

Plain Language Summary of Publication

Clinical activity and safety of the anti-PD-1 monoclonal antibody dostarlimab for patients with recurrent or advanced dMMR endometrial cancer

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Summary

This document provides a short summary of the GARNET trial which was published in *JAMA Oncology* in October 2020. At the end of this document, there are links to websites where you can find more information about this study.

How to say....

- **Dostarlimab:** doh-STAR-luh-mab 
- **Endometrial:** en-dow-MEE-tree-uhl 

The trial enrolled adult participants with advanced solid tumors. This report is restricted to patients with a particular type of endometrial cancer that has a deficient mismatch repair (dMMR) status. Patients received a trial treatment called dostarlimab (also known by the brand name Jemperli). In the US, dostarlimab is approved as a single therapy in adult patients with dMMR recurrent or advanced endometrial cancer that has progressed on or after platinum-based chemotherapy. In the EU, dostarlimab is approved as a single therapy in adult patients with recurrent or advanced dMMR/microsatellite instability-high (MSI-H) endometrial cancer that has progressed on or after treatment with a platinum-containing regimen. The GARNET trial looked at dostarlimab given intravenously to patients with dMMR endometrial cancer from 7 countries. The trial showed that dostarlimab was successful in shrinking the tumor in 42% of these patients. In general, the percentage of participants who experienced medical problems (referred to as side effects) was low and within expectations for this type of treatment.

Who should read this article?

This summary may be helpful for patients with recurrent or advanced endometrial cancer and their family members or caregivers. It may also be helpful for patient advocates and healthcare professionals who are looking for treatment options for patients with recurrent or advanced endometrial cancer.

Why is this study being done?

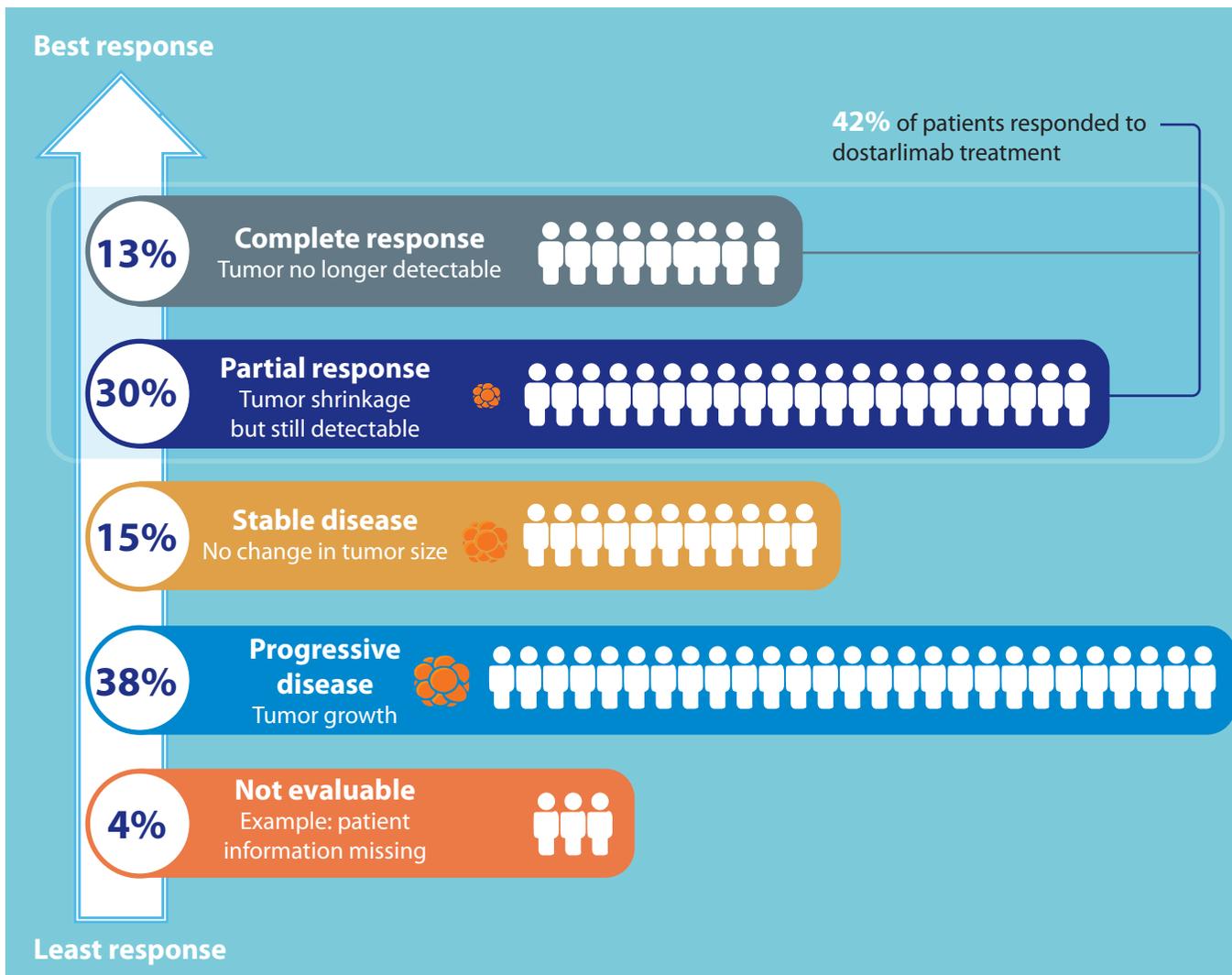
- This study is testing a drug under development for the treatment of various cancer types
- The following analysis looks specifically at one type of cancer called dMMR endometrial cancer (cancer of the womb)
- This document shows the information that led to the approval of dostarlimab in endometrial cancer

