9-1-2021

# 1281O Atezolizumab (atezo) vs platinum-based chemo in blood-based tumour mutational burden-positive (bTMB+) patients (pts) with first-line (1L) advanced/metastatic (m)NSCLC: Results of the Blood First Assay Screening Trial (BFAST) phase III cohort C

R Dziadziuszko

S Peters

Shirish M. Gadgeel
*Henry Ford Health*, sgadgee1@hfhs.org

S M. Shagan

E Felip

*See next page for additional authors*



## Recommended Citation
Dziadziuszko R, Peters S, Gadgeel SM, Mathisen MS, Shagan SM, Felip E, Morabito A, Cheema P, Dols MC, Andric Z, Barrios CH, Yamaguchi M, Dansin E, Danchaivijitr P, Johnson M, Novello S, Gandara DR, Schleifman E, Wang J, and Mok TSK. 1281O Atezolizumab (atezo) vs platinum-based chemo in blood-based tumour mutational burden-positive (bTMB+) patients (pts) with first-line (1L) advanced/metastatic (m)NSCLC: Results of the Blood First Assay Screening Trial (BFAST) phase III cohort C. Ann Oncol 2021; 32:S950-S951.

## Authors

R Dziadziuszko, S Peters, Shirish M. Gadgeel, S M. Shagan, E Felip, A Morabito, P Cheema, M C. Dols, Z Andric, C H. Barrios, M Yamaguchi, E Dansin, P Danchaivijitr, M Johnson, S Novello, D R. Gandara, E Schleifman, J Wang, and T S.K. Mok

## 1207O Bevacizumab + erlotinib vs erlotinib alone as first-line treatment of pts with EGFR mutated advanced non squamous NSCLC: Final analysis of the multicenter, randomized, phase III BEVERLY trial

M.C. Piccirillo[1], L. Bonanno[2], M.C.C. Garassino[3], C. Dazzi[4], L. Cavanna[5], G. Esposito[6], M.A. Burgio[7], F. Rosetti[8], S. Rizzato[9], L. Arenare[1], P. Gargiulo[1], R. Di Liello[1], F. De Marinis[10], L. Crinò[7], F. Morgillo[11], F. Ciardiello[11], N. Normanno[12], C. Gallo[13], C. Gridelli[14], A. Morabito[6]

*[1]Clinical Trial Unit, Istituto Nazionale Tumori, IRCCS, Fondazione G. Pascale, Naples, Italy; [2]Medical Oncology 2, Istituto Oncologico Veneto, IRCCS, Padua, Italy; [3]Department of Medical Oncology, Istituto Nazionale dei Tumori di Milano - Fondazione IRCCS, Milan, Italy; [4]Medical Oncology Unit, AUSL of Romagna, Hospital of Ravenna, Ravenna, Italy; [5]Oncology and Hematology Department, Oncology Unit, Piacenza General Hospital, Piacenza, Italy; [6]Thoracic Medical Oncology, Istituto Nazionale Tumori, IRCCS, Fondazione G. Pascale, Naples, Italy; [7]Department of Medical Oncology, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola, Italy; [8]Medical Oncology and Hematology, Mirano ULSS 3, Serenissima Regione Veneto, Mirano, Italy; [9]Oncology Department, Azienda Sanitaria Universitaria Friuli Centrale, Udine, Italy; [10]Division of Thoracic Oncology, IEO, European Institute of Oncology IRCCS, Milan, Italy; [11]Medical Oncology, Department of Precision Medicine, Università degli Studi della Campania ''Luigi Vanvitelli'', Naples, Italy; [12]Cellular Biology and Biotherapy, Istituto Nazionale Tumori, IRCCS, Fondazione G. Pascale, Naples, Italy; [13]Medical Statistics, Università degli Studi della Campania "Luigi Vanvitelli", Naples, Italy; [14]Division of Medical Oncology, Azienda Ospedaliera "S.G. Moscati", Avellino, Italy*

**Background:** Adding bevacizumab to erlotinib prolonged PFS in NEJ026 and CTONG 1509 trials, but limited data are available in non-Asian patients (pts). BEVERLY is an Italian no-profit, randomized, open-label, multicenter phase III trial of bevacizumab (BEV) plus erlotinib (E) vs E alone as first-line treatment for EGFR-mutated advanced NSCLC.

