

Product Monograph
Including Patient Medication Information

Pr **JEMPERLI**

dostarlimab for injection

Humanized IgG4 monoclonal antibody produced in Chinese hamster ovary cells by recombinant DNA technology

Solution for infusion

For intravenous infusion

500 mg/10 mL vial (50 mg/mL)

Anti-neoplastic agent

ATC Code: L01FF07

GlaxoSmithKline Inc.
100 Milverton Drive
Suite 800
Mississauga, Ontario
L5R 4H1

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Part 1: Healthcare Professional Information

1. Indications

JEMPERLI (dostarlimab for injection) is indicated:

- in combination with carboplatin and paclitaxel for the treatment of adult patients with primary advanced or first recurrent endometrial cancer who are candidates for systemic therapy.

See [14. Clinical Trials](#) for details on eligibility criteria including disease status in the pivotal RUBY study.

- as monotherapy for the treatment of adult patients with mismatch repair deficient (dMMR) or microsatellite instability-high (MSI-H) recurrent or advanced endometrial cancer that has progressed on or following prior treatment with a platinum containing regimen.

1.1. Pediatrics

Pediatrics (<18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

1.2. Geriatrics

Geriatrics (≥ 65 years of age): No overall differences in safety or efficacy were reported between elderly patients (65 years and over) and younger patients (less than 65 years).

There are limited clinical data with dostarlimab in patients aged 75 years or over (see [4.2 Recommended Dose and Dosage Adjustment-Geriatrics](#); [7.1.4 Warnings and Precautions-Geriatrics](#)).

2. Contraindications

Jemperli is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see [6. Dosage Forms, Strengths, Composition, and Packaging](#).

4. Dosage and Administration

4.1. Dosing Considerations

- Jemperli is for intravenous infusion after dilution (see [4.3 Reconstitution](#); [4.4 Administration](#)).
- When Jemperli is used in monotherapy, patients should be selected for treatment based on MSI-H or dMMR tumour status as determined by an accredited laboratory using validated testing methods (see [14.1 Clinical Trials by Indication](#)).

4.2. Recommended Dose and Dosage Adjustment

Jemperli in combination with carboplatin and paclitaxel

The recommended dose as combination therapy is 500 mg Jemperli administered as an intravenous infusion over 30 minutes every 3 weeks for 6 doses followed by 1000 mg every 6 weeks for all cycles thereafter.

The dosage regimen in combination with the chemotherapy is presented in [Table 1](#).

Table 1 Dosage regimen for Jemperli in combination with carboplatin and paclitaxel

500 mg once every 3 weeks in combination with carboplatin and paclitaxel ^a (1 Cycle = 3 weeks)							1000 mg once every 6 weeks until disease progression or unacceptable toxicity (1 Cycle = 6 weeks)			
Cycle	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Cycle 7	Cycle 8	Cycle 9	Continue dosing Q6W
Week	1	4	7	10	13	16	19	25	31	

3 weeks between Cycle 6 and Cycle 7

^a Administer Jemperli prior to the chemotherapy when given on the same day.

Administration of Jemperli should continue according to the recommended dose and schedule until disease progression, unacceptable toxicity, or up to 3 years.

See [14. Clinical Trials](#) for the dosages of the chemotherapy administered in combination with Jemperli in the pivotal study RUBY, and also refer to the Product Monographs of the chemotherapy agents, as appropriate.

Jemperli monotherapy

The recommended dosage of Jemperli as monotherapy in adult patients is:

- Dose 1 through Dose 4: 500 mg every 3 weeks
- Subsequent dosing beginning 3 weeks after Dose 4 (Dose 5 onwards): 1,000 mg every 6 weeks

The dosage regimen as monotherapy is presented in [Table 2](#).

Table 2 Dosage regimen for Jemperli as monotherapy

500 mg once every 3 weeks (1 Cycle = 3 weeks)					1000 mg once every 6 weeks until disease progression or unacceptable toxicity (1 Cycle = 6 weeks)			
Cycle	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Cycle 7	Continue dosing Q6W
Week	1	4	7	10	13	19	25	

3 weeks between Cycle 4 and Cycle 5

Administer Jemperli as an intravenous infusion over 30 minutes. Administration of dostarlimab could continue according to the recommended dose and schedule until disease progression or unacceptable toxicity.

Dose modifications

Dose reduction is not recommended. Dosing delay or discontinuation may be required based on individual safety and tolerability. Recommended dose modifications to manage adverse reactions are provided in [Table 3](#).

Detailed guidelines for the management of immune-mediated adverse reactions and infusion-related reactions are described in [7 Warnings and Precautions, Immune](#).

Table 3 Recommended dose modifications for Jemperli

Immune-mediated adverse reactions	Severity grade ^a	Dose modification
Colitis	2 or 3	Withhold dose. Restart dosing when toxicity resolves to Grade 0 or 1.
	4	Permanently discontinue.
Hepatitis	Grade 2 (AST ^b or ALT ^c > 3 and up to 5 × ULN ^d or total bilirubin > 1.5 and up to 3 × ULN)	Withhold dose. Restart dosing when toxicity resolves to Grade 0 or 1.
	Grade ≥3 (AST or ALT > 5 × ULN or total bilirubin > 3 × ULN)	Permanently discontinue (see exception below). ^e
Type 1 diabetes mellitus (T1DM)	3 or 4 (hyperglycaemia)	Withhold dose. Restart dosing in appropriately managed, clinically and metabolically stable patients.
Hypophysitis or adrenal insufficiency	2, 3 or 4	Withhold dose. Restart dosing when toxicity resolves to Grade 0 or 1. Permanently discontinue for recurrence or worsening while on adequate hormonal therapy.
Hypothyroidism or hyperthyroidism	3 or 4	Withhold dose. Restart dosing when toxicity resolves to Grade 0 or 1.
Pneumonitis	2	Withhold dose. Restart dosing when toxicity resolves to Grade 0 or 1. If Grade 2 recurs, permanently discontinue.
	3 or 4	Permanently discontinue.
Nephritis	2	Withhold dose. Restart dosing when toxicity resolves to Grade 0 or 1.
	3 or 4	Permanently discontinue.
Exfoliative dermatologic conditions (e.g. SJS, TEN, DRESS)	Suspected	Withhold dose for any grade. Restart dosing if not confirmed and when toxicity resolves to grade 0 or 1.
	Confirmed	Permanently discontinue.
Myocarditis	2, 3 or 4	Permanently discontinue.

Immune-mediated adverse reactions	Severity grade^a	Dose modification
Severe neurological toxicities (myasthenic syndrome/myasthenia gravis, Guillain-Barré syndrome, encephalitis, transverse myelitis)	2, 3 or 4	Permanently discontinue.
Other immune-mediated adverse reactions (including but not limited to rash, myositis, sarcoidosis, autoimmune haemolytic anemia, pancreatitis, iridocyclitis, uveitis, diabetic ketoacidosis, arthralgia, solid organ transplant rejection, graft-versus-host disease)	3	Withhold dose. Restart dosing when toxicity resolves to Grade 0 or 1.
	4	Permanently discontinue.
Recurrence of immune-mediated adverse reactions after resolution to ≤ Grade 1 (except for pneumonitis, see above)	3 or 4	Permanently discontinue.
Other adverse reactions	Severity grade^a	Dose modification
Infusion-related reactions	2	Withhold dose. If resolved within 1 hour of stopping, may be restarted at 50% of the original infusion rate, or restart when symptoms resolve with pre-medication. If Grade 2 recurs with adequate pre-medication, permanently discontinue.
	3 or 4	Permanently discontinue.

^a Toxicity graded per National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 5.0.

^b AST = aspartate aminotransferase

^c ALT = alanine aminotransferase

^d ULN = upper limit of normal

^e For patients with liver metastases who begin treatment with Grade 2 increase of AST or ALT, if AST or ALT increases by ≥50% relative to baseline and lasts for at least 1 week, then treatment should be discontinued.

Geriatrics

No dose adjustment is recommended for patients who are 65 years of age or over. There are limited clinical data with Jemperli in patients 75 years of age or over.

Pediatrics

Health Canada has not authorized an indication for pediatric use.

Hepatic Insufficiency

No dose adjustment is recommended for patients with mild hepatic impairment. Data are not sufficient for drawing any conclusion on patients with moderate hepatic impairment and there are no data in patients with severe hepatic impairment (see [10.3 Pharmacokinetics](#)).

Renal Insufficiency

No dose adjustment is recommended for patients with mild or moderate renal impairment. Data are not sufficient for drawing any conclusion on patients with severe renal impairment or end stage renal disease undergoing dialysis (see [10.3 Pharmacokinetics](#)).

4.3. Reconstitution

Jemperli should be inspected visually for particulate matter and discolouration prior to administration. Jemperli is a slightly opalescent colourless to yellow solution. Discard the vial if visible particles are observed.

For the 500-mg dose, withdraw 10 mL of Jemperli from a vial and transfer into an intravenous (IV) bag containing sodium chloride 9 mg/mL (0.9%) solution for injection, or glucose 50 mg/mL (5%) solution for injection. The final concentration of the diluted solution should be between 2 mg/mL and 10 mg/mL. The total volume of the infusion solution must not exceed 250 mL.

For the 1,000-mg dose, withdraw 10 mL of Jemperli from each of two vials (withdraw 20 mL total) and transfer into an IV bag containing sodium chloride 9 mg/mL (0.9%) solution for injection or glucose 50 mg/mL (5%) solution for injection. The final concentration of the diluted solution should be between 4 mg/mL to 10 mg/mL. The total volume of the infusion solution must not exceed 250 mL.

Mix diluted solution by gentle inversion. Do not shake the final infusion bag. Discard any unused portion left in the vial (see [11. Storage, Stability, and Disposal](#)).

4.4. Administration

Jemperli is for intravenous infusion only.

Jemperli should be administered by intravenous infusion using an intravenous infusion pump over 30 minutes. Tubing should be made from polyvinyl chloride (PVC), platinum cured silicon or polypropylene (PP); fittings made from PVC or polycarbonate and needles made from stainless steel. A 0.2 or 0.22 micron in-line polyethersulfone (PES) filter must be used during administration of Jemperli.

Jemperli must not be administered as an intravenous push or bolus injection. Do not co-administer other drugs through the same infusion line.

For instructions on dilution of the medicinal product before administration, see [4.3 Reconstitution](#).

4.5. Missed Dose

It is very important to not miss a dose of this medicine. If a planned dose of Jemperli is missed, it should be administered as soon as possible. The schedule of administration should be adjusted to maintain the prescribed dosing interval.

5. Overdose

There is no information on overdosage with Jemperli. The maximum tolerated dose of Jemperli has not been determined.

If overdose is suspected, the patient should be closely monitored for any signs or symptoms of adverse reactions or effects, and appropriate standard of care measures should be instituted immediately.

For the most recent information in the management of a suspected drug overdose, contact your regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669).

6. Dosage Forms, Strengths, Composition, and Packaging

To help ensure the traceability of biologic products, including biosimilars, health professionals should recognise the importance of recording both the brand name and the non-proprietary (active ingredient) name as well as other product-specific identifiers such as the Drug Identification Number (DIN) and the batch/lot number of the product supplied.

Table 4 Dosage Forms, Strengths, and Composition

Route of Administration	Dosage Form / Strength/Composition	Non-Medicinal Ingredients
Intravenous infusion	Solution for infusion 500 mg/10 mL vial (50 mg/mL)	Citric acid monohydrate; L-arginine hydrochloride; polysorbate 80; sodium chloride; tri-sodium citrate dihydrate; water for injection

Description

Jemperli is packaged in a carton containing one 10mL single-use vial with clear to slightly opalescent colourless to yellow solution, essentially free from visible particles. Each mL of solution for infusion contains 50 mg of dostarlimab. The solution for infusion has a pH of approximately 6.0 and an osmolality of approximately 300 mOsm/kg.

