Mural Oncology, Arsenalbio, Atara Biotherapeutics, Bayer/Celgene/Juno, Genentech, Genmab/Seagen Therapeutics, Gynecologic Oncology Foundation, Kite Pharma, Ludwig Cancer Institute, Lyell Immunopharma, MarkerTherapeutics, Merck, OnCusp Therapeutics, Regeneron, Syndax Pharmaceuticals, TCR2 Therapeutics, Tesaro/GSK; Financial Interests, Personal, Other, payment or honoraria for lectures: Curio/OncLive/PER/MJH/Aptitude Health, GSK, Gynecologic Oncology Canada, Society for Immunotherapy of Cancer; Financial Interests, Personal, Other, support for attending meetings and/or travel: Gathering Around Center Ireland, GOG Foundation, Hitech Health, SGO; Financial Interests, Personal, Officer, participation on a data safety monitoring board or advisory board: 2seventybio; Financial Interests, Personal, Advisory Board, participation on a data safety monitoring board or advisory board: Acrivon, AstraZeneca, Bayer, Carina Biotech, GSK, ImmunoGen, Link Therapeutics, Loxo, Miltenyi, Mural Oncology, OnCusp Therapeutics, R-Pharm, Seattle Genetics/Seagen/Pfizer; Financial Interests, Personal, Leadership Role: NRG Oncology (Chair, Developmental Therapeutics Committee), SGO (Vice-Chair, Clinical Practice Committee). G. Freyer: Financial Interests, Personal, Other, honoraria: GSK. D.M. O'Malley: Financial Interests, Personal and Institutional, Other, grants and contracts: AbbVie, Agenus,Inc, Arcus Biosciences, Inc., AstraZeneca, Boston Biomedical, Clovis Oncology, Eisai, Exelixis, Genentech Inc, GSK, GOG Foundation, Hoffmann-La Roche Inc, ImmunoGen, Inc, Iovance Biotherapeutics, Leap Therapeutics, Inc, Merck & Co, Merck Sharp & Dohme, Mersana Therapeutics, Inc, Novartis, NovoCure, OncoC4, Inc, Regeneron Pharmaceuticals, Inc, Seagen, Sutro Biopharma, Verastem, Inc; Financial Interests, Personal, Other: AdaptImmune, Arquer Diagnostics, Atossa Therapeutics, Cardiff Oncology, Celcuity, Corcept Therapeutics, Duality Bio, Elevar, Genelux, Imvax, InterVenn, INXMED, Janssen, Jazz Pharmaceuticals, Laekna, Luzsana Biotechology, Myriad, Onconova, RepImmune, R Pharm, Roche Diagnostics, Sorrento, Tarveda Therapeutics, Toray, Trillium, Umoja, VBL Therapeutics, Vincerx Pharma, Xencor, Zentalis; Financial Interests, Institutional, Other, grants and contracts: Advaxis, Alkermes, Aravive, Inc, BeiGene USA, Inc, Bristol Myers Squibb, Deciphera Pharma, EMD Serono, Inc, Genmab, Incyte Corporation, Karyopharm, Ludwig Institute for Ca, NCI, NRG Oncology, OncoQuest Inc, Pfizer Inc, Precision Therapeutics, Inc, Prelude Therapeutics, RTOG, Rubius Therapeutics, SWOG. F. Heitz: Financial Interests, Personal, Other, honoraria: AstraZeneca, GSK, ImmunoGen, Merck; Financial Interests, Personal, Speaker, Consultant, Advisor: AstraZeneca, GSK, ImmunoGen, NovoCure, PharmaMar, Roche, Tesaro, Zailabs. M.S. Shahin: Financial Interests, Personal, Speaker, Consultant, Advisor: AstraZeneca, GSK, ImmunoGen, Merck; Financial Interests, Personal, Other, honoraria: AstraZeneca, Eisai, GSK, ImmunoGen, Merck; Financial Interests, Personal, Member of Board of Directors: Unite for Her. W.H. Bradley: Financial Interests, Personal, Speaker, Consultant, Advisor: OncoC4; Financial Interests, Personal, Advisory Board, participation on a data safety monitoring board or advisory board: Imunon. N. Compton: Financial Interests, Personal, Full or part-time Employment, former employee: GSK; Financial Interests, Personal, Speaker, Consultant, Advisor: GSK. I. Malinowska: Financial Interests, Personal, Full or part-time Employment: GSK; Financial Interests, Personal, Stocks or ownership: GSK. A. Redondo: Financial Interests, Personal, Speaker, Consultant, Advisor: AstraZeneca, Boehringer Ingelheim, GSK, MSD, Pharma&; Financial Interests, Personal, Other, honoraria: AstraZeneca, GSK, MSD, Pharma&; Financial Interests, Personal, Other, support for attending meetings and/or travel: AstraZeneca, GSK, MSD. B.J. Monk: Financial Interests, Personal, Speaker, Consultant, Advisor: Acrivon, Adaptimune, Agenus, Akeso Bio, Amgen, Aravive, AstraZeneca, Bayer, Clovis, Easai, Elevar, EMD Merck, Genmab/Seagen, GOG Foundation, Gradalis, Heng Rui, ImmunoGen, Iovance, Karyopharm, Laekna, MacroGenics, Merck, Mersana, Myriad, Novartis, Novocure, OncoC4, Panavance, Pieris, Pfizer, Puma, Regeneron, Roche/Genentech, Sorrento, Teasro/GSK, US Oncology Research, VBL, Verastem, Zentalis; Financial Interests, Personal, Speaker's Bureau: AstraZeneca, Eisai, Myriad, Roche/Genentech, Tesaro/GSK. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2024.08.2268

