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Brigatinib in patients with ALK-positive advanced non-small cell lung cancer treated with sequential ALK inhibitors: A multicentric real-world study (BRIGALK study)

R. Descourt,1 M. Pérol,2 D. Planchard,3 G. Rousseau-Bussac,4 B. Mennecier3
M. Wisté4, J. Cadranel,1 A.B. Cortot,4 F. Guisier,4 P. Do4, R. Schott5,6, A. Buzzi7,8, R. Dansin1,9,10
J. Arrendare1,11,12,13, J.B. Auliac14, C. Chouaid15, L. Galland16

1Medical Oncology Department, CHR Hôpital Augustin Morvan, Brest, France; 2Medical Oncology Department, Centre Léon Bérard, Lyon, France; 3Medical Oncology, Institut Gustave Roussy, Villejuif, France; 4Chest Department, CH Criellet, Creteil, France; 5Pathologie respiratoire, CHU Strasbourg-Nouvel Hôpital Civil, Strasbourg, France; 6Pneumo-Oncology, Hôpital Cochin, Paris, France; 7Chest Department, AP-HP Hôpital Tenson et GRCIM Théranos Sorbonne Université Paris, Paris, France; 8Thoracic Oncology Department, Hospital Albert Calmette, Lille, France; 9Chest Department, Hôpital Charles-Nicotte - CHU de Rouen, Rouen, France; 10Medical Oncology Department, Centre Francois Baclesse, Caen, France; 11Medical Oncology Department, Institut Curie, Paris, France; 12Pneumologie, CH Intermunicipal de Criellet, Creteil, France; 13Chest Department, CH Intercommunal de Criellet, Creteil, France; 14Medical Oncology Department, Hôpital Cochin, Paris, France; 15Pneumologie, CH Intermunicipal de Criellet, Creteil, France; 16Medical Oncology Department, Centre Georges François Leclerc, Dijon, France

Background: Brigatinib is a next-generation ALK inhibitor developed in ALK+ NSCLC initially pretreated with crizotinib and now in first line setting. The objective of this study was to assess efficacy and tolerability of brigatinib administrated in the French early access program (EAP).

Methods: This retrospective multicentric study included ALK+ advanced NSCLC patients pretreated with at least one anti-ALK tyrosine-kinase inhibitor (TKI), enrolled in the brigatinib French EAP. Primary endpoint was investigator-assessed progression-free survival (PFS). The results cover the entire EAP period and are an update of the first data presented at ASCO 2019 (abstract #9045).

Results: 184 patients were included by 66 centers in France: median age: 60 ± 12.7 years; never smokers: 78.3%; adenocarcinoma: 97.8%; median number of previous lines: 3 ± 1.3 and of ALK inhibitors: 2 ± 0.5 (crizotinib: 91.8%, ceritinib: 85.3%, alectinib: 29%). 50.0% of patients had performance status 0-1 and 67.6% more than 3 metastatic sites (brain metastases (BM): 71%, carcinomatous meningitis 7.1%).

Overall response rate was 43.2%. With a median follow up of 27.5 months (95%CI 25-42.9), median duration of brigatinib treatment was 4.9 months (95%CI 4.1-5.9) with 42.4% and 23.4% of patients treated at 6 and 12 months. Median PFS was 4.8 months (95%CI: 3.8-5.6). OS from brigatinib initiation was 19.4 months (95%CI: 15.6-24.5) while 79.1% and 18.2% of patients received 1 and 2 post-brigatinib treatment, respectively. In patients with and without BM, OS was 21.8 (95%CI 15.6-35.4) and 18 (95%CI 12.4-24) months, respectively. In patients who received 1 (n=23), 2 (n=146) or 3 (n=15) TKI before brigatinib start, OS from brigatinib initiation was 15.6 (95%CI 9.7-NR), 19.4 (95%CI 15.7-28.7) and 21.8 (3.3-39) months, respectively. 10.3% of patients had permanent treatment discontinuation due to treatment-related adverse events and 9.7% underwent dose adjustments without definitive interruption.

Conclusions: The analysis of the EAP confirms the efficacy of brigatinib in a cohort of heavily pretreated ALK-positive advanced NSCLC patients.

Legal entity responsible for the study: Groupe Français de Pneumo-Cancérologie.

Funding: Takeda.