7. Warnings and Precautions

General

Jemperli should be administered under the supervision of physicians experienced in the treatment of cancer.

Driving and Operating Machinery

Exercise caution when driving or operating a vehicle or potentially dangerous machinery.

Immune

Immune-mediated adverse reactions, which may be severe or fatal, have occurred in patients treated with antibodies blocking the programmed cell death protein-1 / programmed death-ligand 1 (PD-1/PD-L1) pathway, including Jemperli. While immune-mediated adverse reactions usually occur during treatment with PD-1/PD-L1 blocking antibodies, symptoms can also manifest after discontinuation of treatment. Immune-mediated adverse reactions may occur in any organ or tissue and may affect more than one body system simultaneously. Important immune-mediated adverse reactions listed in this section are not inclusive of all possible severe and fatal immune-mediated reactions.

Early identification and management of immune-mediated adverse reactions are essential to ensure safe use of PD-1/PD-L1 blocking antibodies. Patients should be monitored for symptoms and signs of immune-mediated adverse reactions. Clinical and haematological chemistries, including liver, kidney and thyroid function tests, should be evaluated at baseline and periodically during treatment. For suspected immune-mediated adverse reactions, adequate evaluation including specialty consultation should be ensured.

Based on the severity of the adverse reaction, Jemperli should be withheld or permanently discontinued and corticosteroids (1 to 2 mg/kg/day prednisone or equivalent) or other appropriate therapy administered (see below and [4.2 Recommended Dose and Dosage Adjustment](#)). Upon improvement to Grade 0 or 1, corticosteroid taper should be initiated and continued for at least 1 month or longer. Based on limited data from clinical studies in patients whose immune-mediated adverse reactions could not be controlled with corticosteroid use, administration of other systemic immunosuppressants can be considered. Hormone replacement therapy for endocrinopathies should be instituted as warranted.

Treatment with Jemperli should be permanently discontinued for any Grade 3 immune-mediated adverse reaction that recurs and for any Grade 4 immune-mediated adverse reaction toxicity, except for endocrinopathies that are controlled with replacement hormones and unless otherwise specified in [4.2 Recommended Dose and Dose Adjustment](#).

- **Immune-mediated pneumonitis**

Immune-mediated pneumonitis has been reported in patients receiving Jemperli (see [8.2 Clinical Trial Adverse Reactions](#)). Patients should be monitored for signs and symptoms of pneumonitis. Suspected pneumonitis should be confirmed with radiographic imaging and other causes excluded. Patients should be managed with Jemperli treatment modifications and corticosteroids (see [4.2 Recommended Dose and Dosage Adjustment, Dose Modifications](#) and [8. Adverse Reactions](#)).

- **Immune-mediated colitis**

Jemperli can cause immune-mediated colitis (see [8. Adverse Reactions](#)). Monitor patients for signs and symptoms of colitis and manage with Jemperli treatment modifications, anti-diarrheal agents and corticosteroids (see [4.2 Recommended Dose and Dosage Adjustment](#) and [8. Adverse Reactions](#)).

- **Immune-mediated hepatitis**

Jemperli can cause immune-mediated hepatitis. Monitor patients for changes in liver function periodically as indicated based on clinical evaluation and manage with Jemperli treatment

modifications and corticosteroids (see [4.2 Recommended Dose and Dosage Adjustment](#) and [8. Adverse Reactions](#)).

- **Immune-mediated endocrinopathies**

Immune-mediated endocrinopathies, including hypothyroidism, hyperthyroidism, thyroiditis, hypophysitis, type 1 diabetes mellitus, diabetic ketoacidosis and adrenal insufficiency (primary and secondary), have been reported in patients receiving Jemperli. Long-term hormone replacement therapy may be necessary in cases of immune-mediated endocrinopathies.

Adrenal insufficiency

Immune-mediated adrenal insufficiency (primary and secondary) occurred in patients receiving Jemperli. Patients should be monitored for clinical signs and symptoms of adrenal insufficiency. For symptomatic adrenal insufficiency, patients should be managed as recommended in [4.2 Recommended Dose and Dosage Adjustment](#) (see [8. Adverse Reactions](#)).

Hypophysitis

Jemperli can cause hypophysitis. Monitor patients for signs and symptoms of hypophysitis (including hypopituitarism). Administer corticosteroids and hormone replacement as clinically indicated (See [4.2 Recommended Dose and Dosage Adjustment](#)).

Type 1 diabetes mellitus

Jemperli can cause type 1 diabetes mellitus, including diabetic ketoacidosis. Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Administer insulin for type 1 diabetes and withhold Jemperli in cases of severe hyperglycemia until metabolic control is achieved (See [4.2 Recommended Dose and Dosage Adjustment](#)).

Thyroid disorders (Hypothyroidism and hyperthyroidism)

Immune-mediated thyroid disorders, including hypothyroidism and hyperthyroidism (including thyroiditis) occurred in patients receiving Jemperli. Hypothyroidism may follow hyperthyroidism. Patients should be monitored for changes in thyroid function (at the start of treatment, periodically during treatment and as indicated based on clinical evaluation) and clinical signs and symptoms of thyroid disorders. Hypothyroidism may be managed with hormone replacement therapy (if indicated). Initiate medical management for control of hyperthyroidism.

Immune-mediated hypothyroidism and hyperthyroidism (including thyroiditis) should be managed as recommended in [4.2 Recommended Dose and Dosage Adjustment](#) (see [8. Adverse Reactions](#)).

- **Immune-mediated nephritis**

Jemperli can cause immune-mediated nephritis (see [8. Adverse Reactions](#)). Monitor patients for changes in renal function and manage with Jemperli treatment modifications and corticosteroids (see [4.2 Recommended Dose and Dosage Adjustment](#)).

- **Immune-mediated skin adverse reactions**

Immune-mediated skin reactions including rash, pruritus and pemphigoid been reported in patients receiving Jemperli (see [8.2 Clinical Trial Adverse Reactions](#)). Patients should be monitored for signs and symptoms of severe skin reactions and exclude other causes. Immune-mediated severe skin reactions should be managed as recommended for other immune-mediated adverse reactions (see [4.2 Recommended Dose and Dosage Adjustment](#)).

Cases of Stevens-Johnson Syndrome (SJS) or toxic epidermal necrolysis (TEN), some with fatal outcomes, have been reported in patients treated with PD-1 inhibitors. Exfoliative dermatological conditions should be managed as recommended in [4.2 Recommended Dose and Dosage Adjustment](#). For signs and symptoms of SJS or TEN, withhold treatment and refer the patient for specialized care for assessment and further treatment. If SJS or TEN is confirmed, permanently discontinue treatment.

Caution should be used when considering the use of Jemperli in a patient who has previously experienced a severe or life-threatening skin adverse reaction on prior treatment with other immune-stimulatory anticancer agents.

- **Other immune-mediated adverse reactions**

Given the mechanism of action, Jemperli can cause other clinically important immune-mediated adverse reactions including potentially serious events [e.g. myositis, myocarditis, encephalitis, demyelinating neuropathy (including Guillain Barré syndrome), sarcoidosis, aplastic anemia].

Clinically significant immune-mediated adverse reactions reported in less than 1% of patients treated with Jemperli as monotherapy in clinical trials include encephalitis, autoimmune haemolytic anemia, pancreatitis, uveitis, and iridocyclitis. Patients should be monitored for signs and symptoms of immune-mediated adverse reactions and managed as described in [4.2 Recommended Dose and Dosage Adjustment](#).

Solid organ transplant rejection has been reported in the post-marketing setting in patients treated with PD-1 inhibitors. Treatment with Jemperli may increase the risk of rejection in solid organ transplant recipients. The benefit of treatment with Jemperli versus the risk of possible organ rejection should be considered in these patients.

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

Fatal and other serious complications can occur in patients who receive allogeneic haematopoietic stem cell transplantation (HSCT) before or after being treated with a PD-1/PD-L1–blocking antibody. Transplant-related complications include hyperacute graft-versus-host disease (GvHD), acute GvHD, chronic GvHD, hepatic veno-occlusive disease after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between PD-1/PD-L1 blockade and allogeneic HSCT.

Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/PD-L1–blocking antibody prior to or after an allogeneic HSCT.

- **Infusion-related reactions**

Jemperli can cause infusion-related reactions, including hypersensitivity, which can be severe. For severe (Grade 3) or life-threatening (Grade 4) infusion-related reactions, stop infusion and permanently discontinue Jemperli (see [4.2 Recommended Dose and Dosage Adjustment](#)).

Monitoring and Laboratory Tests

Patients should be monitored for signs and symptoms of immune-mediated adverse reactions and managed as described in [4.2 Recommended Dose and Dosage Adjustment](#).

For suspected immune-mediated adverse reactions, adequate evaluation including specialty consultation should be ensured (see [7. Warnings and Precautions, Immune](#)).

Patients should be evaluated for clinical and haematological chemistries, including liver function tests (hepatic transaminase and bilirubin levels), serum electrolytes and renal and thyroid function tests, at baseline and periodically during treatment.

Reproductive Health

- **Fertility**

Fertility studies have not been conducted with Jemperli (see [16. Non-Clinical Toxicology](#)).

- **Embryo-fetal toxicity**

Jemperli can cause fetal harm. Pregnant women or women with reproductive potential should be advised of the potential risk associated with the administration of Jemperli to the fetus (see [7.1.1 Pregnant Women](#)). Verify pregnancy status in females of reproductive potential prior to initiating Jemperli.

Women of childbearing potential should use effective contraception during treatment with Jemperli and until 4 months after the last dose of Jemperli.

7.1. Special Populations

7.1.1. Pregnancy

There are no available data on the use of Jemperli in pregnant women. Animal reproduction and development studies have not been conducted with Jemperli; however, inhibition of the PD-1/PD-L1 pathway has been shown in murine models of pregnancy to disrupt tolerance to the fetus and to result in an increase in fetal loss (See [16. Non-Clinical Toxicology](#)). These results indicate a potential risk, based on its mechanism of action, that administration of Jemperli during pregnancy could cause fetal harm, including increased rates of abortion or stillbirth. Human IgG4 immunoglobulins (IgG4) are known to cross the placental barrier; therefore, being an IgG4, Jemperli has the potential to be transmitted from the mother to the developing fetus.

Jemperli is not recommended during pregnancy. Women of childbearing potential should use effective contraception during treatment with Jemperli and until 4 months after the last dose of Jemperli.

7.1.2. Breastfeeding

It is unknown if Jemperli is secreted in human milk. A risk to the newborns/infants cannot be excluded. Precaution should be exercised because many drugs can be secreted in human milk. Because of the potential for serious adverse reactions in breastfed children, **Jemperli should not be used during breast-feeding and breast-feeding should be avoided for at least 4 months after the last dose of Jemperli.**

7.1.3. Pediatrics

No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

7.1.4. Geriatrics

No overall differences in safety or efficacy were reported between elderly patients (65 years and over) and younger patients (less than 65 years). No dose adjustment is recommended for patients who are aged 65 years or over.

There are limited clinical data with dostarlimab in patients aged 75 years or over (see [4.2 Recommended Dose and Dosage Adjustment-Geriatrics](#)).

8. Adverse Reactions

8.1. Adverse Reaction Overview

Primary advanced or recurrent endometrial cancer (EC): Jemperli in combination with carboplatin and paclitaxel

The safety of Jemperli in combination with carboplatin and paclitaxel was evaluated in patients with primary advanced or recurrent endometrial cancer in the RUBY study (see [14. Clinical Trials](#)). Patients received Jemperli 500 mg (n = 241) or placebo (n = 246) in combination with carboplatin and paclitaxel every 3 weeks for 6 doses followed by Jemperli 1,000 mg or placebo every 6 weeks until disease progression or unacceptable toxicity. Among the 241 patients, 38.6% were exposed for >1 year and 24.1% were exposed for >2 years.

