LBA9 IMpower150: An exploratory analysis of efficacy outcomes in patients with EGFR mutations

T.S.K. Mok[1], M.A. Socinski[2], M. Reck[3], R.M. Jotte[4], D.W-T. Lim[5], F. Cappuzzo[6], F.J. Orlandi[7], D. Stroyakovskiy[8], N. Nogami[9], D. Rodríguez-Abreu[10], D. Moro-Siblot[11], C.A. Thomas[12], F. Barlesi[13], G. Finley[14], A. Lee[15], G. Shankar[15], W. Yu[16], M. Kowanetz[17], W. Lin[18], M. Nishio[19]

[1]Medical Oncology, Chinese University of Hong Kong, Hong Kong, China, [2]Thoracic Oncology Program, Florida Hospital Cancer Institute, Orlando, FL, USA, [3]Thoracic Oncology, Lung Clinic Grosshansdorf, Airway Research Center North, German Center of Lung Research, Grosshansdorf, Germany, [4]USON Thoracic Committee, Rocky Mountain Cancer Centers, Denver, CO, USA, [5]Division of Medical Oncology, National Cancer Centre Singapore, Singapore, [6]Oncology and Hematology Department, Azienda Unità Sanitaria Locale della Romagna, Ravenna, Italy, [7]Chile and Prosalud Oncologia, Instituto Nacional del Torax, Santiago, Chile, [8]Medical Oncology, Moscow City Oncology Hospital, Moscow, Russian Federation, [9]Department of Thoracic Oncology, National Hospital Organization Shikoku Cancer Center, Matsuyama, Japan, [10]Universidad de Las Palmas de Gran Canaria, Complejo Hospitalario Universitario Insular Materno-Infantil de Gran Canaria, Las Palmas De Gran Canaria, Spain, [11]Thoracic Oncology Unit, Centre Hospitalier Universitaire de Grenoble-Alpes, Grenoble, France, [12]Medical Oncology, New England Cancer Specialists, Scarborough, ME, USA, [13]Assistance Publique-Hôpitaux de Marseille, Aix Marseille University, Marseille, France, [14]Medical Oncology, Allegheny Health Network Cancer Institute, Pittsburgh, PA, USA, [15]Product Development Oncology, Genentech, Inc., South San Francisco, CA, USA, [16]Biometrics, Genentech Inc., South San Francisco, CA, USA, [17]Oncology Biomarker Development, Genentech Inc., South San Francisco, CA, USA, [18]Global Development Team, Genentech Inc., South San Francisco, CA, USA, [19]Department of Thoracic Medical Oncology, The Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan

Background: Atezolizumab (atezo; anti–PD-L1) inhibits PD-L1 to restore anticancer immunity; bevacizumab (bev) may enhance atezo efficacy by inhibiting VEGF immunosuppression and promoting T-cell tumour infiltration. Atezo + bev + chemotherapy (chemo) prolonged PFS and OS vs bev + CP in pts with first-line nonsquamous

Table: LBA9

	mOS, mo			HR (95% CI)	
	ABCP	ACP	BCP	ABCP vs BCP	ACP vs BCP
EGFR-mt	NE n = 34	21.4 n = 45	18.7 n = 45	0.61 (0.29, 1.28)	0.93 (0.51, 1.68)
Sensitising EGFR mutation[a]	NE n = 26	21.2 n = 33	17.5 n = 32	0.31 (0.11, 0.83)	0.90 (0.47, 1.74)
Received prior TKI therapy	NE n = 22	18.4 n = 27	17.5 n = 28	0.39 (0.14, 1.07)	0.99 (0.49, 1.98)
	mPFS, mo			HR (95% CI)	
EGFR-mt	10.2 n = 34	6.9 n = 45	6.9 n = 45	0.61 (0.36, 1.03)	1.14 (0.73, 1.78)
Sensitising EGFR mutation[a]	10.3 n = 26	6.0 n = 33	6.1 n = 32	0.41 (0.23, 0.75)	1.01 (0.61, 1.70)
Received prior TKI therapy	9.7 n = 22	5.7 n = 27	6.1 n = 28	0.42 (0.22, 0.80)	1.20 (0.69, 2.09)

[a]Sensitising EGFR mutations are defined as exon 19 deletions or L858R mutations. NE, not estimable.

NSCLC in the randomised Ph III IMpower150 study, including pts with EGFR or ALK genomic alterations. Here, we further analyse the efficacy of atezo and/or bev with chemo in pts with EGFR mutations (EGFR-mt) in this study.

