GSK receives positive CHMP opinion recommending approval of Jemperli (dostarlimab) plus chemotherapy as a new frontline treatment for dMMR/MSI-H primary advanced or recurrent endometrial cancer

PUBLISHED OCT 16, 2023
BY GSK

For media and investors only

- If approved, dostarlimab would become the first new frontline treatment option in the European Union (EU) in decades and the only immuno-oncology combination regimen available for this patient population with high unmet need

- Decision on EU marketing authorisation expected by the end of the year

GSK plc (LSE/NYSE: GSK) today announced the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion recommending approval of Jemperli (dostarlimab) in combination with carboplatin-paclitaxel (chemotherapy), for the treatment of adult patients with mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H) primary advanced or recurrent endometrial cancer and who are candidates for systemic therapy. The CHMP opinion is one of the final steps prior to a marketing authorisation decision by the European Commission.

Hesham Abdullah, Senior Vice President, Global Head Oncology, R&D, GSK, said:

> We are pleased with this positive CHMP opinion and the

> potential for dostarlimab with chemotherapy to treat patients with this very challenging form of endometrial cancer. If approved, dostarlimab plus chemotherapy will be the first new treatment option in decades for these patients in the European Union, offering long-awaited new hope for improved long-term outcomes. This opinion further reinforces our confidence in dostarlimab's important role in the immuno-oncology treatment landscape.

GSK's application for the authorisation of dostarlimab is based on interim analysis results from Part 1 of the RUBY/ENGOT-EN6/GOG3031/NSGO phase III trial, which were presented at the European Society for Medical Oncology (ESMO) Virtual Plenary and Society of Gynecologic Oncology (SGO) Annual Meeting on 27 March 2023, and simultaneously published in The New England Journal of Medicine. The trial results reflect a robust median duration of follow-up of ≥ 25 months. Part 1 of the RUBY trial met its primary endpoint of investigator-assessed progression-free survival (PFS) in patients treated with dostarlimab plus carboplatin and paclitaxel in the dMMR/MSI-H population. In the dMMR/MSI-H population, a 72% reduction in the risk of disease progression or death was observed (HR: 0.28 [95% CI: 0.16-0.50]).

In a prespecified, exploratory analysis of overall survival (OS) in the dMMR/MSI-H population, the addition of dostarlimab to chemotherapy resulted in a 70% reduction in the risk of death relative to chemotherapy alone (HR: 0.30 [95% CI: 0.13-0.70]).

The safety and tolerability profile for dostarlimab plus carboplatin and paclitaxel was generally consistent with the known safety profiles of the individual agents. The most common adverse reactions (≥ 10%) in patients receiving dostarlimab plus chemotherapy were rash, hypothyroidism (underactive thyroid), increased alanine aminotransferase or increased aspartate aminotransferase (increased liver enzyme levels in the blood), pyrexia (fever) and dry skin.

This opinion follows the July 2023 expansion of the label for Jemperli in the US to include this indication. The new indication for Jemperli was reviewed under the FDA Oncology Center of Excellence Project Orbis framework, which allowed for concurrent submission to and review by US and other international regulatory authorities. As part of Project Orbis, Jemperli was also approved in the United Kingdom

earlier this month in combination with platinum-containing chemotherapy for the treatment of adult patients with dMMR/MSI-H primary advanced or recurrent endometrial cancer and who are candidates for systemic therapy. The application remains under review in Australia, Canada, Switzerland and Singapore.

In the EU, Jemperli currently has conditional approval as a monotherapy for treating adult patients with dMMR/MSI-H recurrent or advanced endometrial cancer that has progressed on or following prior treatment with a platinum-containing regimen. If the European Commission approves the frontline indication for Jemperli plus chemotherapy, this conditional approval is expected to be converted to full approval at the same time. A decision is expected by the end of this year.

Endometrial cancer is found in the inner lining of the uterus, known as the endometrium. Endometrial cancer is the most common gynaecologic cancer in developed countries, with approximately 417,000 new cases reported each year worldwide 1, and incidence rates are expected to rise by almost 40% by 2040. 2, 3 Approximately 15-20% of patients with endometrial cancer will be diagnosed with advanced disease at the time of diagnosis. 4 An estimated 20-29% of all endometrial cancers are dMMR/MSI-H 5. In the EU4 (France, Germany, Italy and Spain), approximately 3,000 people are estimated to be diagnosed with dMMR/MSI-H primary advanced or recurrent endometrial cancer each year 6.

RUBY is a two-part global, randomised, double-blind, multicentre phase III trial of patients with primary advanced or recurrent endometrial cancer. Part 1 is evaluating dostarlimab plus carboplatin-paclitaxel followed by dostarlimab versus carboplatin-paclitaxel plus placebo followed by placebo. Part 2 is evaluating dostarlimab plus carboplatin-paclitaxel followed by dostarlimab plus niraparib versus placebo plus carboplatin-paclitaxel followed by placebo.

