

LBA1
Osimertinib adjuvant therapy in patients (pts) with resected EGFR mutated (EGFRm) NSCLC (ADAURA): Central nervous system (CNS) disease recurrence

M. Tsuboi¹, Y-L. Wu², J. He³, T. John⁴, C. Grohe⁵, M. Majem⁶, J.W. Goldman⁷, K. Laktionov⁸, S-W. Kim⁹, T. Kato¹⁰, H.V. Vu¹¹, C. Akewanlop¹², C-J. Yu¹³, F. de Marinis¹⁴, M. Domine¹⁵, F.A. Shepherd¹⁶, C. Yan¹⁷, A. Atasoy¹⁸, R. Herbst¹⁹

¹ Department of Thoracic Surgery and Oncology, National Cancer Center Hospital East, Kashiwa, Japan, ² Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital and Guangdong Academy of Medical Sciences, Guangzhou, China, ³ Thoracic Surgery Department, National Cancer Center/ National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China, ⁴ Department of Medical Oncology, Austin Health, Melbourne, Australia, ⁵ Department of Respiratory Diseases, Evangelische Lungenklinik, Berlin, Germany, ⁶ Department of Medical Oncology, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, ⁷ David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA, USA, ⁸ Centre of Innovative Technologies and Oncology, N.N Blokhin Russian Cancer Center, Russian Academy of Medical Sciences, Moscow, Russian Federation, ⁹ Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea, ¹⁰ Department of Thoracic Oncology, Kanagawa Cancer Center, Asahi Ward, Japan, ¹¹ Department Thoracic Surgery, Choray Hospital, Ho Chi Minh City, Vietnam, ¹² Division of Medical Oncology, Faculty of Medicine, Siriraj Hospital, Bangkok, Thailand, ¹³ Department of Internal Medicine, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan, ¹⁴ Thoracic Oncology Division, European Institute of Oncology (IEO), IRCCS, Milan, Italy, ¹⁵ Department of Oncology, Instituto de Investigacion Sanitaria-Fundación Jimenez Diaz (IIS- FJD), Madrid, Spain, ¹⁶ Department of Medical Oncology and Hematology, University Health Network, Princess Margaret Cancer Centre and the University of Toronto, Toronto, ON, Canada, ¹⁷ Late Oncology Statistics, AstraZeneca, Cambridge, UK, ¹⁸ Late Oncology Research & Development, AstraZeneca, Cambridge, UK ¹⁹ Medical Oncology, Yale School of Medicine and Yale Cancer Center, New Haven, CT, USA

Background

CNS relapse is common in NSCLC, and is a poor prognostic factor. In the resected EGFRm NSCLC setting, the impact of treatment on sites of recurrence, including the CNS, is a key consideration. Osimertinib is a 3rd-generation EGFR-TKI with demonstrated efficacy in NSCLC CNS metastases. In ADAURA, osimertinib demonstrated a highly statistically significant and clinically meaningful improvement in disease-free survival vs placebo (PBO; DFS, hazard ratio [HR]: 0.20 [99.12% CI 0.14, 0.30; p<0.001) in resected stage IB–IIIA EGFRm (ex19del/L858R) NSCLC (Ph III ADAURA; NCT02511106). We report an exploratory analysis of recurrence patterns.

Methods

Pts with resected stage IB–IIIA EGFRm NSCLC, with/without adjuvant chemotherapy, were randomised 1:1 to receive osimertinib 80 mg once-daily or PBO until recurrence/discontinuation/3 years. Patterns of recurrence and CNS DFS (time to CNS recurrence/death) were exploratory endpoints. An MRI/CT brain scan was mandated at baseline either before surgery or upon enrolment, but was not required in absence of symptoms. Recurrence was categorised as local/regional and/or distant, with sites of relapse recorded. Data cutoff: 17/01/20.

