

# 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.

### Therapies assessed:

- poziotinib
- osimertinib (high and low doses)
- pertuzumab-trastuzumab combination
- mobocertinib
- amivantamab
- erlotinib-onalespib combination
- luminespib
- ado-trastuzumab emtansine
- dacomitinib

- 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.

