MADRID 2026 ESMO congress

LBA12

KEYNOTE-C93/GOG-3064/ENGOT-en15: Phase 3, randomized, open-label study of first-line (1L) pembrolizumab (pembro) vs carboplatin (C) + paclitaxel (P) in mismatch repair-deficient (dMMR) advanced or recurrent endometrial carcinoma (a/rEC)

B.M. Slomovitz[1], F. Backes[2], B. Mackowiak-Matejczyk[3], J. Zhu[4], L. Gilbert[5], K. Hasegawa[6], J-W. Kim[7], J.R. Kroep[8], I. Romero[9], M. Gultekin[10], P-H. Wang[11], Z. Novák[12], O.S. Rosengarten[13], M. Polignano[14], S.E. Baron-Hay[15], L. Yao[16], R. Meng[16], R.J. Orlowski[16], L. Willmott[17], S. Pignata[18]

[1] GOG Foundation and Division of Gynecologic Oncology, Mount Sinai Medical Center, Miami Beach, United States of America, [2] GOG Foundation, Ohio State University Wexner Medical Center and James Cancer Hospital, Columbus, United States of America, [3] PGOG, Bialostockie Centrum Onkologii im Marii Sklodowskiej-Curie, Białystok, Poland, [4] Medical Oncology, Zhejiang Cancer Hospital, Hangzhou, China, [5] Division of Gynecologic Oncology, McGill University Health Centre, Women's Health Research Unit, Research Institute of the McGill University Health Centre, Gerald Bronfman Department of Oncology, McGill University, Montreal, Canada, [6] Gynecologic Oncology Department, Saitama Medical University International Medical Center, Hidaka, Saitama, Japan, [7] Ob-Gyn Department, Seoul National University and Asia-Pacific Gynecologic Oncology Trials Group, Seoul, Republic of Korea, [8] DGOG and Medical Oncology Department, Leiden University Medical Center, Leiden, Netherlands, [9] GEICO, Fundacion Instituto Valenciano de Oncologia, Valencia, Spain, [10] TRSGO and Division of Gynaecological Oncology, Department of Obstetrics and Gynaecology, Hacettepe University Faculty of Medicine, Ankara, Türkiye, [11] Department of Obstetrics and Gynecology, National Yang-Ming University School of Medicine, Taipei Veterans General Hospital and National Yang-Ming University Hospital, Taipei City, Taiwan, [12] CEECOG, National Institute of Oncology, Budapest, Hungary, [13] ISGO and Oncology Institute, Shaare Zedek Medical Center, Jerusalem, Israel, [14] MaNGO and Gynecologic Oncology Department, Fondazione IRCCS – Istituto Nazionale dei Tumori, Milan, Italy, [15] Medical Oncology Department, Royal North Shore Hospital, St Leonards, Australia, [16] Medical Oncology, Merck & Co., Inc., Rahway, United States of America, [17] GOG Foundation and Gynecologic Oncology, Arizona Center for Cancer Care, Phoenix, United States of America[18] MITO and Department of Urology and Gynecology, Istituto Nazionale Tumori IRCCS Fondazione G. Pascale, Naples, Italy

Background

Preferred 1L therapy for dMMR a/rEC is CP + ICI then maintenance ICI. An unmet need exists for a CTx-free option in this setting. The phase 3 KEYNOTE-C93/GOG-3064/ENGOT-en15 study (NCT05173987) assessed 1L pembro vs CP for dMMR a/rEC.

Methods

Participants (pts) had inoperable, stage III/IV, a/rEC that was radiologically evaluable (measurable or non-measurable by investigator unless stage IVB then no evidence of disease was allowed following surgical resection) and centrally confirmed dMMR. Prior systemic therapy was not allowed (except for [neo]adjuvant therapy if recurrence ≥6 mo after last dose). Pts were randomized 1:1 to pembro Q6W for 18 cycles or CP Q3W for 6 cycles. Primary endpoints were PFS by BICR and OS. QoL was assessed by EORTC QLQ-C30 global health status (GHS)/QoL scale.

Results

299 pts were randomized (median follow-up, 36.5 mo). Efficacy results at the prespecified IA (data cutoff: Apr 24, 2026) are in the table. In the CP arm, 85.2% of pts with BICR PD received crossover pembro or subsequent PD-(L)1 inhibitors off study; in the pembro arm, 47.6% of pts with BICR PD received subsequent platinum CTx off study. Clinically meaningful improvement in GHS/QoL scale scores was observed from baseline to week 12 (primary time point) with pembro vs CP, with a between-group difference of 7.02 (95% CI, 2.54–11.50). Grade ≥3 treatment-related AEs occurred in 18.1% in the pembro arm and 50.7% in the CP arm, with the most common being anemia (2.0% vs 18.1%). Grade ≥3 immune-mediated AEs and infusion reactions occurred in 7.4% and 3.5%, respectively.