LBA30 ATHENA-COMBO, a phase III, randomized trial comparing rucaparib (RUCA) + nivolumab (NIVO) combination therapy vs RUCA monotherapy as maintenance treatment in patients (pts) with newly diagnosed ovarian cancer (OC)

B.J. Monk[1], A. Oaknin[2], D.M. O'Malley[3], M. Wilson[4], D. Lorusso[5], S. Westin[6], A.M. Oza[7], F. Zagouri[8], T.J. Herzog[9], O. Mikheeva[10], C. Parkinson[11], R.L. Coleman[12], M.C. Lim[13], A.M. Chudecka-Glaz[14], R.N. Eskander[15], I. Bruchim[16], S. Ghamande[17], D. Despain[18], K. Fujiwara[19], R. Kristeleit[20]

[1]Florida Cancer Specialists & Research Institute, West Palm Beach, FL, USA; [2]Medical Oncology Dept., Medical Oncology Service, Vall d'Hebron Institute of Oncology, Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain; [3]Gyn Oncology, The Ohio State University, James Cancer Center, Columbus, OH, USA; [4]Cancer and Blood Department, Auckland City Hospital, Auckland, New Zealand; [5]Gynecologic Oncology Department, Fondazione Policlinico Universitario Gemelli IRCCS, and Humanitas San Pio X, Milan, Italy; [6]Gynecologic Oncology and Reproductive Medicine Department, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [7]Medical Oncology and Hematology Department, Princess Margaret Hospital Cancer Centre, Toronto, ON, Canada; [8]Clinical Therapeutics, Alexandra Hospital, National and Kapodistrian University of Athens, Athens, Greece; [9]Oncology, University of Cincinnati, Cincinnati, OH, USA; [10]Oncology, Limited Liability Company MedPomosch, Saint-Petersburg, Russian Federation; [11]Oncology, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK; [12]Gynecologic Oncology Department, US Oncology Research, The Woodlands, TX, USA; [13]Oncology, National Cancer Center Korea, Goyang, Republic of Korea; [14]Department of Gynecological Surgery and Gynecological Oncology, Pomeranian Medical University, Szczecin, Poland; [15]Obstetrics, Gynecology and Reproductive Sciences, Gynecology and Reproductive Sciences, University of California, La Jolla, CA, USA; [16]Gynecologic Oncology Department, Hillel Yaffe Medical Center affiliated with the Technion, Institute of Technology, Hadera, Israel; [17]Oncology, Georgia Cancer Center at Augusta University, Augusta, GA, USA; [18]Biostatistics, pharma&, New York, NY, USA; [19]Gynecologic Oncology, Saitama Medical University International Medical Center, Saitama, Japan; [20]Department of Oncology, Guy's and St Thomas' NHS Foundation Trust, London, UK

