

Dostarlimab for Endometrial Cancer: A Comprehensive Review of Clinical Outcomes

Dr. Raviteja S Kanavi¹, Dr. Akash Chathamvelli², Dr. Deepjyoti. Saikia³

^{1,2,3} Dept of Pharmacy Practice, KLE College of Pharmacy, Hubballi, India

Corresponding Author: Dr. Akash Chathamvelli

DOI: <https://doi.org/10.52403/ijshr.20230119>

ABSTRACT

Jemperli (dostarlimab) is an anti-PD-1 mab used to treat endometrial cancer. It is a humanized mab produced using rdna technology in CHO cells. It is approved in the US and EU and was developed by Tesaro, later acquired by GlaxoSmithKline. Clinical trial data on dostarlimab was reviewed using online sources such as PubMed, Cochrane, and Medscape. The review included English language clinical trials, randomized trials, original articles, newsletters, and letters to the editor. Results from the GARNET clinical trial an open-label, multicohort study, which showed reduced progression and recurrence of cancer in treated individuals, led to the approval of dostarlimab. In some cases, the cancer was undetectable during imaging scans during treatment with the drug.

Keywords: Jemperli, Dostarlimab, Anti-PD-1, GARNET clinical trial, Treatment, Endometrial cancer treatment, Cancer therapy

INTRODUCTION

Cancer is a leading cause of death worldwide, accounting for nearly 10 million deaths in 2020, or nearly one in six deaths.[1] Endometrial cancer is sometimes called uterine cancer because it is a type of cancer that begins in the uterus, i.e. in the layer of cells that form the lining (endometrium) of the uterus. Endometrial cancer is the most common gynaecological cancer. According to the results of the WHO survey conducted in 2021, it is estimated that 3 lakh women are

affected by cancer every year and the motility rate was up to 1 lakh women.

Dostarlimab, a drug used to treat endometrial cancer, is marketed under the brand name Jemperli. It is an anti-programmed cell death protein-1 (PD-1) immunoglobulin G4 (IgG4) humanized monoclonal antibody (mAb) derived by rDNA technology in Chinese hamster ovary (CHO) cells. The medication is used to treat adult patients with recurrent or advanced endometrial solid cancer or tumors caused by mismatch repair deficiency (dMMR). MMRd endometrial cancer. ECs with the mismatch deficient / microsatellite unstable molecular subtype account for 25–30% of all ECs, and their prognosis is intermediate. Tumors with this loss of DNA mismatch repair exhibit a high mutational burden ('hypermutated'), with more than 10 mutations per megabase. Advanced endometrial solid cancer refers to an abnormal mass of uterine tissue that usually does not contain cysts or liquid areas and that has spread into the surrounding tissues or organs and is less likely to go into remission (when the signs and symptoms of cancer reduce or disappear). Solid tumors may be benign (not cancer) or malignant (cancer). Different types of solid tumors are named for the type of cells that form them. Examples of solid tumors are sarcomas, carcinomas, and lymphomas.

Dostarlimab was approved for the treatment of endometrial cancer in both the United States and the European Union in April 2021.

Based on the GARNET clinical trial, Dostarlimab (Jemperli) gained accelerated approval from the Food and Drug Administration (FDA) in April 2022. Dostarlimab is developed by Tesaro and was acquired by GlaxoSmithKline in 2019, individuals in the clinical trial which are treated with this compound showed a reduce in progression and reoccurrence, it is been stated that the malignancy is undetectable during endoscopy, positron emission tomography or MRI scans.

There are two types of antibodies in marketed drugs: polyclonal antibody and monoclonal antibody. Dostarlimab is a monoclonal antibody, it is a single antibody species which will only bind to a specific target site by recognizing the particulate targeted proteins. Our body uses the check points which blocks the immune response and are known to be PD-1, PDL-1, CTLA-4 and B71.

MATERIAL AND METHODS

We collected all the data from online source (PubMed, Cochrane and Medscape). The data which are collected are filtered by applying the inclusion and exclusion criteria. The article language is English and the article which are under the clinical trial, randomized trial and original article are added and understand by our review team. News latter, latter to editor and protocol data are extracted from this review.

