

LBA7

CLARITY-Gastric 01 (CG-01): A phase 3 study of sonesitatug vedotin (Sone-Ve) in second or later-line (2L+) advanced or metastatic Claudin 18.2 (CLDN18.2)-positive gastroesophageal carcinoma (GEC)

R-H. Xu¹, Y.Y. Janjigian², M-H. Chen³, J. Lee⁴, J. Zhang⁵, E. Elimova⁶, E. Smyth⁷, T.O. Goetze⁸, W. Guo⁹, M. Furuta¹⁰, K-W. Lee¹¹, G.T.H. Nguyen¹², F. Pietrantonio¹³, M.C. Riesco-Martinez¹⁴, A. Turpin¹⁵, D.R. Castillo¹⁶, J. Ye¹⁷, S. Liu¹⁷, N. Valeri¹⁸, K. Shitara¹⁹

¹ Department of Medical Oncology, Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in South China, Guangdong Provincial Clinical Research Center for Cancer, Sun Yat-sen University, Guangzhou, China, ² Gastrointestinal Oncology Service, Department of Medicine, Memorial Sloan Kettering Cancer Center and Weill Cornell Medical Center, New York, United States of America, ³ Department of Oncology, Taipei Veterans General Hospital, Taipei, Taiwan, ⁴ Division of Hematology-Oncology, Department of Medicine, Sungkyunkwan University School of Medicine, Samsung Medical Center, Seoul, Republic of Korea, ⁵ Department of Oncology, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China, ⁶ Medical Oncology and Hematology, Princess Margaret Cancer Centre, Toronto, Canada, ⁷ NIHR Biomedical Research Centre, Churchill Hospital, Oxford, United Kingdom, ⁸ Hospital Northwest, University Cancer Center Frankfurt, Frankfurt, Germany, ⁹ Department of Medical Oncology, Fudan University Shanghai Cancer Center, Shanghai, China, ¹⁰ Department of Gastroenterology, Kanagawa Cancer Center, Yokohama, Japan, ¹¹ Department of Internal Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Republic of Korea, ¹² Department of Cancer Epidemiology, Vietnam National Cancer Hospital, Ha Noi, Vietnam, ¹³ Medical Oncology Department, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, ¹⁴ Medical Oncology Department, Hospital Universitario 12 de Octubre, Madrid, Spain, ¹⁵ Department of Medical Oncology, CHU Lille, Lille, France, ¹⁶ Division of Medical Oncology and Therapeutic Research, City of Hope National Medical Center, Duarte, United States of America, ¹⁷ R&D China, AstraZeneca, Shanghai, China, ¹⁸ Oncology R&D, Late-Stage Development, AstraZeneca, Cambridge, United Kingdom¹⁹ Department of Gastrointestinal Oncology, National Cancer Center Hospital East, Kashiwa, Japan

Background

CLDN18.2 is a validated therapeutic target in advanced GEC. Sone-Ve, a CLDN18.2-targeting monomethyl auristatin E–based antibody drug conjugate, demonstrated clinical activity in phase 1/2 studies of advanced GEC.

Methods

CG-01 is a randomised, open-label, global, phase 3 study of Sone-Ve vs investigator’s choice of therapy (INV) after ≥1 prior therapy for GEC expressing CLDN18.2 in ≥25% tumour cells with membranous staining at any intensity. Participants (pts) with 2L+ unresectable, locally advanced/metastatic CLDN18.2-positive GEC (intent-to-treat population: ITT) were initially randomised 1:1:1 to Sone-Ve 1.8 mg/kg, Sone-Ve 2.2 mg/kg or INV. Post-dose selection, pts were randomised 1:1 to Sone-Ve 2.2 mg/kg or INV (2L: ramucirumab + paclitaxel, paclitaxel, or docetaxel; 3L+: irinotecan, trifluridine/tipiracil, or apatinib [China only]). Randomisation was stratified by region, prior gastrectomy and line of therapy. Dual primary endpoints are OS in 3L+ and progression-free survival (PFS) by BICR in ITT. Key secondary endpoint is OS in ITT.

