EFFICACY OF THERAPIES IN NON-SMALL-CELL LUNG CANCER WITH EGFR EXON 20 INSERTION MUTATIONS: A SYSTEMATIC REVIEW

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BACKGROUND AND IMPORTANCE

Patients with non-small cell lung cancer (NSCLC) and epidermal growth factor receptor (EGFR) exon 20 insertion mutations have poor prognosis and few therapeutic alternatives.

AIM AND OBJECTIVES

To develop a systematic review of platinum pre-treated NSCLC harboring EGFR exon 20 insertions to assess efficacy of treatments and scientific quality of studies.

MATERIAL AND METHODS

- Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidelines → applied in bibliographic review.
- Search was conducted in Pubmed® database up to September 15, 2022. Filter “clinical trial” on types of articles was applied to the following review strategy: (exon 20 insertion) AND (Therapy/broad[filter]).
- Inclusion criteria: Randomized clinical trials (RCTs) evaluating treatments in patients diagnosed with advanced or metastatic NSCLC harboring EGFR exon 20 insertions who had previously received platinum-based chemotherapy.
- Efficacy endpoints considered → objective response rate (ORR), progression-free survival (PFS) and overall survival (OS).
- Data recorded: publication date, study design, comparator arm, therapies, sample size, treatment line, efficacy data.

RESULTS

- 40 search results were found → 12 RCTs were included.
- Publication dates of studies → between April 2015 and July 2022.
- Design of studies:
  • 9 (75%) phase II RCT (one was basket trial).
  • 3 (25%) phase I/II.
  None of them presented a comparator arm.
- Sample size of RCTs → ranged from 10 to 114 patients.
- Both untreated and platinum-pretreated patients were recruited in 4 (25%) RCTs and the rest comprised exclusively platinum-pretreated population.

- Ado-trastuzumab emtansine → showed the best numerical results according to ORR (54.5%), but the worst PFS (2.8 months; 95% CI 1.4-4.4) and OS (8.1 months; 95% CI 3.5-13.2) of all therapeutic alternatives.

- The highest numerical efficacy results were achieved by:
  ✓ amivantamab [PFS = 8.3 months (95% CI 6.5-10.9); OS = 22.8 months (95% CI 14.6 to not reached)]
  ✓ mobocertinib [PFS = 7.3 months (95%CI 5.5-9.2); OS = 24.0 months (95%CI, 14.6-28.8)]

CONCLUSION AND RELEVANCE

Results of amivantamab and mobocertinib suggested a higher numerical efficacy for clinically relevant endpoints in platinum pre-treated NSCLC harboring EGFR exon 20 insertions. However, comparative RCTs with larger sample sizes are necessary to obtain reliable data.