Clinical pharmacology

Mechanism of action

Dostarlimab, a monoclonal antibody, has high affinity and potential against tumor cells. Inhibiting the binding of both PD-1 receptors on T cells and PD L1/2 ligand on tumor cells results in anticancer activity. Our immune system normally stimulates cytotoxic CD 8+ T cells to kill abnormal cells. However, in cancer, tumor cells expressing PD-L1 (B7-H1, CD247) and PD-L2 (B7-DC, CD273) ligands bind to the PD-1 receptor (CD279). Which sent out strong inhibitory signals, preventing T cell proliferation and immunologic functions. Dostarlimab inhibits the interaction of

binding between the PD-1 receptor and the PD L-1/2 ligands, resulting in decreased tumor growth. [2,3].

Pharmacodynamics

According to the binding of native protein on (PBMC) peripheral blood mononuclear cells, dostarlimab bound to both human and cynomolgus monkey PD-1 with high affinity. At the recommended dose, dostarlimab provides sustained target engagement as measured by PD-1 binding and IL-2 stimulation throughout the dosing interval.

Pharmacokinetics

Cmax, AUC_{0inf}, and AUC₀ with a dose of 500 mg every 3 weeks for the first four doses and later, starting 3 weeks after the fourth dose, 1000 mg every 6 weeks until disease progression or unacceptable toxicity is observed.

Distribution:

At a steady state, the mean (%CV) volume of distribution of dostarlimab is 5.3 L.

Elimination:

Dostarlimab has a mean terminal elimination half-life of 25.4 days and a steady-state clearance of 0.007 L/h.

Metabolism:

Catabolic pathways break down dostarlimab into small peptides and amino acids.

Adverse Reactions:

Frequent side effects: Arthralgia, pyrexia, increased transaminase levels, nausea, vomiting, diarrhoea, rash, pruritis, anaemia, hypothyroidism.

Infrequent side effects: Pneumonitis, colitis, adrenal insufficiency, chills.

Rare side effects: diabetic ketoacidosis, uveitis, hepatitis, nephritis, Type 1 diabetes mellitus.

DISCUSSION

Dostarlimab was approved for the first time on April 22, 2021, for the treatment of adult patients with advanced endometrial cancer or mismatch repair deficient (dMMR) recurrent cancer. Dostarlimab is a monoclonal antibody (PD-1) programmed death-1 receptor antagonist that has been approved by the US-FDA and the European Union for

the treatment of adult patients with advanced endometrial cancer or deficient mismatch repair (dMMR) in endometrial cancer [2]. Dostarlimab as monotherapy was found to be more durable and clinically meaningful in a preliminary analysis of data from the dMMR endometrial cancer cohort of the single-group phase-I GARNET trial. Dostarlimab was approved as a treatment option for patients with advanced dMMR or recurrent tumors who had failed platinum-based doublet chemotherapy [2].

JEMPERLI (dostarlimab) is a sterile, clear to slightly opalescent, colourless yellow solution free of visible particles that is supplied in a single dose vial. JEMPERLI is available in single-dose vials containing 500 mg of JEMPERLI in 10mL of solution and 50 mg of dostarlimab-gxly, L-arginine hydrochloride (21.07 mg), trisodium citrate dihydrate (6.68 mg), sodium chloride (1.81 mg), citric acid monohydrate (0.48mg), polysorbate 80 (0.2mg), and water for injection, USP [4].

The VENTANA MMR RxRx panel has been approved by the US Food and Drug Administration as a companion diagnostic device for selecting endometrial cancer patients for treatment with dostarlimab [4].

PD-1'S ROLE IN ANTITUMOR IMMUNITY

The PD-1 receptor is found on T-cells, and PD-L1/2 ligands are found on tumor cells. The binding of these proteins increases tumor growth and invasiveness, and dostarlimab inhibits this binding by inducing anticancer activity [1]. The expression of PD-L1/L2 on APC after IFN- treatment, as well as the expression of PD-L1 primary cancer cells, led to the hypothesis that blocking the PD-1:PD-L1/2 inhibitory pathway could induce antitumor immunity [7-8].

The observation that overexpression of PD-L1 on a mouse mastocytoma cell line inhibits CD8+ T cell cytolytic activity via PD-1 ligation, which intensifies tumor growth and invasiveness [9] confirmed the hypothesis that activation of the PD-1:PD-L1 pathway may hinder immune responses for tumors.

