Phase III RUBY trial of Jemperli (dostarlimab) plus chemotherapy meets endpoint of overall survival in patients with primary advanced or recurrent endometrial cancer

PUBLISHED OCT 30, 2023
BY GSK

For media and investors only

- Statistically significant and clinically meaningful overall survival benefit observed in the overall population in the trial

- Dostarlimab plus chemotherapy is the only immuno-oncology combination regimen to show an overall survival benefit in this patient population

GSK plc (LSE/NYSE: GSK) today announced positive headline results from a planned analysis of Part 1 of the RUBY/ENGOT-EN6/GOG3031/NSGO phase III trial investigating Jemperli (dostarlimab) plus standard-of-care chemotherapy (carboplatin and paclitaxel), followed by dostarlimab as a single agent, compared to placebo plus chemotherapy followed by placebo in adult patients with primary advanced or recurrent endometrial cancer. The trial met its primary endpoint of overall survival (OS), demonstrating a statistically significant and clinically meaningful benefit in the overall patient population.

A clinically meaningful OS benefit was observed in both prespecified subpopulations in the trial: mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H) and mismatch repair proficient (MMRp)/microsatellite stable (MSS) patient subgroups. OS is one of two primary endpoints in the RUBY Part 1 trial. Previously, the trial met its other primary endpoint of progression-free survival (PFS), demonstrating a 72% and 36% reduction in the risk of disease progression or death observed in the dMMR/MSI-H population (HR:

0.28 [95% CI: 0.16-0.50]) and overall patient population (HR: 0.64 [95% CI: 0.51–0.80]), respectively 1.

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

> With today's headline results from Part 1 of the phase III RUBY trial, dostarlimab plus chemotherapy has become the only immuno-therapy combination to show a survival benefit in this broader patient population in this treatment setting. We look forward to sharing detailed results of this analysis with regulatory authorities and the larger scientific community.

Full results from this latest analysis from the trial will be published in a medical journal and presented at an upcoming scientific meeting.

The safety and tolerability profile of dostarlimab plus carboplatin and paclitaxel was generally consistent with the known safety profiles of the individual agents. The most common treatment-emergent adverse events (≥ 25%) in patients receiving dostarlimab plus chemotherapy were nausea, alopecia, fatigue, peripheral neuropathy, anemia, arthralgia, constipation, diarrhoea and myalgia.

Currently, Jemperli has regulatory approvals in a certain subset of patients with endometrial cancer based on the previously reported positive results for the primary endpoint of progression-free survival in Part 1 of the RUBY trial. In July 2023, Jemperli received FDA approval 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). Jemperli was also approved in the United Kingdom in October 2023 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 the European Union (EU), Australia, Canada, Switzerland and Singapore.

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 2, and incidence

rates are expected to rise by almost 40% between 2020 and 2040. 3, 4 Approximately 15-20% of patients with endometrial cancer will be diagnosed with advanced disease at the time of diagnosis. 5

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 overall population. Pre-specified exploratory analyses of PFS and OS in the MMRp/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. 6

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 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 tumor-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.

Mirza M, et al. N Engl J Med 2023; 388:2145-2158; DOI: 10.1056/NEJMoa2216334

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).

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 30, 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/phase-iii-ruby-trial-of-jemperli-dostarlimab-plus-chemotherapy-meets-endpoint-of-

overall-survival-in-patients-with-primary-advanced-or-recurrent-endometrial-cancer-1728

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/
