# ABSTRAK

**Latar belakang:** Belum diketahui efektivitas klinis dan evaluasi ekonomi biaya terapi target penghambat tyrosine kinase generasi pertama dan generasi kedua yang menggambarkan penerapan hasil RCT dalam praktik pelayanan kesehatan untuk pasien KPKBSK dengan metastasis di Indonesia. Penelitian ini diperlukan untuk mengkaji rasio biaya terhadap manfaat, untuk mendapatkan data efektivitas klinis dan evaluasi ekonomi penatalaksanaan terapi target EGFR TKI pada pasien KPKBSK berdasarkan *standar of care* di Indonesia.
**Metode:** Penelitian observasional dengan desain *dynamic* kohort *ambidirectional*. Responden penelitian adalah pasien KPKBSK dengan EGFRm+ di RSUP Dr. Sarjito dan RSUP Persahabatan berusia minimal 18 tahun, mendapatkan EGFR TKI dengan status naïve minimal dua siklus, dengan dua penilaian respon terapi RECIST, dan menandatangani *informed consent*. Subyek tereksklusi bila data rekam medis tidak lengkap dan tidak dapat dilakukan konfirmasi. Data dikumpulkan menggunakan CRF luaran klinis, instrumen luaran moneter dan humanistik. Dilakukan analisa efektivitas klinis, identifikasi biaya dan perhitungan CEA dalam perspektif payer dengan time horizon waktu pengamatan outcome klinis. Data antar kelompok terapi akan dilakukan uji statistik analisis multivariat.
**Hasil:** Waktu median PFS terapi afatinib (11 vs 10 bulan) lebih panjang dibanding gefitinib, sedangkan erlotinib adalah lebih pendek (9 bulan). Waktu median TTF afatinib (19 bulan) dan erlotinib (20 bulan) lebih panjang dibanding gefitinib (16 bulan). Waktu median OS afatinib (41 bulan) dan erlotinib (40 bulan) lebih pendek dibanding gefitinib (51 bulan). Perbedaan tiga luaran klinis ini secara statistika adalah tidak bermakna (p>0,05). Biaya langsung medis terapi afatinib dan erlotinib lebih rendah dibanding gefitinib. Biaya langsung non-medis terapi afatinib lebih rendah dibanding gefitinib, sedangkan erlotinib lebih tinggi dibanding gefitinib. Biaya tidak langsung terapi afatinib lebih rendah dibanding gefitinib, sedangkan erlotinib lebih tinggi dibanding gefitinib. Perbedaan biaya ini adalah tidak signifikan (p>0,05). Nilai ICER PFS, TTF, dan OS afatinib terhadap gefitinib adalah (Rp26.613.240)/bulan, (Rp5.474.629)/bulan, Rp1.092.943/bulan, lebih rendah dibandingkan erlotinib terhadap gefitinib, Rp40.994.695/bulan, (Rp8.784.197)/bulan. Rp2.614.255/bulan. Kualitas hidup kelompok *health state* progres lebih rendah dibandingkan *health state* stable.
**Kesimpulan:** Luaran klinis PFS, TTF, dan OS afatinib, erlotinib, dan gefitinib adalah similar. Biaya langsung medis, biaya langsung non-medis, dan biaya tidak langsung ketiganya adalah similar. Berdasarkan nilai ICER perbandingan terhadap gefitinib, afatinib memberikan biaya lebih rendah dibanding erlotinib pada setiap tambahan luaran klinis 1 bulan.

Kata kunci : KPKBSK, EGFR TKI, efektivitas, dan evaluasi ekonomi

# ABSTRACT

**Background**: The clinical efficacy and economic evaluation of the cost of targeted therapies for patients with metastatic NSCLC are still unclear. This study is needed to assess the cost-benefit ratio, to obtain data on the clinical effectiveness and economic evaluation of EGFR TKI targeted therapy management in patients with NSCLC based on the standard of care in Indonesia.
**Methods:** Observational study with dynamic ambidirectional cohort design. Respondent were NSCLC EGFRm+ patients at Dr. Sarjito Hospital and Persahabatan Hospital, at least 18 years, receiving EGFR TKIs naive for at least two cycles, with two RECIST response assessments, and signed informed consent. Subjects were excluded if medical record data were incomplete and could not be confirmed. Data were collected using the clinical outcome CRF, monetary and humanistic outcome instruments. Clinical effectivity, cost identification, and CEA on payer perspective were determined. Multivariate statistical analysis will be performed on data between treatment groups.
**Results:** The median PFS time of afatinib therapy (11 vs 10 months) was longer than that of gefitinib, while erlotinib was shorter (9 months). The median TTF of afatinib (19 months) and erlotinib (20 months) was longer than that of gefitinib (16 months). The median OS of afatinib (41 months) and erlotinib (40 months) was shorter than that of gefitinib (51 months). The differences in these three clinical outcomes were not statistically significant (p>0,05). The direct medical costs of treatment with afatinib and erlotinib were lower than those of gefitinib. Direct nonmedical costs were lower with afatinib than with gefitinib, but higher with erlotinib. Indirect costs were lower with afatinib than with gefitinib. Indirect costs were higher with erlotinib than with gefitinib. This cost difference was not significant (p>0,05). The ICER values for PFS, TTF and OS of afatinib versus gefitinib were lower than those of erlotinib versus gefitinib, respectively (Rp26.613.240)/mo vs Rp40.994.695/mo, (Rp5.474.629)/mo vs (Rp8.784.197)/mo, Rp1.092.943/ mo vs Rp2.614.255/mo. The quality of life of the progressing disease group was lower than that of the stable disease group.
**Conclusion:** The clinical outcomes of PFS, TTF, and OS of afatinib, erlotinib, and gefitinib were similar. The direct medical costs, the direct non-medical costs, and the indirect costs were similar. Based on the ICER value compared to gefitinib, afatinib provided lower costs than erlotinib for each additional month of clinical outcomes gained.

**Keywords:** NSCLC, EGFR TKI, effectiveness, and economic evaluation