NSCLC, LOCALLY ADVANCED

LBA3_PR An international randomized trial, comparing post-operative conformal radiotherapy (PORT) to no PORT, in patients with completely resected non-small cell lung cancer (NSCLC) and mediastinal N2 involvement: Primary end-point analysis of LungART (IFCT-0503, UK NCRI, SAKK) NCT00410683

C. Le Pechoux[1], N. Pourel[2], F. Barlesi[3], C. Faivre-Finn[4], D. Lerouge[5], G. Zalcman[6], D. Antoni[7], B. Lamezec[8], U. Nestle[9], P. Boisselier[10], F. Thillays[11], A. Paumier[12], E. Dansin[13], K. Peignaux[14], J. Madelaine[15], E. Pichon[16], A. Larrouy[17], O. Riesterer[18], A. Lavole[19], A. Bardet[20]

[1]Radiation Oncology, Gustave Roussy, Villejuif, France; [2]Radiation Oncology, Institut Sainte Catherine, Avignon, France; [3]France and Institut Gustave Roussy, Aix Marseille Université, Aix-Marseille University, CRCM, AP-HM, Marseille, Villejuif, France; [4]Clinical Oncology, The University of Manchester and The Christie NHS Foundation Trust, Manchester, UK; [5]Radiation Oncology, Centre Baclesse, Caen, France; [6]Department of Thoracic Oncology and CIC1425, Hôpital Bichat-Claude Bernard, Assistance Publique Hôpitaux de Paris, Université Paris-Diderot, Paris, France; [7]Radiation Oncology, Institut de Cancérologie Strasbourg Europe, Strasbourg, France; [8]Radiation Oncology, Clinique Armoricaine de Radiologie, St. Brieuc, France; [9]Radiation Oncology, Universitätsklinikum Freiburg Klinik für Innere Medizin Hämatologie, Onkologie und Stammzelltransplantation, Freiburg Im Breisgau, Germany; [10]Radiation Oncology, ICM Regional Cancer Institute of Montpellier, Montpellier, France; [11]Radiation Oncology, Institut de Cancérologie de l'Ouest, Saint Herblain, France; [12]Radiation Oncology, ICO Site Paul Papin, Angers, France; [13]Medical Oncology, Centre Oscar Lambret, Lille, France; [14]Radiation Oncology, Centre Georges Francois Leclerc, Dijon, France; [15]Medical Oncology, Centre Hospitalier Caen, Caen, France; [16]Pneumology, CHRU Bretonneau, Tours, France; [17]Radiation Oncology, Centre de Cancerologie Paris Nord, Sarcelles, France; [18]Radiation Oncology, University Hospital Zurich and Center for Radiation Oncology KSA-KSB, Cantonal Hospital Aurau, Zurich, Switzerland; [19]Pneumology, Hopital Tenon, Paris, France; [20]Biostatistics, Institut Gustave Roussy, Villejuif, France

Background: Adjuvant PORT has been controversial since publication of a meta-analysis showing PORT could be deleterious especially in pN0 pN1 pts. However, changes have taken place in the management of stage IIIAN2 NSCLC pts including use of adjuvant chemotherapy (CT), patients' workup, quality of surgery and radiotherapy. Therefore the role of PORT warranted further investigations in high risk pts.

Methods: LungART is a multi-institutional randomized phase III trial comparing mediastinal PORT (54 Gy/27-30 fractions) to no PORT. Pts were eligible if they were PS 0-2, had a complete resection with nodal exploration, proven N2 disease; prior (neo)-adjuvant CT was allowed. The main end-point was disease-free survival (DFS). 500 pts and 292 events were required to show an improvement in DFS from 30% to 42% with PORT (bilateral test). Secondary endpoints included toxicity, local control, patterns of recurrence, overall survival (OS), second cancers, prognostic and predictive factors of treatment effect.

Results: Between August 2007 and July 2018, 501 patients were randomized after surgery or after CT: 252 pts allocated to PORT, and 249 to CA. Median age was 61 (range=36-85), 66% male, histology: mostly adenocarcinoma (73%) and work-up included PET scan in 91% pts. Most patients received CT (post op 77%, pre-op 18%). Analysis for DFS was performed with a median FU of 4.8 yrs; toxicity evaluated on 487 pts (246 in CA). Early and late Gr 3-5 cardio-pulmonary toxicity was respectively 7 and 20% in PORT vs 3,2 and 7,7 % in CA. DFS hazard ratio was 0.85 (95% CI 0.67; 1.07); p=0.16; median DFS was 30.5 months in PORT arm [24;48] and 22.8 in CA [17;37]; 3-year DFS was 47.1% with PORT vs 43.8% with no PORT. 3-year OS was 66.5% with PORT vs 68.5% with no PORT.

