RECIST v1.1, as assessed by BICR and OS, and the key secondary end point is time to initiation of subsequent anticancer therapy or death. Other secondary end points include PSA response rate, time to PSA progression, ORR, DOR, time to radiographic soft tissue progression, time to radiographic bone progression, and safety. KEYNOTE-921 is ongoing or planned in 22 countries across, Asia, Australia, Europe, and North and South America.

Results N/A

Conclusions N/A

Ethics Approval The study and the protocol were approved by the Institutional Review Board or ethics committee at each site.

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PHASE 3 TRIAL OF PEMBROLIZUMAB AND ENZALUTAMIDE VERSUS ENZALUTAMIDE IN PATIENTS WITH METASTATIC CASTRATION-RESISTANT PROSTATE CANCER (MCRPC) (KEYNOTE-641)

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Background Antitumor activity with pembrolizumab + enzalutamide was observed in cohort C of the phase 1b/2 KEYNOTE-365 (NCT02861573) study of abiraterone acetate-pretreated patients with mCRPC and in a phase 2 study (NCT02312557) of patients with mCRPC who experienced progression with enzalutamide alone. In KEYNOTE-365 cohort C, prostate-specific antigen (PSA) response rate was 22%, objective response rate (ORR) was 20%, and 12-month PFS and OS rates were 24.6% and 72.8%, respectively. Safety and tolerability of the combination was consistent with individual profiles of each agent. In the phase 2 study of enzalutamide-pretreated patients, 5 of 28 patients (18%) had a PSA decline of $\geq 50\%$, and 3 of 12 patients (25%) with measurable disease achieved objective response. KEYNOTE-641 (NCT03834493) is a randomized, phase 3 trial to assess efficacy and safety of pembrolizumab + enzalutamide versus placebo + enzalutamide in patients with mCRPC.

Methods Enrolled patients have biochemical or radiographic progression with androgen deprivation therapy/after bilateral orchiectomy within 6 months of screening, ECOG PS 0/1, ongoing androgen deprivation with serum testosterone < 50 ng/dL, and tumor tissue availability for biomarker analysis. The study continues to enroll those who previously had abiraterone acetate therapy; the abiraterone-naïve cohort is filled. Exclusion criteria are prior chemotherapy for mCRPC, checkpoint inhibition, or any treatment with a second-generation androgen receptor inhibitor. Treatment stratification factors are prior abiraterone acetate treatment (yes or no), metastases location (bone only or liver or other), and prior docetaxel treatment for metastatic hormone-sensitive prostate cancer (yes or no). Response and progression will be determined by imaging (CT/MRI/bone) per PCWG3-modified RECIST v1.1 on visits Q9W during the first year and Q12W thereafter. Approximately 1200 adults will be randomly assigned 1:1 in a double-blind fashion to receive enzalutamide 160 mg orally once daily + pembrolizumab 200 mg IV Q3W or enzalutamide 160 mg orally once daily + placebo for a maximum of 35 cycles or until disease progression, unacceptable toxicity, or consent withdrawal. Coprimary end points are radiographic

PFS per PCWG3-modified RECIST v1.1, as assessed by blinded independent central review, and OS. The key secondary end point is time to subsequent anticancer therapy or death. Other secondary end points are ORR, DOR, PSA response rate, PSA undetectable rate, time to PSA progression, time to pain progression, time to symptomatic skeletal-related event, time to soft tissue progression, and safety. KEYNOTE-641 is ongoing or planned in 21 countries across Asia, Australia, Europe, and North and South America.

Results N/A

Conclusions N/A

Trial Registration ClinicalTrials.gov, NCT03834493

Ethics Approval The study and the protocol were approved by the Institutional Review Board or ethics committee at each site.

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PHASE 3 STUDY OF COMBINATION PEMBROLIZUMAB + OLAPARIB THERAPY VERSUS ENZALUTAMIDE/ABIRATERONE IN METASTATIC CASTRATION-RESISTANT PROSTATE CANCER (MCRPC) AFTER PROGRESSION ON CHEMOTHERAPY (KEYLYNK-010)

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Background Cohort A of the phase 1b/2 KEYNOTE-365 study (NCT02861573) demonstrated promising antitumor activity with pembrolizumab + olaparib in patients with mCRPC unselected for homologous recombination deficiency. The prostate-specific antigen (PSA) and objective response rates (ORR) were both 9%, progression-free survival (PFS) was 4.3 months, overall survival (OS) was 14.4 months, and 12-month PFS and OS rates were 23.3% and 58.2%, respectively. The safety profile of the combination therapy was also aligned with the individual profiles of each agent. KEYLYNK-010 (NCT03834519) is a phase 3 trial to evaluate efficacy and safety of pembrolizumab + olaparib in molecularly unselected enzalutamide- or abiraterone-pretreated patients with mCRPC who progressed with docetaxel chemotherapy.

