The Medical Letter®

on Drugs and Therapeutics

Volume 65 Published online August 21, 2023

Online Article

IN THIS ISSUE

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IN BRIEF

A New Endometrial Cancer Indication for Dostarlimab *(Jemperli)*

The immune checkpoint inhibitor dostarlimab-gxly (*Jemperli* – GSK) has been approved by the FDA for use in combination with carboplatin and paclitaxel for treatment of adults with mismatch repair deficient (dMMR) or microsatellite instability-high (MSI-H) primary advanced or recurrent endometrial cancer. Dostarlimab was recently granted regular approval for treatment of adults with dMMR recurrent or advanced endometrial cancer that progressed on or following a prior platinum-containing regimen in any setting and who are not candidates for curative surgery or radiation.[1]

MECHANISM OF ACTION — Binding of PD-L1 and PD-L2 to programmed death receptor-1 (PD-1) on T cells supresses T-cell proliferation and cytokine production. Dostarlimab binds to PD-1 on T cells, blocking its interaction with PD-L1 and PD-L2 and restoring T-cell antitumor immune responses. dMMR tumors are more responsive to PD-1 blockade than mismatch repair-proficient tumors.

CLINICAL STUDIES — FDA approval of the new indication was based on the results of a double-blind trial (RUBY) in 494 patients with primary advanced (stage III or IV) endometrial cancer or a first recurrence of endometrial cancer. Patients were randomized to receive dostarlimab or placebo in addition to carboplatin and paclitaxel every 3 weeks for 6 cycles, followed by dostarlimab or placebo alone every 6 weeks for up to 3 years. In the 118 patients with dMMR/MSI-H tumors, estimated progression free survival (PFS) at 24 months was 61.4% in the dostarlimab arm and 15.7% in the placebo arm, a statistically significant difference. In the overall population, estimated PFS at 24 months was also statistically significantly higher in the dostarlimab arm compared to the placebo arm (36.1% vs 18.1%). Overall survival at 24 months was 71.3% with dostarlimab and 56.0% with placebo.[2]

ADVERSE EFFECTS — Infusion-related reactions and severe immune-mediated adverse reactions, including pneumonitis, colitis, hepatitis, endocrinopathies, nephritis with renal dysfunction, and skin reactions, can occur with use of dostarlimab. Serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after a PD-1/PDL1 blocking antibody. Liver enzymes, creatinine, and thyroid function should be assessed before starting and periodically during treatment. The drug should be discontinued in patients who experience grade 4 immune-mediated adverse reactions.

DOSAGE, ADMINISTRATION, AND COST — The recommended dosage of dostarlimab for the new indication is 500 mg administered IV over 30 minutes every 3 weeks for 6 doses with carboplatin and paclitaxel, followed by 1000 mg every 6 weeks until disease progression or unacceptable toxicity occurs or up to 3 years. Dostarlimab should be given before chemotherapy if they are both given on the same day. The label includes dosage modifications that should be made if adverse effects occur. The wholesale acquisition cost of one 1000-mg dose of *Jemperli* is $21,900.[3] ■

1. Dostarlimab (Jemperli) for endometrial cancer. Med Lett Drugs Ther 2023; 65:e64.
2. MR Mirza et al. Dostarlimab for primary advanced or recurrent endometrial cancer. N Engl J Med 2023; 388:2145.
3. Approximate WAC. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. August 5, 2023. Reprinted with permission by First Databank, Inc. All rights reserved. ©2023. www.fdbhealth.com/policies/drug-pricing-policy.

The Medical Letter® Vol. 65 Published online August 21, 2023

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