Conclusions: LungART is the first European randomized study evaluating modern PORT after complete resection, in pts selected predominantly with PET scan and having received (neo)adjuvant CT. 3-year DFS was higher than expected in both arms and PORT was associated with a non-statistically significant 15% increase in DFS among stage IIIAN2 pts.

Clinical trial identification: NCT00410683.

Legal entity responsible for the study: Gustave Roussy.

Funding: French National Cancer Institute (INCa), French Health Ministry (PHRC), Gustave Roussy and CRUK grant (A13969).

Disclosure: C. Le Pechoux: Honoraria (institution): Amgen; Honoraria (institution), Advisory/Consultancy: AstraZeneca; Honoraria (institution): Lilly; Honoraria (self): PrimeOncology; Honoraria (institution): Medscape; Honoraria (institution), Advisory/Consultancy: Roche; Honoraria (institution), Advisory/Consultancy: Nanobiotix. F. Barlesi: Honoraria (self), Personal fees: AstraZeneca; Honoraria (self): Bayer; Honoraria (self): Bristol-Myers Squibb; Honoraria (self): Boehringer-Ingelheim; Honoraria (self): Eli Lilly Oncology; Honoraria (self): F. Hoffmann-La Roche Ltd.; Honoraria (self): Novartis; Honoraria (self): Merck; Honoraria (self): MSD; Honoraria (self): Pierre Fabre; Honoraria (self): Pfizer; Honoraria (self): Takeda. C. Faivre-Finn: Advisory/Consultancy, Research grant/Funding (institution): AstraZeneca; Research grant/Funding (institution): Elekta. G. Zalcman: Research grant/Funding (institution): Fondation Roche; Honoraria (self), Travel/Accommodation/Expenses: AstraZeneca; Honoraria (self), Travel/Accommodation/Expenses: BMS; Honoraria (self): MSD; Honoraria (self), Advisory/Consultancy: Inventiva; Travel/Accommodation/Expenses: Roche; Travel/Accommodation/Expenses: AbbVie; Travel/Accommodation/Expenses: Pfizer; Advisory/Consultancy: Da Volterra. J. Madelaine: Honoraria (self), Dr JM received support: AstraZeneca; Honoraria (self): Chugai Pharma; Honoraria (self): Pfizer; Honoraria (self): Boehringer Ingelheim; Honoraria (self): MSD France; Honoraria (self): Roche SAS; Honoraria (self): Actelion; Honoraria (self): GSK; Honoraria (self): Bristol-Myers Squibb. A. Bardet: Advisory/Consultancy: Roche. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.2280

LBA49 Durvalumab after chemoradiotherapy in stage III NSCLC: 4-year survival update from the phase III PACIFIC trial

C. Faivre-Finn[1], D. Vicente[2], T. Kurata[3], D. Planchard[4], L. Paz-Ares[5], J.F. Vansteenkiste[6], D.R. Spigel[7], M.C. Garassino[8], M. Reck[9], S. Senan[10], J. Naidoo[11,12], A. Rimner[12], Y-L. Wu[13], J.E. Gray[14], M. Özgüroğlu[15], K.H. Lee[16], M. Newton[17], L. Wang[17], P. Thiyagarajah[18], S.J. Antonia[14]

[1]The University of Manchester and The Christie NHS Foundation Trust, Manchester, UK; [2]Hospital Universitario Virgen Macarena, Seville, Spain; [3]Kansai Medical University Hospital, Hirakata, Japan; [4]Department of Medical Oncology, Thoracic Unit, Gustave Roussy, Villejuif, France; [5]Hospital Universitario 12 de Octubre, CiberOnc, Universidad Complutense and CNIO, Madrid, Spain; [6]Department of Respiratory Oncology, University Hospitals KU Leuven, Leuven, Belgium; [7]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN, USA; [8]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [9]Lung Clinic Grosshansdorf, Airway Research Center North, German Center for Lung Research, Grosshansdorf, Germany; [10]Department of Radiation Oncology, Amsterdam University Medical Centers, Vrije Universiteit Amsterdam, Cancer Center Amsterdam, Amsterdam, Netherlands; [11]Sidney Kimmel Comprehensive Cancer Center and Bloomberg-Kimmel Institute for Cancer Immunotherapy, Johns Hopkins University, Baltimore, MD, USA; [12]Department of Radiation Oncology, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [13]Department of Pulmonary Oncology, Guangdong Lung Cancer Institute, Guangdong General Hospital & Guangdong Academy of Medical Sciences, Guangzhou, China; [14]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA; [15]Istanbul University-Cerrahpaşa, Cerrahpaşa School of Medicine, Istanbul, Turkey; [16]Chungbuk National University Hospital, Chungbuk National University College of Medicine, Cheongju, Republic of Korea; [17]AstraZeneca, Gaithersburg, MD, USA; [18]AstraZeneca, Cambridge, UK

