Submitted By:

Alexis Williams, PharmD, RPh
Global Medical Information Manager – Oncology
Global Medical Information
GlaxoSmithKline
5 Moore Drive, PO Box 13398, RTP, NC 27709-3398
alexis.8.williams@gsk.com

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NCCN Guidelines Panel: Uterine Neoplasms

On behalf of GSK, we respectfully resubmit to the NCCN Uterine Neoplasms Panel the enclosed clinical data for *Jemperli* (dostarlimab-gxly) for the Panel's consideration.

FDA Clearance: *Jemperli* (dostarlimab-gxly) is indicated for the treatment of adult patients with mismatch repair deficient (dMMR) recurrent or advanced endometrial cancer (EC), as determined by an FDA-approved test, that has progressed on or following prior treatment with a platinum-containing regimen. 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).[1]

Dostarlimab-gxly is not approved for the treatment of patients with mismatch repair proficient (MMRp) EC.

Rationale: This data is being submitted in response to a standing request from NCCN for new data.

We respectfully ask the NCCN Panel to consider, on page ENDO-D1, adding dostarlimab-gxly as a monotherapy treatment option for patients with recurrent or advanced EC that has progressed on or following prior treatment with a platinum-containing regimen whose tumors are MMRp.

GARNET is currently the largest study specifically evaluating the activity of single agent anti-PD-1 therapy, dostarlimab-gxly, in patients with recurrent or advanced EC that have progressed on or after treatment with a platinum-containing regimen.[2] In the GARNET study, dostarlimab-gxly was administered via intravenous (IV) infusion at a dosage of 500 mg every 3 weeks for the first 4 doses, followed by 1000 mg every 6 weeks until disease progression or unacceptable toxicity.[2] Results of an interim analysis from the MMRp EC cohort (Cohort A2) of the GARNET trial were presented at the 2020 European Society of Medical Oncology Annual Conference and at the 2020 European Society of Gynaecological Oncology Conference.[3,4] In addition, the time course of adverse events during dostarlimab-gxly treatment in patients with MMRp EC enrolled in the GARNET trial was presented at the 2021 Oncology Nursing Society (ONS) Annual Conference.[5] To summarize results:

Efficacy Results[3,4]

- One-hundred and forty-two patients were included in the interim efficacy analysis (data cutoff March 1, 2020).
- After a median follow-up of 11.5 months, the objective response rate (ORR) (primary endpoint) was 13.4% (95% CI, 8.3–20.1). The disease control rate (DCR) (secondary endpoint) was 35.2% (95% CI, 27.4–43.7); 2.1% complete response, 11.3% partial response, 21.8% stable disease.
- Median duration of response (DOR, primary endpoint) was not reached (range, 1.54+ to 30.36+ mos). The Kaplan–Meier estimated probability of remaining in response at 6, 12, and 18 mos was 83.0%, 61.3%, and 61.3%, respectively.

Safety Results

- One-hundred forty-five patients were included in the interim safety analysis.[3,4]
- Most treatment-related adverse events (TRAEs) were grade 1-2. The most common (top 3) any-grade TRAEs were fatigue, nausea, and diarrhea (20.7%, 14.5%, 13.1%, respectively).[3,4]

- Immune-related TRAEs (irTRAEs) reported in ≥ 4 patients were hypothyroidism, diarrhea, aspartate aminotransferase (AST) increased, and hyperglycemia (7.6%, 3.4%, 2.8% and 2.8%; respectively). Grade ≥ 3 irTRAEs reported in ≥ 1% of patients were AST increased (2.1%), hyperglycemia (2.1%), ALT increased (1.4%), diarrhea (1.4%), and amylase increased (1.4%).[3]
- Ten (6.9%) patients discontinued treatment due to TRAEs, including 2 (1.4%) patients due to ALT increased and 1 (0.7%) patient due to AST increased. There were no deaths attributed to dostarlimab-gxly by the investigators.[3,4]
- No increase in the rate of TRAEs or irTRAEs was observed when transitioning from the 500 mg every 3 weeks dose to the 1000 mg every 6 weeks dose of dostarlimab-gxly.[5]

Summary

GARNET is currently the largest prospective study specifically evaluating the activity of single agent anti-PD-1 therapy in recurrent or advanced MMRp EC that has progressed on or after treatment with a platinum-containing regimen.[2] The GARNET study interim analysis demonstrated an ORR of 13.4%, durable antitumor activity, and a disease control rate of 35.2% in a cohort of patients with a high percentage of Type 2 EC histologies (77%)[3,4], which historically have been associated with a poor prognosis.[6] Most TRAEs were grade 1 or 2, and 10 out of 145 patients (6.9%) discontinued treatment due to a TRAE.[3,4] No increase in the rate of TRAEs or irTRAEs was observed when transitioning from the 500 mg every 3 weeks dose to the 1000 mg every 6 weeks dose of dostarlimab-gxly.[5]

We appreciate the Panel's consideration of dostarlimab-gxly as a potential anti-PD-1 monotherapy treatment option for MMRp EC based on the enclosed data. If any questions arise or if you require any additional information, please do not hesitate to contact Alexis Williams, Pharm D, RPh at alexis.8.williams@gsk.com.

Sincerely,

Alexis Williams, PharmD, RPh
Global Medical Information Manager – Oncology
Global Medical Information
GlaxoSmithKline

Tedi Soule, PharmD
Medical Affairs Leader
US Medical Affairs Oncology
GlaxoSmithKline

Please find the attached enclosures in support of this submission.

Bibliography

1. *Jemperli* [package insert]. Research Triangle Park, NC: GlaxoSmithKline, Inc.
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4. Oaknin A, Gilbert L, Tinker AV, et al. Safety and antitumor activity of dostarlimab in patients with recurrent or advanced mismatch repair deficient (dMMR) or proficient (MMRp) endometrial cancer: Results from GARNET. Oral Presentation at the European Society of Medical Oncology (ESMO) Annual Congress (Virtual). September 18th, 2020. Presentation ID LBA36. doi: https://doi.org/10.1016/j.annonc.2020.08.2266.
5. Oaknin A, Gilbert L, Tinker A, et al. The Time Course of Adverse Events During Dostarlimab Treatment in Mismatch Mutation Repair Deficient and Proficient Endometrial Cancer Patients in the GARNET Trial. Oral Presentation by Dr. Pothuri at The 46th Annual Oncology Nursing Society's (ONS) Congress (Virtual). April 20, 22, 27, and 29, 2021. Abstract #10455
6. Kloor M, von Knebel Doeberitz M. The Immune Biology of Microsatellite-Unstable Cancer. *Trends Cancer*. 2016;2(3):121-133. doi:http://dx.doi.org/10.1016/j.trecan.2016.02.004.