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## 605O YL201, a novel B7H3-targeting antibody-drug conjugate (ADC), in patients (pts) with advanced solid tumors: Results from a first-in-human phase I study

H. Zhao[1], Y. Ma[1], X. Meng[2], L. Wu[3], Y. Fan[4], Y. Zheng[5], Z. Liu[6], Y. Ji[7], D. Lv[8], S. Luo[9], D. Sommerhalder[10], S. Fu[11], Y. Huang[12], Y. Yang[12], W. Fang[12], Y. Zhao[12], Y. Wang[5], S. Chin[13], T. Xue[13], L. Zhang[12]

*[1]Department of Clinical Research, State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Guangdong Key Laboratory of Nasopharyngeal Carcinoma Diagnosis and Therapy, Sun Yat-sen University Cancer Center, Guangzhou, China; [2]Radiation Oncology, Shandong Cancer Hospital and Institute, Shandong First Medical University and Shandong Academy of Medical Sciences, Jinan, China; [3]Thoracic Medicine Department II, Hunan Cancer Hospital/The Affiliated Cancer Hospital of Xiangya School of Medicine, Central South University, Changsha, China; [4]Department of Thoracic Medical Oncology, Zhejiang Cancer Hospital - Cancer Research Institute, Hangzhou, China; [5]Department of Medical Oncology, The First Affiliated Hospital of Medical School of Zhejiang University, Hangzhou, China; [6]Medical Oncology, Jiangxi Cancer Hospital, Nanchang, China; [7]Department of Oncology, The First Affiliated Hospital of Xinxiang Medical University, Xinxiang, China; [8]Respiratory Medicine, Taizhou Hospital of Zhejiang Province, Taizhou, China; [9]Phase I Clinical Research Center, Henan Cancer Hospital, Zhengzhou, China; [10]Oncology, NEXT OncologyTM, San Antonio, TX, USA; [11]Investigational Cancer Therapeutics, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [12]Medical Oncology Dept., Sun Yat-sen University Cancer Center, Guangzhou, China; [13]MediLink Therapeutics (Suzhou) Co., Ltd, Suzhou, China*

**Background:** YL201 is a B7H3-targeting ADC with a tumor microenvironment activable linker and a novel topoisomerase I inhibitor payload. Here, we report safety and preliminary efficacy of YL201 monotherapy in pts with advanced solid tumors from phase 1 dose escalation and expansion study.

**Methods:** Pts with metastatic/locally advanced solid tumors with ECOG PS $\leq$1 were treated with YL201 intravenously Q3W. For dose escalation, the 3+3 design was utilized with six dose levels from 0.8 to 3.0 mg/kg. For dose expansion, pts with selected tumor types were treated at the recommended expansion doses (REDs).

**Results:** As of 26 Apr 2024, 276 pts were enrolled and received at least one dose (dose escalation, n=49; dose expansion, n=227). The top 3 tumor types enrolled were small cell lung cancer (SCLC, n=79), nasopharyngeal carcinoma (NPC, n=75), and non-small cell lung cancer without actionable genomic alterations (NSCLC without AGAs, n=44). 60% pts had previously received at least 2 lines of therapy. During dose escalation, DLTs were observed at 2.8 mg/kg (n=1) and 3.0 mg/kg (n=2) including neutropenia, febrile neutropenia and thrombocytopenia, and 2.0 and 2.4 mg/kg were selected as REDs in dose expansion. Among the response-evaluable pts treated at $\geq$2.0 mg/kg (n=146), the response rates were 73.7%, 45.9%, and 32.1% in pts with SCLC, NPC, and NSCLC without AGAs, respectively. The 3-month DoR rates were 77.5% and 91.7% in SCLC and NPC. The most common hematological TRAEs were leukopenia (52.9%; grade [G]$\geq$3: 22.5%), anemia (51.1%; G$\geq$3: 14.9%) and neutropenia (48.9%; G$\geq$3: 23.9%), while decreased appetite (22.5%; G$\geq$3: 1.1%) and nausea (21.0%; G$\geq$3: 0.7%) were the most common non-hematological TRAEs. One (0.4%) interstitial lung disease was reported. The PK, updated DoR and other details will be presented in the meeting.

