KEYLYNK-009: A Phase 2/3, Open-label, Randomized Study of Pembrolizumab + Olaparib vs Pembrolizumab + Chemotherapy After Induction With First-line Pembrolizumab + Chemotherapy in Patients With Locally Recurrent Inoperable or Metastatic Triple-Negative Breast Cancer

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Background

- There is an unmet need for tolerable and effective maintenance treatment regimens after induction therapy for patients with metastatic triple-negative breast cancer (TNBC)
- Here we describe the trial design of KEYLYNK-009 (NCT04191135), a randomized, placebo-controlled, adaptive phase 2/3 trial of pembrolizumab in combination with the PARP inhibitor olaparib after induction therapy for treatment of patients with locally recurrent inoperable or metastatic TNBC that has not been previously treated in the metastatic setting

Study Design

- All enrolled patients will receive 4 to 6 cycles of pembrolizumab + chemotherapy (carboplatin + gemcitabine) as induction therapy
- Patients who achieve complete or partial response or stable disease with induction therapy will be randomized 1:1 to receive pembrolizumab + olaparib or continue pembrolizumab + chemotherapy (**Figure 1**)
  - Toxicities related to induction therapy must be grade ≤1 at randomization (Hb of 9.0 mg/dL; grade 2 hyperthyroidism, hypothyroidism, or hyperglycemia; or any grade alopecia is acceptable)
- This study will enroll ~317 patients in phase 2; if a planned efficacy boundary is met, ~615 additional patients will be enrolled in phase 3

Patient Eligibility Criteria

Key inclusion criteria	Key exclusion criteria
• Locally recurrent, inoperable, centrally confirmed TNBC or metastatic TNBC not previously treated with chemotherapy • Centrally confirmed PD-L1 status • Measurable disease based on RECIST v1.1 • Interval of ≥6 months between completion of treatment with curative intent and first documented local or distant disease recurrence[a] • Aged ≥18 years, with ECOG performance status of 0 or 1 and life expectancy of ≥27 weeks • Treated with anthracycline or taxane in neoadjuvant/adjuvant setting[b]	• Active CNS metastases • Prior therapy with olaparib; another PARP inhibitor; or anti–PD-1, anti–PD-L1, or anti–PD-L2 agent • Immunodeficiency diagnosis or receiving chronic systemic steroids • Active infection requiring systemic therapy • Additional malignancy that is progressing or has required treatment within past 5 years • Pregnant, breastfeeding, or expecting to conceive during the study • History of interstitial lung disease, active tuberculosis, pneumonitis requiring steroids, HIV, hepatitis B virus

CNS, central nervous system; ECOG, Eastern Cooperative Oncology Group; PD-1, programmed cell death receptor 1; PD-L1, PD ligand 1; TNBC, triple-negative breast cancer. [a]Adjuvant radiation therapy is not considered treatment with curative intent for this interval requirement. [b]Unless anthracycline and/or taxane was contraindicated or not considered best treatment option for patient according to treating physician.

