INPLASY PROTOCOL

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Review Stage at time of this submission: Data extraction.

First-line treatment with TKI plus brain radiotherapy vs TKI alone in EGFR-mutated non-small-cell lung cancer with brain metastases: a systematic review and meta-analysis

Song, YW[1]; Lin, SY[2]; Chen, J[3]; Ding, SL[4]; Dang, J[5].

Review question / Objective: It remains uncertain whether first-line treatment with upfront brain radiotherapy (RT) in combination with epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKIs) is superior to EGFR-TKIs alone in EGFR-mutated non-small-cell lung cancer with newly diagnosed brain metastases (BMs). We performed a meta-analysis to address this issue.

Condition being studied: Brain radiotherapy (RT) has been shown to damage the blood-brain barrier (BBB) and improve the concentration of EGFR-TKIs in the CSF. Additionally, RT can result in a reduction of EGFR-TKIs resistance. Therefore, EGFR-TKIs in combination with brain RT should be more effective than EGFR-TKIs alone theoretically. However, results from retrospective studies are inconsistent. There is the possibility that patients characteristics or brain RT technique affect the efficacy of treatments. To date, there is still no randomized controlled trials (RCTs) comparing the two treatment strategies.

INTRODUCTION

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METHODS

Participant or population: Patients with EGFR-mutated non-small-cell lung cancer with newly diagnosed brain metastases.

Intervention: EGFR-TKIs and brain radiotherapy.

Comparator: EGFR-TKIs alone.

Study designs to be included: EGFR-TKIs alone.

Eligibility criteria: (1) study design: prospective or retrospective studies; (2) study population: histologically proven EGFR-mutated NSCLC, with newly diagnosed BMs identified by CT or MRI; (3) intervention: compared first-line treatment with upfront brain RT plus EGFR-TKIs with EGFR-TKIs alone at the time of diagnosis of BMs; (4) outcomes: at least overall survival (OS) or intracranial progression-free survival (iPFS) reported; (5) published in English.

Information sources: PubMed, Embase, Cochrane Library, and Web of Science.

Main outcome(s): Overall survival (OS) or intracranial progression-free survival (iPFS), reported as hazard ratio (HR) and 95% confidence intervals (CIs).

Quality assessment / Risk of bias analysis: Two authors (SY and LS) independently assess the quality of retrospective studies using the Newcastle-Ottawa Scale (NOS).

Strategy of data synthesis: Statistical analysis was performed using the software Review Manager 5.3 (Cochrane Collaboration, Oxford, UK). The outcomes of interest were OS, iPFS, iORR, and iDCR, presented as hazard ratios (HRs) or odds ratios (ORs) with their 95% confidence intervals (CIs). The heterogeneity was assessed by the Chi-square ($\chi2$) and I-square (I2) test. A random-effect model was used when significant heterogeneity existed (P 50%); otherwise, a fixed-effect model was adopted. Subgroup analyses of OS and iPFS. Sensitivity analysis was performed to evaluate the stability of the results. Publication bias was estimated by the funnel plot, Begg's test, and the Egger's linear regression test.

Subgroup analysis: Subgroup analyses of OS and iPFS were performed according to BMs related symptom (asymptomatic and symptomatic), EGFR mutation subtype (19 and 21 deletion mutations), number of BMs (1-3 and >3), and sex (male and female).

Sensitivity analysis: Sensitivity analysis was performed to verify the stability of the pooled results by removing the data of an individual study each time.

Country(ies) involved: China.

Keywords: non-small-cell lung cancer; brain metastases; epidermal growth factor receptor tyrosine kinase inhibitors; brain radiotherapy; meta-analysis.

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