**Methods:** Eligible pts were randomized 1:1 to E (150mg daily) alone or combined with BEV (15mg/kg iv q3w) until disease progression or unacceptable toxicity. Center, ECOG PS and type of mutation (ex19 deletion vs ex21 L858R vs others) were stratification variables. Co-primary endpoints were investigator-assessed PFS (IA-PFS) and blinded-independent centrally-reviewed PFS (BICR-PFS). Secondary endpoints were OS, QoL, IA- and BICR- objective response rate (ORR) and safety; biomarker analyses are also planned. 126 events out of 160 randomized pts were required to detect a PFS prolongation with BEV from 10 to 16.7 mos (HR 0.60), with 2-sided $\alpha$=0.05, 80% power.

**Results:** From Apr 11, 2016 to Feb 27, 2019, 160 pts were randomized to BEV+E (80) or E alone (80). Pts were mainly female (63.8%), never smokers (51.9%), ECOG PS 0-1 (98.1%), median age 66 (IQR 59-73); 55% of pts had ex19Del and 41% L858R mutation. At a median follow-up of 31 mos, 130/160 (81.3%) pts had a PFS event (progression or death) and 84/160 (52.5%) died. BEV+E significantly prolonged IA-PFS over E alone with a median of 15.4 vs 9.7 mos (HR 0.60; 95%CI 0.42-0.85, log-rank P=0.0039). Median OS was 28.4 vs 23.0 mos in BEV+E and E arms, respectively (HR 0.70; 95%CI 0.46-1.10, log-rank P=0.12). One toxic death was reported, due to intracranial hemorrhage with BEV+E. Hypertension (any grade: 49% vs 18%; grade$\geq$3: 24% vs 5%), skin rash (grade$\geq$3: 31% vs 14%), thromboembolic events (any grade: 11% vs 4%), and proteinuria (any grade: 23% vs 6%) were more frequent with the experimental combination treatment.

**Conclusions:** The addition of BEV to E significantly prolonged IA-PFS compared with E alone as first-line treatment in Italian EGFR-mutated NSCLC patients, with no unexpected safety issues. Blinded radiologic revision of PFS and ORR is ongoing and will be presented at the meeting.

**Clinical trial identification:** NCT02633189; EudraCT 2015-002235-17.

**Legal entity responsible for the study:** Clinical Trial Unit, Istituto Nazionale Tumori, IRCCS, Fondazione G. Pascale.

**Funding:** Roche provided partial funding and experimental drugs.

**Disclosure:** M.C. Piccirillo: Financial Interests, Personal, Invited Speaker: Astellas; Financial Interests, Personal, Invited Speaker: AstraZeneca; Financial Interests, Personal, Invited Speaker: Daiichi Sankyo; Financial Interests, Institutional, Research Grant: Roche; Financial Interests, Institutional, Research Grant: AstraZeneca; Financial Interests, Institutional, Research Grant: Bayer. L. Bonanno: Financial Interests, Personal, Advisory Board: Roche; Financial Interests, Personal, Advisory Board: AstraZeneca; Financial Interests, Personal, Invited Speaker: MSD; Financial Interests, Personal, Invited Speaker: BMS; Financial Interests, Personal, Invited Speaker: Boehringer Ingelheim. L. Cavanna: Financial Interests, Personal, Advisory Board: AstraZeneca; Financial Interests, Personal, Advisory Board: Merck; Financial Interests, Personal, Sponsor/Funding: Pfizer; Financial Interests, Personal, Sponsor/Funding: Celgene; Financial Interests, Personal, Sponsor/Funding: Ipsen. F. Rosetti: Financial Interests, Personal, Sponsor/Funding: Roche. S. Rizzato: Financial Interests, Personal, Sponsor/Funding: Roche; Financial Interests, Personal, Sponsor/Funding: Amgen. R. Di Liello: Financial Interests, Personal, Invited Speaker: Astellas. F. Morgillo: Financial Interests, Personal, Advisory Board: MSD; Financial Interests, Personal, Advisory Board: Lilly; Financial Interests, Institutional, Research Grant: AstraZeneca. F. Ciardiello: Financial Interests, Personal, Advisory Board: Roche; Financial Interests, Personal, Advisory Board: Merck; Financial Interests, Personal, Advisory Board: Pfizer; Financial Interests, Personal, Advisory Board: Servier; Financial Interests, Institutional, Research Grant: Merck; Financial Interests, Institutional, Research Grant: Roche; Financial Interests, Institutional, Research Grant: Amgen. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2021.08.1812

