

LBA80

Regorafenib plus nivolumab vs investigator's choice of chemotherapy in previously treated gastric or gastroesophageal cancer: INTEGRATE IIb, a randomized phase 3 AGITG Intergroup [NHMRC-CTC/IKF/AIO, ACCRU, TCOG/NHRI] study

D. Goldstein¹, K. Sjoquist², D. Espinosa³, S.Y. Rha⁴, T.O. Goetze⁵, N. Tebbutt⁶, H. Hara⁷, K-W. Lee⁸, M.H. Ryu⁹, E. Goekkurt¹⁰, P.C. Thuss-Patience¹¹, G.M. Haag¹², S. Lorenzen¹³, J. Simes¹⁴, C.S. Karapetis¹⁵, T.J. Price¹⁶, D. Siu¹⁷, M. Moehler¹⁸, K. Shitara¹⁹, N. Pavlakis²⁰

¹ Medical Oncology, Prince of Wales Hospital - Nelune Comprehensive Cancer Centre, Sydney, Australia, ² Medical Oncology, St George Hospital Cancer Care Centre, Kogarah, Australia, ³ Statistics, NHMRC Clinical Trials Centre, University of Sydney, Camperdown, Australia, ⁴ Medical Oncology Department, Yonsei University, Seoul, Republic of Korea, ⁵ Oncology Department, IKF - Institut für Klinische Krebsforschung GmbH, Frankfurt am Main, Germany, ⁶ Medical Oncology, Austin Health, Heidelberg, Australia, ⁷ Department of Gastroenterology, Saitama Prefectural Cancer Center, Ina, Japan, ⁸ Internal Medicine Dept, Seoul National University Bundang Hospital, Seongnam, Republic of Korea, ⁹ Department of Oncology, Asan Medical Center - University of Ulsan, Seoul, Republic of Korea, ¹⁰ Medical oncology, HOPE Hämatologisch-Onkologische PraxisFacharztzentrum Eppendorf, Hamburg, Germany, ¹¹ Hematology Oncology Dept., Vivantes Klinikum im Friedrichshain, Berlin, Germany, ¹² National Center for Tumor Diseases, Department of Medical Oncology, Heidelberg University Hospital, Heidelberg, Germany, ¹³ Hematology and Oncology Dept., Klinikum Rechts der Isar - Technische Universität München, Munich, Germany, ¹⁴ NHMRC Clinical Trials Centre, University of Sydney, Sydney, Australia, ¹⁵ Medical Oncology Department, Flinders Centre for Innovation in Cancer, Bedford Park, Australia, ¹⁶ Medical Oncology, The Queen Elizabeth Hospital, Woodville, Australia, ¹⁷ Department of Medical Oncology, NHMRC Clinical Trial Centre - The University of Sydney, Sydney, Australia, ¹⁸ Department of Medicine, Universitätsmedizin der Johannes Gutenberg-Universität Mainz, Mainz, Germany, ¹⁹ Department of Gastrointestinal Oncology, National Cancer Center Hospital East, Kashiwa, Japan, ²⁰ Medical Oncology Department, RNSH - Royal North Shore Hospital, St Leonards, Australia

Background

The combination of regorafenib, an oral multi-kinase inhibitor, and nivolumab (RegoNivo) demonstrated promising antitumour activity and manageable safety in an early-phase trial involving participants (pts) with refractory advanced gastric cancer. We present the international phase 3 INTEGRATE IIb trial, comparing RegoNivo with chemotherapy (CT) in pts with refractory advanced gastric or gastro-oesophageal junction cancer.

Methods

Eligible pts who had received ≥ 2 prior lines of CT, including a platinum agent and fluoropyrimidine, were randomised 2:1 to RegoNivo (Rego 90 mg PO on days 1–21 of a 28-day cycle plus Nivo 240 mg IV on day 1 of a 14-day cycle) or investigator's choice CT (taxane, irinotecan, or trifluridine/tipiracil). The primary endpoint was overall survival (OS); secondary endpoints included progression-free survival (PFS), objective response rate (ORR), quality of life (QoL), and safety.

