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ctDNA clearance (CL) during neoadjuvant treatment (neoadj Tx) and its association with outcomes in patients (pts) with resectable/borderline resectable stage IIB–IIIB NSCLC from MDT-BRIDGE

J. Spicer[1], D. Gale[2], M. Reck[3], Z. Zhu[4], C. Gay[5], A.R. Filippi[6], E. Nadal[7], N. Girard[8], C. Petersen[9], L.W. Martin[10], D.A. Cairns[11], M. Majem[12], A. Ardizzoni[13], R.M. Álvarez Álvarez[14], A.G. Robinson[15], U. Emeribe[16], M. Giaj Levra[17], D. Kurtz[18], N.E. Georgoulia[19], M. Diehn[20]

[1] Department of Thoracic Surgery, McGill University, Montreal, Canada, [2] Biomarker Science and Technologies, AstraZeneca, Cambridge, United Kingdom, [3] Lung Clinic Großhansdorf, Airway Research Center North, German Center for Lung Research, Grosshansdorf, Germany, [4] Oncology Bioinformatics, AstraZeneca, Gaithersburg, United States of America, [5] Thoracic/Head and Neck Medical Oncology, University of Texas MD Anderson Cancer Center, Houston, United States of America, [6] Radiation Oncology and Department of Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori and University of Milan, Milan, Italy, [7] Department of Medical Oncology, Institut Català d'Oncologia (ICO), IDIBELL, Bellvitge Healthcare Campus, L'Hospitalet de Llobregat, Barcelona, Spain, [8] Institut du Thorax Curie Montsouris, Institut Curie/UVSQ, Paris, France, [9] Department of Radiotherapy and Radiation Oncology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany, [10] Department of Surgery, Division of Thoracic Surgery, University of Virginia, Charlottesville, United States of America, [11] Leeds Cancer Research UK Clinical Trials Unit, Leeds Institute of Clinical Trials Research, University of Leeds, Leeds, United Kingdom, [12] Medical Oncology Department, Hospital de La Santa Creu I Sant Pau, Barcelona, Spain, [13] Medical Oncology and Department of Medical and Surgical Sciences, IRCCS Azienda Ospedaliero-Universitaria di Bologna and University of Bologna, Bologna, Italy, [14] Medical Oncology Department, Hospital Universitario Gregorio Marañón, Madrid, Spain, [15] Cancer Centre Department, Cancer Centre of Southeastern Ontario at Kingston General Hospital, Kingston, Canada, [16] Oncology Biometrics, AstraZeneca, Wilmington, United States of America, [17] Global Medical Affairs, AstraZeneca, Wilmington, United States of America, [18] Medicine, Foresight Diagnostics, Boulder, United States of America, [19] Global Medical Affairs, AstraZeneca, Gaithersburg, United States of America[20] Radiation Oncology, Foresight Diagnostics, Boulder, United States of America

Background

MDT-BRIDGE is investigating perioperative durvalumab (D) + neoadj CT in pts with resectable/borderline resectable NSCLC and CRT with consolidation D in pts who become unresectable during neoadj Tx. Here, we report analyses of ctDNA CL from baseline (BL) to pre-surgery (Sx)/CRT and other neoadj timepoints (TPs), using an ultrasensitive assay to enhance detection, and its association with outcomes.

Methods

MDT-BRIDGE (NCT05925530) is a phase 2 non-randomized study in Tx-naïve *EGFR*/*ALK* WT pts. After initial MDT resectability assessment, all pts received 2 cycles of neoadj D + CT Q3W IV followed by MDT reassessment. Pts deemed resectable at reassessment received 1–2 more cycles of neoadj D + CT then Sx; pts deemed unresectable received CRT for ⊠6 wk. After Sx/CRT, all pts received D Q4W IV up to 1 yr. ctDNA CL from BL (pre-Tx) to other neoadj TPs was assessed in evaluable pts using the CLARITY™ assay (LoD_{95}: ≤1 ppm variant allele fraction [VAF]).