Background: ATHENA (NCT03522246) consists of 2 studies, MONO and COMBO. In MONO, RUCA monotherapy provided a sustained investigator-assessed progression-free survival (PFS) vs placebo (PBO, median [mdn] 20.2 vs 9.2 months [mo], data cutoff 23 Mar 2022) in pts with newly diagnosed, advanced high-grade OC (AHGOC) after first-line (1L) treatment. COMBO was designed to evaluate if the addition of NIVO to RUCA could further delay time to progression. RUCA + NIVO (COMBO) was compared with RUCA + PBO (MONO) with an additional 2 years (y) of follow up (cutoff 17 May 2024). We report primary efficacy and safety results from COMBO.

Methods: Pts with FIGO stage III–IV AHGOC with response to 1L platinum-based chemotherapy were randomized 1:1 to RUCA 600 mg PO BID + NIVO 480 mg IV Q4W or RUCA + PBO. The primary endpoint was PFS in the intent-to-treat (ITT) population. PFS in homologous recombination deficiency (HRD) subgroups and programmed death-ligand 1 (PD-L1) subgroups were exploratory.

Results: Between 7 Aug 2018 and 26 Oct 2020, 863 pts were randomized. After a mdn follow-up of 48 mo, COMBO was associated with numerically shorter mdn PFS vs MONO in the ITT (15.0 vs 20.2 mo; HR, 1.3; 95% CI, 1.1–1.5), HRD subgroups, and in pts with PD-L1 $\geq$1% and $\geq$5% (table). PFS benefit of 20.2 mo with RUCA MONO was maintained with the additional 2 y follow-up. COMBO had shorter mdn exposure to treatment vs MONO (PO 8.4 vs 14.7 mo, IV 4.6 vs 11.1 mo). Common grade $\geq$3 treatment-related AEs in COMBO vs MONO were anemia/hemoglobin decreased (27.1% vs 28.6%), neutropenia/neutrophil count decreased (25.4% vs 15.4%), and ALT/AST increased (21.2% vs 10.0%).

Table: LBA30

	COMBO vs MONO Data cutoff 17 May 2024			
	RUCA + NIVO (COMBO), n	RUCA + PBO (MONO), n	Median investigator-assessed PFS, mo	HR (95% CI)
ITT	436	427	15.0 vs 20.2	1.3 (1.1–1.5)
HRD	193	185	28.9 vs 31.4	1.1 (0.9–1.5)
BRCA mutation	94	91	48.0 vs NR	1.1 (0.7–1.7)
BRCA wt/LOH^{high}	99	94	17.3 vs 22.3	1.1 (0.7–1.5)
BRCA wt/LOH^{low}	188	189	11.0 vs 12.1	1.3 (1.0–1.7)
BRCA wt/ LOH^{indeterminate}	55	53	9.2 vs 17.5	1.6 (1.0–2.5)
PD-L1 $\geq$ 5%	69	72	22.8 vs 52.2	1.5 (0.9–2.4)
PD-L1 $\geq$ 1%	199	197	18.3 vs 25.8	1.3 (1.0–1.7)

LOH, loss of heterozygosity; NR, not reached; wt, wild-type.