**Table: 605O**

| | YL201 ≥2.0 mg/kg | | |
|---|---|---|---|
| | SCLC | NPC | NSCLC without AGAs |
| ORR (%) | 73.7 (42/57) | 45.9 (28/61) | 32.1 (9/28) |
| DCR (%) | 98.2 (56/57) | 95.1 (58/61) | 85.7 (24/28) |

**Conclusions:** YL201 has demonstrated encouraging efficacy in heavily pretreated advanced solid tumors with manageable safety and tolerability profile.

**Clinical trial identification:** NCT05434234 & NCT06057922.

**Legal entity responsible for the study:** The authors.

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## 606O Initial results from a first-in-human study of the B7-H4-directed antibody-drug conjugate (ADC) AZD8205 (puxitatug samrotecan) in patients with advanced/metastatic solid tumors

F. Meric-Bernstam[1], Y. Naito[2], S. Gaillard[3], T. Shimoi[4], V. Chung[5], A.A. Davis[6], T. Proia[7], A. Ayyoub[8], M. Kulkarni[8], S. Upadhyay[9], N. Miller[9], N. Luheshi[9], A. Varga[9], D-Y. Oh[10], L. Mileshkin[11]

*[1]Investigational Cancer Therapeutics Department, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Department of General Internal Medicine, National Cancer Center Hospital East, Chiba, Japan; [3]Oncology and Gynecology/Obstetrics, Johns Hopkins University, Baltimore, MD, USA; [4]Oncology Department, National Cancer Center Hospital, Chuo-ku, Japan; [5]Medical Oncology Department, City of Hope Comprehensive Cancer Center, Duarte, CA, USA; [6]Medicine Department, Division of Hematology and Oncology, Washington University School of Medicine in St. Louis, St. Louis, MO, USA; [7]AstraZeneca, Waltham, MA, USA; [8]Oncology, AstraZeneca, Gaithersburg, MD, USA; [9]Oncology R&D, AstraZeneca, Cambridge, UK; [10]Internal Medicine Dept., Seoul National University Hospital, Cancer Research Institute, Seoul National University College of Medicine, Seoul, Republic of Korea; [11]Department of Medical Oncology, Peter MacCallum Cancer Centre, Parkville, VIC, Australia*

**Background:** B7-H4 is a promising ADC target with high expression in several solid tumors and limited normal tissue expression. B7-H4 negatively regulates T cell function and high expression of B7-H4 is associated with disease progression. AZD8205 is a novel B7-H4—directed topoisomerase I inhibitor (Top1i) ADC with favorable preclinical antitumor activity in patient-derived xenograft models with an acceptable toxicity profile. This report presents initial results from the dose escalation part of a Phase 1/2a, open-label, multicenter study (NCT05123482; BLUESTAR) of AZD8205 monotherapy in patients (pts) with advanced/metastatic select solid tumors.

**Methods:** Eligible pts were $\geq$18 years old with advanced/metastatic ovarian, breast, endometrial cancer, or cholangiocarcinoma expressing B7-H4 (detected by immunohistochemistry in baseline tumor samples) with progression after available standard of care therapy, had measurable disease by RECIST v1.1 and ECOG PS 0—1. AZD8205 was administered at 0.8—3.2 mg/kg IV every 3 weeks. Safety was a primary objective. Preliminary efficacy was a secondary objective.

**Results:** As of February 23, 2024, 46 pts received AZD8205, 21 during dose escalation and 25 in backfill cohorts. Median age was 56 years (range, 24—88) and pts had received a median number of 4 previous treatment regimens at baseline (range, 2—9). Any grade treatment-emergent adverse events (TEAEs) occurred in 97.8% of pts, most commonly nausea (58.7%), neutropenia (56.5%), and anemia (50.0%). Grade $\geq$3 TEAEs occurred in 82.6% of pts, most commonly neutropenia (37.0%) and anemia (30.4%). Two pts (4.3%) discontinued treatment due to TEAEs. Two pts had dose-limiting toxicities at 3.2 mg/kg (neutrophil count decreased [n=1] and platelet count decreased [n=1]). Of the 43 pts treated at doses $\geq$1.6 mg/kg, 9 pts with ovarian, breast or endometrial cancer had a confirmed partial response (20.9%).