Results

Of 462 pts randomised, 309 were assigned to RegoNivo and 153 to CT. Median time to treatment discontinuation was 1.6 months (mo; RegoNivo) and 1.4 mo (CT). OS was not significantly improved with RegoNivo compared to CT (median 5.9 v 6.3 mo, hazard ratio [HR] 0.88, 95% CI 0.71–1.09, $P = 0.23$), and PFS was similar (1.9 v 1.9 mo). ORR was higher in RegoNivo (7.4%) compared to CT (2.6%), as was median duration of response (9.5 v 5.6 mo). Disease control rate (DCR) was higher in RegoNivo overall (39% v 26%) and at 12-mo (14% v 0%), and global QoL or death was prolonged with RegoNivo (HR 0.74, 95% CI 0.60–0.91). Serious adverse events (SAEs) were reported in both arms, except for disease progression; relatedness was only required for RegoNivo, partially explaining the observed difference (41% RegoNivo v 25% CT).

Conclusions

RegoNivo was not superior to investigator's choice of CT for pts with refractory advanced gastric cancer. The numerically greater response rate and observed longer duration of benefit encourage the search for more effective non-chemotherapy combinations with Regorafenib.

Clinical trial identification

NCT04879368.

Editorial acknowledgement

Editorial assistance Trish Dwight (PhD) of Convey Your Science (Australia).

Legal entity responsible for the study

Australasian Gastrointestinal Trials Group.

Funding

Bayer.