Disclosure: R. Descourt: Advisory/Consultancy, Travel/Accommodation/Expenses, symposium and lectures; Takeda; Advisory/Consultancy, Travel/Accommodation/Expenses, symposium and lectures: Roche; Advisory/Consultancy, Travel/Accommodation/Expenses, symposium and lectures: Pfizer; Advisory/Consultancy, symposium and lectures: Boehringer Ingelheim; Advisory/Consultancy, Travel/Accommodation/Expenses, symposium and lectures: MSD; Advisory/Consultancy, symposium and lectures: Takeda; Advisory/Consultancy, symposium and lectures: BMS; Advisory/Consultancy: Novartis; Advisory/Consultancy, Travel/Accommodation/Expenses, symposium and lectures: AstraZeneca. M. Pérol: Advisory/Consultancy, Research grant/
Conclusions: In our limited series, IO had a scarce impact on the risk of SARS-CoV-2-related mortality, whilst CT, older age, PS 1 and a baseline pro-inflammatory systemic profile could be associated with a higher risk.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.1707

Deep learning model to predict clinical outcomes in patients with advanced non-small cell lung cancer treated with immune checkpoint inhibitors

A. Elkrief1, K. Phan1, L. Di Jonio2, R. Simpson3, M. Chassé3, J. Malo1, C. Richard1, M. Kosyakov2, F. Chandelier2, K. Kafi3, B. Routy1

1Oncology, Centre de recherche de l’Université de Montréal, Montréal, QC, Canada; 2Research Institute, Imagia, Montreal, QC, Canada; 3Medicine, Centre de recherche de l’Université de Montréal, Montréal, QC, Canada

Background: Immune checkpoint inhibitors (ICI) represent a major change in non-small cell lung cancer (NSCLC) treatment, however robust biomarkers are needed. Emerging data suggest that features discovered by deep learning (DL) models from CT scan images using artificial intelligence (AI) algorithms can accurately predict outcomes. In this study, our objective was to explore the potential of AI-based DL radiomics models in patients with advanced NSCLC treated with ICI.

Methods: Pre-ICI CT scans were obtained from n=141 patients with advanced NSCLC. Primary lung cancer lesions were annotated using Weasis medical viewer. PyRadiomics analyses were performed using published known open-source algorithms. In parallel, DeepRadiomics based on convolutional AI neural networks using the Imagia Evidens platform were used. Algorithms were designed by incorporating the baseline clinical characteristics and DL-features in multivariate models to predict overall response rate (ORR), progression-free survival (PFS) and overall survival (OS).

Results: Clinical characteristics (area under the receiver operating characteristic curve (AUC) 0.63, 95% CI 0.53-0.73) or PyRadiomics (AUC 0.67, 95% CI 0.57-0.77) alone were moderately predictive of ORR whereas DeepRadiomics, combined with clinical characteristics, had an AUC of 0.78 (95% CI 0.70-0.85). At a median follow-up of 50 weeks, the association between PFS and clinical characteristics was comparable to that of DeepRadiomics. Further, PFS prediction was not improved when clinical characteristics were combined with DeepRadiomics. With respect to OS, seven DeepRadiomics features were associated with increased hazard of death (HR 1.72-11.50; all p<0.05) while 6 were associated with a decreased hazard (HR 0.08-0.52; p<0.05). Of these 13 features, 11 maintained their association with OS after adjustment with clinical characteristics. Conclusions: These preliminary results reveal the potential of deep learning methods to improve upon standard predictive factors for ICI response. Using DeepRadiomics features to predict clinical outcomes may represent a novel clinical approach in the immuno-oncology arena.

Legal entity responsible for the study: Centre de recherche de l’Université de Montréal.

Funding: Centre de recherche de l’Université de Montréal.

Disclosure: A. Elkrief: Research grant/Funding (institution). Not related to submitted work: Astrazeneca. K. Phan: L. Di Jonio, R. Simpson, M. Kosyakov, F. Chandelier, K. Kafi: Full/Part-time employment: Imagia. B. Routy: Research grant/funding (institution). Imagia. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.1708

1395P Who will maintain as long-term responders more than 3 years with first- or second-generation EGFR TKI among EGFR mutant NSCLC?

J.H. Yeo, S.H. Park, H.A. Jung, J-M. Sun, S.H. Lee, J.S. Ahn, K. Park, M-J. Ahn

Division of Hematology-Oncology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

Background: Although osimertinib is a preferred first-line EGFR tyrosine kinase inhibitor (TKI) in patients with EGFR-mutant non-small cell lung cancer (NSCLC) based on longer progression free survival (PFS) and high CNS efficacy, other first- or second-generation EGFR TKIs (gefitinib, erlotinib or afatinib) still remain as treatment options. Since long-term responders (LTR) with first- or second-generation EGFR TKIs are often noted in proportion of patients in real world, it would be valuable to determine patient characteristics associated with long-term responders considering sequential approach of EGFR TKI in the management of EGFR-mutant NSCLC.