Conclusions

1L pembro showed a statistically significant, clinically meaningful, and durable improvement in PFS and a favorable trend in OS over traditional CTx in pts with dMMR a/rEC. There were no new safety signals in either arm. Single agent pembro can be an option for this patient population.

Table: LBA12

	Pembro (n = 149)	CP (n = 150)
PFS		
Median (95% CI), mo	38.2 (17.9–NR)	8.4 (6.8–10.4)
HR (95% CI)[a]	0.57 (0.42–0.79)	
36-mo rate (95% CI), %	52.8 (44.2–60.7)	30.0 (22.4–37.9)
OS		
Median (95% CI), mo	NR (NR–NR)	NR (38.9–NR)
HR (95% CI)	0.77 (0.52–1.15)	
36-mo rate (95% CI), %	70.7 (62.4–77.5)	62.0 (53.1–69.8)
ORR (95% CI),[b] %	64.1 (55.8–71.9)	62.1 (53.6–70.0)
CR, %	33.8	26.2
PR, %	30.3	35.9
DOR[c]		
Median, mo	NR	10.2
≥24 mo, %	77.0	41.3
≥36 mo, %	70.7	40.0

NR, not reached. [a]Prespecified statistical criterion *p*-value boundary of 1-sided 0.025 was met ($P = 0.0002$) [b]In pts with measurable disease per BICR at baseline (n = 145 per arm). [c]In responders with measurable disease per BICR at baseline (pembro, n = 93; CP, n = 90).

Clinical trial identification

NCT05173987.

Editorial acknowledgement

Medical writing assistance was provided by Young-A Heo, PhD, of ICON plc (Blue Bell, PA, USA). This assistance was funded by Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

Legal entity responsible for the study

Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

Funding

Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

Disclosure

B.M. Slomovitz: Financial Interests, Personal, Advisory Board: AstraZeneca, Eisai, GSK, Genentech, Merck, Immunogen, Novocure, Aadi, Seagen, Incyte, Gilead; Non-Financial Interests, Member of Board of Directors: GOG Foundation. F. Backes: Financial Interests, Personal, Advisory Board: Merck, AstraZeneca, Daiichi Sankyo, AbbVie, GSK, Eisai, BioNTech, Genmab, Tubulis; Financial Interests, Personal, Other, DMC: Macrogenics; Financial Interests, Personal, Royalties: UpToDate; Financial Interests, Institutional, Trial Chair: Merck, AbbVie, GSK; Financial Interests, Institutional, Local PI: Genmab, AstraZeneca, GSK, Daiichi Sankyo, AstraZeneca, Genmab; Financial Interests, Trial Chair: BioNTech; Financial Interests, Institutional, Coordinating PI: Natera; Non-Financial Interests, Member of Board of Directors: Society of Gynecologic Oncology; Non-Financial Interests, Leadership Role: International Society of Gynecologic Cancer; Non-Financial Interests, Member: Society of Gynecologic Oncology, ASCO, IGCS, ESMO. B. Mackowiak-Matejczyk: Financial Interests, Personal, Other, Honoraria: GSK Commercial Sp zoo, AstraZeneca, HealthQuest sp zoo; Amgen Sp zoo; MSD, AbbVie, Medisonpharma; Financial Interests, Personal, Advisory Board: GSK, AstraZeneca; Medisonpharma; Financial Interests, Personal, Other, Clinical trials: Seagen, INC; Merck Sharp & Dohme LLC, MSD Polska Sp zoo; AstraZeneca AB; Parexel International Limited; Tesaro Bio Netherlands BV; Tesaro, Inc; Clovis Oncology, Inc; AstraZeneca Pharma Poland sp zoo; Quiniles Eastern Holdings; Regeneron Pharmaceuticals; Financial Interests, Personal, Other, Travel Grant: AstraZeneca, Medisonpharma. L. Gilbert: Financial Interests, Personal, Advisory Board: Karyopharm, Corcept Therapeutics, Immunogen, Kora Health Care, Novocure, CanariaBio Inc, Esai, GSK, Merck, AbbVie, Repare Therapeutics, Gilead Sciences; Financial Interests, Personal, Other, Consulting: AbbVie, Merck, GSK; Financial Interests, Institutional, Local PI: IMV, Pfizer, Corcept Therapeutics, ImmunoGen, Shattuck Labs, Roche, Tesaro, K-Group Beta Inc, GOG Foundation, GSK, AstraZeneca, OncoQuest Pharmaceuticals, Novocure, GmbH, Alkermes, Espersas, Mersana Therapeutics, Daiichi Sankyo Inc, Ascendis Pharma, Seagen Inc, Karyopharm, Bayer, CanariaBio Inc, Eisai, Fortrea Inc, Merck, Parexel International (IRL) Ltd, Repare Therapeutics, Sichuan Kelun Biotech Biopharma/Parexel, Pri/Wex Pharma Inc, Sutro Bio Pharma, Gilead Sciences, Macrogenics Inc, Verastem Oncology, Recursion Pharmaceuticals Inc., TORL BioTherapeutics LLC. K. Hasegawa: Financial Interests, Personal, Invited Speaker: MSD, AstraZeneca, Takeda, Genmab, Kaken, Eisai, Regeneron; Financial Interests, Personal,