The dual-primary endpoints in Part 1 are investigator-assessed PFS based on the Response Evaluation Criteria in Solid Tumours v1.1 and OS. The statistical analysis plan included pre-specified analyses of PFS in the dMMR/MSI-H and ITT populations and OS in the ITT population. Pre-specified exploratory analyses of PFS in the mismatch repair proficient (MMRp)/microsatellite stable (MSS) population and OS in the dMMR/MSI-H populations were also performed. RUBY Part

1 included a broad population, including histologies often excluded from clinical trials and had approximately 10% of patients with carcinosarcoma and 20% with serous carcinoma. In Part 2, the primary endpoint is investigator-assessed PFS. Secondary endpoints in Part 1 and Part 2 include PFS per blinded independent central review, overall response rate, duration of response, disease control rate, patient-reported outcomes, and safety and tolerability.

About Jemperli (dostarlimab)

Jemperli is a programmed death receptor-1 (PD-1)-blocking antibody that binds to the PD-1 receptor and blocks its interaction with the PD-1 ligands PD-L1 and PD-L2. 7

In the US, Jemperli is indicated in combination with carboplatin and paclitaxel, followed by Jemperli as a single agent for the treatment of adult patients with primary advanced or recurrent endometrial cancer that is mismatch repair deficient (dMMR), as determined by an FDA-approved test, or microsatellite instability-high (MSI-H), and as a single agent for adult patients with mismatch repair-deficient (dMMR) recurrent or advanced endometrial cancer, as determined by a US FDA-approved test, that has progressed on or following a prior platinum-containing regimen in any setting and are not candidates for curative surgery or radiation. The sBLA supporting the new indication in combination with carboplatin and paclitaxel received Breakthrough Therapy designation from the FDA. Jemperli is also indicated in the US for patients with dMMR recurrent or advanced solid tumours, as determined by a US FDA-approved test, that have progressed on or following prior treatment and who have no satisfactory alternative treatment options. The latter indication is approved in the US under accelerated approval based on tumour response rate and durability of response. Continued approval for this indication in solid tumours may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Jemperli was discovered by AnaptysBio, Inc. and licensed to TESARO, Inc., under a collaboration and exclusive license agreement signed in March 2014. The collaboration has resulted in three monospecific antibody therapies that have progressed into the clinic. These are: Jemperli (GSK4057190), a PD-1 antagonist; cobolimab, (GSK4069889), a TIM-3 antagonist; and GSK4074386, a LAG-3 antagonist. GSK is responsible for the ongoing research,

development, commercialisation, and manufacturing of each of these medicines under the agreement.

Important Information for Jemperli in the EU

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

Refer to the Jemperli EMA Reference Information for a full list of adverse events and the complete important safety information in the EU.

GSK is committed to maximising patient survival through transformational medicines, with a current focus on breakthroughs in immuno-oncology and tumour-cell targeting therapies, and development in haematologic malignancies, gynaecologic cancers and other solid tumours.

GSK is a global biopharma company with a purpose to unite science, technology, and talent to get ahead of disease together. Find out more at gsk.com.

Cautionary statement regarding forward-looking statements

GSK cautions investors that any forward-looking statements or projections made by GSK, including those made in this announcement, are subject to risks and uncertainties that may cause actual results to differ materially from those projected. Such factors include, but are not limited to, those described under Item 3.D 'Risk factors" in the company's Annual Report on Form 20-F for 2022, and Q2 Results for 2023 and any impacts of the COVID-19 pandemic.

Faizan U, Muppidi V. Uterine Cancer. [Updated 2022 Sep 5]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available at: https://www.ncbi.nlm.nih.gov/books/NBK562313/.

Braun MM, et al. Am Fam Physician. 2016;93(6): 468-474.

International Research on Cancer. Global Cancer Observatory. Cancer Tomorrow. https://gco.iarc.fr/tomorrow/en/dataviz/. Accessed 13 July

2022.

Kantar Health, Cust Study (2018).

Cerner Enviza CancerMPact® [Treatment Architecture]. Available from www.cancermpact.com. Accessed 14 Apr 2023.

Based on CMP:CancerMPact® [Patient Metrics], Cerner Enviza. Available from www.cancermpact.com. Accessed 28 Sept 2023.

Laken H, Kehry M, Mcneeley P, et al. Identification and characterization of TSR-042, a novel anti-human PD-1 therapeutic antibody. European Journal of Cancer. 2016;69,S102. doi:10.1016/s0959-8049(16)32902-1.

Press release distributed by Wire Association on behalf of GSK, on Oct 16, 2023. For more information subscribe and follow us.

Media Assets

Embedded Media

Visit the online press release to interact with the embedded media.

https://wireassociation.eu/newsroom/gsk/releases/en/gsk-receives-positive-chmp-opinion-recommending-approval-of-jemperli-dostarlimab-plus-chemotherapy-as-a-new-frontline-treatment-for-dmmrmsi-h-primary-advanced-or-recurrent-endometrial-cancer-1735

GSK

Newsroom: https://wireassociation.eu/newsroom/gsk
Website: https://www.gsk.com/
Primary Email: corporate.media@gsk.com

Social Media

Facebook - https://www.facebook.com/GSK
Twitter - http://twitter.com/GSK
Youtube - http://www.youtube.com/GSK
Linkedin - http://www.linkedin.com/company/glaxosmithkline
Instagram - https://www.instagram.com/gsk/