Conclusions: NIVO in combination with RUCA did not add to the PFS benefit of RUCA observed in MONO. The safety profile of RUCA in combination with NIVO was consistent with previously reported studies and their individually known safety profiles.

Clinical trial identification: NCT03522246.

Editorial acknowledgement: Medical writing and editorial support, funded by pharma&, were provided by Gautam Bijur, PhD, and Celia Nelson of Ashfield MedComms, an Inizio company.

Legal entity responsible for the study: pharma&.

Funding: pharma&.

Disclosure: B.J. Monk: Financial Interests, Personal, Other, Consultant: Agenus, Elevar, GOG Foundation, Genmab/Seattle Genetics, Gradalis, Immunogen, Karyopharm, Mersana, Novocure, Pfizer, Acrivon, Alkemers, Amgen, Bayer, BioNtech, Corcept, Duality, EMD Merck, Genalux, Laekna, Novartis, OncoC4, Panavance, Profound Bio, Sarah Cannon Research Institue, Tubulis; Financial Interests, Personal, Other, Consultant/Speaker: AstraZeneca, Clovis, Easai, Merck, Myriad, Roche/Genentech, TESARO/GSK; Financial Interests, Personal, Other, Honorarium Consultant: Regeneron, Verastem, Zentalis; Financial Interests, Personal, Invited Speaker: Aadi; Financial Interests, Personal, Other, Speaker/Consultant: Adaptimune. A. Oaknin: Financial Interests, Personal, Advisory Board: Agenus, AstraZeneca, Clovis Oncology, Corcept Therapeutics, Deciphera Pharmaceuticals, Eisai, F. Hoffmann-La Roche, GSK, Genmab, Immunogen, Itheos, MSD, Mersana Therapeutics, Novocure, OncoXerna Therapeutics, Inc, PharmaMar, Regeneron, Sattuclabs, Seagen/Pfizer, Sutro Biopharma, Exelisis, Dalichi Sankyo, Debiopharm International, Myriad Genetics, Zentalis, TORL Therapuetics, Zymeworks; Financial Interests, Personal, Other, Travel and accomodation: AstraZeneca, PharmaMar, Roche; Financial Interests, Institutional, Funding: Amgen, AbbVie Deutschland, Advaxis Inc., Aeterna Zentaris, Aprea Therapeutics AB, Regeneron Pharmaceuticals, Clovis Oncology Inc, EISAI limited LTD, F. Hoffmann –La Roche LTD, Immunogen Inc, Merck, Sharp & Dohme de España SA, Millennium Pharmaceuticals Inc, PharmaMar SA, Tesaro Inc., Bristol Myers Squibb; Non-Financial Interests, Leadership Role, on behalf of GEICO: GCIG; Non-Financial Interests, Officer, Chair of Gynaecological Track ESMO 2019. Scientific Track Member Gynaecological Cancers ESMO 2018, ESMO 2020, ESMO 2022. Member of Gynaecological Cancers Faculty and Subject Editor Gyn ESMO Guidelines: ESMO; Non-Financial Interests, Leadership Role, ESMO GYN Co-Chair 2023 - 2025: ESMO; Non-Financial Interests, Leadership Role, Chair de Cervix Committee. 2022-2024: GCIG; Non-Financial Interests, Member: ESMO, ASCO, GCIG, SEOM, GOG. D.M. O'Malley: Financial Interests, Personal, Advisory Role: Adaptimmune, Agenus, Arcus Biosciences, AstraZeneca, Atossa Therapeutics, BBI Healthcare, Celsion, Clovis Oncology, Corcept Therapeutics, DualityBio, Eisai, Elevar Therapeutics, Genelux, Genentech/Roche, GSK, GOG Foundation, Immunogen, Imvax, InxMed, Jazz Pharmaceuticals, Laekna, Merck, Mersana, Novartis, Novocure, OncoC4, Onconova Therapeutics, Regeneron, Roche, Seagen, Sutro Biopharma, Takeda, Toray Industries, Umoja Biopharma, VBL Therapeutics, Verastem Oncology, Vincerx Pharma; Financial Interests, Personal, Research Funding: AbbVie, AbbVie/Stemcentrx, Acerta Pharma, Advaxis, Ajinomoto, Amgen, Arcus Biosciences, Array BioPharma, AstraZeneca, BBI Healthcare, BeiGene, Bristol Myers Squibb, Cerulean Pharma, Clovis Oncology, Deciphera, Eisai, EMD Serono, Ergomed, Exelixis, Genentech/Roche, Genmab, GSK, Immunogen, Incyte, Iovance Biotherapeutics, Janssen Research & Development, Karyopharm Therapeutics, Leap Therapeutics, Ludwig Institute for Cancer Research, Merck, Mersana, Novartis, NovoCure, OncoQuest, Pfizer,