The most common treatment emergent adverse events ($\geq 10\%$) occurring at a higher rate in patients receiving Jemperli in combination with carboplatin and paclitaxel as compared to patients receiving placebo in combination with carboplatin and paclitaxel ([Table 5](#)) were alopecia (55.6%), nausea (54.4%), rash (38.2%), pruritus (20.3%), hypokalemia (19.9%), hypothyroidism (16.2%), hypertension (13.7%), pyrexia (12.9%), alanine aminotransferase increased (12.9%), aspartate aminotransferase increased (12.0%), blood creatinine increased (11.6%), depression (11.2%), and dry skin (10.0%).

Serious adverse reactions occurred in 39.8% of patients receiving Jemperli in combination with carboplatin and paclitaxel; the serious adverse reactions which occurred in $\geq 2\%$ of patients were sepsis (including urosepsis) and pyrexia. Fatal adverse reactions occurred in 2.5% of patients receiving Jemperli, among which septic shock (0.8%), and myelosuppression (0.4%) were considered related to Jemperli.

In patients receiving Jemperli in combination with carboplatin and paclitaxel, Jemperli was permanently discontinued due to adverse reactions in 19.1% of patients. Adverse reactions that required permanent Jemperli discontinuation in ≥ 2 patients (0.8%) included rash (including rash maculo-papular), infusion related reaction, alanine aminotransferase increased, aspartate aminotransferase increased, diarrhea, pancreatitis, and pneumonitis.

Jemperli dosage interruptions due to an adverse reaction occurred in 2.5% of patients who received Jemperli in combination with carboplatin and paclitaxel. An adverse reaction that required Jemperli dosage interruption in ≥ 2 patients (0.8%) was alanine aminotransferase increased.

dMMR or MSI-H recurrent or advanced EC that has progressed on or following prior treatment with a platinum-containing regimen: Jemperli monotherapy

The safety of Jemperli in monotherapy has been evaluated in 605 patients (i.e. pooled safety population) with endometrial cancer or other advanced solid tumours who received dostarlimab monotherapy in the open-label, multi-cohort GARNET study, including 153 patients with dMMR/MSI-H recurrent or advanced endometrial cancer. Patients received doses of 500 mg every 3 weeks for 4 doses followed by 1000 mg every 6 weeks for all cycles thereafter (see [4.2 Recommended Dose and Dosage Adjustment](#)). The median treatment duration for the monotherapy pooled population was 24 weeks (range 1 to 229 weeks), including 31.6% of patients treated for greater than one year and 18.7 % of patients treated for greater than two years.

The most common adverse reactions (≥ 10 %) were anemia (28.6 %), diarrhea (26.0%), nausea (25.8 %), vomiting (19.0 %), arthralgia (17.0 %) pruritus (14.2 %), rash (13.2 %), pyrexia (12.4 %), aspartate aminotransferase increased (11.2 %) and hypothyroidism (11.2 %). Adverse reactions were serious in 11.2 % of patients; most serious adverse reactions were immune-mediated adverse reactions (see [8.2 Clinical Trial Adverse Reactions, Immune-mediated Adverse Reactions](#)). Serious adverse reactions reported in ≥ 1 % of patients were pyrexia (1.7 %), vomiting (1.5 %), nausea (1.3 %), anemia (1.3 %) and pneumonitis (1.3 %). Jemperli was permanently discontinued due to adverse reactions in 38 (6.3 %) patients, most of them were immune-mediated events. Adverse reactions leading to dose interruption were reported in 71 (11.7 %) patients. The safety profile for patients with dMMR/MSI-H endometrial cancer in the GARNET study (N=153) was not different from that of the overall monotherapy population (i.e. monotherapy pooled safety population).

General

Adverse reactions known to occur with dostarlimab or with combination therapy components given alone may occur during treatment with these medicinal products in combination, even if these reactions were not reported in clinical studies with combination therapy.

See [7. Warnings and Precautions](#) for additional information regarding immune-mediated adverse reactions.

8.2. Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. Therefore, the frequencies of adverse reactions observed in the clinical trials may not reflect frequencies observed in clinical practice and

should not be compared to frequencies reported in clinical trials of another drug.

Immune-mediated Adverse Reactions

The selected adverse reactions described below are based on the safety of dostarlimab in a monotherapy pooled safety database of 605 patients in the GARNET study in patients with endometrial cancer or other advanced solid tumours. Immune-mediated adverse reactions were defined as events of grade 2 and above from a pre-specified list of terms; the frequencies below exclude grade 1 events. The management guidelines for these adverse reactions are described in section [4.2 Recommended Dose and Dosage Adjustment](#).

Immune-mediated pneumonitis

Immune-mediated pneumonitis occurred in 14 (2.3 %) patients, including grade 2 (1.3 %), grade 3 (0.8 %) and grade 4 (0.2%) pneumonitis. Pneumonitis led to discontinuation of dostarlimab in 8 (61.3 %) patients.

Systemic corticosteroids (prednisone \geq 40 mg per day or equivalent) were required in 11 (78.6%) patients experiencing pneumonitis. Pneumonitis resolved in 11 (78.6 %) patients.

Immune-mediated colitis

Colitis occurred in 8 (1.3 %) patients, including grade 2 (0.7 %) and grade 3 (0.7 %) colitis. Colitis did not lead to discontinuation of dostarlimab in any patients.

Systemic corticosteroids (prednisone \geq 40 mg per day or equivalent) were required in 5 (62.5 %) patients. Colitis resolved in 5 (62.5 %) patients experiencing colitis.

Immune-mediated hepatitis

Hepatitis occurred in 2 (0.3 %) patients, all were grade 3. Systemic corticosteroids (prednisone \geq 40 mg per day or equivalent) were required in 1 (50.0 %) patient. Hepatitis led to discontinuation of dostarlimab in 1 (0.2 %) patient and resolved in all 2 patients.

Immune-mediated endocrinopathies

Hypothyroidism occurred in 46 (7.6 %) patients, all of which were grade 2. Hypothyroidism did not lead to discontinuation of dostarlimab and resolved in 17 (37.0 %) patients.

Hyperthyroidism occurred in 14 (2.3 %) patients, including grade 2 (2.1 %) and grade 3 (0.2 %). Hyperthyroidism did not lead to discontinuation of dostarlimab and resolved in 10 (71.4 %) patients.

Thyroiditis occurred in 2 (0.3 %) patients; both were grade 2. Neither event of thyroiditis resolved; there were no discontinuations of dostarlimab due to thyroiditis.

Adrenal insufficiency occurred in 7 (1.2 %) patients, including grade 2 (0.5 %), and grade 3 (0.7 %). Adrenal insufficiency resulted in discontinuation of dostarlimab in 1 (0.2 %) patient and resolved in 4 (57.1 %) patients.

Immune-mediated nephritis

Nephritis, including tubulointerstitial nephritis, occurred in 3 (0.5 %) patients; all were grade 2. Systemic corticosteroids (prednisone \geq 40 mg per day or equivalent) were required in 2 (66.7 %) patients experiencing nephritis. Nephritis led to discontinuation of dostarlimab in 1 (0.2 %) patient and resolved in all 3 patients.

Immune-mediated skin adverse reactions

Immune-mediated rash (rash, rash maculo-papular, rash macular, rash pruritic, pemphigoid, drug

eruption, skin toxicity, toxic skin eruption) occurred in 31 (5.1 %) patients, including Grade 3 in 9 (1.5 %) patients receiving dostarlimab. The median time to onset of rash was 57 days (range 2 days to 1485 days). Systemic corticosteroids (prednisone \geq 40 mg per day or equivalent) were required in 9 (29.0 %) patients experiencing rash. Rash led to discontinuation of dostarlimab in 1 (0.2%) patient and resolved in 23 (74.2 %) patients.

Infusion-related reactions

Infusion-related reactions including hypersensitivity occurred in 6 (1.0 %) patients, including grade 2 (0.3 %) and grade 3 (0.2 %) infusion-related reactions. Systemic corticosteroids (prednisone \geq 40 mg per day or equivalent) were required in 1 (16.7 %) patient. All patients recovered from the infusion-related reaction.

Combination Therapy: Endometrial cancer (EC) patient population: Jemperli in combination with carboplatin and paclitaxel

Table 5 summarizes the adverse events that occurred in \geq 10% of patients with primary advanced or recurrent EC and which were higher in patients receiving Jemperli in combination with carboplatin and paclitaxel versus patients receiving placebo in combination with carboplatin and paclitaxel in RUBY.

Table 5 Treatment Emergent Adverse Events (\geq 10%) in Patients with Endometrial Cancer who received Jemperli in Combination with Carboplatin and Paclitaxel, and which occurred at a higher rate than in Patients receiving Placebo with Carboplatin and Paclitaxel (between arm difference of \geq 5% [All Grades] or \geq 2% [Grades 3-4]) (RUBY study)^a

Treatment Emergent Adverse Event	Jemperli with Carboplatin and Paclitaxel N = 241		Placebo with Carboplatin and Paclitaxel N = 246	
	All Grades n (%)	Grade 3 or 4 n (%)	All Grades n (%)	Grade 3 or 4 n (%)
Endocrine disorders				
Hypothyroidism ^b	39 (16.2)	0	17 (6.9)	1 (0.4)
Gastrointestinal disorders				
Nausea	131 (54.4)	7 (2.9)	114 (46.3)	4 (1.6)
General and administration site conditions				
Pyrexia	31 (12.9)	0	15 (6.1)	2 (0.8)
Investigations				
Alanine aminotransferase increased	31 (12.9)	5 (2.1)	16 (6.5)	1 (0.4)
Aspartate aminotransferase increased	29 (12.0)	5 (2.1)	11 (4.5)	2 (0.8)
Blood creatinine increased	28 (11.6)	2 (0.8)	15 (6.1)	0
Metabolism and nutrition disorders				
Hypokalemia ^c	48 (19.9)	13 (5.4)	36 (14.6)	10 (4.1)
Psychological disorders				
Depression ^d	27 (11.2)	0	13 (5.3)	0
Skin and subcutaneous tissue disorders				
Alopecia ^e	134 (55.6)	0	123 (50.0)	3 (1.2)
Rash ^f	92 (38.2)	17 (7.1)	50 (20.3)	3 (1.2)
Pruritus ^g	49 (20.3)	1 (0.4)	36 (14.6)	0
Dry skin	24 (10.0)	0	12 (4.9)	0
Vascular disorders				
Hypertension ^h	33 (13.7)	17 (7.1)	20 (8.1)	8 (3.3)

- ^a Additional adverse reactions known to occur with JEMPERLI or chemotherapy agents given alone may occur during treatment with these medicinal products in combination; refer to the Product Monographs for carboplatin and paclitaxel prior to the initiation of treatment.
- ^b Includes hypothyroidism, immune-mediated hypothyroidism, blood thyroid stimulating hormone increased, thyroxine decreased, tri-iodothyronine decreased.
- ^c Includes hypokalaemia and blood potassium decreased.
- ^d Includes depression, depressed mood, depressive symptom.
- ^e Includes alopecia and alopecia totalis.
- ^f Includes rash, rash maculo-papular, rash macular, rash papular, vulvovaginal rash, palmar-plantar erythrodysesthesia syndrome, rash pruritic, rash pustular, erythema nodosum, skin exfoliation, erythema.
- ^g Includes pruritus, vulvovaginal pruritus, pruritus genital.
- ^h Includes hypertension and blood pressure increased.

Graded per National Cancer Institute Common Terminology Criteria for Adverse Events Version 4.03.

dMMR or MSI-H EC patient population: Jemperli monotherapy

[Table 6](#) summarises adverse reactions that occurred in ≥ 1 % patients with dMMR/MSI-H endometrial cancer who received Jemperli (N=153) in the GARNET study.

