Dostarlimab-gxly

An HCP Tool from AIM with Immunotherapy

Dostarlimab-gxly (Jemperli) is a type of immune checkpoint inhibitor that works by binding to and blocking the programmed death receptor-1 (PD-1).

Indications for dostarlimab-gxly

It is indicated for use in endometrial cancer in combination with carboplatin and paclitaxel, followed by dostarlimab-gxly as a single agent for the treatment of adult patients with primary advanced or recurrent endometrial cancer. It is also approved as a single agent for the treatment of adult patients with mismatch repair deficient (dMMR) recurrent or advanced endometrial cancer, as determined by an FDA-approved test, that has progressed on or following prior treatment with a platinum-containing regimen in any setting and are not candidates for curative surgery or radiation.

Dostarlimab-gxly is also approved as a single agent for the treatment of adult patients with dMMR recurrent or advanced solid tumors, as determined by an FDA-approved test, that have progressed on or following prior treatment and who have no satisfactory alternative treatment options. However, this indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Clinical trial results

In a phase 3 gloabal study, dostarlimab-gxly was shown to significantly improve overall survival at 24 months (73.1%) versus placebo (56.0%) in patients with primary advanced stage III or IV or first recurrent endometrial cancer.

- Among the dMMR–microsatellite instability-high (MSI-H) patient population, the estimated progression-free survival at 24 months was 61.4% in the dostarlimab-gxly-treated group and 15.7% in the placebo group.
- For the overall patient population, the estimated progression-free survival at 24 months was 36.1% in the dostarlimab-gxly-treated group and 18.1% in the placebo group.

Patient eligibility for dostarlimab-gxly

Only patients who have solid tumors with deficient mismatch repair proteins are eligible for dostarlimab-gxly. The biomarker proteins include MLH1, PMS2, MSH2, and MSH6 and are detected using a qualitative immunohistochemistry panel (Ventana MMR) using formalin-fixed, paraffin-embedded tissue specimens that stains positive when the protein is detected by light microscopy. The test should be interpreted by a qualified pathologist in conjunction with histological examination. The Ventana MMR panel is the FDA-approved companion diagnostic for dostarlimab-gxly.

Patients should be tested as soon as possible after diagnosis, since it may take weeks to receive the results back.

This document is intended to assist providers in optimizing the management of dostarlimab-gxly in eligible patients.

DRUG DOSAGE AND ADMINISTRATION

As a precaution, the initial infusions (induction) of Jemperli (dostarlimab-gxly) are typically administered in the hospital to facilitate monitoring and management of toxicities. The most common side effects are immune-mediated adverse reactions, which can be severe or fatal and occur in any organ system or tissue. Toxicities can manifest during treatment and after discontinuation. Early identification and management of toxicities are essential to ensure safe use of dostarlimab-gxly. Among other drug-related adverse effects, elevated liver enzymes are also important to address. The measurement and evaluation of liver enzymes, creatinine, and thyroid function tests are performed at baseline and during treatment. Immune-related toxicities can affect any organ. In the endometrial cancer study, dermatologic toxicities, colitis, and endocrine abnormalities were the most common on this study. It is important to do a CBC, CMP (e.g. electrolytes, liver enzymes, creatinine), and thyroid testing at baseline and throughout treatment. Also monitor for clinical symptoms including diarrhea, jaundice, etc.

Jemperli (dostarlimab-gxly) for adult patients with mismatch repair deficient (dMMR) recurrent or advanced endometrial cancer:

Dosing and administration

Prior to Infusion

- Adequate hydration/euvolemic status
- Adequate liver function (labs prior to initiation and q3 wk throughout treatment)
- For patients on maintenance systemic corticosteroids, consider adjusting the corticosteroid dose given the risk of hypotension

No dose reductions of Jemperli (dostarlimab-gxly) are recommended. Withhold drug for Grade 3 immune-mediated adverse reactions. Permanently discontinue for life-threatening Grade 4 reactions, recurrent severe (Grade 3) immune-mediated reactions that require systemic immunosuppressive treatment, or an inability to reduce corticosteroid dose to 10 mg or less of prednisone equivalent per day within 12 weeks of initiating steroids.

Note: Modification of the corticosteroid dose will be made by the clinician based on the specific toxicity, grade, and clinical/laboratory improvement.

- Jemperli (dostarlimab-gxly) is given as a 30-minute IV infusion
- Premedication of the first dose is not required, but institutional practices vary. Examples of potential premedications include acetaminophen 650 mg PO, ondansetron 8 mg PO, diphenhydramine 25 mg PO, and famotidine 20 mg.
- Jemperli (dostarlimab-gxly) is administered once every three weeks for the first four doses. Then, from the fifth dose onward, it is administered every six weeks until disease progression (unless the patient is otherwise deriving clinical benefit) or unacceptable toxicity.
- The median patient duration of exposure to dostarlimab-gxly was 25 weeks, with the range of 1 – 139 weeks.