Results

Of 142 pts (full analysis set [FAS]), 107 had ctDNA assays developed following sequencing of pre-Tx biopsies. BL characteristics were generally similar to the FAS; 99.1% were ctDNA+ at BL. Median VAF decreases of 96–97% occurred by C2D1 regardless of baseline resectability. Deeper molecular responses were seen in pts resectable vs unresectable at reassessment; ctDNA CL at pre-Sx/CRT was 36.7% (resectable, 40.6%; unresectable, 23.8%). The positive predictive value (PPV) of ctDNA CL at C2D1 for pCR was high (83.3%; 95% CI, 43.6–99.1). Higher CL rates were observed in pCR vs non-pCR pts starting after 1 cycle (e.g., pCR [n=25] pre-Sx CL: 76.0%; non-pCR [n=43] pre-Sx CL: 20.9%). Of resected pts, none with pre-Sx CL had an EFS event, while the 12-mo EFS rate (95% CI) in pts without CL was 88.9% (72.8–95.7); of CRT-treated pts, the 12-mo PFS rate (95% CI) was 100.0% (100.0–100.0) with pre-CRT CL vs 77.5% (44.8–92.3) without.

Conclusions

Using an ultrasensitive assay improved the PPV of ctDNA CL for pCR vs prior studies (Reck, ESMO 2024. LBA49), increasing the utility of ctDNA to assess early neoadj Tx response. Higher rates of ctDNA CL in resectable vs unresectable pts and association with outcomes further support its clinical utility.

Clinical trial identification

NCT05925530 (release date: June 29, 2023).

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Legal entity responsible for the study

AstraZeneca.

