P – 052 A phase 3 study of chemotherapy + pembrolizumab versus chemotherapy + placebo as first-line therapy for patients with advanced esophageal or esophagogastric junction (E/EGJ) cancer: KEYNOTE-590 - Trial in progress

K Kato[1], M Shah[2], P Enzinger[3], J Bennouna[4], L Shen[5], A Adenis[6], J Sun[7], B Cho[8], M Ozguroglu[9], T Kojima[10], V Kostorov[11], C Hierro[12], Y Zhu[13], S Shah[13], P Bhagia[13], T Doi[10]

[1]National Cancer Center Hospital, Chuo-ku, Japan, [2]Weill Cornell Medical College and New York Presbyterian Hospital, New York, New York, USA, [3]Dana-Farber Cancer Institute, Boston, Massachusetts, USA, [4]University Hospital of Nantes, Nantes, France, [5]Beijing Cancer Hospital, Beijing, China, [6]Institut du Cancer de Montpellier, Montpellier, France, [7]Samsung Medical Center, Seoul, Republic of Korea, [8]Severance Hospital, Yonsei University Health System, Seoul, Republic of Korea, [9]Istanbul University, Cerrahpasa School of Medicine, Istanbul, Turkey, [10]National Cancer Center Hospital East, Kashiwa, Japan, [11]Leningrad Regional Oncology Dispensary, Saint Petersburg, Russian Federation, [12]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology, Barcelona, Spain, [13]Merck & Co., Inc., Kenilworth, New Jersey, USA

Introduction: Preferred first-line chemotherapy for advanced E/EGJ cancer is fluoropyrimidine in combination with cisplatin; however, no chemotherapy regimen has shown consistent benefit. In the phase 1b KEYNOTE-028 study, pembrolizumab monotherapy demonstrated manageable safety and durable antitumor activity in heavily pretreated patients with programmed death ligand 1 (PD-L1)–positive advanced esophageal carcinoma. Combining chemotherapy with pembrolizumab may be a potential therapeutic strategy for esophageal cancer. KEYNOTE-590 (ClinicalTrials.gov, NCT03189719) is a phase 3, randomized, double-blind, multicenter study to evaluate the efficacy and safety of cisplatin and 5-fluorouracil plus pembrolizumab versus cisplatin and 5-fluorouracil plus placebo in patients with previously untreated advanced E/EGJ carcinoma.

Methods: Key eligibility criteria are age $\geq$18 years; locally advanced unresectable or metastatic adenocarcinoma or squamous cell carcinoma of the esophagus or metastatic Siewert type 1 adenocarcinoma of the EGJ; no prior therapy for advanced disease; measurable disease per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1); Eastern Cooperative Oncology Group performance status 0-1;

adequate organ function; no autoimmune disease; no active infection; can provide a newly obtained or archival tissue sample for later evaluation of PD-L1 expression and gene expression profiling. Patients will be randomly assigned in a 1:1 ratio to receive cisplatin 80 mg/m 2 IV every 3 weeks (Q3W) (capped at 6 doses) plus 5-fluorouracil 800 mg/m 2 continuous IV on days 1-5 Q3W plus pembrolizumab 200 mg IV Q3W or cisplatin 80 mg/m 2 IV Q3W (capped at 6 doses) plus 5-fluorouracil 800 mg/m 2 continuous IV on days 1-5 Q3W plus placebo Q3W IV. Treatment will be continued for up to 2 years or until confirmed disease progression, unacceptable toxicity, or physician or patient decision to discontinue. Crossover from the placebo arm to the pembrolizumab arm is not permitted. Co–primary end points are overall survival and progression-free survival per RECIST v1.1 by blinded independent central review in all patients and in patients with PD-L1–positive tumor expression (combined positive score $\geq$10%). Secondary end points include objective response rate per RECIST v1.1, duration of response, safety, and health-related quality of life. Response will be assessed using computed tomography (preferred) or magnetic resonance imaging every 9 weeks by central imaging review per RECIST v1.1. Adverse events will be graded per National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0 and will be monitored for at least 30 days (90 days for serious adverse events) after the last dose of trial treatment. Patients will be followed for survival until death, withdrawal of consent, or end of study, whichever occurs first. Enrollment is planned for approximately 700 patients.