SIDE EFFECTS AND MANAGEMENT

The most common adverse reactions (≥20%) of dostarlimab-gxly are fatigue/asthenia, nausea, diarrhea, anemia, and constipation. The most common Grade 3 or 4 adverse reactions (≥2%) were anemia and transaminases increased.

A number of immune-mediated toxicities may occur. These may include colitis, dermatologic rash or dermatitis, hepatitis, nephritis, pneumonitis, and endocrinopathies such as adrenal insufficiency, hyperthyroidism, hypophysitis, thyroid disorders, and type 1 diabetes mellitus. Other toxicities have been observed in patients using different PD-1 agents.

No dose reductions are recommended. Withhold dostarlimab-gxly for severe (Grade 3) immune-mediated adverse reactions. Permanently discontinue dostarlimab-gxly for life-threatening (Grade 4) immune-mediated adverse reactions, recurrent severe (Grade 3) immune-mediated reactions that require systemic immunosuppressive treatment, or an inability to reduce corticosteroid dose to 10 mg or less of prednisone equivalent per day within 12 weeks of initiating steroids, with guidance from the clinician.

Management of administration with notable side effects of dostarlimab-gxly

Adverse event	Common management guidance
Pneumonitis	Grade 2: Withhold Grade 3 or 4: Permanently discontinue
Colitis	Grade 2: Withhold Grade 3: Withhold or permanently discontinue Grade 4: Permanently discontinue
Endocrinopathies	Grade 2, 3 or 4: Withhold until stable (obtain clinical guidance on hormonal therapies)
Hepatitis with no tumors in the liver	Withhold: ALT or AST increases to more than 3 and up to 8 times the upper limit normal (ULN) or total bilirubin increases to more than 1.5 and up to 3 times ULN Permanently discontinue: ALT or AST increases to more than 8 times ULN or total bilirubin increases to more than 3 times the ULN
Hepatitis with liver tumors	Withhold: AST or ALT is more than 1 and up to 3 times ULN at baseline and increases to more than 5 and up to 10 times ULN or AST or ALT is more than 3 and up to 5 times ULN at baseline and increases to more than 8 and up to 10 times ULN Permanently discontinue: ALT or AST increases to more than 10 times ULN or total bilirubin increases to more than 3 times ULN
Intestinal Perforation	Any Grade: Permanently discontinue
Myocarditis	Grade 2, 3 or 4: Permanently discontinue
Nephritis with Renal Dysfunction	Grade 2 or 3 increased blood creatinine: Withhold Grade 4 increased blood creatinine: Permanently discontinue

Other side effects

The table below shows management strategies for other side effects associated with dostarlimab-gxly.

Management of other notable side effects of dostarlimab-gxly

Adverse event	Common management guidance
Exfoliative dermatologic conditions	Suspected Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), or Drug Rash with Eosinophilia and Systemic Symptoms (DRESS): Withhold dostarlimab Confirmed SJS, TEN, DRESS: Permanently discontinue
Neurological toxicities	Grade 2: Withhold Grade 3 or 4: Permanently discontinue
Infusion-related reactions	Grade 1 or 2: Interrupt or slow the rate of the infusion Grade 3 or 4: Permanently discontinue

KEY TAKEAWAY ABOUT DOSTARLIMAB-GXLY ADMINISTRATION

- Educate patients and caregivers about side effects and the importance of reporting symptoms as soon as possible. Remind patients about the importance of staying on schedule.

QUESTIONS & ANSWERS

Q. How long will patients stay on dostarlimab-gxly?

A. The prescribing information indicates until disease progression (unless the patient is otherwise deriving clinical benefit) or unacceptable toxicity. In the clinical trial, some patients with progressive disease continued to benefit. There is currently no consensus on strategies for treatment past progression or at which point the patient should be switched to an alternative treatment

Q. Are there standard dose reductions for adverse events?

A. There are no dosage reductions are recommended. The dose is either withheld until the Grade 2 or Grade 3 event resolves sufficiently (typically to Grade 0 or Grade 1) or, if the event is Grade 4, dostarlimab-gxly is discontinued permanently.

Q. How do you modify doses in a patient experiences a severe adverse event?

A. Patients who experience severe (Grade 3) reactions will have the drug withheld. Sometimes, Grade 2 reactions, in the case of colitis, will also result in the drug being withheld. There are no dose modifications for this drug. It is permanently discontinued in the case of Grade 4 adverse reactions. Doses are not escalated. For some toxicities, dostarlimab-gxly can be restarted at the same dose following resolution to < Grade 1 or baseline.

Q. How often do patients discontinue dostarlimab-gxly due to adverse events?

A. There is a low rate of discontinuation due to adverse events. In the clinical trial, 0.7% of patients discontinued dostarlimab-gxly due to pneumonitis, 0% of patients discontinued dostarlimab-gxly due to colitis or nephritis.

The majority of severe adverse events with dostarlimab-gxly tend to occur early during treatment initiation.

Q. What are possible side effects of dostarlimab-gxly combination therapy vs monotherapy?

A. Patients who were dMMR/MSI-H that were given dostarlimab-gxly with carboplatin and paclitaxel most commonly reported rash, diarrhea, decreased thyroid function, and high blood pressure. Patients who were dMMR/MSI-H that were given dostarlimab-gxly monotherapy most commonly reported tiredness and weakness, low red blood cell counts (anemia), diarrhea, nausea, constipation and vomiting.

