News Release

Health Canada Approves KEYTRUDA® for the treatment of adult patients with FIGO 2014 Stage III-IVA cervical cancer, in combination with chemoradiotherapy (CRT)[1]

Approval is based on the results from phase III KEYNOTE-A18/ENGOT-cx11/GOG-3047[2]

KIRKLAND, QC., July 17, 2025 – Merck (NYSE: MRK), known as MSD outside of the United States and Canada, announced today that Health Canada has granted approval for KEYTRUDA® (pembrolizumab), Merck's anti-PD-1 therapy, in combination with chemoradiotherapy (CRT) for the treatment of FIGO (International Federation of Gynecology and Obstetrics) 2014 Stage III-IVA cervical cancer.[1,2] The approval is based on data from the Phase 3 KEYNOTE-A18 trial, also known as ENGOT-cx11/GOG-3047, which demonstrated statistically significant improvements in progression-free survival (PFS) and overall survival (OS) in patients randomized to KEYTRUDA® in combination with CRT compared with patients randomized to placebo plus CRT.[3]

"The approval of KN-A18 is an important addition to the treatment of gynecological cancers, as it has demonstrated a statistically significant improvement in overall survival and progression-free survival in patients with FIGO 2014 Stage III-IVa," stated Shannon Salvador, Gynecologic Oncologist at the Jewish General Hospital and President of the Society of Gynecologic Oncology of Canada.[4] "This recent approval adds another therapeutic option for patients in an important disease space."

"This approval marks a pivotal moment for patients, as it represents the first indication in Canada for KEYTRUDA® in combination with chemoradiotherapy," said André Galarneau, PhD, Executive Director & Vice President, Oncology Business Unit at Merck Canada. "Reaffirming our commitment to cervical cancer, we are eager to continue expanding treatment options for patients impacted by this disease."[5]

About KEYNOTE-A18 / ENGOT-cx11/GOG-3047

KEYNOTE-A18 is a multicenter, randomized, double-blind, placebo-controlled phase III trial (ClinicalTrials.gov, NCT04221945).[2] The trial investigated the efficacy of pembrolizumab in combination with CRT (cisplatin and external beam radiation therapy [EBRT] followed by brachytherapy [BT]) for the treatment of patients with locally advanced cervical cancer.[1]

The trial enrolled 1,060 newly diagnosed patients with locally advanced squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma of the cervix defined as FIGO 2014 stage IB2 to IIB with positive lymph nodes or stage III to IVA regardless of nodal status.[3] There were 599 patients with FIGO 2014 Stage III-IVA.

Randomization was stratified by planned type of EBRT (Intensity modulated radiation therapy [IMRT] or volumetric modulated arc therapy [VMAT] vs. non IMRT and non VMAT), stage at screening of cervical cancer (FIGO 2014 Stage IB2 IIB vs. FIGO 2014 Stage III-IVA), and planned total radiotherapy dose (EBRT + brachytherapy dose of <70 Gy vs. ≥70 Gy as per equivalent dose [EQD2]).[1]

Patients were randomized (1:1) to one of two treatment arms:

- Pembrolizumab 200 mg IV every 3 weeks (5 cycles) concurrent with cisplatin 40 mg/m2 IV weekly (5 cycles, an optional sixth infusion could be administered per local practice) and radiotherapy (EBRT followed by BT), followed by pembrolizumab 400 mg IV every 6 weeks (15 cycles).[1,3]
- Placebo IV every 3 weeks (5 cycles) concurrent with cisplatin 40 mg/m2 IV weekly (5 cycles, an optional sixth infusion could be administered per local practice), and radiotherapy (EBRT followed by BT), followed by placebo IV every 6 weeks (15 cycles).[1,3]

Treatment continued until RECIST (Response Evaluation Criteria in Solid Tumors) v1.1-defined progression of disease as determined by investigator or unacceptable toxicity.[1]

Assessment of tumour status was performed every 12 weeks from completion of CRT for the first two years, followed by every 24 weeks in year 3, and then annually. The major efficacy outcome measures were PFS as assessed by investigator according to RECIST v1.1, modified to follow a maximum of 10 target lesions and a maximum of 5 target lesions per organ, or histopathologic confirmation, and OS.[1]

The trial demonstrated statistically significant improvements in both PFS (HR (Hazard Ratio) 0.70; 95% CI (confidence interval): 0.55–0.89; p = 0.002) and OS (HR 0.67; 95% CI: 0.50–0.90; p = 0.004) in the overall population. In an exploratory subgroup analysis for the 459 patients (43%) with FIGO 2014 Stage IB2–IIB disease, the PFS and OS HR estimates were 0.91 (95% CI: 0.63–1.32) and 0.89 (95% CI: 0.55–1.44), respectively, suggesting that the improvements in PFS and OS observed in the overall population were primarily driven by the later-stage subgroup of patients with FIGO 2014 Stage III–IVA disease.

