Characterization of adverse reactions in patients with advanced endometrial cancer (AEC) receiving lenvatinib + pembrolizumab (Study 309/KEYNOTE-775)

N Colombo, 1D Lotusso, 2AD Santini, 3YM Kim, 4AC Herreiz, 5Y Nomori, 6KF Fujiwara, 7EC Colombo, 8DS Miller, 9S Pignata, 10BJ Monk, 11EM Guerra, 12HR Kristeleit, 13M Orlando, 14UA Sanli, 15D Dutta, 16Ro Orlovsky, 17M Ren, 18YV Makker. 1Gynecologic Oncology Program, University of Milan-Bicocca, European Institute of Oncology IRCCS, Milan, Italy; 2Gynecologic Oncology Program, University of Milan-Bicocca, European Institute of Oncology IRCCS, Milan, Italy; 3Division of Gynecologic Oncology, Fondazione PoliChinica Universitario Agostino Gemelli IRCCS and Catholic University of Sacred Heart, Rome, Italy; 4Department of Obstetrics, Gynecology and Reproductive Sciences, Yale University School of Medicine, New Haven, USA; 5Department of Obstetrics and Gynecology, Asian Medical Center, University of Ulsan, Seoul, Korea, Rep. of South; 6Department of Medical Oncology, San Carlos University Teaching Hospital, Madrid, Spain; 7Department of Breast and Medical Oncology, National Cancer Hospital: Kokuritsu Gan Kenkyu Center Chuo Byoin, Tokyo, Japan; 8Department of Gynecologic Oncology, Saitama Medical University International Medical Center, Hidaka, Japan; 9Department of Cancer Medicine, Gustave Roussy Cancerology Institute, Villejuif, GINECO group, France; 10Division of Gynecologic Oncology, University of Texas Southwestern Medical Center, Dallas, USA; 11Division of Urology and Gynecology, Istituto Nazionale Tumori IRCCS-Fondazione G. Pascale, Naples, Italy; 12Arizona Oncology (US Oncology Network), University of Arizona, Creighton University, Phoenix, USA; 13Servicio de Oncología Médica, Hospital Universitario Ramón y Cajal, Madrid, Spain; 14Department of Oncology, Guy’s and St Thomas’ NHS Foundation Trust, London, UK; 15Oncologia Clinica, Instituto Alexander Fleming, Buenos Aires, Argentina; 16Department of Medical Oncology, Ege University, Izmir, Turkey; 17Clinical Research, Eisai Inc., Wooddill Lake, USA; 18Late Stage Clinical Development, Merck & Co., Inc., Kenilworth, USA; 19Department of Medicine, Memorial Sloan Kettering Cancer Center; Weill Cornell Medical Center, New York, USA

Methodology In Study 309/KEYNOTE-775, patients were randomized to lenvatinib 20 mg QD PO + pembrolizumab 200 mg IV Q3W (n=411) or TPC (n=416; doxorubicin 60 mg/m2 IV Q3W or paclitaxel 80 mg/m2 IV QW, 3 weeks on/1 week off). Herein, characterization of key ARs is based on incidence and known association with lenvatinib+pembrolizumab, and interventions for ARs in aEC patients. Key ARs are grouped by preferred terms per FDA definitions for ARs in patients with endometrial carcinoma from the US prescribing information; ARs include hypertension, musculoskeletal pain, fatigue, nausea, diarrhea, decreased appetite, stomatitis, vomiting, hypothyroidism, palmar-plantar erythrodysesthesia (PPES), and decreased weight.

Result(s) Median times (weeks) to first onset of key ARs [any grade] were: hypertension (2.1), fatigue (2.3), musculoskeletal pain (3.2), nausea (4.7), decreased appetite (4.9), stomatitis (4.9), vomiting (7.6), diarrhea (7.9), hypothyroidism (8.9), PPES (9.6), and decreased weight (10.7). Among ARs described, those that led to withdrawal of lenvatinib included decreased appetite (2%), fatigue (2%), hypertension (2%), diarrhea (1%), musculoskeletal pain (1%), vomiting (1%), and decreased weight (1%); only decreased appetite (1%) and diarrhea (1%) led to withdrawal of pembrolizumab. Hypertension most frequently led to lenvatinib dose reduction (18%); diarrhea and hypertension most frequently led to dose interruption of lenvatinib (11% each) as last action taken with lenvatinib. Diarrhea most frequently led to pembrolizumab interruption (8%). Change in sum of target lesion diameters over time, exposure-adjusted ARs, and AR management strategies will be reported.