Results

Overall, 682 pts were randomised (osimertinib: 339; PBO: 343). Pts treated with osimertinib had fewer recurrence events vs PBO (Table); 45 pts had CNS DFS events (osimertinib: 6; PBO: 39; median follow-up 22 months [mo]). Conditional probability of CNS recurrence at 12 mo (95% CI): <1% (0%, 2%) with osimertinib vs 7% (4%, 10%) with PBO. Median CNS DFS: not reached (95% CI 39.0 mo, not calculable [NC]) with osimertinib vs 48.2 (NC, NC) mo with PBO. CNS DFS HR: 0.18 (95% CI 0.10, 0.33); p<0.0001. Table: LBA1

	Osimertinib n=339	PBO n=343
CNS DFS events, pts (%):	6 (2)	39 (11)
CNS recurrence	4 (1)	33 (10)
Death*	2 (1)	6 (2)
DFS events, pts (%):	37 (11)	159 (46)
Disease recurrence	37 (11)	157 (46)
Non-CNS recurrence	33 (10)	123 (36)

	Osimertinib n=339	PBO n=343
<i>CNS recurrence</i>	4 (1)	33 (10)
<i>Disease recurrence with missing location</i>	0	1 (0)
Death†	0	2 (1)

*Death in absence of CNS disease recurrence, or death within two visits of baseline where the patient has no evaluable assessments or no baseline data. †Death in the absence of disease recurrence (any site), or death within two visits of baseline where the patient has no evaluable assessments or no baseline data.

Conclusions

There was a clinically meaningful improvement in CNS DFS with osimertinib: 82% reduction in risk of CNS disease recurrence or death. Results support that osimertinib reduces risk of CNS recurrence in the resected EGFRm NSCLC setting.

Clinical trial identification

NCT02511106.

Editorial acknowledgement

Natasha Learmond, BSC, of Ashfield Healthcare Communications, Macclesfield, UK, part of UDG Healthcare plc for medical writing support that was funded by AstraZeneca in accordance with Good Publications Practice (GPP3) guidelines.

Legal entity responsible for the study

AstraZeneca.

Funding

AstraZeneca.

Disclosure

M. Tsuboi: Honoraria (self): Johnson & Johnson Japan; Honoraria (self), Research grant/Funding (institution): AstraZeneca KK; Honoraria (self): Eli Lilly Japan; Honoraria (self), Research grant/Funding (institution): Boehringer-Ingelheim Japan; Honoraria (self): Chugai Pharmaceutical Co., Ltd; Honoraria (self), Research grant/Funding (institution): MSD; Honoraria (self): Bristol-Myers Squibb KK; Honoraria (self): Teijin Pharma; Honoraria (self): Taiho Pharma; Honoraria (self): Medtronic Japan; Honoraria (self): Ono Pharmaceutical Co., Ltd. Y-L. Wu: Speaker Bureau/Expert testimony, Research grant/Funding (institution): AstraZeneca; Speaker Bureau/Expert testimony: Boehringer Ingelheim; Speaker Bureau/Expert testimony, Research grant/Funding (institution): BMS; Speaker Bureau/Expert testimony: Eli Lilly; Speaker Bureau/Expert testimony: MSD; Speaker Bureau/Expert testimony, Research grant/Funding (institution): Pfizer; Speaker Bureau/Expert testimony: Sanofi; Speaker Bureau/Expert testimony, Research grant/Funding (self): Roche. T. John: Honoraria (self), Honoraria (institution), Advisory/Consultancy, Shareholder/Stockholder/Stock options: AstraZeneca; Honoraria (institution): Novartis; Advisory/Consultancy: Roche; Advisory/Consultancy: BMS; Advisory/Consultancy: Merck; Advisory/Consultancy: Ignyta; Advisory/Consultancy: Takeda; Advisory/Consultancy: MSD; Advisory/Consultancy: Specialised Therapeutics; Advisory/Consultancy: Pfizer. C. Grohe: Honoraria (self), Advisory/Consultancy, Speaker Bureau/Expert testimony: AstraZeneca; Honoraria (self), Advisory/Consultancy, Speaker Bureau/Expert testimony, Travel/Accommodation/Expenses: Boehringer Ingelheim; Honoraria (self), Advisory/Consultancy, Speaker Bureau/Expert testimony: MSD. M. Majem: Honoraria (self), Research grant/Funding (self): BMS; Honoraria (self): MSD; Honoraria (self): Boehringer Ingelheim; Honoraria (self): AstraZeneca; Honoraria (self): Roche; Honoraria (self): Kyowa Kyirin; Honoraria (self): Pierre Fabre; Honoraria (self): Takeda; Honoraria (self): Bayer. J.W. Goldman: Speaker Bureau/Expert testimony: Merck; Honoraria (self), Research grant/Funding (self): AstraZeneca; Research grant/Funding (self): AbbVie; Research grant/Funding (self): Merck; Research grant/Funding (self): BMS. S-W. Kim: Advisory/Consultancy, Research grant/Funding (self): AstraZeneca. T. Kato: Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (self): AbbVie; Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (self): Amgen; Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (self): AstraZeneca; Advisory/Consultancy, Research grant/Funding (self): Chugai; Advisory/Consultancy, Research grant/Funding (self): Eli Lilly; Advisory/Consultancy, Research grant/Funding (self): Merck Biopharma; Advisory/Consultancy, Research grant/Funding (self): MSD; Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (self): Ono; Advisory/Consultancy, Speaker Bureau/Expert testimony, Research grant/Funding (self): Pfizer; Advisory/Consultancy, Speaker Bureau/Expert testimony: Daiichi-Sankyo; Advisory/Consultancy: Nippon Kayaku; Advisory/Consultancy: Nitto Denko; Advisory/Consultancy: Sumitomo Dainippon; Advisory/Consultancy: Takeda; Speaker Bureau/Expert testimony, Research grant/Funding (self): Bristol Myers Squibb; Research grant/Funding (self): Novartis; Research grant/Funding (self): Taiho; Speaker Bureau/Expert testimony: Boehringer Ingelheim; Speaker Bureau/Expert testimony: F.Hoffman-La Roche; Speaker Bureau/Expert testimony: Shionogi. F. de Marinis: Advisory/Consultancy: Roche; Advisory/Consultancy: BMS; Advisory/Consultancy: AstraZeneca; Advisory/Consultancy: MSD; Advisory/Consultancy: Pfizer. M. Domine: Advisory/Consultancy, Speaker Bureau/Expert testimony: AstraZeneca; Advisory/Consultancy, Speaker Bureau/Expert