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Disclosure

J. Spicer: Financial Interests, Personal, Advisory Board: AstraZeneca, Merck, Roche, BMS, Novartis, Amgen, Xenetic Biosciences, Regeneron, Eisai, Pfizer; Financial Interests, Personal, Invited Speaker: AstraZeneca, Merck, BMS; Financial Interests, Institutional, Coordinating PI, In kind contribution of investigational drug.: AstraZeneca, BMS; Financial Interests, Institutional, Coordinating PI, Grant to institution for research within my laboratory.: CLS Therapeutics; Financial Interests, Institutional, Coordinating PI, Grant to institution for execution of research within my laboratory.: Protalix Biotherapeutics; Financial Interests, Institutional, Coordinating PI, Grant to institution for execution of multi-center clinical trial.: Roche; Financial Interests, Institutional, Coordinating PI, Grant to institution for execution of clinical trial.: Merck; Non-Financial Interests, Leadership Role, Mesothelioma and Thymoma work group chair and member of executive board for the IND program: Canadian Cancer Trials Group. D. Gale: Financial Interests, Personal, Full or part-time Employment: AstraZeneca; Financial Interests, Personal, Stocks/Shares: AstraZeneca, GSK; Financial Interests, Personal, Other, Patent pending: AstraZeneca. M. Reck: Financial Interests, Personal, Invited Speaker: Amgen, AstraZeneca, BMS, Boehringer-Ingelheim, Lilly, MSD, Merck, Novartis, Regeneron, Roche, Sanofi, GSK, Pfizer, Pierre Fabre; Financial Interests, Personal, Advisory Board: Amgen, AstraZeneca, BMS, BioNTech, Boehringer-Ingelheim, Daiichi Sankyo, Gilead, MSD, Mirati, Pfizer, Regeneron, Roche, Sanofi, GSK, Lilly, Pierre Fabre; Financial Interests, Personal, Other, Member of DMSB: Daiichi Sankyo; Financial Interests, Personal, Other, Member of Data Monitoring Committee: Servier, CureVac; Financial Interests, Personal, Coordinating PI: AstraZeneca; Financial Interests, Institutional, Steering Committee Member: Amgen, Boehringer-Ingelheim, BeiGene, Daiichi Sankyo, GSK, BMS, Lilly, MSD, Regeneron, Roche; Financial Interests, Institutional, Local PI: Pfizer Seagen, Nuvalent. Z. Zhu: Financial Interests, Personal, Full or part-time Employment: AstraZeneca; Financial Interests, Personal, Stocks/Shares: AstraZeneca, Pfizer. C. Gay: Financial Interests, Personal, Advisory Role: Abdera, Amgen, AstraZeneca, BeOne, BioNTech, Boehringer Ingelheim, Daiichi Sankyo, G1 Therapeutics, Jazz Pharmaceuticals, Merck, OncoHost, Pharmacosmos, and Roche/Genentech; Financial Interests, Personal, Other, Honoraria: ACHL, Amgen, AstraZeneca, BeiGene, Dava Oncology, IDEOlogy, IDR, Impact Education, MJH, OncLive, PeerView, Physicians' Education Resource (PER), Targeted Healthcare, and UpToDate; Financial Interests, Personal, Other, Consulting fees: Axiom, Boehringer Ingelheim, Cantor Fitzgerald, Catalyst, Pontifax, Globe Life Sciences, Chugai, Kisoji, Abdera, Amgen, AstraZeneca, Bristol-Myers Squibb, Daiichi Sankyo, G1, Jazz, Monte Rosa, OncoHost, and Roche/Genentech; Financial Interests, Institutional, Research Funding: Amgen, AstraZeneca, BioNTech, IDEAYA, Merck; Financial Interests, Personal, Other, US Patent US11732306B2 Molecular subtyping of small cell lung cancer to predict therapeutic responses: University of Texas MD Anderson Cancer Center. A.R. Filippi: Financial Interests, Personal, Advisory Board: AstraZeneca, Roche; Financial Interests, Personal, Invited Speaker: AstraZeneca, Ipsen, Takeda; Financial Interests, Personal, Other, Consultant: RadiomicsBio; Financial Interests, Personal and Institutional, Coordinating PI: AstraZeneca; Financial Interests, Institutional, Local PI: AstraZeneca, MSD; Financial Interests, Institutional, Research Grant: AstraZeneca; Financial Interests, Personal, Steering Committee Member: AstraZeneca; Financial Interests, Steering Committee Member: EORTC; Non-Financial Interests, Principal Investigator, Academic Study: Fondazione IRCCS Policlinico San Matteo; Non-Financial Interests, Other, Member of the Advanced Radiotherapy Committee: IASLC; Non-Financial Interests, Other, Member of the Radiotherapy/Drug Combinations Focus Group: ESTRO; Non-Financial Interests, Other, Member of the EORTC Lung Cancer Group: EORTC; Non-Financial Interests, Other, Member of European Thoracic Oncology Platform: ETOP. E. Nadal: Financial Interests, Personal, Advisory Role: Boehringer Ingelheim, Pfizer, Roche, Transgene; Financial Interests, Personal, Other, Consulting fees: Amgen, Apollomics, AstraZeneca, BeiGene, Boehringer Ingelheim, Bristol-Myers Squibb, Daiichi Sankyo, Genmab, Gilead, GSK, Janssen, Lilly, Merck Serono, Merck Sharp & Dohme, Pfizer, PharmaMar, Pierre Fabre, Qiagen, Regeneron, Roche, Sanofi, Takeda; Financial Interests, Personal, Research Funding: Roche, Pfizer, Merck-Serono, Bristol-Myers Squibb, Boehringer Ingelheim. N. Girard: Financial Interests, Personal, Stocks/Shares: Owkin, Ninsun, Neotis; Financial Interests, Personal, Other, Honoraria: AbbVie, Amgen, AstraZeneca, BeOne, Bristol-Myers Squibb, Daiichi Sankyo, Johnson & Johnson, Merck Sharp & Dohme, Novocure; Financial Interests, Personal, Other, Consulting fees: AbbVie, Accord, Amgen, AstraZeneca, Bayer, BeOne, Bristol-Myers Squibb, Daiichi Sankyo, Ipsen, Johnson & Johnson, Lilly, Merck Sharp & Dohme, Natera, Neotis, Ninsun, Novocure, Owkin, Pfizer, PharmaMar, Pierre Fabre, Regeneron, Summit; Non-Financial Interests, Personal, Other, Employment of family member: AstraZeneca. C. Petersen: Financial Interests, Personal, Other, Honoraria: AstraZeneca, BrainLab; Financial Interests, Personal, Research Funding: BrainLab, Siemens Healthineers. L.W. Martin: Financial Interests, Personal, Full or part-time Employment: University of Virginia Health System; Financial Interests, Personal, Advisory Role: AstraZeneca; Financial Interests, Personal, Member of Board of Directors, Chair: General Thoracic Surgical Club ; Financial Interests, Personal, Speaker's Bureau: Johnson & Johnson. M. Majem: Financial Interests, Personal, Member of Board of Directors, Vice President:

Asociación para la Investigación del Cáncer de Pulmón en Mujeres; Financial Interests, Personal, Other, Honoraria: Amgen, AstraZeneca, Boehringer Ingelheim, BeOne, Bristol-Myers Squibb, Helsinn Therapeutics, Johnson & Johnson, Merck Sharp & Dohme, Novartis, Pfizer, PharmaMar, F. Hoffmann-La Roche Ltd., Takeda, Sanofi, Regeneron, Cassen Recordatti, Immedica; Financial Interests, Personal, Other, Consulting fees: Amgen, AstraZeneca, Boehringer Ingelheim, BeOne, Bristol-Myers Squibb, Helsinn Therapeutics, Johnson & Johnson, Merck Sharp & Dohme, Novartis, Pfizer, PharmaMar, F. Hoffmann-La Roche Ltd., Takeda, Sanofi, Regeneron, Cassen Recordatti, Immedica; Financial Interests, Personal, Research Funding: AstraZeneca, F. Hoffmann-La Roche Ltd.; Non-Financial Interests, Personal, Other, Board member: Associació Contra el Càncer a Barcelona. A. Ardizzoni: Financial Interests, Personal, Other, Honoraria: Merck Sharp & Dohme, Roche, AstraZeneca, Lilly, Bristol-Myers Squibb, Regeneron, BeOne, Pfizer, Gilead, Amgen, Pierre-Fabre, Daiichi Sankyo, Novartis, Diatech, Johnson & Johnson, AbbVie. R.M. Álvarez Álvarez: Financial Interests, Personal, Advisory Role: Boehringer Ingelheim, Novartis, Roche; Financial Interests, Personal, Speaker, Consultant, Advisor: PharmaMar; Financial Interests, Personal, Other, Conference registration support: Merck Sharp & Dohme Oncology; Financial Interests, Personal, Principal Investigator: AstraZeneca, Boehringer Ingelheim, Cebiotex, Janssen Oncology, Novartis, Rain Therapeutics, Roche. A.G. Robinson: Financial Interests, Personal, Other, Honoraria: Merck Sharp & Dohme, Bristol-Myers Squibb, Amgen, AstraZeneca. U. Emeribe: Financial Interests, Personal, Full or part-time Employment: AstraZeneca. M. Giaj Levra: Financial Interests, Personal, Full or part-time Employment: AstraZeneca; Financial Interests, Personal, Stocks/Shares: AstraZeneca. D. Kurtz: Financial Interests, Personal, Full or part-time Employment: Natera, Foresight Diagnostics; Financial Interests, Personal, Stocks/Shares: Natera, Foresight Diagnostics; Financial Interests, Personal, Other, Consulting fees: Foresight Diagnostics; Financial Interests, Personal, Other, Issued and pending patents relating to cell-free DNA, assigned to Stanford: Foresight Diagnostics. N.E. Georgoulia: Financial Interests, Personal, Full or part-time Employment: AstraZeneca; Financial Interests, Personal, Stocks/Shares: AstraZeneca. M. Diehn: Financial Interests, Personal, Stocks/Shares: CiberMed, Perception Medicine, Resero Bio; Financial Interests, Personal, Member of Board of Directors: Resero Bio; Financial Interests, Personal, Other, Honoraria: Chugai Pharmaceuticals; Financial Interests, Personal, Other, Consulting fees: AstraZeneca, Foresight Diagnostics, Natera; Financial Interests, Personal, Research Funding: AstraZeneca; Financial Interests, Personal, Other: Natera, Resero Bio, Roche; Non-Financial Interests, Personal, Other: Hokkaido University. All other authors have declared no conflicts of interest.

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