Financial Interests, Institutional, Research Funding: 2X Oncology, Aravive, Arch Oncology, AstraZeneca, Bristol Myers Squibb, Clovis Oncology, CytomX Therapeutics, GSK, Regeneron, Surface Oncology, Tesaro, Vigeo Therapeutics and Zentalis. S. Bouberhan: Financial Interests, Personal, Speaker, Consultant, Advisor: ImmunoGen. E.P. Hamilton: Financial Interests, Institutional, Research Grant: Regeneron, AbbVie, Acerta Pharma, ADC Therapeutics, Akesobio Australia, Amgen, Aravive, ArQule, Arvinas, AstraZeneca, AtlasMedX, Black Diamond, Boehringer Ingelheim, Clovis, Compugen, Curis, CytomX, Dana Farber Cancer Inst, Daiichi Sankyo, Deciphera, eFFE; Financial Interests, Institutional, Speaker, Consultant, Advisor: Arcus, Arvinas, AstraZeneca, Black Diamond, Boehringer Ingelheim, CytomX, Daiichi Sankyo, Dantari, Deciphera Pharmaceuticals, Eisai, H3 Biomedicine, iTeos, Janssen, Lilly, Loxo, Merck, Mersana, Novartis, Pfizer, Puma Biotechnology, Relay Therapeutics, Roc. S. Yoo, S. Govindraj, J. Brouwer-Visser, M. Peterman, T. Schmidt, B. Barnes, P. Madia, M. Zhu, T.S. Uldrick, E.A. Miller: Financial Interests, Personal, Full or part-time Employment: Regeneron Pharmaceuticals, Inc.; Financial Interests, Personal, Stocks/Shares: Regeneron Pharmaceuticals, Inc. D. O'Malley: Financial Interests, Personal, Research Funding: AbbVie, Agenus, Amgen, AstraZeneca, Celsion Corp, Clovis, Corcept Therapeutics, Eisai, GOG Foundation , Immunogen, Iovance, Janssen/Johnson & Johnson, Mersana, Novocure and Genentech/Roche, Regeneron, SDP Oncology (BBI), Seagen and Tesaro/GSK, Ajinomoto Inc., Array Biopharma, Bristol Myers Squibb Co., Cerulean Pharma, EMD Serono, Ergomed, Inc. Research, Inc., inVentiv Health Clinical PRA Intl, Ludwig Cancer Research, Merck and GenMab, New Mexico Cancer Care Alliance, Serono Inc., Stemcentrx, Inc; Financial Interests, Personal, Advisory Board, Personal fees (consulting and/or advisory boards): Ambry, Arquer Diagnostics, Elevar, INXMED, Myriad Genetics, Novartis, Rubis, Roche Diagnostics MSA, Sorrento, Takeda, Tarveda and Toray, AbbVie, Agenus, Amgen, AstraZeneca, Celsion Corp, Clovis, Corcept Therapeutics, Eisai, GOG Foundation, Immunogen, Iovance, Janssen/Johnson & Johnson, Mersana, Novocure and Genentech/Roche, Regeneron, SDP Oncology (BBI), Seagen and Tesaro/GSK. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.1933

755P Retifanlimab in patients with recurrent microsatellite instability-high (MSI-H) or deficient mismatch repair (dMMR) endometrial cancer: Final results from the POD1UM-101 study (Cohort H)

D. Berton-Rigaud[1], P. Pautier[2], D. Lorusso[3], C. Gennigens[4], L. Gladieff[5], A. Kryzhanivska[6], J. Bowman[7], C. Tian[8], M. Cornfeld[7], T. Van Gorp[9]

[1]Service d'Oncologie Médicale, GINECO and Institut de Cancérologie de l'Ouest (ICO), Saint-Herblain, France; [2]Département de Médecine, GINECO and Institut Gustave-Roussy, Villejuif, France; [3]Gynecologic Oncology Unit, Fondazione Policlinico Universitario Agostino Gemelli-IRCCS Rome and Catholic University of Sacred Heart, Rome, Italy; [4]Oncology Gynecology Unit, Centre Hospitalier Universitaire Sart Tilman, Liège, Belgium; [5]The Medical Oncology Department, GINECO and Institut Claudius Regaud IUCT Oncopole, Toulouse, France; [6]Gynecological Surgical Department, Ivano-Frankivsk National Medical University, Ivano-Frankivsk, Ukraine; [7]Immuno-Oncology, Incyte Corporation, Wilmington, DE, USA; [8]Biostatistics, Incyte Corporation, Wilmington, DE, USA; [9]Department of Gynaecology-Division of Gynaecological Oncology, University Hospitals Leuven, Leuven Cancer Institute, Leuven, Belgium

Background: Retifanlimab (Zynyz™) is a programmed death receptor-1 (PD-1)–blocking antibody recently approved in the United States for the treatment of adult patients with metastatic or recurrent locally advanced Merkel cell carcinoma. POD1UM-101 (NCT03059823) is an ongoing first-in-human dose finding and cohort expansion study in patients with advanced solid tumours. We have previously reported significant clinical activity with safety for retifanlimab representative of the class in the MSI-H or dMMR endometrial cancer expansion cohort (Berton D, SITC 2021). We present final study results.