**Conclusions:** AZD8205 had a manageable safety profile consistent with other Top1i ADCs and showed preliminary efficacy in heavily pre-treated pts with prior progression on standard treatment. Phase 2 expansion cohorts are ongoing in ovarian, breast, endometrial and biliary tract cancer.

**Clinical trial identification:** NCT05123482; 17/11/2021.

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## 607O Interim results of a phase I study of SGN-PDL1V (PF-08046054) in patients with PDL1-expressing solid tumors

M. Oliva[1], S. Ochsenreither[2], C. Le Tourneau[3], S. Champiat[4], R. Saleh[5], K. Burkitt[6], L. Nabell[7], N. Steeghs[8], A. Spreafico[9], A.R. Minchom[10], A. Patnaik[11], J.A. Call[12], E. Fontana[13], N. Kotecki[14], E. Garralda[15], A. Zivi[16], J.W. Riess[17], S. Gupta[18], R. Zhang[19], M. Gillison[20]

*[1]Medical Oncology, Institut Catala d'Oncologia - Hospital Duran i Reynals (ICO L'Hospitalet), Hospitalet de Llobregat, Spain; [2]Hematology Oncology Tumor Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany; [3]Department of Drug Development and Innovation (D3i), Institut Curie, Paris, France; [4]Drug Development Department (DITEP), Gustave Roussy, Villejuif, France; [5]Medical Oncology Department, McGill University Health Centre - Royal Victoria Hospital, Montreal, QC, Canada; [6]Medical Oncology, University Hospitals Cleveland Medical Center, Cleveland, OH, USA; [7]Hematology & Oncology, University of Alabama at Birmingham, Birmingham, AL, USA; [8]Medical Oncology Department, Netherlands Cancer Institute, Amsterdam, Netherlands; [9]Medical Oncology and Hematology Dept., UHN - University Health Network - Princess Margaret Cancer Center, Toronto, ON, Canada; [10]Medical Oncology and Drug Development Unit, The Royal Marsden Hospital, London, UK; [11]Medical Oncology Dept., The START Center for Cancer Research, San Antonio, TX, USA; [12]Phase I Trials, The START Center for Cancer Research, West Valley City, UT, USA; [13]Drug Development, Sarah Cannon Research Institute SCRI UK, London, UK; [14]Medical Oncology Department, Institute Jules Bordet, Anderlecht, Belgium; [15]Early Drug Development Dept., Hospital Universitari Vall d'Hebron, Barcelona, Spain; [16]Medical Oncology, Azienda Ospedaliera Universitaria Integrata Verona/Centro Ricerche Cliniche di Verona, Verona, Italy; [17]Hematology and Oncology, UC Davis Comprehensive Cancer Center, Sacramento, CA, USA; [18]Oncology Clinical Development, Pfizer Inc, Bothell, WA, USA; [19]Biostatistics, Pfizer Inc, Bothell, WA, USA; [20]Thoracic-Head & Neck Medical Oncology, Division of Cancer Medicine, University of Texas MD Anderson Cancer Center, Houston, TX, USA*

**Background:** To assess the safety/tolerability and antitumor activity of SGN-PDL1V, a novel investigational antibody-drug conjugate that delivers monomethyl auristatin E to cells that express Programmed Cell Death Ligand 1 (PDL1).

**Methods:** SGNPDL1V-001 (NCT05208762) is a phase 1 study enrolling patients (pts) with relapsed/refractory PDL1-expressing solid tumors (non-small cell lung cancer [NSCLC], head and neck squamous cell carcinoma [HNSCC], triple negative breast cancer [TNBC], and esophageal cancer [EC]) who progressed on standard of care therapies. Measurable disease per RECIST v1.1, and ECOG PS of $\leq$1 are required. In dose escalation, pts received doses of SGN-PDL1V from 0.5-1.75 mg/kg on days 1, and 8 of every 21-day cycle using adjusted ideal body weight. The primary objectives of this study are safety/tolerability and pharmacokinetics with antitumor activity as a secondary objective.