Advisory Board: GSK, Daiichi Sankyo, Terumo; Financial Interests, Institutional, Funding, contracted research: MSD, Takeda. J. Kim: Financial Interests, Personal, Advisory Board: Takeda Korea, GSK Korea, Boryung, Vifor Pharma, MSD Korea, LG Pharma; Financial Interests, Personal, Invited Speaker: CMIC, AstraZeneca, Janssen; Non-Financial Interests, Leadership Role, Clinical Chair of the Asia Pacific Gynecologic Oncology Trials Group (APGOT) during the year of 2026⊠2027: Asia Pacific Gynecologic Oncology Trials Group. J.R. Kroep: Financial Interests, Institutional, Advisory Board: AstraZeneca, Daiichi Sankyo, GSK, Lilly, MSD, Novartis, Eisai, AbbVie; Financial Interests, Institutional, Research Grant: AstraZeneca, Novartis, Philips. I. Romero: Financial Interests, Personal, Advisory Board: Roche, PharmaMar, Clovis, GSK, AstraZeneca, Pharma&, Regeneron, AbbVie, Genmab; Financial Interests, Personal, Invited Speaker: Roche, PharmaMar, AstraZeneca, Clovis, GSK, MSD; Financial Interests, Institutional, Funding: AstraZeneca; Financial Interests, Institutional, Research Grant: GSK; Non-Financial Interests, Member of Board of Directors: GEICO; Non-Financial Interests, Advisory Role: GEICO; Non-Financial Interests, Member: SEOM. M. Gultekin: Financial Interests, Personal, Invited Speaker, I have been invited for 3-4 times with honororıum: Prohealth Care Spain. P. Wang: Financial Interests, Advisory Role, consulting or advisory role: AbbVie, Alkermes, Astellas, AstraZeneca, Chugai-pharm, Daiichi Sankyo, Eisai, Eli Lilly and Company, GSK, Merck & Co., Inc., Rahway, NJ, USA, MSD, Regeneron, Roche, Taiwan Female Cancer Foundation, Takeda, and TTY Biopharm Company Limited. Z. Novák: Financial Interests, Personal, Other, Lecture fee: MSD, AbbVie, AstraZeneca, Richter Gedeon, Sofmedica. S.E. Baron-Hay: Financial Interests, Personal, Advisory Board: AstraZeneca, MSD, Pfizer, AbbVie, Daiichi Sankyo, Gilead, Novartis; Financial Interests, Speaker's Bureau: AbbVie, AstraZeneca, MSD; Daiichi Sankyo. L. Yao: Financial Interests, Personal, Full or part-time Employment: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA; Financial Interests, Personal, Stocks/Shares: Merck & Co., Inc., Rahway, NJ, USA. R. Meng: Financial Interests, Personal, Full or part-time Employment: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA; Financial Interests, Personal, Stocks/Shares: Merck & Co., Inc., Rahway, NJ, USA. R.J. Orlowski: Financial Interests, Personal, Full or part-time Employment: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA; Financial Interests, Personal, Stocks/Shares: Merck & Co., Inc., Rahway, NJ, USA. L. Willmott: Financial Interests, Personal, Advisory Board: GSK, Eisai, Lilly, AbbVie, Gilead, Tubulis, Corcept; Financial Interests, Personal, Speaker's Bureau: GSK, AstraZeneca, Corcept, Merck, AbbVie, Pfizer. S. Pignata: Financial Interests, Personal, Advisory Board: Roche, AstraZeneca, MSD, GSK, PharmaMar; Financial Interests, Personal, Invited Speaker: Novartis; Financial Interests, Personal, Advisory Board, platinum resitant OC board: AbbVie; Financial Interests, Institutional, Funding: Roche, MSD, Pfizer, AstraZeneca. All other authors have declared no conflicts of interest.

© European Society for Medical Oncology