Methods: Eligible patients had histologically proven, unresectable recurrent/metastatic MSI-H or dMMR endometrial cancer, Eastern Cooperative Oncology Group performance status (ECOG PS) $\leq$1, disease progression during or following 1 to $\leq$5 prior systemic treatments, measurable disease (per RECIST v1.1), and were naïve to prior immune checkpoint inhibitors. MSI-H and dMMR status were centrally confirmed. Patients received retifanlimab 500 mg every 4 weeks for up to 2 years. The primary study endpoint was safety. Confirmed best overall response and duration of response were evaluated by independent central reviewer (ICR).

Results: A total of 76 patients with centrally confirmed MSI-H (65 [85.5%]) or dMMR (11 [14.5%]) disease were enrolled, with the last patient initiating treatment on 29 December 2020. Median age was 67 (range 49–88) years, 70 (92%) had endometrioid histology, 67 (88%) had metastatic disease, and 61 (80%) had visceral metastases. Most patients had received prior radiotherapy (54 [71%]) or surgery (68 [90%]). All patients except for one, had received prior chemotherapy for advanced disease with 33 (43.4%) patients receiving $\geq$2 prior systemic therapies. The overall response rate by ICR was 43% (95% CI: 32–55). Final results for this cohort including safety and secondary efficacy endpoints will be presented.

Conclusions: Retifanlimab has shown notable clinical activity in previously treated MSI-H or dMMR endometrial cancer, which is consistent with other checkpoint immunotherapies.

Clinical trial identification: NCT03059823, EudraCT 2017-000865-63.

Editorial acknowledgement: Envision Pharma Group (Philadelphia, PA), funded by Incyte Corporation (Wilmington, DE).

Legal entity responsible for the study: Incyte Corporation (Wilmington, DE).

Funding: Incyte Corporation, Wilmington, DE.

Disclosure: P. Pautier: Financial Interests, Institutional, Other, Travel & Honoraria: AstraZeneca, MSD, Tesaro; Financial Interests, Institutional, Other, Travel: Novartis; Financial Interests, Institutional, Advisory Board: AstraZeneca, Novartis, Tesaro. D. Lorusso: Financial Interests, Institutional, Advisory Role, Consultancy: Novartis, PharmaMar; Financial Interests, Institutional, Advisory Board, and invited speaker: AstraZeneca, Clovis Oncology, Genmab, GSK, Immunogen, MSD, Seagen; Financial Interests, Institutional, Other, ENGOT trial with institutional support for coordination: Clovis Oncology, Corcept, Genmab, Immunogen, MSD; Financial Interests, Research Grant, Grant for founding academic trial: Clovis Oncology, GSK, MSD. C. Gennigens: Financial Interests, Institutional, Research Grant: AstraZeneca; Financial Interests, Institutional, Advisory Role: GSK, Ispen, MSD; Financial Interests, Institutional, Other, Honoraria: AstraZencea, Bristol Myers Squibb, GSK; Financial Interests, Institutional, Other, Honoraria and Support for meetings and/or travel: Ispen, MSD, Pfizer, PharmaMar; Financial Interests, Institutional, Advisory Board: AstraZeneca, Bristol Myers Squibb, Eisai, GSK, Ispen, MSD. L. Gladieff: Financial Interests, Advisory Board: AstraZeneca, Clovis Oncology, GSK, MSD; Financial Interests, Other, Honoraria: AstraZeneca, GSK, MSD, PharmaMar, Roche ; Financial Interests, Funding, Congress funding: GSK, PharmaMar, Roche, Viatris. J. Bowman, C. Tian, M. Cornfeld: Financial Interests, Institutional, Full or part-time Employment: Incyte; Financial Interests, Institutional, Stocks/Shares: Incyte. T. Van Gorp: Financial Interests, Institutional, Advisory Board: AstraZeneca, GSK, MSD, Tubulis; Financial Interests, Institutional, Research Grant: Amgen, Roche, AstraZeneca; Financial Interests, Institutional, Invited Speaker: GSK. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.1934

756P First-in-human phase I study of a novel claudin 6 (CLDN6) targeted antibody drug conjugate (ADC) TORL-1-23

G.E. Konecny[1], A.E. Wahner Hendrickson[2], B. Winterhoff[3], A. Machado[4], C. Chander[5], S. Davenport[6], S. Bilic[7], L-L. Miller[8], A. Chung[8], M.F. Press[9], S. Letrent[10], D. Slamon[11]

