European Commission approves GSK's JEMPERLI (dostarlimab), the first anti-PD-1 therapy approved for recurrent or advanced endometrial cancer

PUBLISHED APR 23, 2021
BY GSK

For media and investors only

GlaxoSmithKline (LSE/NYSE: GSK) plc today announced the European Commission has granted conditional marketing authorisation for JEMPERLI (dostarlimab), a programmed death receptor-1 (PD-1)-blocking antibody, for use in women with mismatch repair-deficient (dMMR)/microsatellite instability-high (MSI-H) recurrent or advanced endometrial cancer who have progressed on or following prior treatment with a platinum containing regimen. The approval makes dostarlimab the first anti-PD-1 therapy available for endometrial cancer in Europe.

Dr Hal Barron, Chief Scientific Officer and President R&D, GSK, said:

> Women with recurrent endometrial cancer, or advanced disease that has progressed on or after chemotherapy, currently have limited treatment options and a poor prognosis. Today's approval of dostarlimab means that for the first time in Europe, these women will have access to a new, innovative and much-needed therapy.

Dr Ana Oaknin, Head of the Gynaecologic Cancer Program at Vall d'Hebron Institute of Oncology (VHIO), Vall d'Hebron University Hospital, Barcelona, Spain, and primary investigator for the GARNET Trial, said:

> As we saw in the pivotal GARNET trial that supported this approval, treatment with dostarlimab has the potential to provide clinically significant and durable responses in patients

> who formerly had few treatment options. This approval represents a step forward, providing a new treatment for women with recurrent or advanced dMMR/MSI-H endometrial cancer who have previously failed a platinum-based chemotherapy.

Icó Tóth, Co-Chair of European Network of Gynaecological Cancer Advocacy Groups (ENGAGe), Council member for European Society of Gynaecological Oncology (ESGO), President, Mallow Flower Foundation, Hungary, said:

> Today's approval of dostarlimab offers a new treatment option for women with recurrent or advanced dMMR/MSI-H endometrial cancer. We're inspired by the efforts of companies like GSK who are continuing to innovate for patients in dire need of new options.

Endometrial cancer is found in the inner lining of the uterus, known as the endometrium. It is the most common type of cancer that affects the female reproductive organs and is the sixth most prevalent cancer in women worldwide. Endometrial cancer has the highest rate of the MSI-H phenotype of all tumours.

The European Medicine Agency's approval of dostarlimab is based on results from the multi-cohort GARNET study, which included women with recurrent or advanced dMMR/MSI-H endometrial cancer who progressed on or after a platinum-based chemotherapy regimen in cohort A1 (n=108 evaluable for efficacy). Treatment with dostarlimab resulted in an objective response rate (ORR) of 43.5% (95% CI; 34-53.4) and a disease control rate of 55.6% (95% CI; 45.7-65.1). The median duration of response (DoR) had not been reached (2.6 to 28.1+ months) in these patients, and the probability of maintaining a response at six months and 12 months was 97.9% (95% CI; 85.8, 99.7) and 90.9% (95% CI; 73.7, 97.1), respectively.

In the 515 patients with advanced or recurrent solid tumours who participated in the GARNET study, including 129 patients evaluable for safety from cohort A1, the most common adverse reactions (occurring in more than 10% of patients) were anaemia (25.6%), nausea (25.0%), diarrhoea (22.5%), vomiting (18.4 %), arthralgia (13.8 %), pruritus (11.5%), rash (11.1%), pyrexia (10.5%) and hypothyroidism (10.1%). Dostarlimab was permanently discontinued due to adverse reactions in 17 patients (3.3%); most were immune-

related events. Serious adverse reactions occurred in 8.7% of patients; most were immune-related adverse reactions. The safety profile for patients in cohort A1 was comparable with the overall study population.

GSK is also studying dostarlimab for endometrial cancer in earlier treatment lines and in combination with other therapeutic agents for patients with advanced solid tumours or metastatic cancer as we work to expand our oncology pipeline and reinforce our portfolio of cancer treatments.

The ongoing phase 1 GARNET trial is evaluating dostarlimab as monotherapy in patients with advanced solid tumours. Part 2B of the study includes five expansion cohorts: dMMR/MSI-H endometrial cancer (cohort A1), mismatch repair proficient/microsatellite stable (MMRp/MSS) endometrial cancer (cohort A2), non-small cell lung cancer (cohort E), dMMR/MSI-H non-endometrial or POLE-mut solid tumour basket cohort (cohort F), and platinum-resistant ovarian cancer without BRCA mutations (cohort G). GARNET is ongoing and enrolling patients in certain cohorts.

About JEMPERLI (dostarlimab)

Dostarlimab is a programmed death receptor-1 (PD-1)-blocking antibody that binds with high affinity to the PD-1 receptor and blocks its interaction with the ligands PD-L1 and PD-L2. In addition to GARNET, dostarlimab is being investigated in other registrational-enabling studies, as monotherapy and as part of combination regimens for women with recurrent or primary advanced endometrial cancer stage III or IV non-mucinous epithelial ovarian cancer for patients with advanced solid tumours or metastatic cancer.