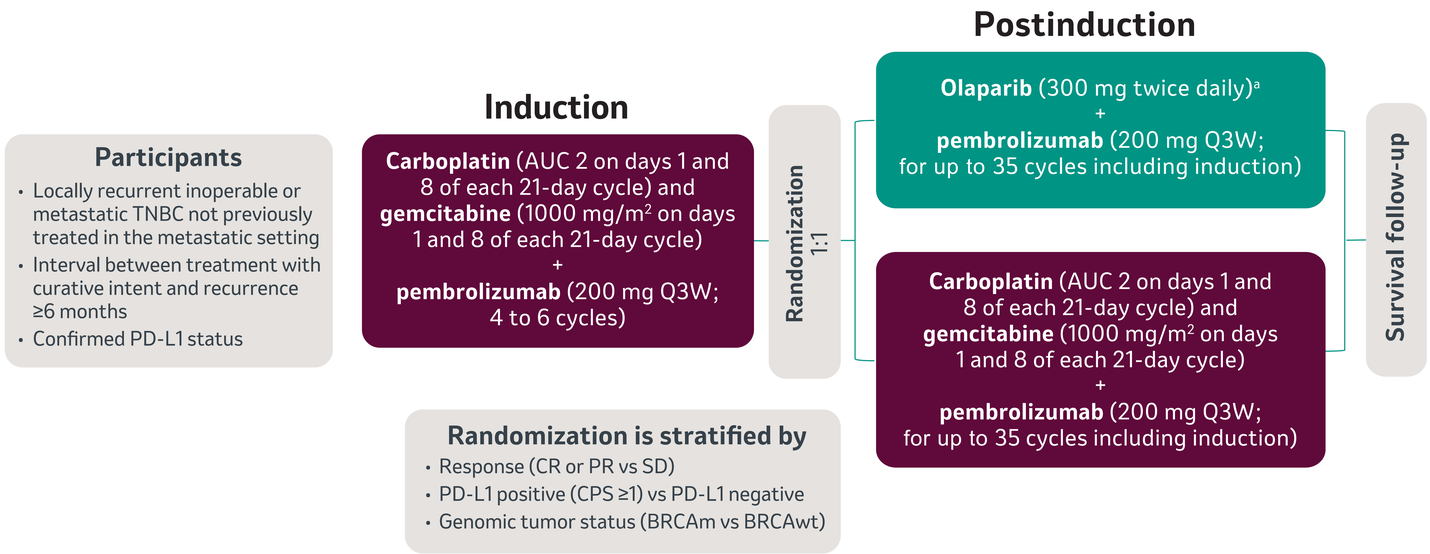
Endpoints and Assessments

- Primary endpoints
  - Progression-free survival (PFS) per RECIST v1.1 by blinded independent central review (BICR)
  - Overall survival (OS)
- Secondary endpoints
  - PFS and OS in patients with BRCA-mutated (BRCAm) tumors
  - Health-related quality of life and time to deterioration using the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) and the breast cancer module (EORTC QLQ-BR23)
  - Visual analog scale using the EuroQoL 5-Dimension, 5-Level Questionnaire in patients with BRCAm tumors
  - Safety and tolerability
- Key exploratory endpoints per RECIST v1.1 by BICR
  - Objective response rate
  - Duration of response
  - Disease control rate
- Postinduction imaging assessments will be performed every ~6 weeks for the first year and every ~12 weeks thereafter

Status

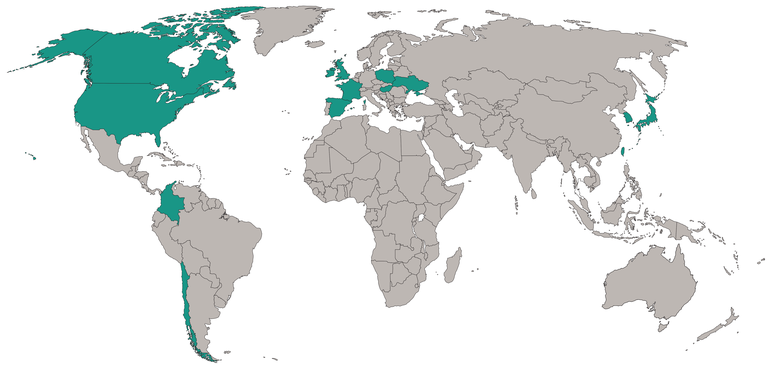
- Enrollment is ongoing at sites in Canada, Chile, Colombia, France, Hungary, Japan, Poland, Republic of Korea, Spain, Taiwan, Ukraine, the United Kingdom, and the United States (**Figure 2**)

Figure 1. Study Design



Olaparib, carboplatin, and gemcitabine may continue until disease progression or treatment discontinuation for any reason. AUC, area under concentration-time curve; BRCAm, BRCA mutated; BRCAwt, BRCA wild-type; CPS, combined positive score; CR, complete response; PD-L1, programmed cell death ligand 1; PR, partial response; Q3W, every 3 weeks; SD, stable disease; TNBC, triple-negative breast cancer. [a]Olaparib will be administered postinduction and given concurrently with pembrolizumab.

Figure 2. Countries With Current and Planned Enrollment Sites for KEYLYNK-009



Disclosures

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