吉非替尼联合阿帕替尼一线治疗EGFR敏感突变的晚期非小细胞肺癌患者的疗效及安全性

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Title: **Efficacy and safety of gefitinib combined with apatinib in the first-line treatment of patients with advanced non-small cell lung cancer with EGFR-sensitive mutations**

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摘要: 目的：探讨吉非替尼联合阿帕替尼对比吉非替尼一线治疗EGFR敏感突变的晚期非小细胞肺癌患者的疗效及安全性，以明确阿帕替尼能否延迟吉非替尼的耐药时间。方法:选取2015年1月至2016年12月期间我院收治的EGFR敏感突变的晚期NSCLC患者50例进行回顾性分析，分为观察组和对照组，每组各25人。观察组：吉非替尼（0.25 g，口服，1次/日）联合阿帕替尼（0.5 g，口服，1次/日）；对照组：吉非替尼（0.25 g，口服，1次/日）。评价无进展生存时间、客观缓解率、疾病控制率和不良反应发生率。结果：观察组、对照组客观缓解率分别为76.0%、68.0%，疾病控制率分别为96%、92%。观察组的近期疗效似有优于对照组的趋势，但差异均无统计学意义。观察组中位PFS为14.3个月（95%CI 11.3~17.2），对照组中位PFS为10.3个月（95%CI 8.5~12.0），差异有统计学意义。观察组1年的PFS率为64%，95%CI为44.4%~83.6%；对照组为20%，95%CI为4.3%~35.6%。两组主要不良反应为皮疹、高血压、蛋白尿、消化道反应、手足综合征、肝酶升高、间质性肺炎以及乏力，最为突出的不良反应为皮疹，观察组发生率为88%，对照组为84%（P > 0.05）。两组主要不良反应有统计学差异的为1-4度的高血压（P=0.004）、蛋白尿（P=0.027）、手足综合征（P=0.040），但严重不良反应（3-4度）均无统计学差异。结论：吉非替尼联合阿帕替尼一线治疗EGFR基因敏感突变的晚期NSCLC患者似乎是一种有效且耐受良好的治疗策略，可能延迟吉非替尼的耐药时间，还需大规模多中心的临床随机对照试验证实。

Abstract: Objective:To evaluate the efficacy and safety of gefitinib when combined with apatinib as first-line therapy in patients with advanced non-small cell lung cancer with EGFR-sensitive mutations,and to assess whether this strategy might prolonged the resistance time of gefitinib.Methods:This was a retrospective analysis of 50 cases of advanced NSCLC admitted to the medical group of Zhengzhou First Pepple's Hospital from January 2015 to December 2016.Patients were assigned to observation group or control group.Patients who received gefitinib (0.25 g per day) combined with apatinib (0.5 g per day) was considered as observation group,and patients who were administered at gefitinib 0.25 g per day was considered as control group.To estimate the progression-free survival time (PFS), objective response rate(ORR),disease control rate(DCR),and incidence of adverse effect.Results:The objective response rate(ORR) in the observation group and the control group was 76.0% and 68.0% respectively,and the disease control rate (DCR) was 96% and 92.0% respectively.The short-term efficacy of the observation group seemed to be better than that of the control group,but the difference was not statistically significant.The median PFS was 14.3 months (95%CI 11.3~17.2) in the observation group and 10.3 months (95%CI 8.5~12.0) in the control group.The difference was statistically significant.The 1-year PFS rate of the experimental group and the control group was 64%(95%CI 44.4%~83.6%),20%(95%CI 4.3%~35.6%) respectively.The main adverse reactions in the two groups were rash,hypertension,proteinuria,nausea and vomiting,hand-foot syndrome,aspartate transaminase/alanine aminotransferase increase,pulmonary interstitial

fibrosis,and fatigue.The most prominent adverse reaction was rash,88% in the observation group and 84% in the control group (P > 0.05).Other common adverse event was hypertension (P=0.004),proteinuria (P=0.027),and hand-foot syndrome (P=0.040) of any grade,but serious adverse reactions of grade 3-4 were not significant.Conclusion:Gefitinib combined with apatinib as a first-line treatment of advanced NSCLC patients with EGFR gene-sensitive mutations appears to be an effective and well-tolerated treatment strategy,and may extend the resistance time of gefitinib.Large-scale,multicenter randomized controlled clinical trials are needed to confirm this conclusion.

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