## 1281O Atezolizumab (atezo) vs platinum-based chemo in blood-based tumour mutational burden-positive (bTMB+) patients (pts) with first-line (1L) advanced/metastatic (m)NSCLC: Results of the Blood First Assay Screening Trial (BFAST) phase III cohort C

R. Dziadziuszko[1], S. Peters[2], S.M. Gadgeel[3], M.S. Mathisen[4], S.M. Shagan[5], E. Felip[6], A. Morabito[7], P. Cheema[8], M. Cobo Dols[9], Z. Andric[10], C.H. Barrios[11], M. Yamaguchi[12], E. Dansin[13], P. Danchaivijitr[14], M. Johnson[15], S. Novello[16], D.R. Gandara[17], E. Schleifman[5], J. Wang[18], T.S.K. Mok[19]

*[1]Oncology and Radiotherapy, Medical University of Gdansk, Gdansk, Poland; [2]Oncology, Centre Hospitalier Universitaire Vaudois, Lausanne University, Lausanne, Switzerland; [3]Internal Medicine, Henry Ford Cancer Institute/Henry Ford Health System, Detroit, MI, USA; [4]Product Development Oncology, Genentech, Inc., South San Francisco, CA, USA; [5]Oncology Biomarker Development, Genentech, Inc., South San Francisco, CA, USA; [6]Medical Oncology Service (Lung Cancer Unit), Hospital Universitari Vall d'Hebron, Barcelona, Spain; [7]Thoracic, Istituto Nazionale Tumori 'Fondazione G Pascale', IRCCS, Naples, Italy; [8]Medical Oncology, William Osler Health System, University of Toronto, Toronto, ON, Canada; [9]Medical Oncology, Unidad de Gestión Clínica Intercentros de Oncología Médica, Hospitales Universitarios Regional y Virgen de la Victoria, IBIMA, Málaga, Spain; [10]Medical Oncology, University Hospital Medical Center Bezanijska Kosa, Belgrade, Serbia; [11]Internal Medicine, Oncology Research Center HSL/PUCRS, Porto Alegre, Brazil; [12]Department of Thoracic Oncology, National Hospital Organization Kyushu Cancer Center, Otsu, Japan; [13]Medical Oncology, Center Oscar Lambret, Lille, France; [14]Department of Medicine, Faculty of Medicine, Siriraj Hospital, Bangkok, Thailand; [15]Lung, Sarah Cannon Research Institute, Nashville, TN, USA; [16]Oncology, University of Turin, S. Luigi Gonzaga Hospital, Orbassano, Italy; [17]Internal Medicine & Hematology-Oncology Dept., UC Davis Comprehensive Cancer Center, Sacramento, CA, USA; [18]Biostatistics, Genentech Inc., South San Francisco, CA, USA; [19]Department of Clinical Oncology, The Chinese University of Hong Kong, Hong Kong, China*

**Background:** TMB is a promising biomarker for immunotherapy in NSCLC, but current data are mostly retrospective. As not all pts may have sufficient tissue for comprehensive biomarker testing, bTMB was prospectively tested as a novel biomarker using targeted next-generation sequencing. BFAST (NCT03178552), a global, open-label, multi-cohort trial, evaluated safety and efficacy of targeted therapies or immunotherapy in biomarker-selected pts with unresectable mNSCLC. Here we present results from Cohort C of 1L atezo vs platinum-based chemo in pts with bTMB+ mNSCLC.

**Methods:** We planned to randomise $\approx$440 pts with 1L mNSCLC with measurable disease per RECIST 1.1 and bTMB $\geq$10 (9.1 mut/Mb; FMI bTMB assay) 1:1 to atezo 1200 mg IV every 3 weeks or chemo and stratified by tissue availability, ECOG PS, bTMB and histology. The primary endpoint was INV-PFS per RECIST 1.1 in bTMB $\geq$16 (14.5 mut/Mb) pts. Key secondary endpoints included OS in bTMB $\geq$10 (intent to treat, ITT) and bTMB $\geq$16 pts, and INV-PFS in ITT pts.

