Systematic Literature Review (SLR) and Meta-Analysis of Crizotinib Versus Conventional Chemotherapy in First-Line Treatment for ROS-1 Rearranged Non-Small Cell Lung Cancer

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Introduction

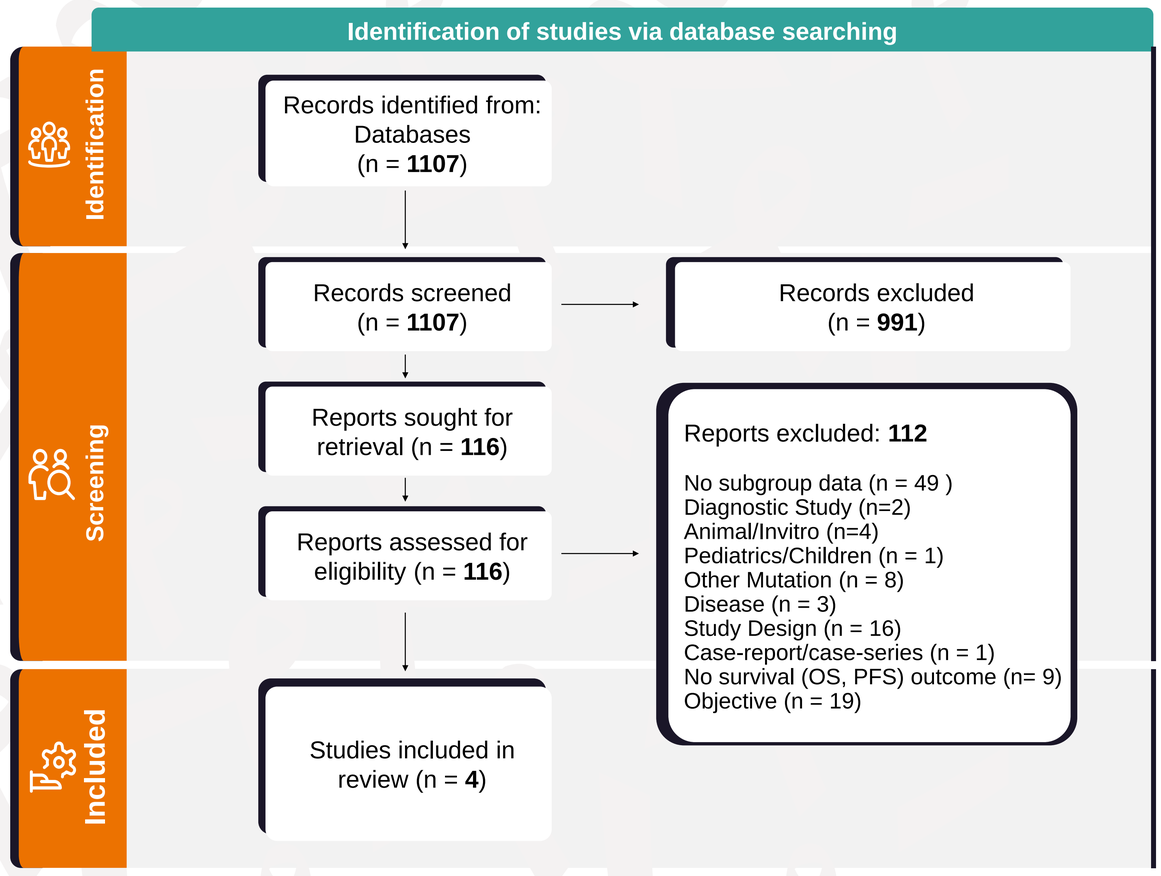
- Lung cancer is the most common cancer with 2.5 million new cases worldwide, accounts for 12.4% of all cancers and is the main cause of cancer-related mortality worldwide. Non-small cell lung cancer (NSCLC) is the major histologic subtype and accounts for 80% of all lung cancers[1, 2]
- In 2024, American Cancer Society estimated 234,580 new cases of lung cancer (116,310 in men and 118,270 in women) in the US[2]
- Current treatments available for NSCLC includes surgery, radiation therapy, chemotherapy, immunotherapy, and targeted therapy[3] that encounters challenges like drug resistance, disease progression, high cost of the agent, toxicity etc.[4]
- Approximately 1%-2% of patients with NSCLC harbor ROS-1 rearrangement, which has now become a successful target of multiple tyrosine kinase inhibitors (TKIs).[5]
- Crizotinib showed high efficacy in ROS1-positive NSCLC patients with 72% objective response rate in phase I PROFILE 1001 trial.[6]
- The aim of our SLR/meta-analysis was to assess the impact of newer therapies such as crizotinib in comparison to traditional chemotherapies in real world setting.

Methods

- We conducted a systematic literature review (SLR) in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[5]. Biomedical databases; Medline®, Embase® (via Ovid®) and Cochrane Library were searched from database inception to May 2023 supplemented with hand searches
- Two independent reviewers performed screening and data extraction, and any conflicts were resolved by a third independent reviewer, when necessary, to ensure methodological rigor
- Meta-analysis was performed using the Metaprop package in R-4.1.3 software. The effect size for Hazard Ratio (HR) and ORR were all pooled with 95% confidence intervals (CIs). Heterogeneity was considered significant for I^2 - statistic greater than or equal to 50% or the p value was ≥ 0.10, and then the random-effects model was adopted.