Several cancer studies have confirmed that tumours use PD-1-mediated immune suppression to avoid immune surveillance. Ovarian, urothelial, breast, colon, pancreatic, cervical, gastric glioblastoma, melanoma, non-small cell lung cancer, and hematologic malignancies have all been shown to express PD-1 and, to a lesser extent, PD-2. The presence of PD-L1 in the tumour microenvironment (TME) has also been linked to a better clinical response to PD-1/PD-L1 checkpoint blockade therapy [10]. PD-L1 expression on tumor-infiltrating immune cells, like cancer cell-specific expression, correlates with clinical responses to PD-1:PD-L1 blockade therapy. A lack of PD-L1 upregulation in tumor cells or tumor-infiltrating immune cells, on the other hand, is associated with a lack of therapeutic response and disease progression. Through a cell-intrinsic mechanism, oncogenic mutations mediate PD-L1 expression in cancer cells [6]. Programmed cell death 1 (PD-1) is involved in the maintenance and induction of peripheral tolerance and is critical in tumor immunity regulation.

Dosage and administration

Dostarlimab may be used to treat patients with advanced or recurrent endometrial cancer that has not responded to previous treatment with a platinum-based regimen, if the tumor tissue exhibits dMMR. The recommended dosage is 500 mg every 3 weeks for the first 4 doses, and then 1,000 mg every 6 weeks for subsequent doses. No dose reductions are recommended. If a patient experiences severe (Grade 3) immune-mediated side effects, treatment with dostarlimab should be withheld. The medication should be permanently discontinued for life-threatening (Grade 4) immune-mediated side effects, recurrent severe immune-mediated side effects that require systemic immunosuppressive treatment, or if the patient is unable to reduce their corticosteroid dose to 10 mg or less of prednisone equivalent per day within 12 weeks of starting steroids. For adverse reactions that require a different management

approach than the general guidelines, the dosage modifications for dostarlimab are summarized in Table 1.

Table 1. Recommended Dosage Modifications for Adverse Reactions

Adverse Reaction	Severity	Dosage Modifications
Pneumonitis	Grade 2	Withhold
	Grade 3 or 4 or recurrent Grade 2	Permanently discontinue
Colitis	Grade 2 or 3	Withhold
	Grade 4	Permanently discontinue
Hepatitis with no tumor involvement of the liver	AST or ALT increases to more than 3 and up to 8 times ULN or Total bilirubin increases to more than 1.5 and up to 3 times the ULN	Withhold ^b
	AST or ALT increases to more than 8 times the ULN or Total bilirubin increases to more than 3 times the ULN	Permanently discontinue
Hepatitis with tumor involvement of the liver ^c	Baseline AST or ALT is more than 1 and up to 3 times ULN and increases to more than 5 and up to 10 times ULN or Baseline AST or ALT is more than 3 and up to 5 times ULN and increases to more than 8 and up to 10 times ULN	Withhold ^b
	AST or ALT increases to more than 10 times ULN or Total bilirubin increases to more than 3 times ULN	Permanently discontinue
Endocrinopathies	Grade 2, 3, or 4	Withhold if not clinically stable ^b
Nephritis with renal dysfunction	Grade 2 or 3 increased blood creatinine	Withhold ^b
	Grade 4 increased blood creatinine	Permanently discontinue
Exfoliative dermatologic conditions	Suspected SJS, TEN, or DRESS	Withhold ^b
	Confirmed SJS, TEN, or DRESS	Permanently discontinue
Myocarditis	Grade 2, 3, or 4	Permanently discontinue
Neurological toxicities	Grade 2	Withhold ^b
	Grade 3 or 4	Permanently discontinue
Other Adverse Reactions		
Infusion-related reactions [see Warnings and Precautions (5.2)]	Grade 1 or 2	Interrupt or slow the rate of infusion
	Grade 3 or 4	Permanently discontinue

AST = aspartate aminotransferase, ALT = alanine aminotransferase, ULN = upper limit of normal, SJS = Stevens-Johnson syndrome, TEN = toxic epidermal necrolysis, DRESS = drug rash with eosinophilia and systemic symptoms.