What were the overall results?

In total, **71 patients had the 6 months of enrollment** required to be analyzed for how well dostarlimab worked at **reducing tumor size**

Responses were long lasting

In the 30 patients who had a response, **25 (83%) were still in response** when the data were analyzed. The average time for which we have been following the patients and their results was 11.2 months



Background Information



Endometrial cancer is the most common gynecologic cancer

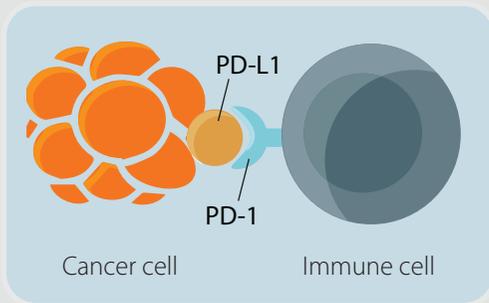


About **1 out of 3** cases of **endometrial cancer** has a particular defect called **DNA mismatch repair deficiency (dMMR)**. DNA repair happens in all human bodies, but in dMMR, the process to repair broken DNA no longer works correctly



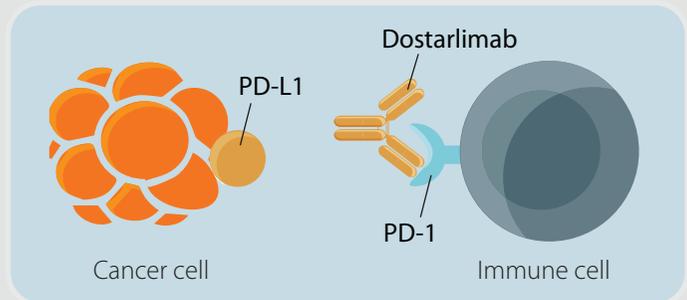
Patients with this disease **do not have many options** if the chemotherapy they receive does not fully treat the cancer

- One class of promising new drugs, called **immunotherapy**, works by helping the patient's immune system **find and kill cancer cells**
- One type of immunotherapy is called **programmed death 1 (PD-1) inhibitors**



When cancer cells have a protein called PD-L1 on their surface, immune cells that have PD-1 will find them, and they connect. Through this 'handshake', the immune system is tricked into not attacking the cancer cells

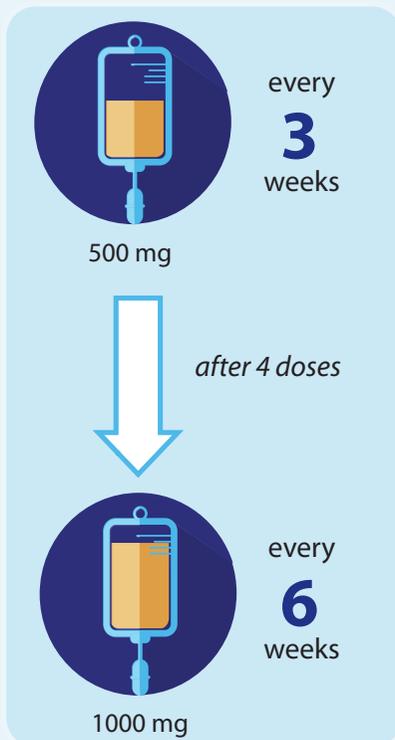
Dostarlimab attaches to PD-1 and prevents the 'handshake'. This immune cell can now signal to the rest of the immune cells that there are cancer cells that should be attacked



What medicine was tested?