Table 6 Adverse Reactions (incidence $\geq 1\%$) in dMMR/MSI-H EC Patients who Received Jemperli in GARNET study

Adverse Reaction	Jemperli (N = 153)	
	All Grades n (%)	Grade 3 or 4 n (%)
Blood and Lymphatic System		
Anemia	51 (33.3)	26 (17.0)
Endocrine disorders		
Hypothyroidism	18 (11.8)	0
Hyperthyroidism	8 (5.2)	0
Adrenal insufficiency	2 (1.3)	1 (0.7)
Gastrointestinal		
Nausea	50 (32.7)	1 (0.7)
Diarrhea	45 (29.4)	4 (2.6)
Vomiting	34 (22.2)	1 (0.7)
Gastritis	5 (3.3)	1 (0.7)
Colitis	3 (2.0)	2 (1.3)
General and Administration Site		
Pyrexia	21 (13.7)	0
Chills	10 (6.5)	0
Hepatobiliary disorders		
Hypertransaminasaemia	3 (2.0)	0
Investigations		
Alanine aminotransferase increased	14 (9.2)	4 (2.6)
Aspartate aminotransferase increased	13 (8.5)	1 (0.7)
Transaminases increased	4 (2.6)	2 (1.3)
Musculoskeletal and Connective Tissue		
Arthralgia	33 (21.6)	3 (2.0)
Myalgia	16 (10.5)	0
Respiratory, Thoracic, and Mediastinal		
Pneumonitis	6 (3.9)	2 (1.3)
Skin and Subcutaneous Tissue		
Pruritus	29 (19.0)	2 (1.3)
Rash	24 (15.7)	0
Erythema	6 (3.9)	0
Rash maculo-papular	3 (2.0)	0

Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events Version 4.03.

8.3. Less Common Clinical Trial Adverse Reactions

The following adverse reactions were reported in $<1\%$ of patients with recurrent or advanced dMMR/MSI-H endometrial cancer, treated with Jemperli in the GARNET study (N=153). Adverse reactions presented elsewhere in this section are excluded.

Endocrine disorders: hypophysitis
Eye disorders: iridocyclitis, uveitis
Gastrointestinal: immune-mediated enterocolitis, pancreatitis, pancreatitis acute
Hepatobiliary disorders: hepatic cytolysis
Infections and infestations: encephalitis
Musculoskeletal and connective tissue: immune-mediated arthritis, immune-mediated myositis
Renal and urinary: nephritis, tubulointerstitial nephritis
Respiratory, thoracic and mediastinal: immune-mediated lung disease, interstitial lung disease
Skin and subcutaneous: drug eruption, pemphigoid, rash pruritic, skin toxicity

The following clinically important adverse reactions were reported in <10 % of patients with primary advanced or recurrent endometrial cancer treated with Jemperli in the RUBY study (N=241). Adverse reactions presented elsewhere in this section are excluded.

Cardiovascular disorders: myocarditis
Endocrine disorders: adrenal insufficiency, thyroiditis, type 1 diabetes mellitus, hypophysitis, hyperthyroidism
Eye disorders: uveitis, iritis
Gastrointestinal disorders: pancreatitis, colitis, autoimmune hepatitis
Immune system disorders: sarcoidosis
Musculoskeletal and connective tissue disorders: immune-mediated arthritis, myositis
Nervous System disorders: encephalitis
Respiratory, thoracic and mediastinal disorders: pneumonitis

8.4. Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data

Clinical Trial Findings

Table 7 summarizes laboratory abnormalities in patients with EC who received Jemperli in combination with platinum-containing chemotherapy (RUBY study).

Table 7 Laboratory Abnormalities that Worsened from Baseline in $\geq 10\%$ of Patients with Endometrial Cancer Receiving Jemperli with carboplatin and paclitaxel and at a Higher Incidence Rate than in those Receiving placebo with carboplatin and paclitaxel (Between Arm Difference of $\geq 5\%$ [All Grades] or $\geq 2\%$ [Grades 3-4]) (RUBY study)

Laboratory Test	Jemperli with Carboplatin and Paclitaxel N = 241		Placebo with Carboplatin and Paclitaxel N = 246	
	All Grades ^a %	Grade 3 or 4 ^a %	All Grades ^a %	Grade 3 or 4 ^a %
Hematology				
Decreased lymphocytes	117 (48.5)	41 (17.0)	100 (40.7)	35 (14.2)
White blood cell decreased	153 (63.5)	35 (14.5)	144 (58.5)	27 (11.0)

Laboratory Test	Jemperli with Carboplatin and Paclitaxel N = 241		Placebo with Carboplatin and Paclitaxel N = 246	
	All Grades ^a %	Grade 3 or 4 ^a %	All Grades ^a %	Grade 3 or 4 ^a %
Chemistry				
Alanine Aminotransferase increased	77 (32.0)	11 (4.6)	48 (19.5)	3 (1.2)
Alkaline phosphatase increased	73 (30.3)	10 (4.1)	54 (22.0)	2 (0.8)
Aspartate Aminotransferase increased	96(39.8)	13 (5.4)	58 (23.6)	5 (2.0)
Creatinine increased	186 (77.2)	9 (3.7)	202 (82.1)	2 (0.8)
Hyperglycemia	119 (49.4)	30 (12.4)	108 (43.9)	25 (10.2)
Hypoalbuminemia	76 (31.5)	8 (3.3)	54 (22.0)	1 (0.4)
Serum amylase increased	61 (25.3)	22 (9.1)	32 (13.0)	9 (3.7)
Blood bilirubin increased ^b	15 (6.2)	7 (2.9)	8 (3.3)	2 (0.8)
Electrolytes				
Hypokalemia	77 (32.0)	20 (8.3)	71 (28.9)	11 (4.5)
Hypomagnesemia	112 (46.5)	11 (4.6)	117 (47.6)	6 (2.4)
Hyponatremia	74 (30.7)	19 (7.9)	55 (22.4)	10(4.1)

^a Consists of new onset of laboratory abnormality or worsening of baseline laboratory abnormality, or missing values. Patients with missing post-baseline values were included in worsening as a conservative approach.

^b Blood bilirubin increase was observed in <10% of patients with endometrial cancer receiving Jemperli with carboplatin and paclitaxel.

Table 8 summarizes laboratory abnormalities worsening from baseline to Grade 3 or 4 in ≥1 % of patients with dMMR/MSI-H EC on Jemperli monotherapy (GARNET study).

Table 8 Laboratory Abnormalities that Worsened from Baseline to Grade 3 or 4 Occurring in ≥1% of Patients with dMMR/MSI-H Endometrial Cancer Receiving Jemperli in monotherapy (GARNET Study)

Laboratory Test	Jemperli N=153	
	All Grades ^a n (%)	Grades 3 or 4 n (%)
Hematology		
Decreased lymphocytes	71 (46.4)	22 (14.4)
Decreased leukocytes	31 (20.3)	3 (2.0)
Decreased neutrophils	26 (17.0)	4 (2.6)
Decreased hemoglobin	77 (50.3)	28 (18.3)
Chemistry		
Decreased albumin	54 (35.3)	4 (2.6)
Increased creatinine	49 (32.0)	5 (3.3)
Increased alkaline phosphatase	46 (30.1)	4 (2.6)
Increased aspartate aminotransferase	48 (31.4)	3 (2.0)
Increased alanine aminotransferase	38 (24.8)	7 (4.6)
Electrolytes		
Decreased sodium	45 (29.4)	9 (5.9)
Decreased magnesium	41 (26.8)	3 (2.0)

Decreased potassium	33 (21.6)	3 (2.0)
Increased calcium	11 (7.2)	3 (2.0)

^a Consists of new onset of laboratory abnormality or worsening of baseline laboratory abnormality.

8.5. Post-Market Adverse Reactions

Guillain Barré syndrome including demyelinating polyneuropathy has been reported in <1% of patients, across clinical trials of dostarlimab in combination with other anti-cancer agents.

9. Drug Interactions

9.2. Drug Interactions Overview

No formal drug-drug interaction studies have been conducted with dostarlimab. Dostarlimab is considered to have low potential to affect pharmacokinetics of other drugs based on the lack of effect on cytokines, cytochrome P450, and active substance transporters.

9.4. Drug-Drug Interactions

Immunosuppression

The use of systemic corticosteroids or immunosuppressants before starting Jemperli should be avoided because of their potential interference with the pharmacodynamic activity and efficacy of Jemperli. However, systemic corticosteroids or other immunosuppressants can be used after starting Jemperli to treat immune-mediated adverse reactions (See [7. Warnings and Precautions](#)).

9.5. Drug-Food Interactions

Interactions with food have not been established.

9.6. Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7. Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10. Clinical Pharmacology

10.1. Mechanism of Action

Dostarlimab is an anti-programmed cell death protein-1 (PD-1) immunoglobulin G4 (IgG4) humanised monoclonal antibody (mAb), derived from a stable Chinese hamster ovary (CHO) cell line.

Binding of the PD-1 ligands, PD-L1 and PD-L2, to the PD-1 receptor found on T cells inhibits T-cell proliferation and cytokine production. Upregulation of PD-1 ligands occurs in some tumours and signaling through this pathway can contribute to inhibition of active T-cell immune surveillance of tumours.

Dostarlimab binds to PD-1 and blocks its interaction with PD-L1 and PD-L2, releasing inhibition of PD-1 pathway-mediated immune response, including the anti-tumour immune response. In syngeneic mouse tumour models, blocking PD-1 activity resulted in decreased tumour growth.

10.2. Pharmacodynamics

Dostarlimab provides sustained target engagement as measured by direct PD-1 binding and IL-2 production throughout the dosing interval at the recommended therapeutic dosing regimen.

Cardiac Electrophysiology

In a phase 1, open-label, single-arm study of Jemperli administered to patients with multiple tumour types, no large mean increase from baseline in QTc interval (i.e. >10 ms) was detected following treatment with Jemperli at the recommended therapeutic dose, when assessed at 0.5 hours postdose.

10.3. Pharmacokinetics

Dostarlimab pharmacokinetics (PK) as monotherapy or in combination with platinum-containing chemotherapy were assessed using non-compartmental analysis (NCA) and population PK (n=546) in endometrial cancer, based approach for both single agent Jemperli (monotherapy) and Jemperli in combination with carboplatin and paclitaxel. The pharmacokinetics of dostarlimab is linear in the dose range of 1 to 10 mg/kg. NCA PK parameters corresponding to the 500 mg (single dose) is summarized in Table 9. At the recommended therapeutic dose for monotherapy (500 mg administered intravenously every 3 weeks for 4 doses, followed by 1,000 mg every 6 weeks), or at the recommended therapeutic dose for combination with platinum-containing chemotherapy (500 mg administered intravenously every 3 weeks for 6 doses, followed by 1000 mg every 6 weeks), dostarlimab shows an approximate two-fold accumulation (C_{min}), consistent with the terminal half-life. The exposures of dostarlimab administered as a monotherapy and in combination with carboplatin and paclitaxel were comparable.

Table 9 Summary of Dostarlimab Non-Compartmental pharmacokinetic parameters in Patients with Solid Tumours

	C_{max} ($\mu\text{g/mL}$) ^a	C_{min} ($\mu\text{g/mL}$) ^a	T_{max} (h) ^b	$t_{1/2}$ (h) ^a	$AUC_{0-\infty}$ / $AUC_{(0-tao)}$ ^c ($\mu\text{g}\cdot\text{h/mL}$) ^a	CL (mL/h) ^a	Vd/Vdss (mL) ^a
Monotherapy							Vd
Single Dose Mean (500 mg Q3W) [N=6]	171.1 (20.0)	39.17 (26.7)	0.96 (0.5-3.02)	346.8 (12.3)	$AUC_{0-\infty}$ 55510 (24.2)	9.007 (24.2)	4506 (20.5)

^a Geometric mean and geometric coefficient of variation (%), when applicable

^b Median (range), when applicable

C_{max} : maximum drug concentration, C_{min} : minimum drug concentration, T_{max} : time when maximum drug concentration is attained, $t_{1/2}$: drug half life, $AUC_{0-\infty}$: area under the concentration-time curve between times zero and infinity, CL: systemic drug clearance, Vd : volume of distribution after single dose, Q3W: every three weeks

Absorption

Jemperli is administered via the intravenous route and therefore is immediately and expected to be completely bioavailable.