Preparation for Intravenous Infusion

The intravenous infusion of Dostarlimab should be prepared by withdrawing 10 mL of the solution from a single vial for the 500-mg dose or from two vials for the 1,000-mg dose. The solution should be clear to slightly opalescent and colorless to yellow, and any vials with visible particles should be discarded. The solution should not be shaken and should be mixed by gentle inversion. It should then be diluted in an intravenous bag containing 0.9% Sodium Chloride Injection or 5% Dextrose Injection to a concentration between 2 to 10 mg/mL for the 500-mg dose or 4 to 10 mg/mL for the 1,000-mg dose, and the resulting solution should not be shaken. The prepared solution can be stored at room temperature for no more than 6 hours or

under refrigeration for no more than 24 hours, but it should be brought to room temperature before administration if it has been refrigerated. The prepared solution should not be frozen and should be discarded after 6 hours at room temperature or 24 hours under refrigeration.

Administration

The infusion should be administered over 30 minutes through an intravenous line with appropriate tubing (made of polyvinyl chloride or platinum cured silicon), fittings (made of polyvinyl chloride or polycarbonate), and a sterile, non-pyrogenic filter.

Warnings and Precautions

Immune-Mediated Adverse Reactions

As a monoclonal antibody, dostarlimab targets either programmed death receptor-1 (PD-1) or PD-ligand 1 (PD-L1), blocking their pathway, thereby removing inhibition of the immune response, potentially breaking peripheral tolerance, and leading to immune-mediated adverse reactions. These reactions can be severe or even life-threatening, and all may not be listed in these warning and precautions for the drug.

Immune-mediated adverse reactions, including severe or fatal ones, can affect any part of the body and can occur at any time during or after treatment with a monoclonal antibody that blocks the PD-1 or PD-L1 proteins. These reactions are more likely to occur while the patient is taking a PD-1/PD-L1-blocking antibody, but they can also occur after treatment with the antibody has been stopped. It is important to be aware of the potential for immune-mediated adverse reactions and to closely monitor for signs and symptoms.

Early detection and management of immune-mediated adverse drug reactions are essential to ensure safe use of PD-1/PD-L1-blocking antibodies. It is important to closely monitor for symptoms and signs that could be related to immune-mediated adverse reactions. It is also recommended to regularly check liver enzymes, creatinine, and thyroid function tests during treatment. Start the necessary workup in situations of suspected immune-mediated adverse reactions to rule out other causes, such as infection. Implement medical management as soon as possible, along with specialty advice as required.

If a patient experiences an adverse reaction while taking Dostarlimab, treatment may need to be temporarily or permanently stopped depending on the severity of the reaction. In general, if Dostarlimab must be interrupted or discontinued, the patient should receive systemic corticosteroids (such as prednisone at a dose of 1 to 2 mg/kg/day) until the reaction improves to Grade 1 or less. Once the reaction has improved to Grade 1 or less, the corticosteroid dose should be gradually reduced over a period of at least one month. If the immune-mediated adverse

reaction is not controlled with corticosteroids, the use of other immunosuppressive medications may be considered. Toxicity management guidelines for adverse reactions that do not necessarily require systemic steroids (such as endocrine disorders and dermatologic reactions) are discussed below.

Immune-Mediated Pneumonitis

Dostarlimab can cause immune-mediated pneumonitis, which can be severe or even fatal. This type of pneumonitis may be more common in patients who have received thoracic radiation in the past. In clinical trials, immune-mediated pneumonitis occurred in 1.1% of patients taking Dostarlimab, and required systemic corticosteroids in all cases. Pneumonitis led to discontinuation of treatment in 0.7% of patients and resolved in 80% of cases. Of the three patients who resumed treatment after improvement of symptoms, one had a recurrence of pneumonitis.

Immune-Mediated Colitis

Dostarlimab can cause immune-mediated colitis, which may be accompanied by cytomegalovirus infection or reactivation. In clinical trials, immune-mediated colitis occurred in 1.4% of patients taking Dostarlimab and required systemic corticosteroids in 17% of cases. Colitis did not lead to discontinuation of treatment in any patients and resolved in 50% of cases. Of the two patients in whom Dostarlimab was withheld due to colitis, both resumed treatment after improvement. If a patient experiences corticosteroid-refractory colitis while taking Dostarlimab, it may be necessary to exclude other potential causes through further infectious testing.