Methods Eligibility criteria include histologically confirmed mCRPC unselected for homologous recombination repair (HRR) gene mutation, progression on docetaxel chemotherapy, progression on androgen deprivation therapy within 6 months before screening, received either abiraterone for metastatic castration-sensitive prostate cancer/mCRPC or enzalutamide for mCRPC (but not both) for ≥ 8 weeks (≥ 14 weeks with bone progression), and Eastern Cooperative Oncology Group performance status of 0 or 1. Patients will also be required to provide tumor tissue for biomarker analysis. Approximately 780 adults will be randomized in a 2:1 ratio to pembrolizumab 200 mg IV Q3W (maximum 35 cycles) + olaparib 300 mg PO QD or abiraterone 1000 mg PO QD + prednisone or prednisolone 5 mg PO BID (enzalutamide-pretreated patients) or enzalutamide 160 mg PO QD (abiraterone-pretreated patients). Randomization will be stratified by prior treatment (abiraterone or enzalutamide) and measurable disease (yes/no). Treatment for all patients will continue until disease progression, unacceptable toxicity, or withdrawal. Response will be assessed by imaging (CT/MRI/bone) per Prostate Cancer

Working Group 3 (PCWG3)-modified RECIST v1.1 by blinded independent central review (BICR) Q9W during the first year and then Q12W thereafter. The dual primary end points are radiographic PFS per PCWG3-modified RECIST v1.1, as assessed by BICR and OS. The key secondary end point is time to initiation of subsequent anticancer therapy or death. Other secondary end points include ORR, duration of response, time to PSA progression, time to first symptomatic skeletal-related event, and safety and tolerability. Patient-reported outcomes and identification of molecular biomarkers for treatment response are exploratory end points. KEYLYNK-010 is ongoing or planned in 19 countries across Asia, Australia, Europe, and North and South America.

Results N/A

Conclusions N/A

Trial Registration ClinicalTrials.gov, NCT03834519

Ethics Approval The study and the protocol were approved by the Institutional Review Board or ethics committee at each site.

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KEYNOTE-991: PHASE 3 STUDY OF PEMBROLIZUMAB PLUS ENZALUTAMIDE AND ANDROGEN DEPRIVATION THERAPY (ADT) FOR PATIENTS WITH METASTATIC HORMONE-SENSITIVE PROSTATE CANCER (MHSPC)

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Background Combination of pembrolizumab, an anti-PD-1 antibody, added to enzalutamide, a nonsteroidal antiandrogen agent, has shown antitumor activity in abiraterone-resistant mCRPC (KEYNOTE-365, NCT02861573) and in patients with mCRPC for whom enzalutamide was ineffective (KEYNOTE-199, NCT02787005). These data indicate that the combination of pembrolizumab + enzalutamide with ADT warrants phase 3 evaluation. Also, efficacy in enzalutamide may be proimmunogenic, suggesting that it may be additive or synergistic in antitumor activity when combined with pembrolizumab.

Methods The KEYNOTE-991 (NCT04191096) phase 3 trial will evaluate the efficacy and safety of enzalutamide + ADT (LHRH agonist/antagonist during study treatment or bilateral orchiectomy) + pembrolizumab or placebo in patients with mHSPC. Eligibility criteria include age ≥ 18 years, mHSPC, ≥ 2 bone lesions or visceral disease, no prior treatment with next-generation hormone agents, adequate organ function, and ECOG PS 0 or 1. Patients must provide tissue for biomarker analysis. Approximately 1232 patients will be randomized in a 1:1 ratio to receive enzalutamide 160 mg orally once daily + ADT + pembrolizumab 200 mg IV every 3 weeks (Q3W) or enzalutamide 160 mg orally once daily + ADT + placebo IV Q3W. Treatment will continue with pembrolizumab up to 35 cycles and treatment with enzalutamide will proceed continuously from day 1 of cycle 1 until disease progression, unacceptable toxicity, or withdrawal of consent. The stratification factors are prior docetaxel therapy (yes or no) and presence of high-volume disease (yes or no). CT or MRI and radionuclide bone imaging will be used to assess response according to Prostate Cancer Working Group 3 (PCWG3)-modified RECIST v1.1 by blinded independent central review (BICR) Q12W from the date of randomization. Imaging will continue

until the end of treatment and will resume Q12W during the posttreatment period. The co-primary end points are BICR-assessed radiographic PFS (according to PCWG3-modified RECIST v1.1) and OS. Key secondary end points are time to first subsequent anticancer therapy and time to symptomatic skeletal-related event. Other end points are PFS2 (progression after next line of therapy or death), PSA response rate, time to PSA progression, PSA undetectable rate, ORR, duration of response, time to soft tissue and radiographic bone progression per PCWG3-modified RECIST v1.1, safety, and patient-reported outcomes (eg, time to pain progression). Safety and tolerability will be evaluated using a tiered approach. KEYNOTE-991 is enrolling at 40 sites in Australia, Chile, Colombia, Israel, Japan, Poland, South Korea, Spain, Switzerland, Taiwan, and the United States.

Results N/A

Conclusions N/A

Trial Registration ClinicalTrials.gov: NCT04191096

Ethics Approval The study and the protocol were approved by the Institutional Review Board or ethics committee at each site.

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CLINICAL OUTCOMES OF OVARIAN CANCER PATIENTS TREATED WITH ALKS 4230, A NOVEL ENGINEERED CYTOKINE, IN COMBINATION WITH PEMBROLIZUMAB: ARTISTRY-1 TRIAL

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Background ALKS 4230 is a novel engineered cytokine that selectively targets the intermediate-affinity interleukin-2 receptor complex to activate CD8+ T cells and natural killer cells.¹ The ARTISTRY-1 trial (NCT02799095) has shown encouraging efficacy and acceptable tolerability of ALKS 4230 among patients with advanced solid tumors.² We report a detailed analysis of ovarian cancer (OC) patients who received combination therapy in ARTISTRY-1.

Methods ARTISTRY-1 is an ongoing multicohort phase 1/2 trial exploring intravenous ALKS 4230 as monotherapy and combined with pembrolizumab. OC patients were enrolled into a cohort with mixed anti PD 1/L1 unapproved tumor types who had progressed on prior chemotherapy. OC patients received ALKS 4230 (3 μ g/kg) on days 1–5 and pembrolizumab (200 mg) on day 1 of a 21 day cycle. Outcomes