Distribution

The geometric mean volume of distribution of dostarlimab at steady state is approximately 5.81 L (% Coefficient of Variation (%CV): 14.9%).

Metabolism

The metabolic pathway of dostarlimab has not been characterized. As a humanized IgG4 monoclonal antibody, dostarlimab is expected to be degraded into small peptides and amino acids via catabolic non-specific pathways in the same manner as endogenous IgG.

Jemperli in combination with carboplatin and paclitaxel: When dostarlimab was administered at 500 mg every 3 weeks in combination with carboplatin and paclitaxel, followed by 1000 mg every 6 weeks, the CL parameter was decreased by 7.8% based on population PK modelling. There was no meaningful impact on dostarlimab exposure.

Elimination

The geometric mean clearance (CL) parameter at steady state and terminal half-life are 6.81 mL/h (30.2% CV) and 23.2 days (20.8% CV), respectively.

Special populations and conditions

Based on population pharmacokinetic analysis, age (24-86 years), sex, race, ethnicity, and tumour type did not have an effect on pharmacokinetic parameters of dostarlimab.

- **Hepatic Insufficiency:** No dose adjustment is needed in patients with mild hepatic impairment (total bilirubin (TB) 1.0 to 1.5 x ULN or AST > ULN as defined using the National Cancer Institute criteria of hepatic dysfunction) based on a population PK analysis. Data are not sufficient for drawing any conclusion on patients with moderate hepatic impairment (TB > 1.5 to 3 x ULN and any AST) and no data in patients with severe hepatic impairment (TB > 3 x ULN and any AST).
- **Renal Insufficiency:** No dose adjustment is needed in patients with mild (estimated Glomerular Filtration Rate (eGFR) < 90 and ≥ 60 mL/min/1.73 m²) or moderate (eGFR < 60 and ≥ 30 mL/min/1.73 m²) renal impairment based on a population PK analysis. Data are not sufficient for drawing a conclusion on patients with severe (eGFR < 30 and ≥ 15 mL/min/1.73 m²) renal impairment.

10.4. Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity.

Anti-drug antibodies (ADA) were tested in 384 patients who received dostarlimab monotherapy as 500 mg Q3W for the first 4 cycles followed by 1000 mg Q6W dostarlimab and the incidence of dostarlimab treatment-emergent ADAs was 2.1%. Neutralizing antibodies were detected in 1.0% of patients.

Co-administration with carboplatin and paclitaxel did not affect dostarlimab immunogenicity. In the RUBY study, there was no incidence of dostarlimab treatment-emergent ADAs or treatment-emergent neutralizing antibodies in 225 patients who were treated with dostarlimab at a dose of 500 mg every 3 weeks for 6 doses in combination with carboplatin and paclitaxel followed by 1000 mg of dostarlimab every 6 weeks thereafter.

Due to the limited number of patients who tested positive for ADAs, no conclusions can be drawn concerning a potential effect of immunogenicity on efficacy or safety.

11. Storage, Stability, and Disposal

Store undiluted vial refrigerated at 2°C to 8°C in the original carton in order to protect from light until time of preparation.

The diluted dose may be stored either:

- At room temperature up to 25°C for no more than 6 hours from the time of dilution until the end of infusion.
- Under refrigeration at 2°C to 8°C for no more than 24 hours from time of dilution until end of infusion. If refrigerated, allow the diluted solution to come to room temperature prior to administration.

Do not freeze.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Part 2: Scientific Information

13. Pharmaceutical Information

Drug Substance

Proper name: dostarlimab

Chemical name: Immunoglobulin G4-kappa, anti-[Homo sapiens PDCD1(programmed cell death 1, PD1, PD1 CD279)], humanized monoclonal antibody

Molecular formula and molecular mass: C₆₄₂₀H₉₈₃₂N₁₆₈₀O₂₀₁₄S₄₄ (non-glycosylated form with C-terminal lysine residues) and 143.9 kDa.

Structure/Structural formula: Dostarlimab is a humanized IgG4 monoclonal antibody. It is a glycosylated homodimer consisting of two identical heavy chains and two identical light chains, with 12 intra-chain disulfide bonds and 4 inter-chain disulfide bonds.

Physicochemical properties: Formulated drug substance: dostarlimab is a clear to slightly opalescent, colorless to yellow solution, essentially free from visible particles.

Product characteristics:

Dostarlimab is produced from recombinant-DNA technology in a Chinese Hamster Ovary (CHO)-derived cell line.

14. Clinical Trials

14.1. Clinical Trials by Indication

Primary advanced or recurrent endometrial cancer (EC): JEMPERLI in combination with carboplatin and paclitaxel

The efficacy and safety of dostarlimab in combination with carboplatin-paclitaxel were investigated in RUBY, a multicentre, randomized, double-blinded, placebo-controlled Phase 3 study conducted in patients with primary advanced or recurrent EC.

Table 10 Summary of Patient Demographics for Clinical Trials in primary advanced or recurrent EC

Study #	Study Design	Dosage, Route of Administration, Duration	Study Subjects (n)	Mean Age (range)	Sex
213361, RUBY	Multicentre, randomized, double-blind, controlled study	Part 1 Arm 1: Dostarlimab: 500 mg IV Q3W (Cycles 1 to 6) and 1000 mg IV Q6W (Cycle 7 and thereafter) Carboplatin: AUC 5 mg•mL/min IV Q3W (Cycles 1 to 6 only) Paclitaxel: 175 mg/m ² IV Q3W (Cycles 1 to 6 only)	Part 1: n=494	63.5 (39-85)	Female

Study #	Study Design	Dosage, Route of Administration, Duration	Study Subjects (n)	Mean Age (range)	Sex
		<p>Arm 2: Placebo: IV Q3W (Cycles 1 to 6) and IV Q6W (Cycle 7 and thereafter)</p> <p>Carboplatin: AUC 5 mg•mL/min IV Q3W (Cycles 1 to 6 only)</p> <p>Paclitaxel: 175 mg/m² IV Q3W (Cycles 1 to 6 only)</p>			

Q3W: every 3 weeks; Q6W: every 6 weeks; IV: intravenous; AUC: area under curve

The key eligibility criteria for the study were International Federation of Gynaecology and Obstetrics (FIGO) primary Stage III or Stage IV disease, including Stage IIIA to IIIC1 disease with presence of evaluable or measurable disease per RECIST v.1.1, Stage IIIC1 patients with carcinosarcoma, clear cell, serous, or mixed histology (containing ≥10% carcinosarcoma, clear cell, or serous histology) regardless of presence of evaluable or measurable disease on imaging, Stage IIIC2 or Stage IV disease regardless of presence of evaluable or measurable disease. The study also included patients with first recurrent EC with a low potential for cure by radiation therapy or surgery alone or in combination, including patients who had first recurrent disease and were naïve to systemic anticancer therapy or who had received prior neo-adjuvant/adjuvant systemic anticancer therapy and had a recurrence or progressive disease ≥6 months after completing treatment (first recurrence).

The study excluded patients who had received prior therapy with an anti-PD-1, anti PD-L1, or anti PD-L2 agent, patients who had received prior anticancer therapy (chemotherapy, targeted therapies, hormonal therapy, radiotherapy, or immunotherapy) within 21 days or <5 times the half-life of the most recent therapy prior to Study Day 1, whichever is shorter, patients with uterine sarcoma, patients with known uncontrolled central nervous system metastases, carcinomatosis meningitis, or both.

Treatment continued for up to 3 years or until unacceptable toxicity, disease progression or investigator decision. Treatment could continue beyond 3 years or beyond disease progression if the patient was clinically stable and considered to be deriving clinical benefit by the investigator. Assessment of tumour status was performed every 6 weeks through week 25, every 9 weeks through week 52 and every 12 weeks thereafter.

Patients were randomized (1:1) to receive dostarlimab 500 mg plus carboplatin AUC 5 mg/mL/min and paclitaxel 175 mg/m² every 3 weeks for 6 cycles followed by dostarlimab 1000 mg every 6 weeks or placebo plus carboplatin AUC 5 mg/mL/min and paclitaxel 175 mg/m² every 3 weeks for 6 cycles followed by placebo every 6 weeks. Randomization was stratified by MMR/MSI status, prior external pelvic radiotherapy, and disease status (recurrent, primary Stage III, or primary Stage IV).

The identification of dMMR/MSI-H tumour status (dMMR/MSI-H vs. mismatch repair proficient (MMRp)/microsatellite stable (MSS)) was prospectively determined based on local testing assays (immunohistochemistry [IHC], polymerase chain reaction [PCR] or next generation sequencing [NGS]), or central testing (IHC) when no local result was available. Efficacy data is presented per MMR/MSI status at randomization.

The primary efficacy outcomes were investigator-assessed PFS according to RECIST v1.1 in the dMMR/MSI-H population and in the overall population, and overall survival (OS) in the overall population. Secondary efficacy outcome measures included objective response rate (ORR), and duration of response (DOR).

A total of 494 patients with EC were evaluated for efficacy in the RUBY study. Demographic and baseline characteristics are summarized in [Table 11](#).

Table 11 Demographic and baseline characteristics of patients with endometrial cancer (RUBY study)

Characteristic	Overall Population N = 494		dMMR/MSI-H Population N = 122	
	Jemperli with Carboplatin and Paclitaxel N = 245	Placebo with Carboplatin and Paclitaxel N = 249	Jemperli with Carboplatin and Paclitaxel N = 60	Placebo with Carboplatin and Paclitaxel N = 62
Race, n (%)				
White	189 (77.1)	191 (76.7)	49 (81.7)	52 (83.9)
Black or African American	28 (11.4)	31 (12.4)	4 (6.7)	7 (11.3)
Asian	7 (2.9)	8 (3.2)	3 (5.0)	0
Others ^a	21 (8.6)	19 (7.6)	4 (6.7)	3 (4.8)
Age (years)				
Median	64.0	65.0	61.0	66.0
Min, max	41, 81	28, 85	45, 81	39, 85
ECOG performance status, n (%)				
0	145 (60.2)	160 (65.0)	33 (55.9)	36 (58.1)
1	96 (39.8)	86 (35.0)	26 (44.1)	26 (41.9)
Disease status, n (%)				
Primary Stage III	48 (19.6)	51 (20.5)	13 (21.7)	14 (22.6)
Primary Stage IV	80 (32.7)	80 (32.1)	17 (28.3)	17 (27.4)
Recurrent	117 (47.8)	118 (47.4)	30 (50.0)	31 (50.0)
Histology at Diagnosis, n (%)				
Endometrioid ^b	134 (54.7)	136 (54.6)	48 (80.0)	51 (82.3)
Serous adenocarcinoma	50 (20.4)	52 (20.9)	3 (5.0)	3 (4.8)
Carcinosarcoma	25 (10.2)	19 (7.6)	5 (8.3)	1 (1.6)
Other ^c	36 (14.7)	42 (16.9)	4 (6.7)	7 (11.3)
Previous Therapy, n (%)				

Characteristic	Overall Population N = 494		dMMR/MSI-H Population N = 122	
	Jemperli with Carboplatin and Paclitaxel	Placebo with Carboplatin and Paclitaxel	Jemperli with Carboplatin and Paclitaxel	Placebo with Carboplatin and Paclitaxel
Surgery	224 (91.4)	224 (90.0)	56 (93.3)	57 (91.9)
Received Previous Radiotherapy for Endometrial Cancer	71 (29.0)	69 (27.7)	20 (33.3)	23 (37.1)
Any Prior Anticancer Systemic Treatment	48 (19.6)	52 (20.9)	10 (16.7)	12 (19.4)
Residual disease at baseline^d, n (%)	212 (86.5)	219 (88.0)	53 (88.3)	57 (91.9)

^a American Indian or Alaska Native, Native Hawaiian, or other Pacific Islander, Mixed Race, Unknown, Not Reported.