**Results:** As of March 6, 2024, 55 pts were dosed with a median age of 60 years (range 24–72); 54.5% were male, 72.7% had ECOG PS 1, 54.5% had HNSCC, 29.1% NSCLC, 14.5% TNBC, and 1.8% EC. No dose-limiting toxicities (DLTs) were seen; 1.75 mg/kg was the highest dose evaluated. Peripheral sensory neuropathy (21.8%), asthenia (18.2%), fatigue (18.2%), and nausea (18.2%), were the most common treatment-related adverse events (TRAEs); the majority were grade 1-2 in severity. No immune-related TRAEs were seen. Overall grade $\geq$ 3 TRAEs was 30.9%. The most common grade $\geq$ 3 TRAE was decreased neutrophil count (7.3%). Treatment discontinuation due to treatment-emergent AEs was seen in 14.5% of pts. The investigator-assessed objective response rate (ORR) across all doses and tumor types was 27.3% (12.7% confirmed), and the median duration of confirmed responses was 7.9 months. Objective responses were observed starting at 1.25 mg/kg and independent of PDL1 expression.

**Conclusions:** Single agent SGN-PDL1V was generally well tolerated with a manageable safety profile. Encouraging preliminary antitumor activity was observed. Enrollment in the phase 1 study continues.

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## 608O Preliminary safety and clinical activity of ASP3082, a first-in-class, KRAS G12D selective protein degrader in adults with advanced pancreatic (PC), colorectal (CRC), and non-small cell lung cancer (NSCLC)

W. Park[1], A. Kasi[2], A.I. Spira[3], J.D. Berlin[4], J.S. Wang[5], B. Herzberg[6], Y. Kuboki[7], S. Kitano[8], M. Pelster[9], J.W. Goldman[10], D. Morgensztern[11], S. Kondo[12], P.A. Jänne[13], H. Fujii[14], H-J. Lee[15], S. Gill[16], A. Saci[17], P. Lorusso[18], A.W. Tolcher[19]

*[1]Gastrointestinal Oncology Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Department of Medicine, Division of Medical Oncology, University of Kansas Medical Center, Westwood, CA, USA; [3]Research Department, Virginia Cancer Specialists Research Institute, Fairfax, VA, USA; [4]Division of Hematology/Oncology, Vanderbilt-Ingram Cancer Center, Nashville, TN, USA; [5]Drug Development Unit, Florida Cancer Specialists/Sarah Cannon Research Institute, Sarasota, FL, USA; [6]Division of Hematology/Medical Oncology, Department of Medicine, Columbia University Irving Medical Center, Herbert Irving Comprehensive Cancer Center, New York, NY, USA; [7]Department of Experimental Therapeutics, National Cancer Center Hospital East, Kashiwa, Japan; [8]Advanced Medical Development Center, The Cancer Institute Hospital of Japanese Foundation for Cancer Research, Koto-ku, Japan; [9]GI Cancer Research, Sarah Cannon Research Institute, Nashville, TN, USA; [10]Medicine, David Geffen School of Medicine, Los Angeles, CA, USA; [11]Medical Oncology Dept., Washington University School of Medicine in St. Louis, St. Louis, MO, USA; [12]Department of Experimental Therapeutics, National Cancer Center - Tsukiji Campus, Chuo-ku, Japan; [13]Lowe Center for Thoracic Oncology, Dana Farber Cancer Institute, Boston, MA, USA; [14]Medical Science, Astellas Pharma USA, Northbrook, IL, USA; [15]Biostatistics, Astellas Pharma Inc., Northbrook, IL, USA; [16]Global Clinical Pharmacology & Exploratory Development Science, Astellas Pharma Global Development, Inc., Northbrook, IL, USA; [17]Translational Medicine, Astellas Pharma Global Development, Inc., Deerfield, IL, USA; [18]15Department of Internal Medicine, Section of Medical Oncology, Yale School of Medicine - Radiology and Biomedical Imaging, New Haven, CT, USA; [19]Clinical Research, South Texas Accelerated Research Therapeutics, San Antonio, TX, USA*

**Background:** ASP3082 is a novel protein degrader selectively targeting KRAS G12D. Here, we describe the preliminary safety and antitumor activity of ASP3082 monotherapy in patients (pts) with previously treated advanced solid tumors.