PATIENT RESOURCES

ADDITIONAL INFORMATION RESOURCES

American Cancer Society
Patient programs, services, 24/7 hotline, etc
https://www.cancer.org/

National Cancer Institute
Information about cancer types, treatment, side effects, find a clinical trial, etc
https://www.cancer.gov/

FINANCIAL ASSISTANCE

Cancer Financial Aid Coalition
Facilitates communication, educates and advocates for patients.
www.cancerfac.org

Centers for Medicare and Medicaid Services (CMS)
Apply to determine if you are eligible for government assistance.
www.cms.gov or www.medicare.gov
800-633-4227

Lazarex Foundation
Provides assistance with travel costs for clinical trial participation. Ask your social work counselor for a referral if you have been consented to a clinical trial for melanoma.
www.lazarex.org

Needymeds
Database to search for free or low-cost medications, help with medical transportation and other resources.
www.needymeds.org

Patient Advocate Foundation
Provides assistance with mediation, financial stability, and other assistance. Funds subject to availability. Patient must meet their eligibility for financial assistance.
www.patientadvocate.org
800-532-5274

The Sam Fund for Young Adult Survivors of Cancer
Assists cancer survivors ages 21-39 with their transition into post-treatment life. This program distributes grants and scholarships in an effort to enable survivors to pursue goals.
www.thesamfund.org
info@thesamfund.org

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PRESCRIPTION ASSISTANCE

CancerCare Co-Payment Assistance Foundation
Helps with the cost of medication. Availability of funds for patients with specific cancers is subject to availability.
www.cancercarecopay.org
1-866-552-6729

Medicine Assistance Tool
Database to search for patient assistance resources offered by pharmaceutical companies.
www.medicineassistancetool.org/

Patient Advocate Foundation Co-Pay Relief
Provides direct financial support to patients who medically qualify. Funds subject to availability.
https://copays.org
1-866-512-3861

Good Days
Provides assistance with insurance co-pays, and prescription medications. Funds subject to availability.
www.mygooddays.org

Health Well Foundation
For patients who cannot afford insurance premiums, co-payments, co-insurance, or other out-of-pocket health care costs. Funds for patients subject to availability. Patient must also meet eligibility for financial assistance.
www.healthwellfoundation.org or grants@healthwellfoundation.org
1-800-675-8416

The Assistance Fund, Inc
Provides prescription copay and financial assistance, including health insurance premiums. Funds subject to availability.
www.theassistancefund.org
https://tafcares.org
1-855-845-3663

PAN Foundation
Provides financial assistance to cover out-of-pocket treatment costs. Funds subject to availability.
www.panfoundation.org
1-866-316-PANF (7263)

Patient Assistance Program
Comprehensive database of patient assistance programs offering free medications.
www.rxassist.org
info@rxassist.org

HOUSING

American Cancer Society – Hope Lodge
Provides free housing during treatment appointments. Requires a referral from your social worker.
www.cancer.org/
1-800-227-6333.

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American Cancer Society – Extended Stay America
Partnership to offer discounted rooms for patients who have to be away from home for cancer treatment.
https://www.cancer.org/about-us/our-partners/extended-stay-america.html
1-800-227-2345

Healthcare Hospitality Network
Connects patients and their caregivers looking for lodging near their healthcare provider
https://members.hhnetwork.org/locate-a-house
1-800-318-8861

Joe's House
Helping patients with cancer find lodging throughout the U.S.
https://www.joeshouse.org/lodging?state=0
1-877-563-7468

National Council of State Housing Agencies
Emergency rental assistance programs available by state. Federal grants still available in some areas.
https://www.ncsha.org/emergency-housing-assistance/

TRANSPORTATION (AIR AND GROUND)

Air Charity Network
Provides access for people in need who are seeking free air transportation to specialized health care facilities
http://aircharitynetwork.org/
1-877-621-7177

Corporate Angel Network
Nonprofit organization that helps cancer patients by arranging free travel on corporate aircraft
https://www.corpangelnetwork.org/
info@corpangelnetwork.org
1-914-328-1313

Medicaid
Ground transportation only. Sets up rides and provides mileage reimbursement for Medicaid patients only.
1-877-633-8747

Mercy Medical Angels
Provides free medical transportation (flights, gas cards, bus and train tickets) for patients with financial needs who need to travel more than 50 miles. Patients must meet their eligibility for financial assistance.
www.mercymedical.org/

Pilots for Patients
Provides free flights to people in need of medical treatment. Patient must be medically stable to fly and be ambulatory. Ask your social worker about a referral.
www.pilotsforpatients.org
318-322-5112

ADDITIONAL RESOURCES

Mirza MR, Chase DM, Slomovitz BM et al. Dostarlimab for Primary Advanced or Recurrent Endometrial Cancer. *N Engl J Med*. 2023;388(23):2145-2158. doi: 10.1056/NEJMoa2216334.

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