^b Adenocarcinoma or adenocarcinoma-variants.

^c Clear cell adenocarcinoma, mixed, undifferentiated carcinoma, mucinous adenocarcinoma, mixed carcinoma with $\geq 10\%$ of carcinosarcoma, clear cell or serous histology.

^d Subjects with measurable or evaluable disease at baseline.

Study Results

Efficacy results are shown in [Table 12](#) and [Figure 1-3](#).

Table 12 Efficacy Results in the Endometrial Cancer population (RUBY study)

Endpoint	Overall Population		dMMR/MSI-H Population ^a	
	Jemperli with Carboplatin and Paclitaxel N = 245	Placebo with Carboplatin and Paclitaxel N = 249	Jemperli with Carboplatin and Paclitaxel N = 60	Placebo with Carboplatin and Paclitaxel N = 62
Progression Free Survival (PFS)^b				
Number (%) of patients with event	135 (55.1)	177 (71.1)	23 (38.3)	47 (75.8)
Median in months (95% CI) ^c	11.8 (9.6, 17.1)	7.9 (7.6, 9.5)	30.3 (11.8, NR)	7.7 (5.6, 9.7)
Hazard ratio (95% CI) ^d	0.64 (0.51, 0.80)		0.29 (0.17, 0.50)	
p-value ^e	<0.0001		<0.0001	
Overall survival (OS)^{f,g}				
Number (%) of patients with event	109 (44.5)	144 (57.8)		
Median in months (95%) ^c	44.6 (32.6, NR)	28.2 (22.1, 35.6)		
Hazard Ratio (95% CI) ^d	0.69 (0.54, 0.89)			
p-value ^e	0.0020			

dMMR = Mismatch Repair Deficient, MSI-H = Microsatellite Instability-High, NR = Not Reached

^a MMR/MSI status as defined at randomization.

^b Median follow-up of 25 months. PFS is a primary endpoint for the overall population and the dMMR/MSI-H population respectively.

^c By Brookmeyer and Crowley method.

^d Based on stratified Cox regression model.

^e One-sided p-value based on stratified log-rank test.

^f Median follow-up of 37 months.

^g OS is a primary endpoint for the overall population only.

Figure 1. Progression-Free Survival per RECIST v1.1, as assessed by Investigator in Patients with dMMR/MSI-H Endometrial Cancer (RUBY study)

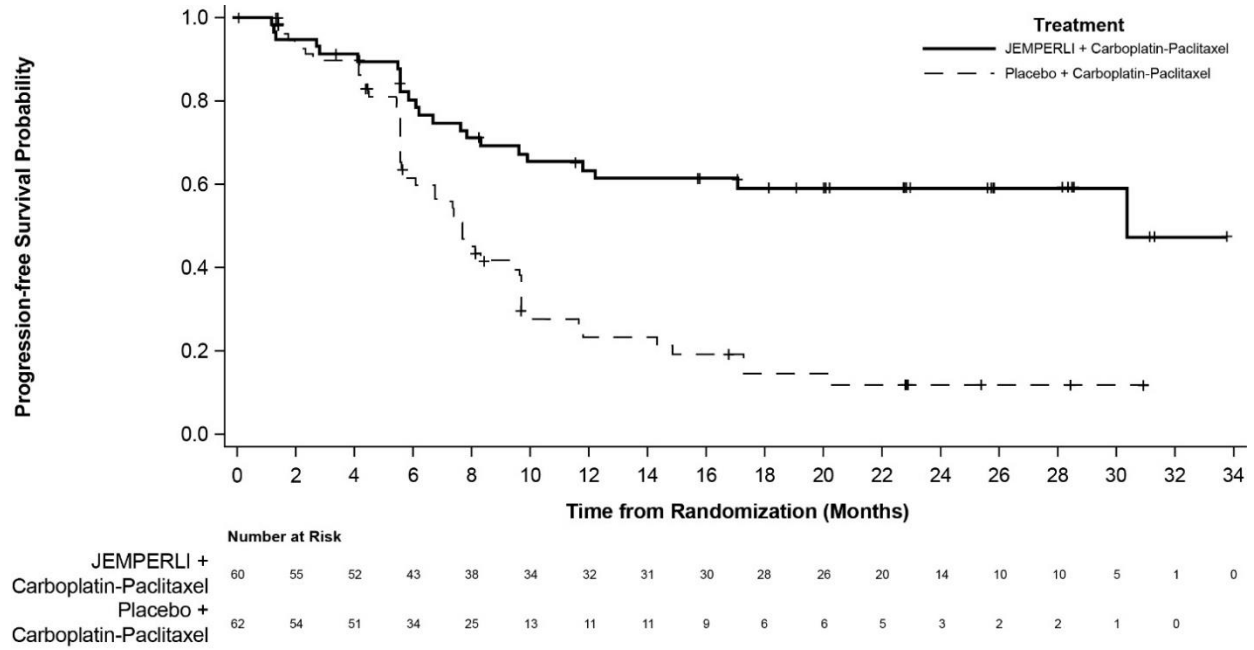


Figure 2. Progression-free Survival per RECIST v1.1, as assessed by Investigator in Patients with Endometrial Cancer (RUBY study, overall population)

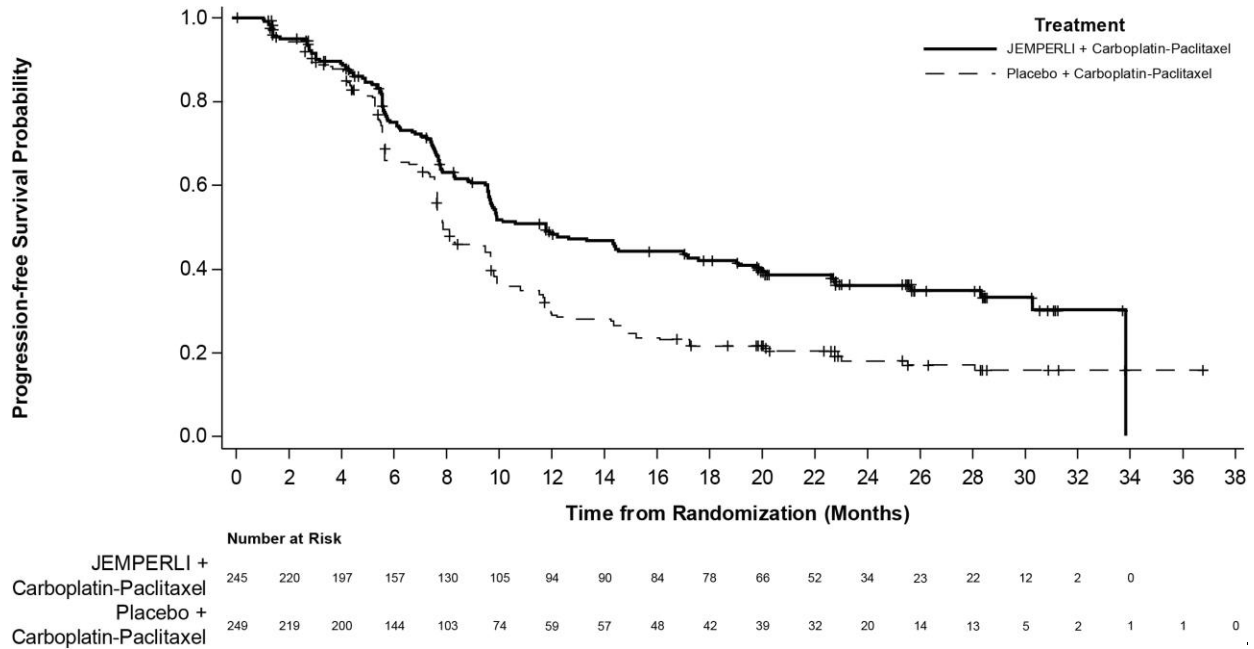
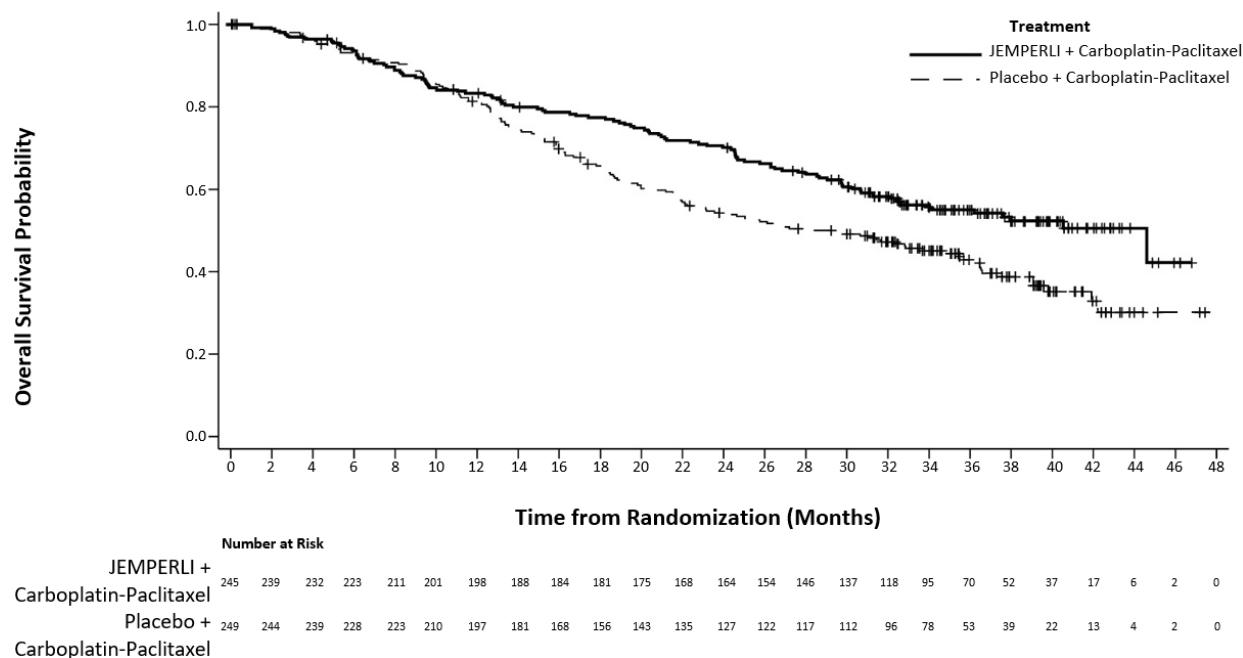


Figure 3. Overall Survival in Patients with Endometrial Cancer (RUBY study, overall population)



In a pre-specified exploratory analysis of OS in the dMMR/MSI-H population with a median follow-up of 37 months, the HR was 0.34 (95% CI: 0.18, 0.62) with median OS not reached for the Jemperi plus carboplatin-paclitaxel arm (n=60) versus a median OS of 30.8 months (95% CI: 18.7, NR) for the placebo plus carboplatin-paclitaxel arm (n=62).

In a pre-specified exploratory analysis of PFS in the MMRp/MSS population with a median follow-up of 25 months, the HR was 0.78 (95% CI: 0.6, 1.0) with a median PFS of 9.8 months (95% CI: 9.0, 12.6) for the Jemperi plus carboplatin-paclitaxel arm (n=185) versus 7.9 months (95% CI: 7.6, 9.8) for the placebo plus carboplatin-paclitaxel arm (n=187). In a pre-specified exploratory analysis of OS in the MMRp/MSS population with a median follow-up of 37 months, the HR was 0.82 (95% CI: 0.62, 1.08) with a median OS of 32.5 months (95% CI: 28.6, NR) for the Jemperi plus carboplatin-paclitaxel arm (n=185) versus 28.2 months (95% CI: 21.9, 36.1) for the placebo plus carboplatin-paclitaxel arm (n=187).