PharmaMar, Precision Therapeutics, Regeneron, Roche, Sanofi, Seagen, Sumitomo Dainippon Pharma Oncology, Inc., Sutro Biopharma, Tesaro, Tracon Pharma, Verastem. D. Lorusso: Financial Interests, Personal, Advisory Board, Participation in Advisory Boards and Invited Speakers: AstraZeneca, MSD; Financial Interests, Personal, Advisory Board, Participation in Advisory Boards and Invited Speaker: Clovis Oncology, GSK; Financial Interests, Personal, Advisory Board, Invited member of advisory board: Corcept, Oncoinvest, Sutro; Financial Interests, Personal, Advisory Board: Daiichi Sankyo; Financial Interests, Personal, Advisory Board, Invited member of advisory board and invited speaker: Genmab, Immunogen, Seagen; Financial Interests, Personal, Advisory Board, Invited Speaker of advisory board: Novocure; Financial Interests, Personal, Other, Consultancy: AstraZeneca, Clovis Oncology, GSK, Genmab, Immunogen, MSD, Novartis, PharmaMar, Seagen; Financial Interests, Personal, Other, Colsuntancy: Novartis; Financial Interests, Institutional, Funding, Clnical trial/contracted research: Alkermes, AstraZeneca, Clovis Oncology, GSK, MSD, Seagen, Corcept; Financial Interests, Institutional, Coordinating PI, ENGOT trial with institutional support for coordination: Clovis Oncology; Financial Interests, Institutional, Funding, Grant for founding academic trials: Clovis Oncology, GSK, MSD, Pharma&, PharmaMar; Financial Interests, Institutional, Coordinating PI, ENGOT trial with insitutional support for coordination: Genmab, MSD; Financial Interests, Institutional, Funding, Clinical trials/contracted research: Genmab, Immunogen, Incyte, Novartis, Roche; Non-Financial Interests, Principal Investigator, PI of several trials. No personal compensation received: AstraZeneca, Genmab, Cercept; Non-Financial Interests, Principal Investigator, PI of clinical trial. No personal compensation received: Clovis Oncology, Immunogen, Incyte, Roche; Non-Financial Interests, Principal Investigator, PI of several trials, no compensation received: GSK; Non-Financial Interests, Principal Investigator, PI in several trials. No personal compensation received: MSD; Non-Financial Interests, Principal Investigator, PI of several trials, no personal compensation received: Novartis; Non-Financial Interests, Principal Investigator, PI of clinical trials, no personal compensation received: PharmaMar; Non-Financial Interests, Principal Investigator, PI of clinical trial, no personal compensation received: Seagen; Non-Financial Interests, Member, Board of Directors: GCIG; Non-Financial Interests, Member, President Elected: MITO; Non-Financial Interests, Member, Coordinating: ENGOT; Other, Grants for traveling: AstraZeneca, Menarini, Clovis Oncology, GSK. S. Westin: Financial Interests, Personal, Advisory Board: AstraZeneca, Caris, Clovis Oncology/Pharma&, Corcept, Eisai, EQRX, Gilead, GSK, Immunocore, Immunogen, Lilly/Loxo, Merck, Mereo, Mersana, NGM Bio, Nuvectis, Roche/Genentech, Seagen, Verastem, Vincerx, Zentalis, ZielBio; Financial Interests, Institutional, Research Grant: AstraZeneca, AvengeBio, Bayer, Bio-Path, Clovis/Pharma&, GSK, Jazz Pharma, Mereo, Novartis, Nuvectis, Roche/Genentech, Zentalis. A.M. Oza: Financial Interests, Institutional, Research Grant, Funding for investigator initiated studies received within the last 36 months: AstraZeneca; Financial Interests, Institutional, Coordinating PI: U.S NCI, Department of Defense, Cancer Care Ontario, Ontario Institute for Cancer Research; Non-Financial Interests, Other, Uncompensated Steering Committee member: AstraZeneca, Clovis Oncology; Non-Financial Interests, Advisory Role, Uncompensated: AstraZeneca, GSK; Non-Financial Interests, Principal Investigator, Investigator-initiated studies with agents from AstraZeneca: AstraZeneca; Non-Financial Interests, Principal Investigator, Investigator-initiated trials with agents from Clovis Oncology: Clovis Oncology; Non-Financial Interests, Principal