Conclusion In general, ARs due to lenvatinib+pembrolizumab were as expected and often occurred within 3 months of treatment initiation. As will be presented, clinicians play a critical role in prompt identification and AR-directed management of patients with aEC; such management may potentially reduce treatment interruption(s) and/or lenvatinib dose reduction.

Increased survival in non-endometrioid endometrial cancer after introduction of Swedish national guidelines

12Å Åkesson, 3C Adok, 1P Dahm-Kähler. 1Inst of Clinical Sciences, Sahlgrenska Academy at the University of Gothenburg, Obstetrics and gynecology, Göteborg, Sweden; 2Sahlgrenska University Hospital, Gynecology, Göteborg, Sweden; 3Regionalt cancercentrum väst, Göteborg, Sweden

Introduction/Background The first Swedish national guidelines for endometrial cancer (NGEC) recommended adequate staging with pelvic and paraaortic lymphadenectomy for patients with high-risk disease, including non-endometrioid endometrial cancer (EC). The recommended adjuvant oncological treatment protocol was chemotherapy to all non-endometrioid EC and radiotherapy only for those with stage IIIIC. Before the NGEC, the stipulated surgery was solely hysterectomy and bilateral salpingectomy followed by adjuvant chemono-radiotherapy to all non-endometrioid ECs. The aim of this study was to investigate the outcome in survival and recurrence of this shift in treatment strategy.

A78 Int J Gynecol Cancer 2021;31(Suppl 3):A1–A395
Introduction/Background: Pembrolizumab, an anti-PD-1 antibody, has demonstrated activity in patients with previously treated mismatch repair (MMR) deficient (dMMR; 57.1% objective response rate [ORR] as monotherapy and 63.6% ORR as combination therapy with lenvatinib) and MMR proficient (pMMR; 36.2% ORR as combination therapy with lenvatinib) endometrial cancer. ENGOT-en11/GOG-3053/KEYNOTE-B21 (NCT04634877) is a phase 3, randomized, double-blind study of pembrolizumab or placebo in combination with adjuvant chemotherapy with/without radiotherapy in patients with endometrial cancer.

Methodology: Eligible patients are ≥18 years old with newly diagnosed, high-risk (stage I/II non-endometrioid or with ps5 abnormality and any histology, stage III/IVA), previously untreated endometrial cancer following surgery with curative intent with no evidence of disease post-operatively. Approximately 990 patients are randomized to receive pembrolizumab 200 mg or placebo every 3 weeks (Q3W) for 6 cycles plus chemotherapy (carboplatin area under the curve [AUC] 5/6 plus paclitaxel 175 mg/m² Q3W or carboplatin AUC 2/2.7 plus paclitaxel 60 mg/m² QW) in stage 1. Patients receive pembrolizumab 400 mg or placebo Q6W for 6 cycles in stage 2. Radiotherapy (external beam radiotherapy [EBRT] and/or brachytherapy) ± radiosensitizing cisplatin 50 mg/m² (days 1 and 29) may be administered after completion of chemotherapy. Randomization is stratified by MMR status (pMMR vs dMMR) and, within pMMR, by planned radiation therapy (cisplatin-EBRT vs EBRT vs no EBRT), histology (endometrioid vs non-endometrioid), and International Federation of Gynecology and Obstetrics surgical stage (I/II vs III/IVA). Dual primary endpoints are disease-free survival (DFS; per investigator assessment) and overall survival (OS). Secondary endpoints include DFS (per blinded independent central review), DFS (per investigator assessment) and OS by biomarker status (PD-L1 and tumor mutational burden), safety (per National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0), and quality of life (per European Organization for Research and Treatment of Cancer: first published on http://ije.bmj.com/ Int J Gynecol Cancer: first published as 10.1136/ijgc-2021-ESGO.121 on 12 October 2021. Downloaded from Int J Gynecol Cancer 2021;31(Suppl 3):A1–A395 A79