Methods: We analyzed EGFR-mutant advanced NSCLC patients treated with first-line gefitinib, erlotinib or afatinib from Jan 2013 to Dec 2016. LTRs were defined as patients whose PFS is longer than 36 months. We compared patient characteristics and other clinical outcomes between LTR group and control group.

Results: Of the 931 patients treated with first-line EGFR-TKI other than osimertinib, 140 (15.0%) patients were LTRs; gefitinib (n=85, 60.7%), erlotinib (n=22, 15.7%), and afatinib (n=33, 23.6%), respectively. With median follow-up of 59.5 months, median PFS was 54.1 months and overall survival was not reached in the LTR group. Patients with recurrent disease (OR 0.40, p<0.001), Exon 19 deletion (OR 0.58, p<0.007) and without wet pleura (OR 3.11, p=0.001) were more common in the LTR patients. In contrast, bone (OR 1.93, p<0.001) and peritoneal metastases were associated with LTRs.

Conclusions: In real world data, 15% of patients can achieve more than 3 years of treatment duration with first- or second-generation EGFR TKI alone. Given insufficient availability of osimertinib as first-line therapy in many countries and lack of established salvage therapy against osimertinib-resistant NSCLC, our results suggest that first- or second-generation EGFR TKIs can be considered for patients with recurrent disease, exon 19 deletion, and without wet pleura metastases as well as extrathoracic metastases.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.1709

1396P Development and validation of a host-dependent, PD-L1-independent, biomarker to predict 6-month progression-free survival in metastatic non-small cell lung cancer (mNSCLC) patients treated with anti-PD1 immune checkpoint inhibitors (ICIs) in the CERTIM cohort: The ELY study

P. Boudou Rouquette1, J. Arrondeau1, C. Gervais1, A. Jouinot1, E. Fabre1, S. De Perro2, A-C. Pickety1, C. Vaquin Villemin1, N. Al-Rassy3, G. Ulmann2, D. Damotte1, A. Lupo-Mansuet2, K. Leroy1, F. Giraud1, J. Alexandre3, M. Alfano3, L. Cynober1, M. Wislez1, J-P. Durand4, F. Goldwasser5

1Medical Oncology, Hôpital Cochin, Paris, France; 2Medical Oncology, Hôpital Cochin, Paris, France; 3Thoracic Oncology, Hôpital Européen Georges Pompidou, Paris, France; 4Laboratoire de Biologie de la Nutrition, Hôpital Cochin, Paris, France; 5Pathology, Hôpital Cochin, Paris, France; 6Service de genetique et biologie moleculaire, Hôpital Cochin, Paris, France; 7Pneumo-Oncology, Hôpital Cochin, Paris, France; 8Thoracic surgery, Hôpital Cochin, Paris, France

Background: Immunotherapy with ICI is active in a minority of NSCLC patients. The identification of new biomarkers of efficacy is needed. We studied the relationship between the metabolism of the patient and the effectiveness of ICI.

Legal entity responsible for the study: CERTIM cohort: The ELY study.

Funding: Not received.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.1709

Table: 1395P

| Patients, no. | IO = 39 (62%) | CT+IO = 24 (38%) | P value |
|---------------|---------------|-----------------|--------|
| FU, median (95% CI) | 19.4 (15.4-23.4) | 10.5 (10.3-10.7) |        |
| Death rate, No. (%) | 8 (21%) | 8 (33%) |        |
| Death rate, HR (95%) | 1.0 | 4.05 (1.31-12.56) | 0.015 |
| Deaths, causes: PD Chest infection COVID-19 | 6 (75%) 2 (25%) 0 (0%) | 5 (62.5%) 0 (0%) 3 (37.5%) |        |

FU: Follow Up; No: Number; PD: Progressive Disease. aNot SARS-CoV-2-related. bSARS-CoV-2-related. cValue (range)

Table: 1396P

| Characteristics | IO (No. 8) | CT+IO (No. 5) | P value |
|----------------|-----------|---------------|--------|
| Age | 70 (65-78) | 67 (52-79) |        |
| PS: 0 1 | 3 (37.5%) 5 (62.5%) | 4 (80%) 1 (20%) | 1 (33%) 2 (67%) |
| Smoking: current former | 7 (87.5%) 1 (12.5%) | 2 (40%) 3 (60%) | 2 (67%) 1 (33%) |
| NLR | 3.4 | 2.6 | 4.5 |
| SII | 1169 | 735 | 1610 |

1First-line treatment of NSCLC (no. 63)