Investigator, Investigator-initiated studies with agents from GSK: GSK; Non-Financial Interests, Principal Investigator: Bristol Myers Squibb; Non-Financial Interests, Advisory Role: Bristol Myers Squibb. F. Zagouri: Financial Interests, Personal, Invited Speaker: Roche, Novartis, Gilead, Genesis Pharma, AstraZeneca, Daiichi, Eli Lilly, Merck, MSD, Pfizer; Non-Financial Interests, Principal Investigator: Roche, Eli Lilly, Pfizer, MSD. T.J. Herzog: Financial Interests, Personal, Leadership Role: GOG Foundation; Financial Interests, Personal, Advisory Role: Aravive, AstraZeneca, Caris MPI, Clovis Oncology, Eisai, Epsilogen, GSK, Johnson & Johnson, Merck, Mersana, Roche/Genentech, Seagen. R.L. Coleman: Financial Interests, Personal, Advisory Board: AstraZeneca, Alkermes, Immunogen, roche/genentech, GSK, Genmab/Seagen, Epsilogen, Myriad Genetics, Panavance, Profoundbio; Financial Interests, Personal, Invited Speaker: AstraZeneca; Financial Interests, Personal, Trial Chair: Immunogen; Financial Interests, Personal, Steering Committee Member: Merck, Roche-Genentech, Verastem, AstraZeneca, Gsk; Financial Interests, Personal, Coordinating PI: Karyopharm; Non-Financial Interests, Principal Investigator: abbvie, immunogen, Roche/Genentech, Merck, Genmab; Non-Financial Interests, Project Lead, MyLung Consortium: US Oncology Research. M.C. Lim: Financial Interests, Personal, Advisory Role: AstraZeneca, Boryung, Chong Kun Dang Pharma, Genexine, GI Innovation, Hospicare, Takeda; Financial Interests, Personal, Research Funding: AbbVie, Amgen, Astellas Pharma, BeiGene, CelliD, Chong Kun Dang Pharma, Clovis Oncology, Eisai, Genexine, GSK, Incyte, Merck, MSD, OncoQuest, Pfizer, Roche. A.M. Chudecka-Glaz: Financial Interests, Personal, Research Grant: GSK; Financial Interests, Personal, Other, honoraria: AstraZeneca, GSK; Financial Interests, Personal, Speaker's Bureau: AstraZeneca, GSK; Financial Interests, Personal, Advisory Board: AstraZeneca, GSK; Financial Interests, Personal, Principal Investigator: Clovis Oncology, AstraZeneca, MSD, Roche, GSK. R.N. Eskander: Financial Interests, Personal, Advisory Role: AstraZeneca, Clovis Oncology, Eisai, Genmab, GSK, GOG Foundation, Immunogen, MSD, PMV Pharma, Daiichi Sankyo, Elevar Therapeutics, Repare Therapeutics, Seagen, Regeneron. S. Ghamande: Financial Interests, Personal, Other, Consultant: GSK; Financial Interests, Personal, Invited Speaker: GSK. D. Despain: Financial Interests, Personal, Full or part-time Employment: pharma&. K. Fujiwara: Financial Interests, Personal, Advisory Board: Genmab, Nano Carrier, Daiichi Sankyo, Seagen; Financial Interests, Personal, Invited Speaker: Takeda; Financial Interests, Personal, Other, Travel Expense: Clovis; Financial Interests, Institutional, Coordinating PI: MSD, AstraZeneca; Non-Financial Interests, Leadership Role: GOTIC, NRG Oncology-Japan. R. Kristeleit: Financial Interests, Personal, Advisory Board: GSK, Eisai, Basilea Pharmaceutica, Clovis Oncology, Shattuck Labs, AstraZeneca, Seattle Genetics, Celcuity, Immunogen, Pharma&; Financial Interests, Personal, Invited Speaker: GSK, Zydus Cadila, Clovis Oncology, AstraZeneca, MSD; Financial Interests, Personal, Advisory Board, Consultancy and steering committee: Duke St Bio; Financial Interests, Personal, Steering Committee Member: GSK; Financial Interests, Institutional, Coordinating PI: GSK, Clovis Oncology, InCyte, AstraZeneca, MSD, Allarity, IoVance; Financial Interests, Institutional, Trial Chair: Clovis Oncology; Financial Interests, Institutional, Local PI: Eisai, BerGenBio, Artios, Regeneron; Financial Interests, Institutional, Research Grant: MSD; Financial Interests, Steering Committee Member: Eisai, AstraZeneca, Merck; Financial Interests, Coordinating PI: Tubulis, Merck, Epsilogen; Financial Interests, Trial Chair: Leucid Bio; Non-Financial Interests, Advisory Role: OHEAG Advisor, CRUK NAC Committee member. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2024.08.2269