**Results:** 471 pts were assigned to atezo (n=234) or chemo (n=237). At baseline, 72% had non-squamous histology, 2% never smoked and median SLD was 103 mm. 145 pts with bTMB $\geq$16 were assigned to atezo and 146 to chemo. At data cutoff (21 May 2020) minimum follow up was 6 mo. INV-PFS difference in bTMB $\geq$16 pts for atezo vs chemo was not significant ($P$=0.053; Table). Grade 3-4 TRAEs occurred in 18% (atezo) vs 46% (chemo) of pts. Serious TRAEs occurred in 12% (atezo) vs 14% (chemo). Results at other bTMB thresholds and by F1L CDx will also be presented as an exploratory analysis.

**Conclusions:** The primary PFS endpoint in bTMB $\geq$16 pts was not met. OS was numerically better with atezo vs chemo but the difference was not statistically significant. The safety profile of atezo vs chemo was favourable and consistent with atezo monotherapy across indications.

**Clinical trial identification:** NCT03178552.

**Editorial acknowledgement:** Medical writing support for this abstract was provided by Chris Lum, PhD, of Health Interactions Inc and funded by F. Hoffmann-La Roche, Ltd.

**Legal entity responsible for the study:** F. Hoffmann-La Roche, Ltd.

**Funding:** F. Hoffmann-La Roche, Ltd.

**Disclosure:** R. Dziadziuszko: Financial Interests, Personal, Advisory Role, Advisory/Consultancy: Roche, AstraZeneca, Pfizer, MSD, BMS, Boehringer Ingelheim, Takeda, Foundation Medicine, Seattle Genetics, Beigene, Regeneron. S. Peters: Consultation / Advisory role: AbbVie, Amgen, AstraZeneca, Bayer, Beigene, Biocartis, Bio Invent, Blueprint Medicines, Boehringer Ingelheim, Bristol Myers Squibb, Clovis, Daiichi Sankyo, Debiopharm, Eli Lilly, Elsevier, F. Hoffmann-La Roche/Genentech, Foundation Medicine, Illumina, Incyte, IQVIA, Janssen, Medscape, Merck Sharp & Dohme, Merck Serono, Merrimack, Mirati, Novartis, PharmaMar, Phosplatin Therapeutics, Pfizer, Regeneron, Sanofi, Seattle Genetics, Takeda, Vaccibody Talk in a company's organized public event: AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, e-cancer, Eli Lilly, F. Hoffmann-La Roche/Genentech, Illumina, Medscape, Merck Sharp & Dohme, Novartis, PER, Pfizer, Prime, RTP, Sanofi, Takeda. Receipt of grants/research supports: (Sub)investigator in trials (institutional financial support for clinical trials) sponsored by Amgen, AstraZeneca, Biodesix, Boehringer Ingelheim, Bristol Myers Squibb, Clovis, F. Hoffmann-La Roche/Genentech, GSK, Illumina, Lilly, Merck Sharp & Dohme, Merck Serono, Mirati, Novartis, Pfizer, Phosplatin Therapeutics. S.M. Gadgeel: Financial Interests, Personal, Other, Honoraria: AstraZeneca, Roche/Genentech, Takeda, Pfizer, Bristol Myers Squibb, Novartis, Janssen, Merck, Eli Lilly, Blueprint; Non-Financial Interests, Personal, Other, Serve on IDMC of a phase III trial: AstraZeneca. M.S. Mathisen: Financial Interests, Personal, Full or part-time Employment: Genentech; Financial Interests, Personal, Stocks/Shares: Roche/Genentech. S.M. Shagan: Financial Interests, Personal, Full or part-time Employment: Genentech; Financial Interests, Personal, Stocks/Shares: Roche. E. Felip: Financial Interests, Personal, Advisory Board: Amgen, AstraZeneca, Bayer, Beigene, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, F. Hoffmann-La Roche, GlaxoSmithKline,

**Table: 1281O**

| Endpoint | Population | Atezo | Chemo[a] | HR (95% CI)[b] | *P* value |
|---|---|---|---|---|---|
| INV-PFS, median, mo | bTMB ≥16 | 4.5 (n=145) | 4.3 (n=146) | 0.77 (0.59, 1.00) | 0.053 |
| | ITT[c] | 4.1 (n=234) | 4.4 (n=237) | 0.91 (0.74, 1.11) | 0.35 |
| OS, median, mo | bTMB ≥16[c] | 13.3 | 10.3 | 0.87 (0.64, 1.17) | 0.35 |
| | ITT[c] | 10.8 | 10.4 | 0.99 (0.79, 1.25) | 0.92 |