Among patients with target or non-target lesions at baseline in the overall population, in the Jemperi plus carboplatin-paclitaxel arm (n=212), ORR was 70.3% (95% CI: 63.6%, 76.3%), consisting of 53 patients (25.0 %) with complete responses and 96 patients (45.3 %) with partial responses. The median DOR was 10.6 months (95% CI: 8.2, 17.6) among the 149 responders. In the placebo plus carboplatin-paclitaxel arm (n=219), ORR was 64.8% (95% CI: 58.1%, 71.2%), consisting of 43 patients (19.6 %) with complete responses and 99 patients (45.2 %) with partial responses. The median DOR was 6.2 months (95% CI: 4.4, 6.7) among the 142 responders.

In a pre-specified exploratory analysis of OS (with a median follow-up of 37 months) for the subgroups in the overall population defined by disease status (primary Stage III, primary Stage IV, and recurrent), the HRs (Jemperi plus carboplatin-paclitaxel vs. placebo plus carboplatin-paclitaxel) were 1.32 (95% CI: 0.66, 2.66), 0.78 (95% CI: 0.52, 1.17) and 0.51 (95% CI: 0.36, 0.74) for the patients with primary Stage III, primary Stage IV and recurrent EC, respectively.

dMMR or MSI-H recurrent or advanced EC that has progressed on or following prior treatment with a platinum containing regimen: Jemperli monotherapy

The efficacy and safety of Jemperli as monotherapy were investigated in the GARNET study, a multicentre, uncontrolled, multiple parallel cohort, open-label phase-1 study. The GARNET study included expansion cohorts in subjects with recurrent or advanced solid tumours who have limited available treatment options.

GARNET study Cohort A1 enrolled 153 patients with dMMR/MSI-H endometrial cancer who have progressed on or after a platinum containing regimen, with 143 assessed for efficacy. The identification of dMMR/MSI-H tumour status was prospectively determined based on local testing. Local diagnostic assays (IHC, PCR or NGS) available at the sites were used for the detection of the dMMR/MSI-H status in tumour material. Most of the sites used IHC as it was the most common assay available.

Patients with the following status were excluded from the GARNET study: ECOG baseline performance score ³2; uncontrolled central nervous system metastases or carcinomatous meningitis; other malignancies within the last 2 years; immunodeficiency or receiving immunosuppressive therapy within 7 days; active HIV, hepatitis B or hepatitis C infection; active autoimmune disease requiring systemic treatment in the past 2 years excluding replacement therapy; history of interstitial lung disease; or receiving live vaccine within 14 days.

Patients received Jemperli 500 mg every 3 weeks for 4 cycles followed by 1000 mg every 6 weeks. Treatment continued until unacceptable toxicity or disease progression that was either symptomatic, rapidly progressive, required urgent intervention, or occurred with a decline in performance status. The median duration of treatment was 34 weeks, with a minimum of 3 weeks and a maximum of 220 weeks (51 months), and 37 (24%) of subjects who received any amount of dostarlimab received treatment >102 weeks (2 years).

The major efficacy outcome measures were objective response rate (ORR) and duration of response (DOR) as assessed by blinded independent central radiologists' (BICR) review according to Response Evaluation Criteria in Solid Tumors (RECIST v1.1). The efficacy population (N=143) was defined as patients who had measurable disease by BICR at baseline and had minimum of 24 weeks follow-up or had less than 24 weeks of follow-up and discontinued due to adverse events or disease progression.

Demographic and baseline characteristics are summarized in [Table 13](#).

Table 13 Demographic and baseline characteristics of patients with dMMR/MSI-H endometrial cancer in GARNET study

Demographic Characteristics	
Characteristic	Total (N=143)
Race, n (%)	
White	110 (76.9)
Black	4 (2.8)
Asian	5 (3.5)
American Indian or Alaska Native	3 (2.1)
Unknown	1 (0.7)

Demographic Characteristics	
Not Reported	20 (14.0)
Age (years)	
n	143
Median	65.0
Min, max	39, 85
Age group, n (%)	
<65 years	68 (7.6)
≥65 years to <75 years	61 (42.7)
≥75 years	14 (9.8)
ECOG performance status	
0	56 (39.2)
1	87 (60.8)
Primary Cancer History	
Variable, n (%)	Total (N=143)
Grade of disease at diagnosis	
Grade 1	38 (26.6)
Grade 2	56 (39.2)
Grade 3	44 (30.8)
Not assessable	5 (3.5)
FIGO stage at diagnosis	
Stage I	49 (34.3)
Stage II	13 (9.1)
Stage III	51 (35.7)
Stage IV	30 (21.0)
Prior Anticancer Treatment	
Variable, n (%)	Total (N=143)
Any prior anticancer treatment	143 (100)
Prior surgery for study indication	127 (88.8)
Any prior anticancer radiotherapy	101 (70.6)
Prior bevacizumab use	5 (3.5)
Any prior adjuvant/neo-adjuvant anticancer treatment	75 (52.4)
Number of prior anticancer regimens	
1	90 (62.9)
2	35 (24.5)
3	15 (10.5)
≥4	3 (2.1)
Number of prior regimens for metastatic disease ^a	
0	61 (42.7)
1	68 (47.6)
2	13 (9.1)
3	1 (0.7)

Abbreviations: BMI=body mass index; dMMR=mismatch repair-deficient; EC=endometrial cancer; FIGO=International Federation of Gynecology and Obstetrics; ECOG=Eastern Cooperative Oncology Group; max=maximum; min=minimum; MMR-unk=unknown mismatch repair tumour status; MSI-H=microsatellite instability high.

^a Excluding neo-adjuvant, adjuvant regimens, and hormonal agents.

Study Results

A total of 143 patients (18 years or older) with dMMR/MSI-H EC, at least one target lesion at baseline and 24 weeks of tumour assessment data were assessed for efficacy in the GARNET study. A total of 10 patients were excluded from primary efficacy analysis due to no measurable disease at baseline by RECIST 1.1 per BICR. At the time of analysis, 70.6% of subjects and 49% of subjects had discontinued treatment and discontinued from the study respectively.

The efficacy results of GARNET study for dMMR /MSI-H endometrial cancer patients are shown in [Table 14](#).

Table 14 Efficacy results in GARNET study for patients with dMMR/MSI-H endometrial cancer

Endpoint	Jemperli (N=143) ^a
Primary endpoints	
Objective response rate (ORR)	
ORR n (%) (95% CI)	65 (45.5) (37.1, 54.0)
Complete response rate n (%)	23 (16.1)
Partial response rate n (%)	42 (29.4)
Duration of response (DOR)^b	
Median in months (range)	Not reached (1.18+, 47.21+)
Patients with duration ≥12 months n (%)	52 (80.0)
Patients with duration ≥ 24 months, n (%)	29 (44.6)

CI: Confidence interval

^a Efficacy data with a median follow-up of 27.6 months (cut-off date 01 Nov 2021)

^b For patients with a partial or complete response.

+ongoing at last assessment

15. Microbiology

No microbiological information is required for this drug product.

16. Non-Clinical Toxicology

General Toxicology: Dostarlimab was administered by IV to cynomolgus monkeys in a single dose study and two repeat-dose studies: 4-weeks and 13-weeks. Dostarlimab was generally well tolerated in cynomolgus monkeys in the single- and 4-weeks repeat-dose toxicity studies and the no observed adverse effect level (NOAEL) in both studies was considered to be 100 mg/kg, the top dose. The NOAEL could not be determined in the 13-weeks repeat-dose study.

In Study 4010-09-003, dostarlimab was administered by IV to cynomolgus monkeys (4 animals/sex/group) at dose levels of 10, 30, and 100 mg/kg once weekly over 13 weeks (14 doses in total). After completion of dosing, 2 animals/sex/group from the control and high-dose groups were assigned to an 8-week treatment-free recovery period. One male receiving 10 mg/kg dostarlimab was euthanized on Day 89 due to chronic, unresolved, generalized skin findings (first recorded on Day 5) and secondary swollen and firm inguinal lymph nodes. The skin findings were indicative of an immune reaction and

they could be exaggerated pharmacological effects of dostarlimab based on the mechanism of action. Additionally, liquid feces observed in all groups, including control, was considered a possible drug-related effect at ≥ 30 mg/kg/week dose given the increased incidence over concurrent controls and timing relative to dosing. However, there were no correlated changes in body weight and food consumption, or associated pathology findings, thus, it was not considered adverse. Also, sporadic and dose-unrelated macroscopic and/or microscopic findings of an immune-mediated nature were observed in the skin, kidney, liver, or heart of 1-2 animals per group, dosed with dostarlimab. These findings could be the anticipated pharmacological effects or drug-related exacerbation of background findings.

Genotoxicity: No studies have been performed to assess the potential of dostarlimab for genotoxicity.

Carcinogenicity: No studies have been performed to assess the potential of dostarlimab for carcinogenicity.

Reproductive and developmental toxicology: Animal reproduction studies have not been conducted with dostarlimab. The PD-1/PD-L1 pathway is thought to be involved in maintaining tolerance to the fetus throughout pregnancy. Blockade of PD-L1 signalling has been shown in murine models of pregnancy to disrupt tolerance to the fetus and to result in an increase in fetal loss. These results indicate a potential risk that the administration of Jemperli during pregnancy could cause fetal harm, including increased rates of abortion or stillbirth.

Animal fertility studies have not been conducted with dostarlimab. In 1-month and 3-month repeat-dose toxicology studies in cynomolgus monkeys, there were no notable effects in the male and female reproductive organs; however, these results may not be representative at all of the potential clinical risks because of the immaturity of the reproductive system of animals used in the studies. Therefore, fertility toxicity remains unknown.

Juvenile toxicity: No studies have been performed to assess the potential of Jemperli for juvenile animal toxicity.

Special toxicology: No immunotoxicity or local tolerance studies have been performed with dostarlimab. Tissue cross-reactivity studies were performed in human and cynomolgus monkey tissues in two Jemperli doses, 0.5 or 5.0 $\mu\text{g}/\text{mL}$. Dostarlimab-specific binding was observed at 0.5 or 5.0 $\mu\text{g}/\text{mL}$ in both human and cynomolgus monkey tissues. Binding in cynomolgus monkey tissues was similar to that of human tissues; however, a greater amount of staining was present in the human tissue panel. In both the human and cynomolgus monkey studies, there was no unexpected binding, and hence no tissue cross-reactivity was observed.

Patient Medication Information

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Pr JEMPERLI (jem-PER-lee)

dostarlimab for injection

This Patient Medication Information is written for the person who will be taking **Jemperli**. This may be you or a person you are caring for. Read this information carefully. Keep it as you may need to read it again.

This Patient Medication Information is a summary. It will not tell you everything about this medication. If you have more questions about **Jemperli**, talk to a healthcare professional.

What Jemperli is used for:

Jemperli is a prescription medicine used in adults to treat:

- a kind of cancer called endometrial cancer (cancer of the lining of the womb) in adults that is shown by a laboratory test to be mismatch repair deficient (dMMR) or microsatellite instability-high (MSI-H) that has progressed on or following prior treatment with a platinum containing regimen.
- a kind of cancer called endometrial cancer (cancer of the lining of the womb) in combination with carboplatin and paclitaxel, if the cancer has spread outside your uterus (womb) and you have not received any systemic anti-cancer treatment for the advanced disease, or if your cancer has returned for the first time and cannot be cured by surgery or radiation.

How Jemperli works:

Jemperli contains the active substance dostarlimab, which is a monoclonal antibody, a type of protein designed to recognise and attach to a specific target substance in the body.

Jemperli works by helping your immune system fight your cancer.

Jemperli may be given in combination with other anticancer medicines. It is important that you also read the package leaflets for the other anticancer medicines you may be receiving. If you have any questions about these medicines, ask your doctor.

