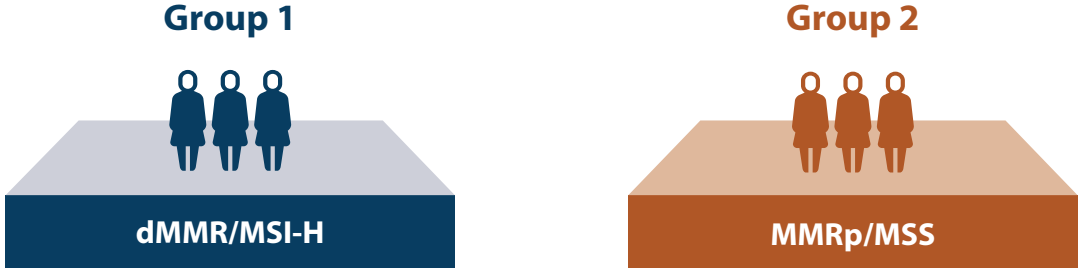
- All patients who received at least 1 dose of dostarlimab were included in a safety analysis to look at side effects.
- Patients were included in the analysis even if they did not receive dostarlimab treatment for the entire time that they participated in the study.

What were the results of the study?

Dostarlimab was found to reduce tumor size in both groups of patients.

44% of patients with **dMMR/MSI-H** status responded to dostarlimab treatment

14% of patients with **MMRp/MSS** status responded to dostarlimab treatment



Responses were long lasting

Of the patients whose cancer responded to treatment, after 1 year, **91%** (Group 1) and **62%** (Group 2) of patients were still responding to treatment (responding to treatment means that their cancer shrunk and did not start growing again).

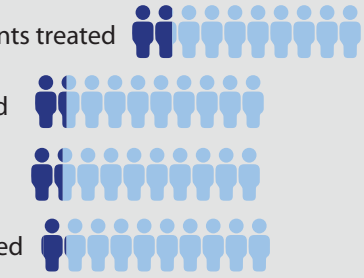
What were the most common side effects?

- A total of 290 patients received at least 1 dose of dostarlimab. The side effects experienced by patients were similar to what researchers expected.
- No patient died because of a side effect caused by dostarlimab treatment.

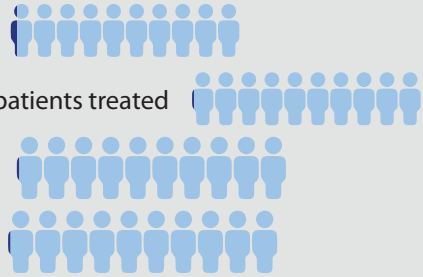
17% of patients experienced severe side effects that were treatment-related

6% of patients were required to stop taking dostarlimab because of a treatment-related side effect

- The most common side effects included:
  - fatigue (tiredness) – 18% of patients treated
  - diarrhea – 14% of patients treated
  - nausea – 14% of patients treated
  - weakness – 11% of patients treated



- Severe side effects (defined as those requiring medical support) included:
  - anemia – 3% of patients treated
  - increased liver enzymes – 1% of patients treated
  - diarrhea – 1% of patients treated
  - fatigue – 1% of patients treated



How do these results help patients and researchers?

Dostarlimab is an important new option for patients with certain types of endometrial cancer and may provide long-term benefits.

Although these results are encouraging, more research is still needed. For example, the study did not compare dostarlimab with other therapies or determine if it is effective in all forms of endometrial cancer.

GARNET is a phase 1 clinical study, which means dostarlimab is still in the early phase of development. Because dostarlimab has shown benefit in this phase 1 study, it can move on to be tested in larger studies (phases 2 and 3), and be compared with other therapies.

These results are important because patients with this type of cancer do not currently have many treatment options

Where can readers find more information on this study?

More information about the GARNET study is available at the following websites:

- GARNET: www.clinicaltrials.gov/ct2/show/NCT02715284
- RUBY, a follow-up study to GARNET: www.clinicaltrials.gov/ct2/show/NCT03981796
- Earlier results from the GARNET study (free to access): https://jamanetwork.com/journals/jamaoncology/fullarticle/2771011
- A plain language summary of the earlier results from the GARNET study (free to access): www.futuremedicine.com/doi/epdf/10.2217/fon-2021-0598

Read more about endometrial cancer on these websites:

- The American Cancer Society: www.cancer.org/cancer/endometrial-cancer.html
- The International Gynecologic Cancer Society: www.igcs.org/womens-cancers/
- ENGAGe: www.engage.esgo.org/brochures/cancer-fact-sheets/uterine-endometrial-cancer/

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