F1L CDx, FoundationOne Liquid companion diagnostic; FMI, Foundation Medicine, Inc.; INV-PFS, investigator-assessed progression-free survival; OS, overall survival; SLD, sum of longest diameters; TRAE, treatment-related adverse event. [a] Cisplatin/carboplatin + pemetrexed (non-squamous) or cisplatin/carboplatin + gemcitabine (squamous). [b] Stratified Cox HR. Brookmeyer-Crowley 95% CIs. [c] Not formally tested.

Janssen, Merck Sharpe & Dohme, Merck Serono, Peptomyc, Pfizer, Puma, Regeneron, Sanofi, Syneos Health, Takeda; Financial Interests, Personal, Invited Speaker: Amgen, AstraZeneca, Bristol Myers Squibb, Eli Lilly, F. Hoffmann-La Roche, Janssen, Medscape, Merck Sharpe & Dohme, Merck Serono, Peervoice, Pfizer, Springer, Touch Medical; Financial Interests, Personal, Other: Medical Trends; Non-Financial Interests, Personal, Leadership Role, Dr. Felip is President Elect (2021-2023) of Spanish Society of Medical Oncology; Non-Financial Interests, Personal, Member, Dr. Felip is member of the ESMO Nominating Committee and Compliance Committee: ESMO; Non-Financial Interests, Personal, Member, Dr. Felip is member of the Scientific Committee: ETOP; Non-Financial Interests, Personal, Leadership Role, Dr. Felip is member of the Board of Directors and the Executive Committee (2017-September 2021): IASLC. A. Morabito: Financial Interests, Personal, Speaker's Bureau: Roche, AstraZeneca, Boehringer Ingelheim, Pfizer, BMS; Financial Interests, Personal, Expert Testimony: Roche, AstraZeneca, Boehringer Ingelheim, Pfizer, BMS; Financial Interests, Personal, Advisory Role, Advisory/Consultancy: Eli Lilly, Takeda, MSD. P. Cheema: Financial Interests, Personal, Advisory Role, Advisory/Consultancy: Roche, Pfizer, EMD (Serono), Bristol Myers Squibb, Takeda, Merck; Financial Interests, Institutional, Other, Honoraria: AstraZeneca, Merck; Financial Interests, Institutional, Research Grant, Research Grant/Funding: Merck, AstraZeneca, BMS. C.H. Barrios: Financial Interests, Personal, Advisory Board, Consulting scientific presentations: AstraZeneca, Bayer, Boehringer Ingelheim, Eisai, GSK, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi, Zodiac; Financial Interests, Personal, Ownership Interest, Pathology Lab: Biomarker; Financial Interests, Personal, Stocks/Shares, Clinical Research Company: MedSIR; Financial Interests, Personal, Stocks/Shares, Application: Tummi; Financial Interests, Institutional, Research Grant: AB Sciences, AbbVie, Abraxis, Amgen, Asana, Astellas, AstraZeneca, BioMarin, BMS, Boehringer Ingelheim, Daiichi Sankyo, Exelixis, GSK, IMclone, Leo Pharma, Lilly, Medivation, Merck KGaA, Merck, Merrimack, Millennium, Mylan, Novartis, Pfizer, PharmaMar, Pol. P. Danchaivijitr: Financial Interests, Personal, Advisory Role, Advisory/Consultancy: MSD, Roche, BMS; Financial Interests, Institutional, Research Grant, Research Grant/Funding: MSD, Roche, AstraZeneca. M. Johnson: Financial Interests, Institutional, Advisory Board: AbbVie, Amgen, Daiichi Sankyo, Editas Medicine, Eisai, G1 Therapeutics, GlaxoSmithKline, Ideaya Biosciences, Incyte, Ribon Therapeutics, and Roche; Financial Interests, Principal Investigator: AbbVie, Acerta, Adaptimmune, Amgen, Apexigen, Arcus Biosciences, Array BioPharma, Artios Pharma, AstraZeneca, Atreca, BeiGene, BerGenBio, Boehringer Ingelheim, Calithera, Checkpoint Therapeutics, Corvus Pharmaceuticals, Curis, CytomX, Daiichi