Immune-Mediated Hepatitis

Dostarlimab can cause immune-mediated hepatitis, which can be fatal and in clinical trials studies Immune-mediated hepatitis occurred in 0.2% (1/444) of patients receiving the drug, which was Grade 3. Systemic corticosteroids were required and the event resolved.

Immune-Mediated Endocrinopathies

Dostarlimab can cause immune-mediated endocrinopathies such as adrenal insufficiency, hypophysitis, thyroid disorders, and type 1 diabetes mellitus. Adrenal insufficiency occurred in 0.9% of patients taking Dostarlimab and required symptom management and hormone replacement in some cases. It led to discontinuation of treatment in one patient and resolved in 25% of cases. Hypophysitis can cause symptoms such as headache, photophobia, and visual field cuts and can result in hypopituitarism. Thyroiditis occurred in 0.5% of patients and did not resolve, while hypothyroidism occurred in 5.6% of patients and resolved in 40% of cases. Hyperthyroidism occurred in 1.8% of patients and resolved in 63% of cases. Type 1 diabetes mellitus, which can present with diabetic ketoacidosis, occurred in a small number of patients and may require treatment with insulin. If a patient experiences any of these endocrinopathies while taking Dostarlimab, treatment may need to be withheld or permanently discontinued depending on the severity of the condition. [See Dosage and Administration].

Immune-Mediated Nephritis with Renal Dysfunction

Dostarlimab can cause immune-mediated nephritis, which can be severe or even fatal. In clinical trials, nephritis occurred in 0.5% (2/444) of patients taking Dostarlimab and resolved in both cases. Systemic corticosteroids were required in one of the two patients with nephritis. It is important to monitor for signs of nephritis and to promptly initiate appropriate treatment if it occurs.

Immune-Mediated Dermatologic Adverse Reactions

Dostarlimab can cause immune-mediated rash or dermatitis, including severe reactions such as Stevens-Johnson syndrome, toxic epidermal necrolysis, and DRESS syndrome. Mild to moderate rashes may be treated with topical emollients or corticosteroids. If a patient experiences a rash or dermatitis while taking Dostarlimab, treatment may need to

be withheld or permanently discontinued depending on the severity of the reaction.

Other Immune-Mediated Adverse Reactions

The following clinically significant immune-mediated adverse reactions occurred in <1% of the 444 patients treated with dostarlimab. Severe or fatal cases have been reported for some of these adverse reactions. Dostarlimab can cause a variety of other immune-mediated adverse reactions, including those affecting the nervous system (meningitis, encephalitis, myelitis, myasthenic syndrome, Guillain-Barre syndrome, nerve paresis, autoimmune neuropathy), cardiovascular system (myocarditis, pericarditis, vasculitis), eyes (uveitis, iritis, other ocular inflammatory toxicities), gastrointestinal system (pancreatitis, gastritis, duodenitis), musculoskeletal and connective tissue (myositis, rhabdomyolysis, arthritis, polymyalgia rheumatica), endocrine system (hypoparathyroidism), and hematologic/immune system (hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, Kikuchi lymphadenitis, sarcoidosis, immune thrombocytopenia, solid organ transplant rejection). Some of these reactions can be severe or even fatal. If a patient experiences any of these adverse reactions while taking Dostarlimab, appropriate medical management should be initiated.

Infusion-Related Reactions

Severe or life-threatening infusion reactions have been reported with the use of PD-1/PD-L1 blocking drugs like Dostarlimab. In clinical trials, severe infusion reactions occurred in 0.2% of patients taking Dostarlimab, and all patients recovered from these reactions. It is important to monitor patients for signs and symptoms of infusion reactions and to interrupt or slow the rate of infusion or permanently discontinue Dostarlimab as needed based on the severity of the reaction.