Results

At data cutoff (31 May 2026), 532 of 594 total pts were randomised to Sone-Ve 2.2 mg/kg (n=267) or INV (n=265); median follow-up was 8.6 months (mo). Sone-Ve 2.2 mg/kg significantly improved OS vs INV in 3L+ (median 10.0 vs 5.0 mo, HR 0.47 [95% CI 0.36–0.62]; p<0.001) and in 2L+ (ITT) (median 10.6 vs 6.4 mo, HR 0.58 [95% CI 0.47–0.73]; p<0.001). PFS by BICR in ITT did not meet the threshold for statistical significance (Table). OS benefit in ITT was consistent in CLDN18.2 ≥75% (HR 0.59 [95% CI 0.45–0.78]) and ≥25–<75% (HR 0.63 [95% CI 0.42–0.94]) expression subgroups. Safety is summarised in the table.

Table: LBA7

	3L+	
	Sone-Ve (n=178) INV (n=177)	
Median OS (95% CI), mo	10.0 (7.2–11.4)	5.0 (4.2–6.4)
HR (95% CI)	0.47 (0.36–0.62)	
p-value	<0.001	
	ITT (2L+)	
	(n=267)	(n=265)
Median OS (95% CI), mo	10.6 (9.1–12.0)	6.4 (5.8–7.6)
HR (95% CI)	0.58 (0.47–0.73)	

	3L+ Sone-Ve (n=178) INV (n=177)	
p-value	<0.001	
Median PFS by BICR (95% CI), mo	4.2 (3.5–5.3)	3.8 (3.0–4.2)
HR (95% CI)	0.77 (0.62–0.96)	
p-value	0.05	
	SAS* (n=261) (n=252)	
TRAE, n (%)		
Any	224 (85.8)	205 (81.3)
Grade ≥3	95 (36.4)	113 (44.8)
Gastrointestinal toxicity	29 (11.1)	16 (6.3)
Haematology	20 (7.7)	40 (15.9)
Leading to death	3 (1.1)	2 (0.8)
Leading to discontinuation	8 (3.1)	11 (4.4)

*SAS, safety analysis set; all pts who received ≥1 dose. TRAE, treatment-related adverse event.

Conclusions

CG-01 showed a significant OS benefit with Sone-Ve vs INV in 3L+ and ITT, with a manageable safety profile. These findings support Sone-Ve as a potential 2L+ treatment for a broad patient population with advanced CLDN18.2-positive GEC.

Clinical trial identification

NCT06346392.

Editorial acknowledgement

Medical writing support under the direction of the authors was provided by Mhairi Macfadyen, PhD, Publications and Medical Affairs Division of Omnicom Health Medical Communications, and was funded by AstraZeneca.

Legal entity responsible for the study

AstraZeneca.

Funding

AstraZeneca.