Sankyo, Drac; Financial Interests, Principal Investigator: Therapeutics, Kadmon Pharmaceuticals, Loxo Oncology, Lycera, Merck, Mirati, Neovia Oncology, Novartis, OncoMed, Pfizer, PMV Pharmaceuticals, Regeneron, Ribon, Rubius, Sanofi, Seven & Eight Biopharmaceuticals, Shattuck Labs, Silicon Therapeutics, Stem Cent; Financial Interests, Institutional, Advisory Role: AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, CytomX, EMD Serono, Genentech, Gritstone Oncology, Janssen, Lilly, Merck, Mirati, Novartis, Pfizer, Sanofi-Aventis and WindMIL Therapeutics. S. Novello: Financial Interests, Personal, Advisory Role, Advisory/Consultancy: Sanofi, Eli Lilly, Boehringer Ingelheim, Pfizer, Beigene, BMS; Financial Interests, Personal, Speaker's Bureau: Eli Lilly, AstraZeneca, Roche, Takeda, MSD; Financial Interests, Personal, Expert Testimony: Eli Lilly, AstraZeneca, Roche, Takeda, MSD. D.R. Gandara: Financial Interests, Institutional, Research Grant: Amgen, AstraZeneca, Genentech, Merck; Financial Interests, Institutional, Advisory Board, Advisory/Consultancy: AstraZeneca, Roche/Genentech, Guardant Health, IO Biotech, Oncocyte; Financial Interests, Personal, Advisory Board, Advisory/Consultancy: Inivata, Lilly, Merck, Novartis. E. Schleifman: Financial Interests, Personal, Stocks/Shares: Genentech/Roche; Financial Interests, Personal, Full or part-time Employment: Genentech/Roche. J. Wang: Financial Interests, Personal, Full or part-time Employment: Genentech; Financial Interests, Personal, Stocks/Shares: Genentech/Roche. T.S.K. Mok: Financial Interests, Personal, Other, Honoraria: Abbie, Inc., ACEA Pharm, Alpha Biopharma Co. Ltd., Amgen, Amoy Diagnostics Co. Ltd., AstraZeneca, BeiGene, Berry Oncology, Boehringer Ingelheim, Bristol Myers Squibb, Blueprint Medicines Corporation, CStone Pharmaceuticals, Curio Science, Daiichi Sankyo, E; Financial Interests, Personal, Advisory Role, Advisory/Consultancy: Abbie, Inc., ACEA Pharm, Alpha Biopharma Co. Ltd., Amgen, Amoy Diagnostics Co. Ltd., AstraZeneca, BeiGene, Berry Oncology, Boehringer Ingelheim, Bristol Myers Squibb, Blueprint Medicines Corporation, CStone Pharmaceuticals, Curio Science, Daiichi Sankyo, E; Financial Interests, Personal, Other, Lecture: ACEA Pharma, Alpha Biopharma Co. Ltd., Amoy Diagnostics Co. ltd., Boehringer Ingelheim, Bristol Myers Squibb, Daiichi Sankyo, Fishawack Facilitate Ltd., InMed Medical Communication, Lilly, MD Health (Brazil), Medscape/WebMD, Merck Serono, Merck Sharpe & Dohme, Financial Interests, Institutional, Research Grant: Clovis Oncology, SFJ Pharmaceuticals, XCovery; Other, Other, Non-remunerated Activities: geneDecode; Financial Interests, Personal, Stocks/Shares: Lunit Inc., Aurora Tele-Oncology Ltd., Sanomics Ltd.; Financial Interests, Personal, Leadership Role, Board of Directors/Office: Aurora Tele-Oncology Ltd., Hutison ChiMed, Sanomics Ltd., AstraZeneca PLC.All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2021.08.1883

## 1192MO Amivantamab monotherapy and in combination with lazertinib in post-osimertinib EGFR-mutant NSCLC: Analysis from the CHRYSALIS study

N.B. Leighl[1], C.A. Shu[2], A. Minchom[3], E. Felip[4], S. Cousin[5], B.C. Cho[6], K. Park[7], J-Y. Han[8], M. Boyer[9], C.K. Lee[10], V. Moreno Garcia[11], P. Tomasini[12], S. Viteri[13], J. Xie[14], J. Mertz[15], E. Artis[15], R.W. Schnepp[15], R.E. Knoblauch[15], M. Thayu[15], J.M. Trigo Perez[16]