Dostarlimab was discovered by AnaptysBio and licensed to TESARO, Inc., under a Collaboration and Exclusive License Agreement signed in March 2014. The collaboration has resulted in three monospecific antibody drugs that have progressed into the clinic. These are: dostarlimab (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 manufacture of each of these products under the Agreement.

Important Information for JEMPERLI in the EU

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

Immune-Mediated Adverse Reactions

Immune-related adverse reactions, which may be severe or fatal, can occur in patients treated with antibodies blocking the programmed cell death protein-1 / programmed death-ligand 1 (PD-1/PD-L1) pathway, including JEMPERLI. While immune-related adverse reactions usually occur during treatment with PD-1/PD-L1 blocking antibodies, symptoms can also manifest after discontinuation of treatment. Immune-related adverse reactions may occur in any organ or tissue and may affect more than one body system simultaneously. Important immune-related adverse reactions listed in this section are not inclusive of all possible severe and fatal immune-related reactions.

Early identification and management of immune-related adverse reactions are essential to ensure safe use of PD-1/PD-L1 blocking antibodies. Patients should be monitored for symptoms and signs of immune-related adverse reactions. Clinical chemistries, including liver tests and thyroid function tests, should be evaluated at baseline and periodically during treatment. For suspected immune-related adverse reactions, adequate evaluation including specialty consultation should be ensured.

Based on the severity of the adverse reaction, treatment with JEMPERLI should be withheld or permanently discontinued and corticosteroids (1 to 2 mg/kg/day prednisone or equivalent) or other appropriate therapy administered. Upon improvement to Grade ≤1, corticosteroid taper should be initiated and continued for 1 month or longer. Based on limited data from clinical studies in patients whose immune-related adverse reactions could not be controlled with corticosteroid use, administration of other systemic immunosuppressants can be considered. Hormone replacement therapy for endocrinopathies should be instituted as warranted.

Treatment with JEMPERLI should be permanently discontinued for any Grade 3 immune-related adverse reaction that recurs and for any Grade 4 immune-related adverse reaction toxicity, except for

endocrinopathies that are controlled with replacement hormones and unless otherwise specified in the Summary of Product Characteristics (SmPC).

Immune-Related Pneumonitis

Pneumonitis has been reported in patients receiving JEMPERLI. Patients should be monitored for signs and symptoms of pneumonitis. Suspected pneumonitis should be confirmed with radiographic imaging and other causes excluded. Patients should be managed with JEMPERLI treatment modifications and corticosteroids.

Immune-related pneumonitis occurred in 7 (1.4%) of 515 patients, including Grade 2 (1.2%) and Grade 3 (0.2%) pneumonitis. Pneumonitis led to discontinuation of JEMPERLI in 3 (0.6%) patients. Systemic corticosteroids (prednisone ≥ 40 mg per day or equivalent) were required in all 7 patients experiencing pneumonitis. Pneumonitis resolved in 6 (85.7%) patients.

JEMPERLI can cause immune-related colitis. Patients should be monitored for signs and symptoms of colitis and managed with treatment modifications, anti-diarrhoeal agents and corticosteroids.

Colitis occurred in 8 (1.6%) patients, including Grade 2 (1.0%) and Grade 3 (0.6%) colitis. Colitis did not lead to discontinuation of JEMPERLI in any patients. Systemic corticosteroids (prednisone ≥ 40 mg per day or equivalent) were required in 2 (28.6%) patients. Colitis resolved in 6 (75.0%) patients experiencing colitis.

JEMPERLI can cause immune-related hepatitis. Patients should be monitored for changes in liver function periodically as indicated, based on clinical evaluation and managed with JEMPERLI treatment modifications and corticosteroids.

Hepatitis occurred in 1 (0.2%) patient, which was Grade 3. Systemic corticosteroids (prednisone ≥ 40 mg per day or equivalent) were required. Hepatitis did not lead to discontinuation of JEMPERLI and resolved.

Immune-Mediated Endocrinopathies

Hypothyroidism occurred in 37 (7.2%) patients, all of which were Grade 2. Hypothyroidism did not lead to discontinuation of JEMPERLI

and resolved in 13 (35.1%) patients.

Hyperthyroidism occurred in 10 (1.9%) patients, including Grade 2 (1.7%) and Grade 3 (0.2%). Hyperthyroidism did not lead to discontinuation of JEMPERLI and resolved in 8 (80%) patients.

Thyroiditis occurred in 2 (0.4%) patients; both were Grade 2. Neither event of thyroiditis resolved; there were no discontinuations of JEMPERLI due to thyroiditis.

Adrenal insufficiency occurred in 7 (1.4%) patients, including Grade 2 (0.8%), and Grade 3 (0.6%). Adrenal insufficiency resulted in discontinuation of JEMPERLI in 1 (0.2%) patient and resolved in 2 (28.6%) patients.