Disclosure

R. Xu: Financial Interests, Personal, Advisory Board: BeiGene, Astalas, Junshi, AstraZeneca, MSD, CSPC, Innovent. Y.Y. Janjigian: Financial Interests, Personal, Advisory Board: AbbVie, Arcus Biosciences, Ask- Gene Pharma, Inc., AstraZeneca, Bayer, Bristol-Myers Squibb, Daiichi Sankyo, Eisai, Inc., Eli Lilly, GSK, Guardant Health, Inc., Imugene, Lynx Health, Merck, Sanofi Genzyme, Seagen, Zymeworks Inc., Gilead Sciences; Financial Interests, Personal, Other, Consulting: Amerisource Bergen, Astellas, Basilea Pharmaceutica, Geneos Therapeutics, Imedex, Inspirna, Mersana Therapeutics, Paradigm Medical Communications, Pfizer, Silverback Therapeutics; Financial Interests, Personal, Other, Consulting and Invited Speaker: Arcus Biosciences, AstraZeneca, Clinical Care Options, HMP Education, Merck Serono, PeerView Institue, Research to Practice; Financial Interests, Personal, Invited Speaker: Bristol-Myers Squibb, Ed MedResources (OncInfo), H.C. Wainwright & Co., LLC, Merck, TotalCME, Talem Health, BeiGene, Boehringer Ingelheim, Gilead Sciences; Financial Interests, Personal, Other, Consulting, Invited Speaker and Chair of Giants of Cancer Care Steering Committee: Michael J. Hennessy Associates; Financial Interests, Personal, Other, Consulting and Moderator: Physicians' Education Resource, LLC; Financial Interests, Personal, Stocks/Shares: OncoDaily; Financial Interests, Personal and Institutional, Research Grant: NCI, Cycle for Survival, Fred's Team, Inspirna, Bayer, Genetech/Roche, Bristol-Myers Squibb, Eli Lilly, Merck, Transcenta, Stand Up To Cancer, AstraZeneca, Arcus Biosciences, Astellas; Financial Interests, Personal, Steering Committee Member: AstraZeneca, Transcenta Holding Limited. M. Chen: Financial Interests, Personal, Invited Speaker: MSD, AstraZeneca; Financial Interests, Personal, Advisory Board: ONO, Astellas, Eli Lilly, TTY; Financial Interests, Personal, Steering Committee Member: Roche; Financial Interests, Personal and Institutional, Local PI: Roche, MSD, Amgen, Ono; Financial Interests, Personal and Institutional, Steering Committee Member: AstraZeneca; Financial Interests, Personal and Institutional, Research Grant: Boehringer Ingelheim; Financial Interests, Institutional, Local PI: Pfizer. J. Lee: Financial Interests, Steering Committee Member: BMS, AZ, AbbVie, Daiichi Sankyo, Immunoncيا; Financial Interests, Research Grant: Merck, Samsung Bioepis, Samsung Electronics, Samsung Biologics; Non-Financial Interests, Principal Investigator: AstraZeneca, Daichi Sankyo, Merck MSD, BMS; Non-Financial Interests, Project Lead: Genome and