Eligibility criterions are listed below:

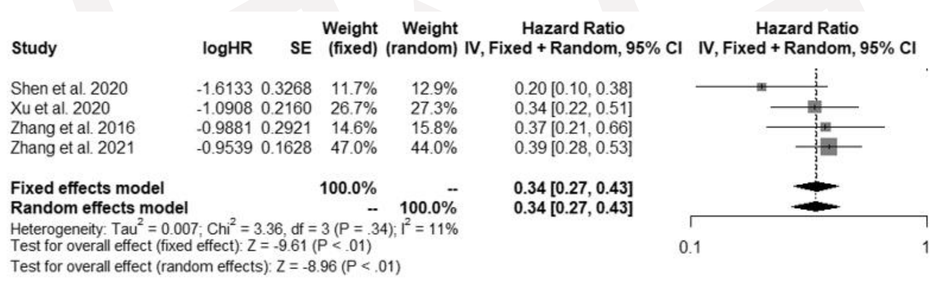
Population	Adult patients with unresectable locally-advanced, metastatic ROS1 NSCLC cancer in first line setting
Intervention & Comparator	Crizotinib compared to traditional chemotherapy
Time frame	Inception to May 2023
Study design	Observational studies (excluding case reports and case series)
Language	English language publications
Country	No restrictions



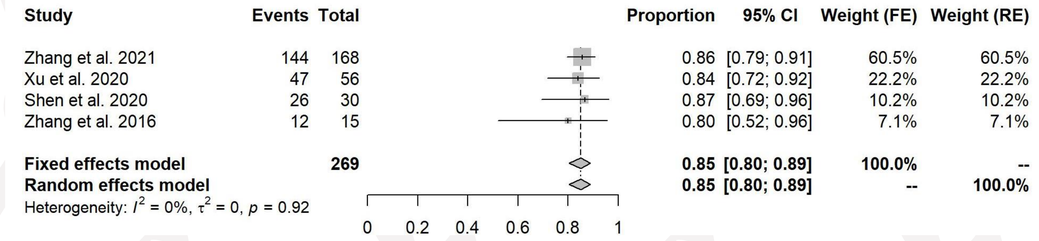
Results

- Of 1107 publications screened, four studies met the predefined eligibility criteria assessing the comparison between crizotinib and traditional chemotherapy in patients with unresectable locally-advanced, metastatic ROS1 NSCLC cancer in first line setting
- Our meta-analysis of observational studies revealed a pooled PFS HR of 0.34 (95% CI: 0.27-0.43) for crizotinib compared to conventional chemotherapy. Crizotinib demonstrated a significantly higher ORR of 85% (95% CI: 80%-89%) compared to 42% (95% CI: 30%-45%) observed with conventional chemotherapy. The relative difference in ORR between the TKI and conventional chemotherapy was notable at 41% (95% CI: 29%-63%).

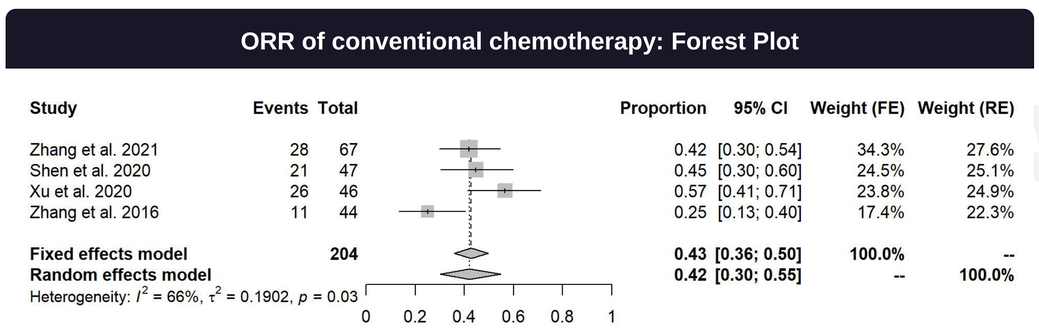
PFS-HR: Forest Plot



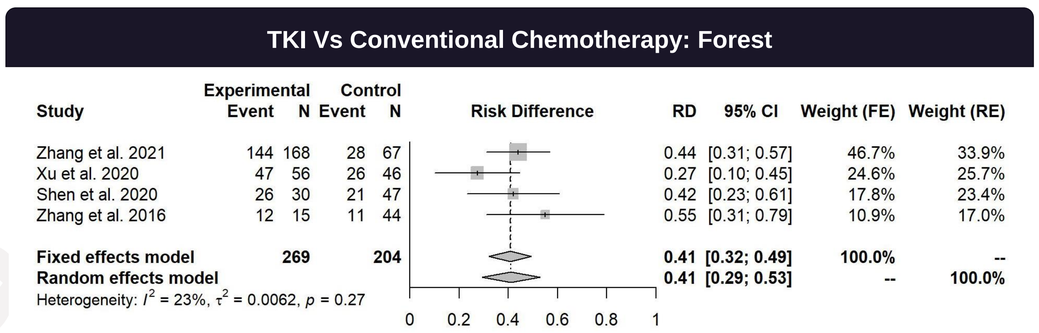
ORR of TKI: Forest Plot



ORR of conventional chemotherapy: Forest Plot



TKI Vs Conventional Chemotherapy: Forest



Note: Most studies present the outcomes for chemotherapy and crizotinib in first-line (1L) setting, with the exception of Zhang et al. (2016) which reports PFS-HR and ORR for chemotherapy in first-line (1L) setting, and for crizotinib in second-line (2L) setting. Sub-group analysis was used to adjust for the differences in reporting between first-line and second-line therapies for crizotinib.

Conclusion

In conclusion, our meta-analysis of four observational studies indicates that crizotinib outperforms traditional chemotherapy as a first-line treatment for unresectable locally-advanced, metastatic ROS1 NSCLC. Crizotinib shows significantly improved progression-free survival (HR: 0.34, 95% CI: 0.27-0.43) and a markedly higher objective response rate (85% vs. 42%). These findings support the preferential use of crizotinib in this patient population.

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