The ingredients in Jemperli are:

Medicinal ingredients: dostarlimab

Non-medicinal ingredients: trisodium citrate, dihydrate; citric acid, monohydrate; L-arginine hydrochloride; sodium chloride; polysorbate 80; and water for injection (see “Do not use Jemperli if”).

Jemperli comes in the following dosage form:

Solution for infusion, 500 mg dostarlimab per vial

Do not use Jemperli if:

- if you are allergic to dostarlimab or any of the other ingredients of this medicine (listed in “The ingredients in Jemperli are:”). Talk to your doctor before you are given Jemperli if you are not sure

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Jemperli. Talk about any health conditions or problems you may have, including if you:

- have immune system problems
- have lung or breathing problems
- have liver or kidney problems
- have serious skin problems
- have any other medical problems including but not limited to:
 - had an allergic reaction to other monoclonal antibody therapies;
 - have or have had chronic viral infection of the liver, including hepatitis B (HBV) or hepatitis C (HCV);
 - have human immunodeficiency virus (HIV) infection or acquired immune deficiency syndrome (AIDS);
 - have had a solid organ transplant or a bone marrow (stem cell) transplant that used donor stem cells (allogeneic); or
 - take other medicines that make your immune system weak. Examples of these may include steroids, such as prednisone.

Pregnancy

- **You must not be given Jemperli if you are pregnant** unless your doctor specifically recommends it.
- If you are pregnant, think you may be pregnant or are planning to become pregnant, ask your doctor for advice before you are given this medicine.
- You should not become pregnant while you are being treated with Jemperli. Jemperli can cause harmful effects or death to your unborn baby.
- If you are a woman who could become pregnant, you must use effective contraception while you are being treated with Jemperli and for at least 4 months after your last dose.

Breast-feeding

- **You must not breast-feed during treatment and for at least 4 months after your last dose of Jemperli.**
- A risk to the newborns/infants cannot be excluded.
- If you are breast-feeding, ask your doctor for advice before you are given this medicine.
- The active ingredient of Jemperli may pass into your breast milk.
- You and your doctor should decide if you will take Jemperli or breast-feed, you should not do both.

Children:

- It is not known if Jemperli is safe and effective in children less than 18 years of age. Therefore, **Health Canada has not authorized an indication for children less than 18 years of age.**

Elderly

- No overall differences in safety or efficacy were reported between elderly patients (65 years and over) and younger patients (less than 65 years). No dose adjustment is recommended for patients who are aged 65 years or over. There are limited clinical data with dostarlimab in patients aged 75 years or over.

Other warnings you should know about:

There are possible side effects of Jemperli treatment in people who have received a transplant

- **Rejection of a transplanted organ.** People who have had an organ transplant may have an increased risk of organ transplant rejection. Your doctor should tell you what signs and symptoms you should report and monitor you, depending on the type of organ transplant that you have had.
- **Jemperli can cause complications, including graft-versus-host-disease (GVHD), in people who have received a bone marrow (stem cell) transplant that uses donor stem cells (allogeneic).** These complications can be serious and can lead to death. These complications may happen if you underwent transplantation either before or after being treated with Jemperli. Your healthcare professional will monitor you for these complications.

Jemperli can have serious side effects, which can sometimes become life-threatening and can lead to death. These side effects may happen at any time during treatment, or even after your treatment has ended. You may get more than one side effect at the same time.

You need to be aware of possible symptoms, so your doctor can give you treatment for side effects if necessary.

Driving and using machines:

If you experience side effects that affect your ability to concentrate and react, do not drive or use machines until you feel better.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with Jemperli:

- *Some medicines may interfere with the effect of Jemperli, especially medicines that make your immune system weak-for example corticosteroids, such as prednisone.*

Once you are treated with Jemperli, your doctor may give you corticosteroids to reduce any side effects that you may have.

How to take Jemperli:

Jemperli will be given to you in a hospital or clinic under the supervision of a doctor experienced in cancer treatment.

Your doctor will give you Jemperli as a drip into a vein (*intravenous infusion*) for about 30 minutes.

Your doctor will decide how many treatments you need.

Usual dose:

When Jemperli is given on its own, the recommended dose of Jemperli is 500 mg every 3 weeks for first 4 doses, followed by 1000 mg every 6 weeks for all doses thereafter, for up to 3 years.

When Jemperli is given in combination with chemotherapy, the recommended dose of Jemperli is 500 mg every 3 weeks for 6 doses, followed by 1000 mg every 6 weeks for all doses thereafter.

Overdose:

If you think you, or a person you are caring for, have taken too much Jemperli, contact a healthcare professional, hospital emergency department, regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no signs or symptoms.

Missed dose:

If you miss an appointment to receive Jemperli

- Contact your doctor or hospital immediately to reschedule your appointment.
- It is very important that you do not miss a dose of this medicine.

Possible side effects from using Jemperli:

When you get Jemperli, you can have some serious side effects. These side effects can sometimes become life-threatening and can lead to death. These side effects may happen anytime during treatment or even after your treatment has ended. You may experience more than one side effect at the same time. The following lists do not include all the possible side effects you may feel when taking Jemperli. If you experience any side effects not listed here, contact your healthcare professional.

The following side effects have been reported with dostarlimab alone or in combination with chemotherapy:

Very Common

- feeling sick (*nausea*); being sick (*vomiting*)
- skin redness or rash; blistering of the skin or mucous membranes; itchy skin; dry skin
- high temperature; fever
- feeling sad or depressed
- hair loss
- changes in test results: high blood pressure, increased creatinine levels in blood, decreased potassium levels in blood

Common

- muscle or joint pain
- chills

If you are being treated with Jemperli and have any of the following serious side effects, call or see your doctor or nurse right away. Your doctor may give you other medicines in order to prevent more severe complications and reduce your symptoms. Your doctor may withhold the next dose of Jemperli or stop your treatment with Jemperli.

Serious side effects and what to do about them

Symptom / effect		Talk to your healthcare professional		Stop taking this drug and get immediate medical help
		Only if severe	In all cases	
VERY COMMON (monotherapy*)	Low red blood cells count (<i>anemia</i>)		X	
VERY COMMON (monotherapy, combination*)	Increased liver enzyme levels in the blood: feeling tired or weak		X	
VERY COMMON (monotherapy)	Skin problems Inflammation of the skin: rash, itching, peeling or skin sores; ulcers in the mouth, nose, throat or genital area		X	
VERY COMMON (combination)	Skin conditions: dry skin, skin rash		X	
VERY COMMON (combination)	Thyroid gland problems Underactive thyroid gland: weight gain, feeling cold, constipation, abdominal pain, deeper voice, muscle aches, fatigue, dizziness or fainting, headache that will not go away or unusual headache		X	
COMMON (monotherapy, combination)	Overactive thyroid gland: rapid heartbeat, feeling anxious, weight loss, increased sweating, hair loss		X	
UNCOMMON (combination)	Inflammation of the thyroid gland: weight gain, constipation, dry skin, muscle weakness, fatigue		X	
COMMON (monotherapy, combination)	Inflammation of the lungs (<i>pneumonitis</i>): shortness of breath, chest pain, new or worse cough		X	
COMMON (monotherapy, combination)	Food pipe, stomach or bowel problems Inflammation of the lining of the bowel (<i>colon</i>): diarrhea, or more bowel movements than usual; black, tarry, sticky stools, blood or mucus in stools; severe stomach pain or tenderness; feeling sick (<i>nausea</i>), being sick (<i>vomiting</i>)		X	
COMMON (monotherapy)	Inflammation of the stomach: decreased appetite, upper belly pain, feeling sick (<i>nausea</i>), being sick (<i>vomiting</i>)		X	
COMMON (combination)	Decreased secretion of adrenal hormones: Feeling tired, muscle weakness, loss of appetite, weight loss, abdominal pain		X	

Symptom / effect		Talk to your healthcare professional		Stop taking this drug and get immediate medical help
		Only if severe	In all cases	
UNCOMMON (monotherapy, combination)	Inflammation of the eye: changes in the coloured part of the eye (<i>the iris</i>) and the area around the iris, changes to eyesight, pain		X	
UNCOMMON (monotherapy)	Inflammation of the kidneys: changes in amount or colour of urine, swelling of the ankles, loss of appetite, blood in the urine		X	
COMMON (combination)	Inflammation of the pancreas: upper belly pain, feeling sick (nausea) being sick (vomiting)		X	
UNCOMMON (monotherapy)				
UNCOMMON (monotherapy, combination)	Inflammation of the pituitary gland, in the base of the brain: rapid heartbeat, weight loss or weight gain, increased sweating, hair loss, feeling cold, constipation, abdominal pain, deeper voice, muscle aches, dizziness or fainting, headache that will not go away or unusual headache		X	
FREQUENCY UNKNOWN (monotherapy)	Brain and nervous system (<i>Guillain-Barré syndrome, encephalitis</i>): inflammation of the nerves that can cause pain, weakness, or paralysis in the extremities. Neck stiffness, headache, fever, chills, vomiting, eye sensitivity to light, dry mouth, impaired speech, confusion pricking or pins and needles sensations in the hands and feet, difficulty walking or lifting objects, abnormal heart beat/rate or blood pressure		X	
UNCOMMON (combination)		<i>(Encephalitis)</i> : confusion, fever, memory problems, seizures		X
UNCOMMON (combination)	Inflammation of the Heart muscle (<i>myocarditis</i>): trouble breathing, dizziness or fainting, fever, chest pain and chest tightness, flu-like symptoms		X	
FREQUENCY UNKNOWN (monotherapy)				
FREQUENCY UNKNOWN (monotherapy)	Muscle weakness and rapid fatigue of the muscles (<i>myasthenic syndrome/myasthenia gravis</i>): aching muscles, weakness of eye muscles, drooping eyelids, dry eyes and blurred vision, difficulty speaking or swallowing, sleepiness, dizziness		X	

Symptom / effect		Talk to your healthcare professional		Stop taking this drug and get immediate medical help
		Only if severe	In all cases	
UNCOMMON (combination) FREQUENCY UNKNOWN (monotherapy)	Inflammation of the liver (<i>hepatitis</i>): feeling sick (<i>nausea</i>), being sick (<i>vomiting</i>); loss of appetite; pain on the right side of the abdomen (stomach); yellowing of the skin or the whites of the eyes; dark-coloured urine; bleeding or bruising more easily than normal		X	
UNCOMMON (combination) FREQUENCY UNKNOWN (monotherapy)	Inflammation of other organs: (sarcoidosis): swollen lymph nodes, rash or tender lumps on skin, cough, or eye pain severe or persistent muscle or joint pains, severe muscle weakness, swollen or cold hands or feet, feeling tired		X	
FREQUENCY UNKNOWN (monotherapy)	Infusion-related reactions: shortness of breath or wheezing, itching or rash, flushing, dizziness, chills or shaking, fever, drop in blood pressure (feeling like passing out)		X	
FREQUENCY UNKNOWN (monotherapy)	Spinal cord (<i>myelitis</i>): pain, numbness, tingling or weakness in the arms or legs, bladder or bowel problems including needing to urinate more frequently, urinary incontinence, difficulty urinating and constipation		X	
FREQUENCY UNKNOWN (monotherapy) UNCOMMON (combination) FREQUENCY UNKNOWN (monotherapy)	Diabetes Problems Type 1 diabetes Diabetic complications (<i>diabetic ketoacidosis</i>)		X	
			X	

*In the table, when Jemperli is given on its own, this is called 'monotherapy'. When Jemperli is given in combination with chemotherapy, this is called 'combination'.

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting side effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (canada.ca/drug-device-reporting) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

It is unlikely that you will be asked to store Jemperli yourself. It will be stored in the hospital or clinic where it is given to you.

Store in a refrigerator (2°C – 8°C). Do not freeze. Store in the original package in order to protect from light. Keep out of reach and sight of children.

If you want more information about Jemperli:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: ([Drug Product Database: Access the database](#)); the manufacturer's website www.gsk.ca, or by calling 1-800-387-7374.

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