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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: Characterisation of PORT efficacy in lung ART (IFCT-0503, UK NCRI, SAKK)

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Background

Primary analysis of Lung ART trial has shown (ESMO 2020) a non-statistically significant effect of PORT on disease-free survival (DFS) in N2 NSCLC patients (HR = 0.86 (95% CI 0.68-1.08); p=0.18). However PORT was associated with a reduction of 51% in the risk of mediastinal relapse (MR). Patterns of relapse as well as prognostic factors of PORT efficacy warranted further investigations to determine which patients could benefit more from PORT.

Methods

Patients were eligible in Lung ART if they had a WHO performance status ≤ 2 , considered to have undergone complete resection with lymph node exploration, proven N2 disease +/- prior neo-adjuvant or adjuvant CT. DFS components (metastatic, mediastinal relapses and deaths) were analysed using competing risks approaches. Prognosis factors for DFS and OS were explored based on prespecified analyses coupled with an exploratory approach.

Results

501 patients were randomised. Among DFS events, there are 161 (54%) metastatic relapses (including 61 (21%) brain metastases), 106 (36%) MR, and 29 (10%) deaths. Three-year metastatic relapse-free survival is 72.31% [66.5;77.1] and 68.47% [61.7;74] in the control and PORT arms, respectively; 3-year MR-free survival is 72.26% [65.9;77.4] and 86.06% [81.2;89.7], respectively. MR occurs mainly within initially involved nodes (66% in control arm, 47% in PORT arm) and significantly less in PORT arm (unadjusted sub-distribution HR= 0.46 (95% CI [0.3;0.7])). The 3 most frequent sites of MR are stations 7 (47%), 4L (42%), 4R (37%) for left-sided tumours; stations 4R (48%), 2R (44%) and 7 (41%) for right-sided tumours. Prognostic factors for DFS include quality of resection, extent of mediastinal involvement and lymph node ratio (involved / explored), with differential effects according to DFS components. With regards to overall survival, extent of nodal involvement is a significant prognostic factor whereas PORT (HR = 0.98 [0.7;1.4]) is not.

Conclusions

Use of PORT in N2 NSCLC patients reduces the risk of MR, but has no significant impact on DFS. Prognostic factors associated with different DFS components were identified which may allow a personalized prescription of PORT.

Clinical trial identification

NCT00410683.

Legal entity responsible for the study

Gustave Roussy.

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Disclosure

C. Le Pechoux: Non-Financial Interests, Institutional, Advisory Board, Outside the submitted work: AstraZeneca, Nanobiotix, Roche; Non-Financial Interests, Institutional, Invited Speaker, Outside the submitted work: Amgen, Eli Lilly, Medscape; Financial Interests, Personal, Invited Speaker, Outside the submitted work: PriME Oncology. F. Barlesi: Financial Interests, Personal, Other: AstraZeneca, Bayer, Bristol Myers Squibb, Boehringer Ingelheim, Eli Lilly Oncology, F. Hoffmann-La Roche Ltd., Novartis, Merck, Mirati, MSD, Pierre Fabre, Pfizer, Sanofi-Aventis, Seattle Genetics, Takeda; Financial Interests, Institutional, Other, Outside the submitted work: AbbVie, ACEA, Amgen, AstraZeneca, Bayer, Bristol Myers Squibb, Boehringer Ingelheim, Eisai, Eli Lilly Oncology, F. Hoffmann-La Roche Ltd., Genentech, Ipsen, Ignyta, Innate Pharma, Loxo, Novartis, MedImmune, Merck, MSD, Pierre Fabre, Pfizer, Sanofi-Aventis. N. Pourel: Non-Financial Interests, Institutional, Research Grant, Outside the submitted work: Pfizer, Varian. C. Faivre-Finn: Financial Interests, Institutional, Research Grant, Outside the submitted work: AstraZeneca, Elekta. G. Zalcman: Financial Interests, Personal, Advisory Board, All outside the submitted work: BMS, MSD, AstraZeneca, Boehringer Ingelheim; Non-Financial Interests, Institutional, Research Grant, All outside the submitted work: Roche, Takeda AstraZeneca, AbbVie. A. Bardet: Financial Interests, Personal, Other, Consultancy fees: Roche. All other authors have declared no conflicts of interest.

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