Nephritis, including tubulointerstitial nephritis, occurred in 3 (0.6%) patients; all were Grade 2. Systemic corticosteroids (prednisone ≥ 40 mg per day or equivalent) were required in 2 (66.7%) patients experiencing nephritis. Nephritis led to discontinuation of JEMPERLI in 1 (0.2%) patient and resolved in 2 of 3 (66.7%) patients.

Immune-related rash occurred in 17 (3.3%) patients, including Grade 3 in 6 (1.2%) patients receiving JEMPERLI. The median time to onset of rash was 41 days (range 2 days to 407 days). Systemic corticosteroids (prednisone ≥ 40 mg per day or equivalent) were required in 5 (29%) patients experiencing rash. Rash did not lead to discontinuation of JEMPERLI and resolved in 13 (76.5%) patients.

Immune-related arthralgia occurred in 21 (4.1%) patients. Grade 3 immune-related arthralgia was reported in 3 (0.6%) patients receiving JEMPERLI. The median time to onset of arthralgia was 87 days (range 1 day to 783 days). Systemic corticosteroids (prednisone ≥ 40 mg per day or equivalent) were required in 2 (9.5%) patients experiencing arthralgia. Arthralgia did not lead to discontinuation of JEMPERLI and resolved in 8 (38%) patients experiencing arthralgia.

Other Immune-Related Adverse Reactions

Given the mechanism of action of JEMPERLI other potential immune-related adverse reactions may occur, including potentially serious events [e.g. myositis, myocarditis, encephalitis, demyelinating neuropathy (including Guillain Barré syndrome), sarcoidosis].

Clinically significant immune-related adverse reactions reported in less than 1% of patients treated with JEMPERLI as monotherapy in clinical studies include autoimmune haemolytic anaemia, pancreatitis, iridocyclitis, uveitis and diabetic ketoacidosis. Patients should be monitored for signs and symptoms of immune-related adverse reactions and managed as described in the SmPC.

Solid organ transplant rejection has been reported in the post-marketing setting in patients treated with PD-1 inhibitors. Treatment with JEMPERLI may increase the risk of rejection in solid organ transplant recipients. The benefit of treatment with JEMPERLI versus the risk of possible organ rejection should be considered in these patients.

Fatal and other serious complications can occur in patients who receive allogeneic haematopoietic stem cell transplantation (HSCT) before or after being treated with a PD-1/PD-L1–blocking antibody. Transplant-related complications include hyperacute graft-versus-host disease (GvHD), acute GvHD, chronic GvHD, hepatic veno-occlusive disease after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between PD-1/PD-L1 blockade and allogeneic HSCT. Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/PD-L1–blocking antibody prior to or after an allogeneic HSCT.

Infusion-Related Reactions

Infusion-related reactions including hypersensitivity occurred in 7 (1.4%) patients, including Grade 2 (1.2%) and Grade 3 (0.2%) infusion-related reactions. All patients recovered from the infusion-related reaction.

Anti-drug antibodies (ADA) were tested in 315 patients who received JEMPERLI and the incidence of JEMPERLI treatment-emergent ADAs was 2.5%. Neutralising antibodies were detected in 1.3% of patients. In the patients who developed anti-JEMPERLI antibodies, there was no evidence of altered efficacy or safety of JEMPERLI.

Of the 515 patients treated with JEMPERLI monotherapy, 50.7% were under 65 years, 37.9% were 65-75 years, and 11.5% were 75 years or older. No overall differences in safety were reported between elderly

(≥ 65 years) and younger patients (

Pregnancy, Lactation and Fertility

JEMPERLI is not recommended during pregnancy and in women of childbearing potential not using contraception. JEMPERLI should not be used during breast-feeding and breast-feeding should be avoided for at least 4 months after the last dose of JEMPERLI. Fertility studies have not been conducted with JEMPERLI.

JEMPERLI is most commonly associated with immune-related adverse reactions. Most of these, including severe reactions, resolved following initiation of appropriate medical therapy or withdrawal of JEMPERLI.

In patients with advanced or recurrent solid tumours (N = 515), the most common adverse reactions (> 10%) were anaemia (25.6%), nausea (25.0%), diarrhoea (22.5%), vomiting (18.4%), arthralgia (13.8%), pruritus (11.5%), rash (11.1%), pyrexia (10.5%) and hypothyroidism (10.1%). JEMPERLI was permanently discontinued due to adverse reactions in 17 (3.3%) patients; most of them were immune-related events. Adverse reactions were serious in 8.7% of patients; most serious adverse reactions were immune-related adverse reactions.

Refer to the JEMPERLI Prescribing Information for a full list of adverse events and the complete important safety information.

GSK is focused on maximising patient survival through transformational medicines. GSK's pipeline is focused on immuno-oncology, cell therapy, cancer epigenetics and synthetic lethality. Our goal is to achieve a sustainable flow of new treatments based on a diversified portfolio of investigational medicines utilising modalities such as small molecules, antibodies, antibody drug conjugates and cells, either alone or in combination.

GSK is a science-led global healthcare company with a special purpose: to help people do more, feel better, live longer. For further information please visit www.gsk.com/about-us.

Cautionary statement regarding forward-looking statements

GSK cautions investors that any forward-looking statements or

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