Methods: The 1202 enrolled pts received atezo (A) 1200 mg + bev (B) 15 mg/kg + carboplatin (C) AUC 6 + paclitaxel (P) 200 mg/m^2 (ABCP) or A + C + P (ACP) or B + C + P (BCP) by IV q3w for 4 or 6 cycles per investigator (INV) decision, then q3w maintenance with atezo + bev, atezo or bev, respectively. Co-primary endpoints were OS and INV-assessed PFS in the ITT–wild-type population (excluded pts with EGFR or ALK genomic alterations). Exploratory analyses included OS and INV-assessed PFS in pts with EGFR-mt disease, pts with sensitising EGFR mutations and pts with EGFR-mt disease who had prior TKI therapy.

Results: These data represent $\geq$ 20-mo follow-up (data cutoff: 22 Jan 2018) in the ITT population. 124 pts were EGFR-mt, including 91 with a sensitising mutation. Baseline characteristics of EGFR-mt pts across the treatment arms were generally comparable to the ITT population. OS was improved with ABCP vs BCP in EGFR-mt pts, especially in pts with sensitising EGFR mutations (HR, 0.31 [95% CI: 0.11, 0.83]). This benefit extended to PFS (HR, 0.41 [95% CI: 0.23, 0.75]). See table for full efficacy results. Safety was similar between the EGFR-mt subgroup and the ITT population.

Conclusions: IMpower150 is the first randomised Ph III trial of a checkpoint inhibitor to show a benefit in pretreated EGFR-mt pts. Adding atezo to standard-of-care bev and chemo provided survival benefit in EGFR-mt pts who have failed TKIs, for whom this regimen may represent a new treatment option.

Editorial acknowledgement: Jessica Bessler of Health Interactions, funded by F. Hoffmann-La Roche.

Clinical trial identification: NCT02366143.

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

Funding: F. Hoffmann-La Roche.

Disclosure: T.S.K. Mok: Honor/Speaker B: AZ, BI, Roche, Pfizer, Lilly, Merck, MSD, Novartis, SFJ, ACEA, Vertex, BMS, geneDecode, OncoGenex, Celgene, Ignyta, Cirina, Fishawack, Sanomics*, Janssen, Takeda, Chi-Med*, OrigiMed, Hengrui, Sanofi, Yuhan(*Stock) Employee: CUHK. M.A. Socinski: Honoraria, Speakers' bureau, Research funding: Genentech. M. Reck: Advisor/Board member: Lilly, Roche, BI, BMS, MSD, AstraZeneca, Merck, Novartis, Pfizer, Celgene; Speakers' bureau: Roche, Lilly, Pfizer, BI, AstraZeneca, MSD, BMS, Merck, Novartis, Pfizer, Celgene. R.M. Jotte: Speakers' bureau, Travel and accommodation expenses, Honoraria: Bristol-Myers Squibb. F. Cappuzzo: Speakers or advisory board: Roche, AZ, BMS, Pfizer, MSD, Takeda. F.J. Orlandi: Consulting/advisory role: AZ, Roche, BMS, MSD, Lilly, Pfizer Travel and accommodation expenses: Pfizer, MSD, AZ, Roche, BMS; Research funding: AZ, Amgen, Roche, BI, Astellas Medivation, MSD, BMS, Celltrion; Speakers: AstraZeneca. N. Nogami: Honoraria: AstraZeneca, Pfizer Inc., Ono Pharmaceutical CO., Ltd., Kyowa Hakko Kirin, Taiho Phamaceutical Co.,Ltd., Chugai Pharmaceutical Co., Ltd, Eli Lilly Japan, Boehringer Ingelheim, MSD KK. D. Rodríguez-Abreu: Speakers' bureau: MSD, Roche, BMS, AstraZeneca, Pfizer. D. Moro-Siblot: Honoraria, consulting/advisory role: Roche, MSD, Pfizer, Novartis, BMS, AstraZeneca, Lilly; Travel and accommodation expenses: Roche, MSD, Pfizer, BMS, AstraZeneca. F. Barlesi: Personal fees: AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Clovis Oncology, Eli Lilly Oncology, F. Hoffmann–La Roche Ltd, Novartis, Merck, MSD, Pierre Fabre, Pfizer. G. Finley: Promotional speaking: Bristol Meyers, Boehringer Ingleheim, Astellas Medivation, Merck. A. Lee: Employee, owner of stock: Genentech. G. Shankar, W. Yu: Employee: Genentech. M. Kowanetz: Genentech Employee with Roche Stock. Patent biomarkers and methods of treating PD-1 and PD-l1 related conditions pending. W. Lin: Employee: Genentech; Stock owner: Roche. M. Nishio: Speakers/advisory: Ono Pharma, BMS, Pfizer, Chugai Pharma, Lilly, Taiho Pharma, AZ, BI, MSD, Novartis, Daiichi Sankyo, Merck Serono; Research funding: MSD, Novartis, Ono Pharma, Chugai Pharma, BMS, Taiho Pharma, Lilly, AZ, Pfizer, Astellas. All other authors have declared no conflicts of interest.