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

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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.

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%), monio-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).

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 on-going.