LBA32 A randomized, phase II, dose optimization of gotistobart, a pH-sensitive anti-CTLA-4, in combination with standard dose pembrolizumab in platinum-resistant recurrent ovarian cancer: Safety, efficacy and dose optimization (PRESERVE-004/GOG-3081)

J.N. Barlin[1], P.C. Lim[2], J. Thomes Pepin[3], E.E. Hopp[4], N.G. Cloven[5], C. Lee[6], H.D. Eshed[7], D. Black[8], H.M. Cottrill[9], L. Hand[10], D.M. O'Malley[11], L.T. Chuang[12], L. Willmott[13], M. Chisamore[14], S. Shpyro[15], J. Durbin[16], P. Zheng[17], Y. Liu[18], B.J. Monk[19]

[1]Gynecologic Oncology, Women's Cancer Care Associates, Albany, NY, USA; [2]Obstetrics and Gynecology, Center of Hope Reno, Reno, NV, USA; [3]Gynecology Oncology, Minnesota Oncology, Minneapolis, MN, USA; [4]Obstetrics and Gynecology, Froedtert Hospital & Medical College of Wisconsin, Milwaukee, WI, USA; [5]Gynecologic Oncology Department, Texas Oncology, Fort Worth, TX, USA; [6]Gynecologic Oncology, Texas Oncology - The Woodlands, Huston, TX, USA; [7]Gynecologic Oncology, Texas Oncology - Austin North, Austin, TX, USA; [8]Gynecologic Oncology, LSU Health Shreveport, Shreveport, LA, USA; [9]Gynecologic Oncology, Baptist Health, Lexington, KY, USA; [10]Gynecologic Oncology, Baptist Health Jacksonville, Jacksonville, FL, USA; [11]Gyn Oncology, OSUCCC - The Ohio State University Comprehensive Cancer Center - James, Columbus, OH, USA; [12]Gynecologic Oncology, Danbury Hospital, part of Nuvance Health, Danbury, CT, USA; [13]Gynecologic Oncology, Arizona Center for Cancer Care, Phoenix, AZ, USA; [14]Oncology Early Clinical Development, Merck & Co., Inc., Rahway, NJ, USA; [15]Clinical Development, BioNTech SE, Mainz, Germany; [16]Clinical Operations, OncoC4, Inc., Rockville, MD, USA; [17]Clinical Development, OncoC4, Inc., Rockville, MD, USA; [18]Research, OncoC4, Inc., Rockville, MD, USA; [19]Gynecologic Oncology Department, Florida Cancer Specialists and Research Institute, West Palm Beach, FL, USA