Complications of Allogeneic HSCT after PD-1/PD-L1-Blocking Antibody

Patients who receive allogeneic hematopoietic stem cell transplants (HSCT) before or after treatment with PD-1/PD-L1 blocking drugs like Dostarlimab may be at risk for serious and potentially fatal complications. These complications may include hyperacute graft-versus-host disease, acute GVHD, chronic GVHD, hepatic veno-occlusive disease after reduced intensity conditioning, and steroid-requiring febrile syndrome. These complications can occur even if there is a gap between treatment with PD-1/PD-L1 blockers and allogeneic HSCT. It is important to closely monitor patients for evidence of transplant-related complications and to intervene promptly if they occur. Consider the potential benefits and risks of treatment with a PD-1/PD-L1 blocking drug before or after an allogeneic HSCT.

Embryo-Fetal Toxicity

Dostarlimab can cause harm to a developing fetus. Animal studies have shown that blocking the PD-1/PD-L1 pathway can increase the risk of immune-mediated rejection of the fetus, resulting in fetal death.

Women who are pregnant or planning to become pregnant should be warned of the potential risk to their fetus and should use effective contraception during treatment with dostarlimab and for 4 months after their last dose.

ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Immune-mediated adverse reactions
- Infusion-related reactions

Clinical Trials Experience

The safety of jemperli (dostarlimab) was evaluated in 444 patients with advanced or recurrent solid tumors. Jemperli was given as a single agent intravenously at doses of 500 mg every 3 weeks for 4 doses followed by 1,000 mg every 6 weeks until disease progression or unacceptable toxicity. Of the 444 patients, 38% were treated for over 6 months and 12% were treated for over 1 year. It is not possible to directly compare adverse reaction rates between clinical trials.

Table 2 summarizes the adverse reactions that occurred in $\geq 10\%$ of patients with dMMR EC on JEMPERLI in the GARNET study.

Adverse Reaction	JEMPERLI N = 104	
	All Grades %	Grade 3 or 4 %
Blood and Lymphatic System Anemia ^a	24	13
Gastrointestinal		
Nausea	30	0
Diarrhea	26	1.9
Constipation	20	0.9
Vomiting	18	0
General and Administration Site		
Fatigue ^b	48	1
Infections		
Urinary tract infection	13	1.9
Metabolism and Nutrition	14	0
Decreased appetite		
Musculoskeletal and Connective Tissue	12	0
Myalgia		
Respiratory, Thoracic, and Mediastinal	14	0
Cough		
Skin and Subcutaneous Tissue		
Pruritus	14	1

Mismatch Repair Deficient (dMMR) Endometrial Cancer

The safety of jemperli was evaluated in a clinical trial (named Garnet trial) involving 104 patients with advanced or recurrent endometrial cancer caused by mismatch repair deficiency who received the drug. Adverse reactions occurred in 34% of patients taking jemperli, with serious

reactions occurring in more than 2% of patients, including sepsis, kidney injury, urinary tract infection, abdominal pain, and fever. JEMPERLI was permanently discontinued in 5% of patients due to adverse reactions, including increased transaminases, sepsis, bronchitis, and pneumonitis. Dosage was interrupted in 23% of patients due to adverse reactions, including anemia,

diarrhea, increased lipase, and fever. The most common adverse reactions, occurring in more than 20% of patients, were fatigue, nausea, diarrhea, anemia, and constipation.

The most common Grade 3 or 4 adverse reactions, occurring in more than 2% of patients, were anemia and increased transaminases.

Table 3. Laboratory Abnormalities that Worsened from Baseline to Grade 3 or 4 Occurring in ≥1% of Patients with dMMR EC Receiving JEMPERLI in GARNET

Laboratory Test	JEMPERLI N = 104	
	All Grades ^a %	Grade 3 or 4 ^a %
Hematology		
Lymphopenia	37	9
Leukopenia	21	2.9
Chemistry		
Hypoalbuminemia	30	2.9
Increased alkaline phosphatase	25	2.9
Increased creatinine	27	2.9
Hyponatremia	26	4.8
Hypercalcemia	15	1.9
Increased alanine aminotransferase	15	2.9
Hypokalemia	15	1.9
Increased aspartate aminotransferase	16	1.9

CONCLUSION

In conclusion, Dostarlimab (Jemperli) is an immunotherapy drug approved for the treatment of endometrial cancer in both the United States and the European Union. The drug works by targeting the PD-1 protein, which can help to increase the effectiveness of the immune system against cancer cells. The approval of Dostarlimab was based on results from the GARNET clinical trial, which showed a reduction in progression and recurrence of cancer in individuals treated with the drug. This drug is developed by Tesaro and was acquired by GlaxoSmithKline in 2019. Our review of the available clinical trial data on Dostarlimab found that the drug can provide significant benefits for patients with endometrial cancer, including the ability to make the cancer undetectable during imaging scans.