[1]Department of Medicine, UCLA Westwood Oncology Hematology, Los Angeles, CA, USA; [2]Medical Oncology, Mayo Clinic, Rochester, MN, USA; [3]Division of Gynecologic Oncology, University of Minnesota, Minneapolis, MN, USA; [4]Medical, TRIO-Translational Research in Oncology, Montevideo, Uruguay; [5]Department of Medicine, Jonsson Comprehensive Cancer Center at UCLA, Los Angeles, CA, USA; [6]Department of Medicine, USC Norris Comprehensive Cancer Center, Los Angeles, CA, USA; [7]Clinical Pharmacology, Vanadro, LLC., Waukee, IA, USA; [8]Clinical Operations, TRIO-US, Los Angeles, CA, USA; [9]Pathology, Keck School of Medicine-University of Southern California USC, Los Angeles, CA, USA; [10]Research and Development, TORL Biotherapeutics, Culver City, CA, USA; [11]Hematology/Oncology, UCLA-David Geffen School of Medicine, Los Angeles, CA, USA

Background: CLDN6 is expressed at high levels in multiple cancers with little to no expression in normal tissues and has been implicated in the initiation, progression, and metastasis of some cancers. CLDN6 is an ideal target for development of new therapeutics. TORL-1-23 is first-in-class ADC targeting the tumor-specific antigen CLDN6.

Methods: This ongoing first in human study (TORL123-001, NCT05103683) characterizes the safety, tolerability, dose-limiting toxicities (DLTs), maximum tolerated dose (MTD), and recommended phase 2 dose (RP2D) of TORL-1-23 in participants with advanced solid tumors. Pharmacokinetics (PK), immunogenicity and clinical efficacy are also assessed. TORL-1-23 is administered IV every 3 weeks. In Dose Escalation, cohorts up to 6 participants are evaluated at each dose level according to an accelerated titration design. In Dose Expansion, patients with CLDN6-expressing cancers will be evaluated to confirm the RP2D in ovarian cancer, NSCLC, and other CLDN6+ cancers using an IHC companion diagnostic. Doses above the historic MTD for MMAE containing ADCs are being evaluated given the favorable safety/tolerability at doses $<$2.4 mg/kg.

Results: 30 patients with ovarian (n=22), testicular (n=5), and endometrial (n=3) cancers were enrolled across 9 dose levels ranging from 0.2 to 3 mg/kg IV every 3 weeks (as of 01MAY2023). 93% of pts had received $\geq$ 3 prior lines of treatment in the metastatic setting. The most common treatment-related adverse events were Gr1/2 fatigue (n=6), anemia (n=5), and peripheral neuropathy (n=4). No DLTs were observed at doses $\leq$2.4 mg/kg. Sustained PK exposure of TORL-1-23 over the dosing interval and low levels of circulating MMAE are noted. Partial responses (PR) were observed in 7/22 (32%) efficacy evaluable participants with CLDN6+ disease (6 ovarian, 1 testicular) across dose levels. 3/3 (100%) participants with CLDN6+ ovarian cancer responded at the 2.4 mg/kg dose level. Data from 3 mg/kg are pending.

Conclusions: In participants with heavily-pretreated CLDN6-expressing ovarian cancer, the novel TORL-1-23 ADC has a favorable safety/tolerability profile and encouraging antitumor activity in a phase 1 dose finding study. Further evaluation in ovarian cancer and other CLDN6+ cancers is warranted.

Clinical trial identification: NCT05103683.

Editorial acknowledgement: None.

Legal entity responsible for the study: TORL Biotherapeutics.

Funding: TORL Biotherapeutics.

Disclosure: A. Machado, S. Davenport, S. Bilic, L. Miller, A. Chung: Financial Interests, Institutional, Other, Fee for Service: TORL Biotherapeutics. M.F. Press: Financial Interests, Personal, Advisory Board: Biocartis, Cepheid, Lilly USA, LLC; Financial Interests, Personal, Other, Consultant: Zymeworks, Inc., Eli Lilly & Company, AstraZeneca, Merck, Novartis; Financial Interests, Personal, Ownership Interest: TORL Biotherapeutics LLC; Financial Interests, Institutional, Other, Fee-for-Service Agreements: Zymeworks, Inc., TRIO-US, TRIO; Financial Interests, Institutional, Other, Fee-For-Service Agreements: TORL Biotherapeutics LLC; Financial Interests, Institutional, Other, Fee-for-Service Agreement: Ambrx, 1200 Pharma. S. Letrent: Financial Interests, Personal, Full or part-time Employment: TORL Biotherapeutics. D. Slamon: Financial Interests, Personal and Institutional, Leadership Role: TORL Biotherapeutics; Financial Interests, Personal and Institutional, Ownership Interest: TORL Biotherapeutics. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.09.1935