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ENGOT-cx11/GOG 3047/KEYNOTE-A18: A Phase 3, Randomized, Double-blind Study of Pembrolizumab With Chemoradiotherapy in Patients With High-Risk Locally Advanced Cervical Cancer

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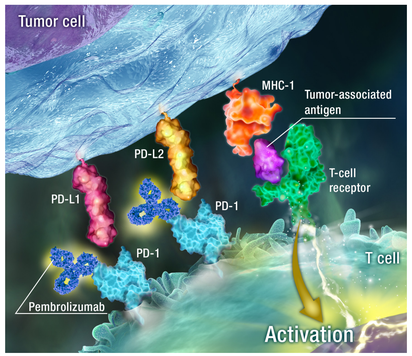
INTRODUCTION

- The current standard of care for patients with high-risk locally advanced cervical cancer is chemoradiotherapy (CRT) composed of external beam radiotherapy (EBRT) with concurrent chemotherapy followed by brachytherapy[1]
- Pembrolizumab is a selective, humanized immunoglobulin G4κ monoclonal antibody against programmed cell death receptor 1 (PD-1) (**Figure 1**) approved for the treatment of patients with PD-L1–positive recurrent or metastatic cervical cancer that progressed during or after chemotherapy on the basis of data from KEYNOTE-158[2,3]

Figure 1. Pembrolizumab and the PD-1 Pathway



MHC-1, major histocompatibility complex 1; PD-1, programmed cell death receptor 1; PD-L1, PD ligand 1; PD-L2, PD ligand 2.

STUDY OBJECTIVES

- To compare progression-free survival (PFS), overall survival (OS), response rates, health-related quality of life, and safety between pembrolizumab plus CRT vs placebo plus CRT

STUDY DESIGN

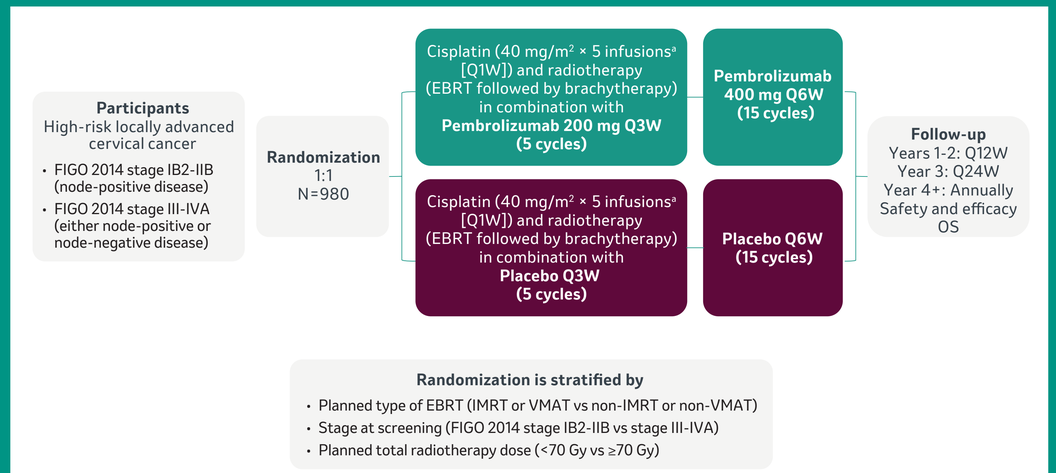
- Approximately 980 patients with advanced cervical cancer will be randomized to receive CRT combined with pembrolizumab or placebo, followed by pembrolizumab monotherapy or placebo (**Figure 2**)

Table. Patient Eligibility Criteria

Key inclusion criteria	Key exclusion criteria
• Females aged ≥18 years • High-risk locally advanced cervical cancer (FIGO 2014 stage IB2-IIB [node-positive disease] or FIGO 2014 stage III-IVA [node-positive or node-negative disease]) • Histologically confirmed squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma of the cervix • No prior definitive surgical, radiation, or systemic therapy and no prior immunotherapy	• Histological subtypes other than those allowed in the inclusion criteria • FIGO 2014 stage IVB disease • History of or planned total hysterectomy • Prior systemic anticancer therapy within 4 weeks prior to randomization

FIGO, International Federation of Gynecology and Obstetrics.

Figure 2. ENGOT-cx11/GOG 3047/KEYNOTE-A18 Study Design



EBRT, external beam radiotherapy; FIGO, International Federation of Gynecology and Obstetrics; IMRT, intensity-modulated radiotherapy; OS, overall survival; QnW, every n weeks; VMAT, volumetric-modulated arc therapy. [a]An optional 6th dose may be administered according to local practice.

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STUDY DESIGN (cont)

- Treatment will continue until disease progression, unacceptable toxicity, or withdrawal or until the patient has received 20 cycles (~2 years) of pembrolizumab (5 cycles of 200 mg Q3W given with CRT, then 15 cycles of 400 mg Q6W as monotherapy) or matching placebo plus CRT

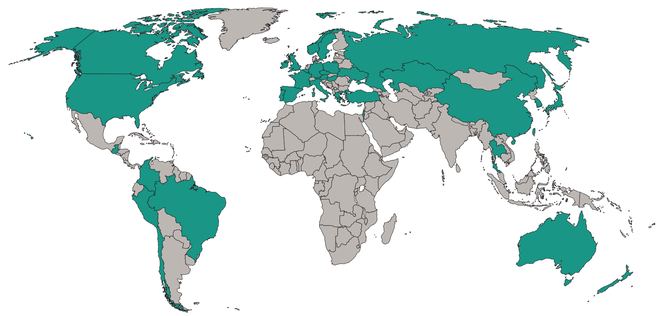
Endpoints

- Primary endpoints
  - PFS per RECIST v1.1, assessed by blinded independent central review (BICR) or histopathologic confirmation of suspected local disease progression
  - OS
- Secondary endpoints
  - PFS per RECIST v1.1, assessed by BICR or histopathologic confirmation at 2 years
  - OS at 3 years
  - Complete response rate 12 weeks after CRT
  - Objective response rate
  - OS and PFS per RECIST v1.1, assessed by BICR, in patients with PD-L1–positive tumors
  - Time from randomization to disease progression on next-line treatment or death
  - Health-related quality of life
    - EORTC QLQ-C30
    - EORTC QLQ-CX24
  - Adverse events
  - Discontinuations due to adverse events

STATUS

- Enrollment is ongoing in the Republic of Korea and is planned to begin soon in Australia, Austria, Belgium, Brazil, Canada, Chile, China, Colombia, Czechia, France, Germany, Greece, Guatemala, Hungary, Ireland, Israel, Italy, Japan, Norway, Peru, Russia, Spain, Sweden, Taiwan, Thailand, Turkey, Ukraine, the United Kingdom, and the United States (**Figure 3**)

Figure 3. Countries With Current and Planned Enrollment Sites for ENGOTcx11/GOG 3047/KEYNOTE-A18



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