The Dostarlimab does come with some adverse reactions that are associated with immunotherapy drugs and some of them are life-threatening, such as Immune-mediated adverse reactions. These can include pneumonitis, colitis, nephritis, endocrinopathies, and other serious complications. In addition to these immune-mediated adverse reactions, Dostarlimab can also cause infusion-related reactions and transplant-related complications in patients who receive allogeneic hematopoietic stem cell transplantation before or after treatment

with the drug. Furthermore, based on the drug mechanism of action, it can cause fetal harm when administered to a pregnant woman.

In summary, Dostarlimab is a promising treatment option for patients with endometrial cancer that can improve outcomes and quality of life. However, it is important to closely monitor patients for potential adverse reactions and complications and to carefully weigh the benefits and risks of treatment before starting therapy.

Disclosure of ethical statements

Approval of the research protocol: N/A

Informed consent: N/A

Approval data of Registry and Registration No: N/A

Animal Studies: N/A

Conflict of interest: N/A

Funding: N/A

Author's contribution

Dr. Raviteja S Kanavi: data curation, writing, reviewing & editing, methodology

Dr. Akash. Chathamvelli: data curation, writing, resources, supervision

Dr. Deepjyoti. Saikia: resources, writing-original draft, investigation

Conflict of interest: The authors whose names are listed, certified that they have no affiliation's with or involvement in any

organization or entity with any financial interests or non-financial interests in the subject matter or materials discussed in this manuscript.

REFERENCES

1. <https://www.who.int/news-room/fact-sheets/detail/cancer#:~:text=Cancer%20is%20a%20leading%20cause,and%20rectum%20and%20prostate%20cancers>.
2. Laken H, Kehry M, McNeeley P, et al. Identification and characterization of TSR-042, a novel anti-human PD-1 therapeutic antibody. *Eur J Cancer*. 2016;69(Suppl 1):S102.
3. Markham A. Dostarlimab: First Approval. *Drugs*. 2021 Jul;81(10):1213-1219. doi: 10.1007/s40265-021-01539-5. PMID: 34106455.
4. Food & Drug Administration. FDA grants accelerated approval to dostarlimab-gxly for dMMR endometrial cancer [media release]. 22 Apr 2021.
5. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761174s000lbl.pdf
6. <https://doi.org/10.3389/fimmu.2016.00550>
7. Dong H, Strome SE, Salomao DR, Tamura H, Hirano F, Flies DB, et al. Tumor associated B7-H1 promotes T-cell apoptosis: a potential mechanism of immune evasion. *Nat Med* (2002) 8(8):793–800. doi:10.1038/nm0902-1039c
8. Latchman Y, Wood CR, Chernova T, Chaudhary D, Borde M, Chernova I, et al. PD-L2 is a second ligand for PD-1 and inhibits T cell activation. *Nat Immunol* (2001) 2(3):261–8. doi:10.1038/85330
9. Iwai Y, Ishida M, Tanaka Y, Okazaki T, Honjo T, Minato N. Involvement of PD-L1 on tumor cells in the escape from host immune system and tumor immunotherapy by PD-L1 blockade. *Proc Natl Acad Sci U S A* (2002) 99(19):12293–7. doi:10.1073/pnas.192461099
10. Thompson RH, Gillett MD, Cheville JC, Lohse CM, Dong H, Webster WS, et al. Costimulatory B7-H1 in renal cell carcinoma patients: indicator of tumor aggressiveness and potential therapeutic target. *Proc Natl Acad Sci U S A* (2004) 101(49):17174–9. doi:10.1073/pnas.0406351101

How to cite this article: Raviteja S Kanavi, Akash Chathamvelli, Deepjyoti Saikia. Dostarlimab for endometrial cancer: a comprehensive review of clinical outcomes. *International Journal of Science & Healthcare Research*. 2023; 8(1): 136-144. DOI: <https://doi.org/10.52403/ijshr.20230119>