testimony: BMS; Advisory/Consultancy, Speaker Bureau/Expert testimony: Boehringer Ingelheim; Advisory/Consultancy, Speaker Bureau/Expert testimony: MSD; Advisory/Consultancy, Speaker Bureau/Expert testimony: Pfizer; Advisory/Consultancy, Speaker Bureau/Expert testimony: Roche. F.A. Shepherd: Honoraria (self), Shareholder/Stockholder/Stock options: AstraZeneca. C. Yan, A. Atasoy: Full/Part-time employment: AstraZeneca. R. Herbst: Honoraria (self): AbbVie; Honoraria (self): Armo Biosciences; Honoraria (self), Research grant/Funding (self): AstraZeneca; Honoraria (self): Biodesix; Honoraria (self): Bolt Biotherapeutics; Honoraria (self): Bristol-Myers Squibb; Honoraria (self), Research grant/Funding (self): Eli Lilly; Honoraria (self): Cybrexa; Honoraria (self): EMD Serrano; Honoraria (self), Research grant/Funding (self): Genentech/Roche; Honoraria (self): Genmab; Honoraria (self): Halozyme; Honoraria (self): Heat Biologics; Honoraria (self): IMAB Biopharma; Honoraria (self): Immunocore; Honoraria (self): Infinity Pharmaceuticals; Honoraria (self): Loxo Oncology; Honoraria (self), Research grant/Funding (self): Merck; Honoraria (self): Mirati Therapeutics; Honoraria (self): Nektar; Honoraria (self): Neon Therapeutics; Honoraria (self): NextCure; Honoraria (self): Novartis; Honoraria (self): Pfizer; Honoraria (self): Sanofi; Honoraria (self): Seattle Genetics; Honoraria (self): Shire PLC; Honoraria (self): Spectrum Pharmaceuticals; Honoraria (self): Symphogen; Honoraria (self): Takeda, Tesaro, Tocagen, WindMIL Therapeutics; Officer/Board of Directors: Junshi Pharmaceuticals. All other authors have declared no conflicts of interest.

© European Society for Medical Oncology