Real-world management of patients with EGFR exon 20-mutant NSCLC in the precision oncology era: First report from the European EXOTIC registry

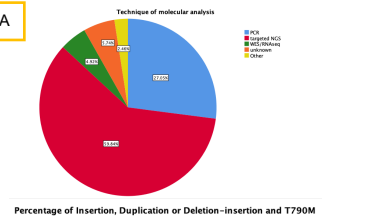
Giannis Mountzios (1), David Planchard (2), Giulio Metro (3), Arsela Prelaj (4), Dora Tsiouda (5), Walid Shalata (6), Mariona Riudavets (2), Petros Christopoulos (7), Nicolas Girard (8), Victor Albarran (9), Rosario Garcia Campelo (10), Samitas Konstantinos (11), Giuseppe Banna (12) Ioannis Boukovinas (13), Abed Agbarya (14), Anna Koumarianou (15), Perdikouri Eleni-Isidora (16), Kosmidis Paris (17), Martin Reck (18) and Giuseppe Lo Russo (4)

(1) Fourth Oncology Department and Clinical Trials Unit, Henry Dunant Hospital Center, Athens, Greece; (2) Department of Medical Oncology, Thoracic group, Institut Gustave-Roussy, Villejuif, France; (3)Ospedale Santa Maria della Misericordia, Perugia, Italy; (4) Thoracic Oncology Unit, Medical Oncology Department 1, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy; Department of Electronics, Information, and Bioengineering, Politecnico di Milano, Milan, Italy; (5) Department of Thoracic Oncology, Theageneion Hospital, Thessaloniki, Greece; (6) The Legacy Heritage Center & Dr. Larry Norton Institute, Soroka Medical Center and Ben-Gurion University of the Negev, Beer Sheva, Israel; (7) Department of Thoracic Oncology, University Hospital Heidelberg, Heidelberg, Germany; (8) Department of Medical Oncology, Curie-Montsouris Thorax Institute, Paris, France, (9), Thoracic Oncology Group, Medical Oncology Department, Hospital Clinic Barcelona, Spain; (10) Medical Oncology Department, Thoracic Tumors Unit, University Hospital A Coruña and Biomedical Research Institute (INIBIC, A Coruña), Spain; (11) 7th department of Pneumonology, Sotiria Hospital, Athens, Greece, (12) Candiolo Cancer Institute, FPO-IRCCS, Candiolo, Turin, Italy; (13) Department of Medical Oncology, Bioclinic Hospital, Thessaloniki, Greece; (14) Institute of Oncology, Bnai Zion Medical Center, Haifa, Israel; (15) Department of Medical Oncology, University Hospital Attikon, Athens, Greece; (16) Department of Medical Oncology, Hospital of Volos, Volos, Greece; (17) Second department of Medical Oncology, Hygeia Hospital, Athens, Greece; (18) Lung Clinic, Airway Research Center North, German Center of Lung Research, Grosshansdorf, Germany.

Background: Real-world evidence (RWE) regarding molecular epidemiology and management patterns of patients with epidermal growth factor receptor (EGFR) exon-20 mutated, advanced non-small-cell lung cancer (NSCLC) outside the context of clinical trials in Europe are lacking.

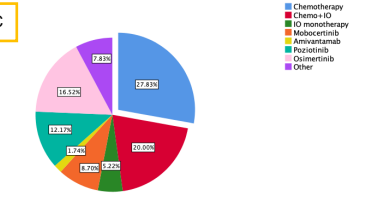
Methods: We created a European registry for patients with advanced EGFR exon 20-mutant NSCLC diagnosed from January 2019 to December 2021. Patients enrolled in clinical trials were excluded. Clinical, pathological and molecular epidemiology data were collected and treatment patterns were recorded. Clinical endpoints according to treatment assignment were assessed using Kaplan-Meier curves and Cox-regression models.

1A



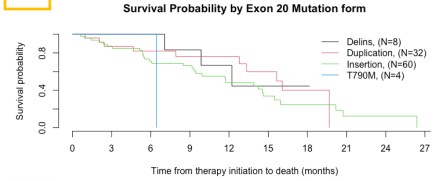
1B

1C

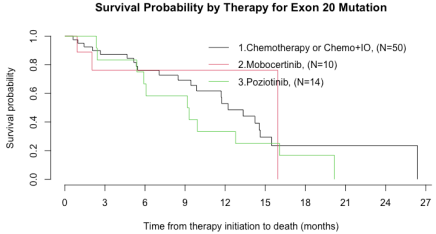


Results: Data on 126 patients from 31 centers across 8 European countries are presented. Median age was 65.4 years (range 29.7-87.8); Main features included female sex (61.6%), never smokers (60.3%), adenocarcinoma histology (93.7%) and tropism for bone (56.5%) and brain (32.2%) metastases. Mean PD-L1 TPS score was 20.5% (range 0-95) and mean TMB was 6.71 mut/MB DNA (range 0-14). Exon 20 was detected in tissue (90.3%), in plasma (8.1%) or both (1.6%), using mostly targeted NGS (57.9%) or PCR (26.2%), **(Fig.1A)**. Mutations were mainly insertions (59.1%) followed by duplications (29.1%), deletions-insertions (7.3%) and the T790M (4.5%), **(Fig.1B).** The vast majority of mutations (98.1%) were located in the adjacent loop (codons 767-775) and only 1.9% within the C-helix (codons 761-766). Main co-alterations included mutations in TP53 (61.3%) and MET amplifications (8.1%). Treatment included chemotherapy (CT), (27.8%), CT-IO (20%), osimertinib (16.5%), poziotinib (12.2%), mobocertinib (8.7%), mono-IO (5.2%) and amivantamab (1.7%), **(Fig.1C)**. Disease control rates were 67.8% with CT+/- IO, 59.8% with osimertinib, 64.2% with poziotinib and 75% with mobocertinib. Corresponding median survival (OS) was 12.2, 7.9, 9.2 and 15.9 months respectively. Type of treatment (new targeted agents vs Chemo+/-IO) significantly affected OS (p=0.03) **(Fig.2A and 2B)**.

2A



2B



Conclusions: EXOTIC represents the largest RWE dataset on EGFR exon 20 mutant NSCLC in Europe. Indirectly compared, treatment with new exon 20-targeting agents confers survival benefit over chemo+/-immunotherapy. Analysis is ongoing.

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