- **Dostarlimab** is a PD-1 inhibitor
- Dostarlimab is being **tested in the GARNET study in several types of cancer**, as well as in other ongoing trials

Dostarlimab is given intravenously (IV) over a 30-minute period



Which patients were included in this analysis?



All patients in this analysis had endometrial cancer with the dMMR defect

The presence of the dMMR defect was identified using a type of test called **immunohistochemistry**



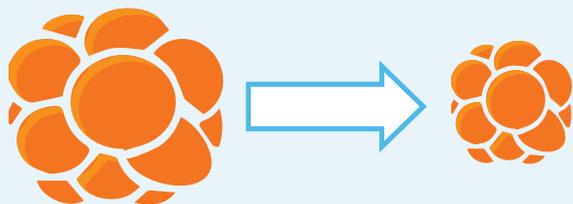
The test **looks at the properties of a tumor** sample using a microscope and specialized stains to find particular proteins

The patients in this trial must have been **treated with at least 1 prior platinum-based chemotherapy regimen** and either have not responded to the treatment or responded but the cancer came back

≈ 7 out of every 10

patients had endometrioid carcinoma, a subtype of endometrial cancer

How was the analysis done?



The analysis was done to see if dostarlimab could **reduce the size of the tumor and to test the safety of the treatment**

Reducing the size of the tumor

- Because of the way this analysis was done, only patients who had been enrolled in the trial for **at least 6 months** were included
- This was done **to allow enough time to make sure the tumor reduction lasts**

Safety

- An analysis was also done to **look at side effects**
 - All patients who received at least 1 dose of dostarlimab were **included in the safety analysis**
 - Patients were included in the analysis even if they did not get dostarlimab treatment for the entire time that they were enrolled

What were the side effects?

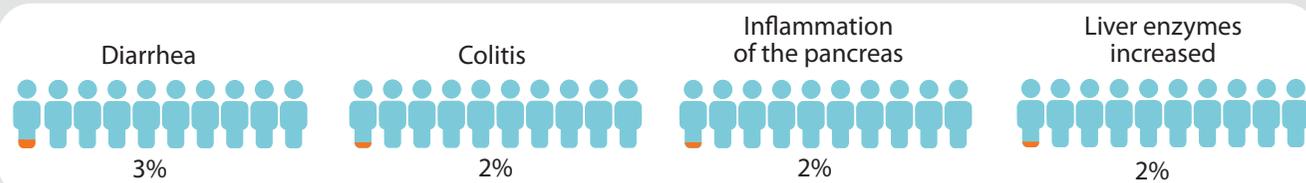
- In total, **104 patients received at least 1 dose** and were included in the safety analysis
- Most of the side effects were **mild**

Patients who experienced mild side effects (% of 104 patients)



Patients who experienced severe side effects (% of 104 patients)

- Although most side effects were mild, **there were some severe side effects** that required medical support to recover from



23%

of patients skipped at least 1 dose of dostarlimab because of a side effect, but they were able to continue treatment later

2%

of patients were required to stop taking dostarlimab because of a side effect (liver enzymes increased, both cases)

No patient died as a result of a side effect of dostarlimab treatment

How do these results help patients and researchers?

This analysis provides data that **dostarlimab is capable of reducing tumor size** in patients with advanced or recurrent dMMR endometrial cancer



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

42%

of patients had a response in their tumors, and many responses were long-lasting

The **side effects were generally mild** and were consistent with other PD-1 inhibitor drugs

Educational resources

Read more about endometrial cancer on the American Cancer Society website at:

www.cancer.org/cancer/endometrial-cancer.html

Where can I find more information about this study?

The original article discussed in this summary entitled ‘Clinical Activity and Safety of the Anti-programmed Death 1 Monoclonal Antibody Dostarlimab for Patients With Recurrent or Advanced Mismatch Repair-Deficient Endometrial Cancer: A Nonrandomized Phase 1 Clinical Trial’ was published in *JAMA Oncology* in 2020. You can read the original, free-to-access article [here](#).

The full name of the GARNET study is:

Study of Dostarlimab (TSR-042), an Anti-programmed Cell Death-1 Receptor (PD-1) Monoclonal Antibody, in Participants With Advanced Solid Tumors (GARNET)

You can read more about the GARNET study at the following websites:

- GARNET:
<https://clinicaltrials.gov/ct2/show/NCT02715284>
- RUBY, a follow-up study to GARNET:
<https://clinicaltrials.gov/ct2/show/NCT03981796>

General information about this study

The GARNET trial is ongoing

Study number: NCT02715284

Study name: GARNET

Sponsored by: GlaxoSmithKline

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