*[1]Medicine, Princess Margaret Cancer Centre, Toronto, ON, Canada; [2]Medicine, Columbia University Medical Center, New York, NY, USA; [3]Drug Development Unit, Royal Marsden Hospital/ Institute of Cancer Research, Sutton, UK; [4]Oncology, Vall d'Hebron University Hospital, Barcelona, Spain; [5]Oncologie Medicale, Institut Bergonie, Bordeaux, France; [6]Medical Oncology, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea; [7]Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [8]Center for Lung Cancer, National Cancer Center, Goyang, Republic of Korea; [9]Medical Oncology, Chris O'Brien Lifehouse, Camperdown, NSW, Australia; [10]Medical Oncology, St George Hospital, Sydney, NSW, Australia; [11]START Madrid FJD, Early Phase Clinical Trials Unit, Hospital Universitario Fundacion Jimenez Diaz, Madrid, Spain; [12]Multidisciplinary Oncology and Therapeutic Innovations, Aix Marseille Univ, APHM, INSERM, CNRS, CRCM, Hôpital Nord, Marseille, France; [13]Oncology, Instituto Oncológico Dr. Rosell, Hospital Universitari Dexeus, Grupo Quironsalud, Barcelona, Spain; [14]Clinical Biostatistics, Janssen R&D, Spring House, PA, USA; [15]Oncology, Janssen R&D, Spring House, PA, USA; [16]Medical Oncology, Hospital Universitario Virgen de la Victoria y Regional, IBIMA, Malaga, Spain*

**Background:** Amivantamab (ami), an epidermal growth factor receptor (EGFR)-MET bispecific antibody, has demonstrated efficacy in EGFR mutant non-small cell lung cancer (NSCLC) that progressed on osimertinib (osi), both as monotherapy and in combination with lazertinib (laz), a 3rd-generation tyrosine kinase inhibitor. Clinical outcomes of patients (pts) treated with ami monotherapy (mono) and ami in combination with laz (combo) are presented here.

**Methods:** CHRYSALIS is an ongoing study of ami in pts with advanced EGFR mutant NSCLC (NCT02609776). Pts who progressed on osi were pooled to form the mono group, a majority of whom were preselected for C797S/other resistance mutations or *MET* amplification. The combo group comprised unselected pts who had progressed on osi but were chemotherapy-naïve. Response was assessed by the investigator per RECIST v1.1.

**Results:** As of 19 Apr 2021, 121 pts in the mono group (85% with EGFR/MET-based resistance) and 45 in the combo group (38% with EGFR/MET-based resistance) were efficacy-evaluable, with median follow-up of 6.9 and 11.1 months, respectively. Antitumor activity was observed in the mono group, with 33 achieving partial response (PR) as best response, of which 23 were confirmed, for an overall response rate (ORR) of 19% (95% CI, 12—27). In the combo group, 1 complete response and 15 PRs were observed, all of which confirmed, for an ORR of 36% (95% CI, 22—51). Median duration of response was 5.9 months with mono, 9.6 months with combo (Table). The safety profile for both mono and combo was consistent with previously-reported safety. No new safety signals were identified.

**Table: 1192MO Efficacy of amivantamab monotherapy and in combination with lazertinib among efficacy-evaluable[a] patients**

| | Efficacy | |
|---|---|---|
| | Monotherapy (n=121) | Combination (n=45) |
| ORR (95% CI) | 19% (12—27) | 36% (22—51) |
| CBR (95% CI) | 48% (39—57) | 64% (49—78) |
| mDOR, month (95% CI) | 5.9 (4.2—12.6) | 9.6 (5.3—NR) |

[a]Patients who had at least 2 post-baseline disease assessment or discontinued before the second assessment. CBR, clinical benefit rate (complete response, partial response, or stable disease of at least 11 weeks); mDOR, median duration of response; ORR, overall response rate; NR, not reached

**Conclusions:** Antitumor activity of ami + laz in the post-osi setting appears favorable even without molecular selection post osimertinib failure, supporting that simultaneous targeting of the extracellular and catalytic domains of EGFR provides additive benefits.