The efficacy results in the exploratory subgroup analysis of 599 patients with FIGO 2014 Stage III-IVA disease showed that pembrolizumab plus CRT demonstrated improvements in PFS (Hazard Ratio (HR) 0.59; 95% CI 0.43, 0.81) and OS (HR 0.58; 95% CI 0.40, 0.85) in the overall population.[1]

For the FIGO 2014 Stage III-IVA population, the most common treatment-related adverse events (reported in at least 20% of patients) were anemia, nausea, diarrhea, white blood cell count decreased, neutrophil count decreased, vomiting, platelet count decreased, and hypothyroidism.[6]

For complete information, refer to the KEYTRUDA® product monograph.

About cervical cancer

Cervical cancer forms in the cells lining the cervix, which is the lower part of the uterus.[7] Despite concerted efforts in screening and prevention across Canada, cervical cancer has become the fastest growing cancer type in females.[8,9] In 2024 alone, it was estimated that there were approximately 1,600 women diagnosed with cervical cancer and an estimated 400 deaths as a result of the disease.[10]

About KEYTRUDA®

KEYTRUDA® is an anti-programmed death receptor-1 (anti-PD-1) therapy that works by helping increase the ability of the body's immune system to help detect and fight tumour cells. KEYTRUDA® is a humanized monoclonal antibody that blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2, thereby activating T lymphocytes which may affect both tumour cells and healthy cells.[11,12,13]

KEYTRUDA® was first approved in Canada in 2015 and currently has indications in several disease areas, including advanced renal cell carcinoma, bladder cancer, non-small cell lung carcinoma, primary mediastinal B-cell lymphoma, classical Hodgkin lymphoma, colorectal cancer, endometrial carcinoma, cervical cancer, esophageal cancer, triple-negative breast cancer, melanoma, and head and neck squamous cell carcinoma.[14]

About Merck

At Merck, known as MSD outside of the United States and Canada, we are unified around our purpose: We use the power of leading-edge science to save and improve lives around the world. For more than 130 years, we have brought hope to humanity through the development of important medicines and vaccines. We aspire to be the premier research-intensive biopharmaceutical company in the world – and today, we are at the forefront of research to deliver innovative health solutions that advance the prevention and treatment of diseases in people and animals. We foster a diverse and inclusive global workforce and operate responsibly every day to enable a safe, sustainable, and healthy future for all people and communities. For more information about our operations in Canada, visit www.merck.ca and connect with us on LinkedIn @MerckCanada.

Forward-Looking Statement of Merck & Co., Inc., Rahway, N.J., USA

This news release of Merck & Co., Inc., Rahway, N.J., USA (the "company") includes "forward-looking statements" within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company's management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline candidates that the candidates will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company's Annual Report on Form 10-K for the year ended December 31, 2023 and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site (www.sec.gov).

###

CA-NON-04142

References:

1. KEYTRUDA® Product Monograph, page 285-286.
2. https://clinicaltrials.gov/study/NCT04221945
3. The ASCO Post. KEYNOTE-A18: Overall Survival in Cervical Cancer Improved by Pembrolizumab Plus Chemoradiotherapy. https://ascopost.com/issues/october-10-2024/keynote-a18-overall-survival-in-cervical-cancer-improved-by-pembrolizumab-plus-chemoradiotherapy/
4. Pembrolizumab or placebo with chemoradiotherapy followed by pembrolizumab or placebo for newly diagnosed, high-risk, locally advanced cervical cancer (ENGOT-cx11/GOG-3047/KEYNOTE-A18): overall survival results from a randomised, double-blind, placebo-controlled, phase 3 trial, page 1329. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(24)00317-9/fulltext
5. https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1426
6. KEYTRUDA® Product Monograph, page 146.

7. Canadian Cancer Society. What is cervical cancer? https://cancer.ca/en/cancer-information/cancer-types/cervical/what-is-cervical-cancer
8. Canadian Cancer Statistics 2023, page 22. https://cdn.cancer.ca/-/media/files/research/cancer-statistics/2023-statistics/2023_pdf_en.pdf?rev=7e0c86ef787d425081008ed22377754d&hash=DBD6818195657364D831AF0641C4B45C
9. Canadian Cancer Statistics 2023, page 80. https://cdn.cancer.ca/-/media/files/research/cancer-statistics/2023-statistics/2023_pdf_en.pdf?rev=7e0c86ef787d425081008ed22377754d&hash=DBD6818195657364D831AF0641C4B45C
10. Canadian Cancer Society. Cervical cancer statistics. https://cancer.ca/en/cancer-information/cancer-types/cervical/statistics
11. KEYTRUDA® Product Monograph, page 300.
12. KEYTRUDA® Product Monograph, page 188.
13. KEYTRUDA® Product Monograph, page 192.
14. KEYTRUDA® Product Monograph, pages 1-3.