Background: In the phase III PACIFIC trial of patients (pts) with unresectable Stage III NSCLC without disease progression after concurrent chemoradiotherapy (cCRT), durvalumab significantly improved progression-free survival (PFS; stratified HR 0.52, 95% CI 0.42–0.65; P<0.0001; median 16.8 vs 5.6 months; data cutoff [DCO], 13 Feb 2017) and overall survival (OS; stratified HR 0.68, 95% CI 0.53–0.87; P=0.0025; median not reached vs 28.7 months; DCO, 22 Mar 2018) vs placebo (pbo), with manageable safety. We report updated, exploratory analyses of survival outcomes at 4 years, including the first estimate of median OS for the durvalumab arm.

Methods: Pts with WHO PS 0/1 (any tumour PD-L1 status) who had received ≥2 cycles of platinum-based cCRT (RT dosage typically 60–66 Gy in 30–33 fractions) were enrolled and randomised (2:1), 1–42 days post-cCRT, to IV durvalumab 10 mg/kg or pbo (q2w for ≤12 months), stratified by age, sex, and smoking history. Primary endpoints were PFS (blinded independent central review; RECIST v1.1) and OS (both measured from the time of randomisation). HRs and 95% CIs were estimated using a stratified log-rank test in the ITT population. Medians and OS/PFS rates at 48 months were estimated by Kaplan–Meier method.

Results: In total, 709/713 randomised patients received durvalumab (n/N=473/476) and pbo (n/N=236/237). The last pt had completed study treatment in May 2017, almost 3 years prior to the current DCO. As of 20 Mar 2020 (current DCO; median follow up, 34.2 months [range, 0.2–64.9]), updated PFS (stratified HR 0.55, 95% CI 0.44–0.67; median 17.2 vs 5.6 months) and OS (stratified HR 0.71, 95% CI 0.57–0.88) remained consistent with previous reports. Median OS for the durvalumab arm was determined for the first time: 47.5 months (pbo, 29.1 months). The 48-month OS rates were 49.6% vs 36.3% for durvalumab vs pbo, and PFS rates were 35.3% vs 19.5% respectively. Updates to treatment effects for pt subgroups will be reported.

Conclusions: These updated analyses of PFS and OS demonstrate durable benefit with durvalumab after cCRT. Approximately half of patients randomised to durvalumab in PACIFIC remain alive at 4 years, and about a third remain both alive and progression free, almost 3 years after the last pt completed study treatment.

Clinical trial identification: NCT02125461.

Editorial acknowledgement: Medical writing support, which was in accordance with Good Publication Practice (GPP3) guidelines, was provided by Aaron Korpal, PhD, of Cirrus Communications (Manchester, UK), an Ashfield company, and was funded by AstraZeneca.

Legal entity responsible for the study: AstraZeneca.

Funding: AstraZeneca.

Disclosure: C. Faivre-Finn: Advisory/Consultancy, Research grant/Funding (institution), Travel/Accommodation/Expenses: AstraZeneca; Research grant/Funding (institution), Travel/Accommodation/Expenses: Elekta. D. Vicente: Honoraria (self), Research grant/Funding (institution): AstraZeneca; Honoraria (self), Research grant/Funding (institution): Pfizer; Honoraria (self): Bristol-Myers Squibb; Honoraria (self), Research grant/Funding (institution): MSD; Honoraria (self), Research grant/Funding (institution): Roche. T. Kurata: Honoraria (self), Research grant/Funding (institution): AstraZeneca; Honoraria (self): Eli Lilly; Honoraria (self), Research grant/Funding (institution): MSD; Honoraria (self): Ono; Honoraria (self): Boehringer Ingelheim; Honoraria (self), Research grant/Funding (institution): Bristol-Myers Squibb; Honoraria (self), Research grant/Funding (institution): Chugai; Research grant/Funding (institution): Novartis; Research grant/Funding (institution): Takeda. D. Planchard: Advisory/Consultancy: AstraZeneca; Advisory/Consultancy: Bristol-Myers Squibb; Advisory/Consultancy: Boehringer Ingelheim; Advisory/Consultancy: Celgene; Advisory/Consultancy: Daiichi Sankyo; Advisory/Consultancy: Eli Lilly; Advisory/Consultancy: Merck; Advisory/Consultancy: Novartis; Advisory/Consultancy: Pfizer; Advisory/Consultancy: prIME Oncology; Advisory/Consultancy: Peer CME; Advisory/Consultancy: Roche; Advisory/Consultancy: Samsung. L. Paz-Ares: Advisory/Consultancy, Speaker Bureau/Expert testimony, Travel/Accommodation/Expenses: MSD;