Background: Gotistobart (ONC-392/BNT316) is a humanized anti-CTLA-4 mAb that preserves CTLA-4 immune checkpoint activity by avoiding lysosomal degradation. The safety and clinical activity of gotistobart monotherapy in ovarian cancer was previously reported [https://doi.org/10.1136/jitc-2022-SITC2022.0564]. We report safety and efficacy results of gotistobart + pembrolizumab in a randomized, open-label, multicenter phase 2 trial in patients with PROC.

Methods: Patients with platinum-resistant high-grade serous OC, tubal or peritoneal cancer who previously received 1 line of platinum-based therapy and progressed between 3-6 months, or received ≥1 line and progressed within 6 months of last dose, were randomized 1:1 to receive different doses of gotistobart + pembrolizumab 200 mg, Q3W. Primary endpoints are ORR (RECIST 1.1) and safety. Secondary endpoints include PFS and OS.

Results: As of May 24, 2024, 83 patients had received ≥1 dose of gotistobart + pembrolizumab with 33 and 29 patients in 1 mg/kg and 2 mg/kg gotistobart + pembrolizumab groups, respectively. At the safety and efficacy cutoff date of May 10, 2024, with a median follow-up of 2.1 months (range 0.1-9.2), grade ≥3 treatment-related adverse events (TRAEs) were observed in 35.7% and 31.0% patients in 1 mg/kg or 2 mg/kg groups, respectively. No grade 5 TRAEs were observed. Common grade 3 TRAEs from combined groups were increased ALT and AST (both 7.0%), and diarrhea (5.3%). Unconfirmed ORR was 31.8% (7/22; 95% CI 13.9-54.9) and 36.4% (8/22; 95% CI 17.2-59.3) in 1 mg/kg and 2 mg/kg groups, respectively.

Table: LBA32

Gotistobart + 200 mg Pembrolizumab Q3W Cutoff date: 10 May 2024	1 mg/kg n=28	2 mg/kg n=29
Safety		
Treatment cycles, Mean (Range)	3.6 (1-9)	3.4 (1-9)
Treatment duration in months, Mean (Range)	2.71 (0.1-7.6)	2.55 (0.3-7.1)
Any TEAEs, N (%)	25 (89.3)	26 (89.7)
TRAEs: All grades, N (%)	21 (75.0)	20 (69.0)
TRAEs: Grade ≥ 3, N (%)	10 (35.7)	9 (31.0)
irAE All grades, N (%)	11 (39.3)	13 (44.8)
irAE: Grade ≥ 3, N (%)	5 (17.9)	8 (27.6)
TRAE leading to study drug discontinuation	4 (14.3)	3 (10.3)
Efficacy		
Efficacy-evaluable population	22	22
Unconfirmed ORR, N (%)	7 (31.8)	8 (36.4)
CR	1 (4.5)	1 (4.5)
PR	6 (27.3)	7 (31.8)
SD	6 (27.3)	2 (9.0)
PD*	9 (40.9)	12 (54.5)

*PD included those without post baseline disease assessment