Disclosure

D. Goldstein: Non-Financial Interests, Institutional, Non remunerated activity, biliary guidelines-project partially supported by an independent grant: AstraZeneca; Non-Financial Interests, Institutional, Non remunerated activity, local gastric guidelines: AstraZeneca; Financial Interests, Institutional, Coordinating PI, investigator initiated trial: Pfizer; Financial Interests, Institutional, Local PI, clinical trials: Pfizer; Financial Interests, Institutional, Local PI, clinical trial: Amgen, Boehringer, Deciphera; Financial Interests, Personal, Advisory Board, international clinical trials sop: Boehringer Ingelheim; Financial Interests, Institutional, Coordinating PI, international gastric trial: bayer; Financial Interests, Personal, Other, DSMB: panbela, ANZUP, OMICO; Financial Interests, Institutional, Local PI, Clinical trial: MSD; Financial Interests, Institutional, Trial Chair, clinical trial: Amplificare. K. Sjoquist: Financial Interests, Personal, Invited Speaker, oesophageal cancers dinner meeting - speaker May 2025: BeiGene; Financial Interests, Personal, Other, consultancy: Glenmark Specialty SA; Financial Interests, Personal, Advisory Board: MSD Australia, BMS, Servier, Astellas; Financial Interests, Institutional, Steering Committee Member, Untied grant to institution for study conduct (independent of the presented work): Lisata Therapeutics; Financial Interests, Institutional, Trial Chair, provision of drug and portion funding for unrelated investigator initiated trial, to institution: AstraZeneca; Financial Interests, Institutional, Steering Committee Member, untied grant to institution for conduct of study, as detailed in the submission: Bayer; Other, Other, payment to institution for role as IDSMC member for trial unrelated to the submitted work: Novotech; Other, Other, Conference travel - ESMO Asia 2024: Astellas. S.Y. Rha: Financial Interests, Personal, Advisory Board: Indivumed, Amgen, LG Biochemical, Astellas, Boehringer Ingelheim, BeiGene, Ono Pharmaceuticals, qureator; Financial Interests, Personal, Invited Speaker: MSD, Daiichi Sankyo, AstraZeneca; Financial Interests, Institutional, Steering Committee Member: Amgen; Financial Interests, Institutional, Funding: MSD; Financial Interests, Institutional, Research Grant: BMS, Daichii Sankyo; Financial Interests, Institutional, Funding, drug supply for IIT: Lilly; Financial Interests, Institutional, Local PI: Indivumed, AstraZeneca, Ono Pharmaceuticals; Financial Interests, Other, Durg supply for clinical trial: Merck; Financial Interests, Institutional, Coordinating PI, Drug supply for clincial trial: MSD; Financial Interests, Institutional, Local PI, drug supply for clinical trial: Jazz Pharmaceuticals; Financial Interests, Institutional, Local PI, drug supply for clincial trial: BeiGene; Financial Interests, Local PI: Roche. 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, Reserach 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. N. Tebbutt: Financial Interests, Personal, Advisory Board: AstraZeneca, BMS, BeiGene, MSD, Takeda, Amgen; Financial Interests, Personal, Invited Speaker: Amgen, Roche, Takeda Pharmaceuticals; Financial Interests, Institutional, Coordinating PI: AstraZeneca. H. Hara: Financial Interests, Personal, Invited Speaker: Astellas, Bristol Myers Squibb, Chugai, Daiichi Sankyo, Lilly, MSD, Merck Biopharma, Nippon Kayaku, Ono, Taiho, Takeda, Yakult, miyarisano, otsuka; Financial Interests, Personal, Advisory Board: Boehringer Ingelheim, Chugai, Daiichi Sankyo; Financial Interests, Institutional, Coordinating PI: ALX oncology, AbbVie, Amgen, Astellas, AstraZeneca, Bayel, Chugai, Daiichi Sankyo, Janssen, MSD, Merck Biopharma, Ono, Taiho, henlius, innovent, jazz pharmaceuticals. K. Lee: Financial Interests, Personal, Advisory Board: AbbVie (Korea), Astellas, Daiichi Sankyo (Korea), Merck Sharp & Dohme (Korea), Metafines, Ono Pharmaceuticals (Korea), BeiGene (Korea), PIN therapeutics, Takeda (Korea); Financial Interests, Personal, Invited Speaker: Bayer (Korea), Merck KCaA (Korea), Celltrion; Financial Interests, Institutional, Local PI, For conducting clinical trials: ALX Oncology, Amgen, Arcus Biosciences, Astellas Pharma, AstraZeneca, Avelos Therapeutics, Bayer, BeiGene, Boehringer Ingelheim, Bolt therapeutics, Daiichi Sankyo, Erasca, Inc, Exelixis, Genome & Company, GSK, Hanmi, IDRx, IgM Biosciences, Ildong Pharmaceutical, InventisBio, Jazz Pharmaceuticals, Jiangsu Hengrui, Leap therapeutics, MedPacto, Medicenna, Merck KGaA, Merck Sharp & Dohme, Metafines, Ono pharmaceutical, Panolos Bioscience, Pfizer, Roche, Taiho Pharmaceutical, Tori Biotherapeutics, Trishula therapeutics, Wellmarker Bio; Non-Financial Interests, Leadership Role, SMC chair of ASPEN-06 study: ALX Oncology. M.H. Ryu: Financial Interests, Personal, Advisory Board: DAE HWA Pharmaceutical, BMS, Lilly, Ono Pharmaceuticals, MSD, Taiho Pharmaceutical, Novartis, Daiichi Sankyo, AstraZeneca, Astellas; Financial Interests, Personal and Institutional, Research Grant: Ono Pharmaceuticals, BMS; Financial Interests, Personal, Research Grant: AstraZeneca. E. Goekkurt: Financial Interests, Institutional, Advisory Board: MSD, BMS, Daiichi, Servier; Financial Interests, Institutional, Local PI: msd, Daiichi, AstraZeneca, BMS, Novartis. P.C. Thuss-Patience: Financial Interests, Personal, Advisory Board, upper GI: Roche, AstraZeneca, Astellas, Daiichi Sankyo, Lilly, Servier, BeiGene; Financial Interests, Personal, Advisory Board, upper GI adboard and speaker: BMS; Financial Interests, Personal, Advisory Board, MSD: Upper GI Adboard and speaker: Merck; Financial Interests, Personal, Other, Travel to conference: Celltrion. G.M. Haag: Financial Interests, Institutional, Advisory Board: Bristol Myers Squibb, MSD Sharp & Dohme; Financial Interests, Personal, Advisory Board: Lilly, Daiichi Sankyo, Servier, AstraZeneca, AbbVie, BeiGene; Financial Interests, Personal, Invited Speaker: Servier, MSD Sharp & Dohme, Bristol Myers Squibb, AstraZeneca, Astellas, BeiGene, Deciphera, StreamedUp; Financial Interests, Personal, Other, Reviewer committee: Swiss Cancer League; Financial Interests, Institutional, Research Grant: MSD Sharp & Dohme; Financial Interests, Institutional, Coordinating PI: DKFZ Heidelberg; Other, Other, Travel Support: Lilly, Amgen, MSD Sharp & Dohme, Daiichi Sankyo, BeiGene, AstraZeneca. S. Lorenzen:

Financial Interests, Personal, Invited Speaker: Servier, Lilly, MSD, BMS, AstraZeneca; Financial Interests, Personal, Advisory Board: Astellas. J. Simes: Financial Interests, Institutional, Advisory Board, Advisory Board Member: Detsamma FivepHusion; Financial Interests, Institutional, Research Grant, Research funding for clinical trials: Bayer, Roche; Financial Interests, Institutional, Research Grant, Research Funding for Clinical Trials: BMS, MSD, AstraZeneca, Pfizer. C.S. Karapetis: Financial Interests, Personal, Advisory Board: BMS, Eisai, Takeda, BeiGene, Astellas, Janssen; Financial Interests, Personal, Invited Speaker: Eli Lilly, MSD, Gilead; Financial Interests, Institutional, Coordinating PI: Takeda, Roche, Mirati, Daiichi Sankyo, Gilead, BeiGene, Boston Pharmaceuticals Inc, Servier; Non-Financial Interests, Leadership Role, Chair, Scientific Advisory Committee: Australasian Gastrointestinal Trials Group; Non-Financial Interests, Member: Medical Oncology Group of Australia, American Society of Clinical Oncology. T.J. Price: Financial Interests, Personal, Invited Speaker: AMGEN; Financial Interests, Personal, Advisory Board, Asia Pacific advisory board: Takeda; Non-Financial Interests, Advisory Role, Australian Advisory Board: Takeda; Non-Financial Interests, Advisory Role: Servier, Duo Oncology, AMGEB, BMS. M. Moehler: Financial Interests, Personal, Advisory Board: BMS, Servier, Amgen, Lilly, BeiGene, Novartis, Taiho, Daiichi, Amgen, MD; Financial Interests, Personal, Invited Speaker: MSD, BMS, Falk foundation, AIO, BeiGene, Amgen; Financial Interests, Institutional, Advisory Board: Bayer, Sanofi; Financial Interests, Personal, Other, Chair: EORTC. K. Shitara: Financial Interests, Personal, Advisory Board: Bristol Myers Squibb, Takeda, Ono Pharmaceutical, MSD, Novartis, Daiichi Sankyo, Amgen, Guardant Health Japan Corp, Astellas Pharma Inc., Astellas, Bayer, AstraZeneca, Zymeworks Biopharmaceuticals Inc, ALX Oncology Inc, GSK K.K., Janssen, Healios K.K., Moderna.Inc, Arcus Biosciences Inc.; Financial Interests, Personal, Invited Speaker: Bristol Myers Squibb, Janssen, AstraZeneca, Eli Lilly, Astellas, Ono Pharmaceutical; 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. N. Pavlakis: Financial Interests, Personal, Advisory Board: Boehringer Ingelheim, MSD, Merck KgA, BMS, AstraZeneca, Takeda, Pfizer, Roche, Amgen, BeiGene, Gilead, Zymeworks, BioNtech, Daiichi Sankyo, Duo Oncology, Johnson and Johnson; Financial Interests, Institutional, Trial Chair: Bayer, Roche, Pfizer. All other authors have declared no conflicts of interest.