Company; Non-Financial Interests, Advisory Role: Trutino Bioscience, Daichi Sankyo; Non-Financial Interests, Member: KSMO; Non-Financial Interests, Other, AP Council: ASCO. J. Zhang: Financial Interests, Personal, Invited Speaker: Roche, HengRui Pharmacy, MSD; Financial Interests, Personal, Advisory Board: AstraZeneca. E. Elimova: Financial Interests, Personal, Invited Speaker: Roche, Daiichi Sankyo; Financial Interests, Institutional, Advisory Board: BMS; Financial Interests, Personal, Advisory Board: BeiGene, Signatera, AbbVie, Astellas, Viracta Tx, Amgen; Financial Interests, Personal, Other, Steering committee and Meet investigator and GI Summit Panel: AstraZeneca; Financial Interests, Institutional, Steering Committee Member, Institution receives: Jazz; Financial Interests, Institutional, Local PI: Jazz, Zymeworks, Amgen, AstraZeneca, BMS, Trio-Oncology, Arcus Biosciences, AbbVie; Other, Other, A family member employed by Merck Vaccines.: Merck. E. Smyth: Financial Interests, Personal, Advisory Board: AbbVie, Astellas, AstraZeneca, Avalere Health, Boehringer Ingelheim, Bristol-Myers Squibb, Clarivate, Elevation Oncology, Ellipses, EsoBiotec, Gilead, J&J, MSD, My Personal Therapeutics, Natera, Novartis, Owkin, Roche, Servier, TCypherBio, Viracta, Zymeworks, Bristol-Myers Squibb, RCM Health Consultancy; Financial Interests, Personal, Invited Speaker: Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Cor2Ed, Daiichi Sankyo, Elsevier, Imedex, Index Conferences, Jazz Pharmaceuticals, MSD, Merck, Novartis, Peervoice, Prova Education, Servier, Suzhou Lianghui Network Technology Company Ltd, TouchIME, Wiley; Financial Interests, Personal, Invited Speaker, Speaker at GTG 2026: Brazilian GI Clinical Trials Group; Financial Interests, Personal, Invited Speaker, EIOC Meeting Dubai 2025: Excellence in Oncology Care Meeting; Financial Interests, Personal, Other, TSC: Amgen, Astellas, Daiichi Sankyo; Financial Interests, Personal, Other, TSC for ROSETTA Gastric Trial: BMS; Financial Interests, Personal, Other, Travel to meeting: BeOne Medicines; Financial Interests, Personal, Other, IDMC: BeiGene, Daiichi Sankyo, Zymeworks; Financial Interests, Personal, Other, IDMC chair: Everest Clinical Research; Financial Interests, Personal, Other, IDMC Chair: Jazz Pharmaceuticals; Financial Interests, Personal, Other, Online Education: Medscape; Financial Interests, Personal, Other, Rapid Peer Review: Elsevier; Financial Interests, Personal, Writing Engagement: Connexiant; Financial Interests, Personal, Officer: EORTC GI Clinical Trials Group; Financial Interests, Personal, Other, Contract as external Principal Investigator to allow opening of clinical trials. Nominal monthly payment.: Sarah Cannon Research Institute; Financial Interests, Personal, Full or part-time Employment, Clinical Lead Oxford University Oncology Clinical Trials Office: Oxford Oncology Clinical Trials Office (OCTO); Financial Interests, Personal, Other, GI Associate Editor of ESMO Open Journal: ESMO; Financial Interests, Personal, Full or part-time Employment, National Research Delivery Network Oncology Speciality co-Lead: NIHR; Financial Interests, Institutional, Coordinating PI: Amgen, AstraZeneca, Roche, Astellas, Astellas, Iambic; Financial Interests, Institutional, Local PI: Arcus, Basilea, Daiichi Sankyo, MSD, Merus, Mirati, AbbVie, Infinitopes; Financial Interests, Institutional, Research Grant: AstraZeneca, Bristol-Myers Squibb; Financial Interests, Institutional, Funding, To EORTC: BeiGene; Financial Interests, Institutional, Research Grant, To EORTC: Novartis, Roche; Financial Interests, Institutional, Other, Grant for ctDNA testing in cholangiocarcinoma patients: Incyte; Financial Interests, Institutional, Coordinating PI, National co-ordinating PI for LUCERNA trial: Astellas; Financial Interests, Institutional, Coordinating PI, National Co-ordinating PI for DESTINY Gastric 05 trial: Daiichi Sankyo; Financial Interests, Institutional, Coordinating PI, National Co-ordinating PI for Phase I trial: BeOne Medicines; Financial Interests, Institutional, Coordinating PI, National Co-ordinating PI for ROSETTA Gastric Trial: BMS; Non-Financial Interests, Leadership Role, Trustee: UK & Ireland Oesophagogastric Group (UKIOG); Other, Other, My spouse is an employee of HCA International and director of Sarah Cannon Research Institute, London. Spousal DOI is submitted and reviewed by ESMO.: HCA International. T.O. Goetze: Financial Interests, Personal, Invited Speaker: Lilly, Servier; Financial Interests, Personal, Advisory Board: MSD Oncology, Bayer, Roche, BMS, Sanofi, Jazz Pharmaceuticals, Amgen; Financial Interests, Personal and Institutional, Funding, Research grant: Deutsche Forschungsgemeinschaft (DFG); Financial Interests, Personal and Institutional, Funding, Research Grant: Gemeinsamer Bundesausschuss, Deutsche Krebshilfe, Lilly, AstraZeneca; Financial Interests, Personal and Institutional, Funding: Incyte, Taiho Oncology, Servier. M. Furuta: Financial Interests, Personal, Invited Speaker: Bristol myers squibb, Merck & Co., Inc., Ono Pharmaceutical Co., Ltd., Astellas Pharma Inc., BeOne Medicines, Taiho Pharmaceutical, Daiichi Sankyo; Financial Interests, Institutional, Local PI: AstraZeneca, Daiichi Sankyo, Innovent Biologics, Astellas Pharma Inc., Ono Pharmaceutical Co., Ltd., Nippon Kayaku, Merck KGaA. K. Lee: Financial Interests, Personal, Advisory Board: Amgen, Astellas, BeOne (Korea), Daiichi Sankyo (Korea), ImmuneOncia, Merck Sharp & Dohme (Korea), Ono Pharmaceuticals (Korea), Takeda (Korea); Financial Interests, Personal, Invited Speaker: Astellas, Bayer (Korea), Celltrion, Merck KCaA (Korea), Merck Sharp & Dohme (Korea); Financial Interests, Institutional, Local PI, For conducting clinical trials: ALX Oncology, AbbVie, Amgen, ApatBio, Arcus Biosciences, Astellas Pharma, AstraZeneca, Avelo Therapeutics, Bayer, BeiGene, Boehringer Ingelheim, Bolt therapeutics, Celltrion, Daiichi Sankyo, Exelixis, GSK, Hanmi, IDRx, IgM Biosciences, Ildong Pharmaceutical, ImmuneOncia, Jazz Pharmaceuticals, Jiangsu Hengrui, Leap therapeutics, MedPacto, Medicenna, Merck KGaA, Merck Sharp & Dohme, Metafines, Minneamrita Therapeutics, Ono pharmaceutical, Oscotec, Panolos Bioscience, Pfizer, Roche, STCube, Taiho Pharmaceutical, Toray, Tori Biotherapeutics, Yuhon; Non-Financial Interests, Leadership Role, SMC chair of ASPEN-06 study: ALX Oncology. F. Pietrantonio: Financial Interests, Personal, Advisory Board: Amgen, Merck-Serono, MSD, Bayer, Astellas, Takeda, Ipsen, GSK, Johnson&Johnson, Rottapharm, AstraZeneca, Pierre Fabre, Gilead, Agenus, Incyte, Daiichi Sankyo, BMS, Jazz Pharmaceuticals, BeiGene, Revolution Medicine, 3T Biosciences, Takeda; Financial Interests, Personal, Invited Speaker: Amgen, Merck-Serono, BMS, Servier, Bayer, Pierre-Fabre, AstraZeneca, Astellas, Daiichi Sankyo, Takeda, MSD, BeiGene, Johnson and Johnson, Incyte; Financial Interests, Institutional, Research Grant: BMS, AstraZeneca, Incyte, Agenus, Johnson and Johnson, GSK, BeOne; Financial Interests, Institutional, Coordinating PI: Lilly, Amgen; Financial Interests, Institutional, Funding: Rottapharm; Financial Interests, Personal, Steering Committee Member: Johnson and Johnson, AstraZeneca, MSD; Financial Interests, Personal, Coordinating PI: Rottapharm. J. Ye: Financial Interests, Personal, Full or part-time Employment: AstraZeneca; Financial Interests, Personal, Stocks/Shares: AstraZeneca. S. Liu: Financial Interests, Personal, Full or part-time Employment: AstraZeneca; Financial Interests, Personal, Stocks/Shares: AstraZeneca. N. Valeri: Financial Interests, Personal, Full or part-time Employment: AstraZeneca; Financial Interests, Personal, Stocks/Shares: AstraZeneca. K. Shitara: Financial Interests, Personal, Advisory Board: Takeda, MSD, Novartis, Daiichi Sankyo, Amgen, Astellas, AstraZeneca, GSK K.K., HEALIOS K.K., Moderna Inc, Arcus Biosciences Inc., Boehringer Ingelheim, AbbVie, Sanofi, Oncolys, Elevation Oncology, Suzhou Liangyihui Network Technology Co., Ltd, CMIC CO.,LTD, ALX Oncology Inc, Bayer, Bristol-Myers Squibb International, Janssen, Ono Pharmaceuticals, Zymeworks Biopharmaceuticals Inc., Gilead Sciences, eChinaHealth, Inc., Leap Therapeutics,

Phanes Therapeutics, Inc., Scandion Oncology, Levolution Medicines, Inc., Guardant Health; Financial Interests, Personal, Invited Speaker: Bristol-Myers Squibb, AstraZeneca, Astellas, Ono Pharmaceutical, Janssen, Eli Lilly; Financial Interests, Personal, Writing Engagement: Eli Lilly; Financial Interests, Institutional, Research Grant: Astellas, Ono Pharmaceutical, Daiichi Sankyo, Taiho Pharmaceutical, Chugai Pharmaceutical, MSD, Eisai, Amgen, PRA Health Sciences, AstraZeneca, PPD-SNBL K.K., TORAY, Medpace Japan KK, Incyte Biosciences Japan G.K. All other authors have declared no conflicts of interest.

© *European Society for Medical Oncology*