



EP12.18:Efficacy Analysis of EGFR-TKI Combined with Antiangiogenic Agents versus Anlotinib Monotherapy in EGFR-TKI-Resistant Non-Small Cell Lung Cancer

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INTRODUCTION

DISCUSSION AND CONCLUSION

RESULTS

This research uses clinical retrospective analysis with in vitro and animal experiments to explore treatments for EGFR-TKI-resistant NSCLC. It verifies that EGFR-TKI combined with antiangiogenic drugs achieves better PFS than anlotinib monotherapy, whose synergistic anti-tumor effect relies on inhibition of multiple pathways.

METHODS

Design:

This study retrospectively collected 80 EGFR-TKI-resistant NSCLC patients and split them into three treatment groups. Kaplan-Meier curves and Cox regression were used to analyze PFS and prognostic factors. In vitro PC-9/GR resistant cell lines and nude mouse xenograft models were established. CCK8, colony formation, Transwell and Western blot experiments were performed to detect cell proliferation, migration and key oncogenic signaling changes for mechanism exploration.

Actionable Take Away Message

This paper interprets the synergistic anti-tumor mechanism of EGFR-TKI combined with antiangiogenic therapy through dual-signal blockade. It compares relevant clinical studies, analyzes prognostic risk factors and treatment safety, and elaborates the study's retrospective limitations. Future research needs large prospective trials and biomarker screening to optimize individualized treatment regimens for resistant NSCLC patients.

INCLUSION AND EXCLUSION CRITERIA

INCLUSION CRITERIA

18–75 y, stage IIIB–IV EGFR+ NSCLC (AJCC 9th); EGFR-TKI resistant without actionable T790M or clear resistance mechanism.; chemo-progressed/ chemo-intolerant; ECOG 0–2; ≥1 RECIST 1.1 measurable lesion; intact cardiac/hepatic/renal function.

EXCLUSION CRITERIA

Severe vital organ failure, hemorrhagic coagulopathy, incomplete follow-up data, concurrent other malignancies.

The mPFS was 7.0 months in the EGFR-TKI plus anlotinib group (A) and 9.0 months in the EGFR-TKI plus bevacizumab group (B). Both were significantly longer than the 4.0 months observed in the anlotinib monotherapy group (A vs C, P=0.0090; B vs C, P=0.0016). But there was no statistically significant difference between the combined treatment group (Group A and Group B) (P=0.4058). Multivariate analysis shows ≥3 treatment lines and bone metastasis are independent adverse prognostic factors. In vitro and in vivo experiments confirm gefitinib plus anlotinib exerts synergistic anti-tumor activity. Combination therapy suppresses multiple signaling pathways to inhibit cell proliferation/migration and trigger apoptosis.

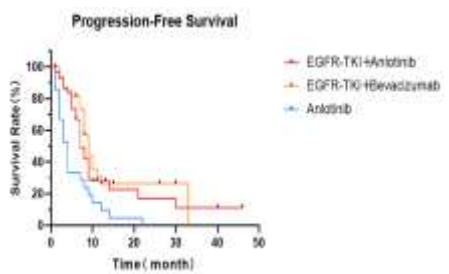


Figure 1.PFS curves for three regimens: EGFR-TKI+Anlotinib (red), EGFR-TKI+Bevacizumab (orange), single Anlotinib (blue).

Influencing Factor	HR95%CI	P value for PFS
≥3 lines of combined therapy	2.289 (1.120,4.680)	0.023
Co-occurrence of tumor suppressor gene mutation	1.945 (0.954,3.963)	0.067
Smoking history	1.951 (0.844,4.512)	0.118
Bone metastasis	2.002 (1.024,3.914)	0.042

Table 1.Multivariate PFS analysis of combined regimens post EGFR-TKI resistance

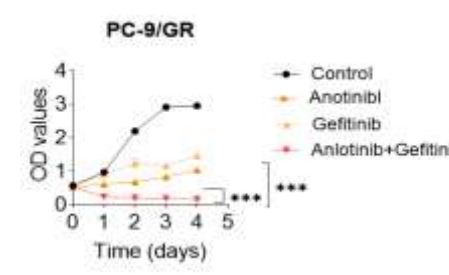


Figure3. presents gefitinib-anlotinib combined inhibition on PC-9/GR cells; combination group shows significantly better efficacy than gefitinib monotherapy.

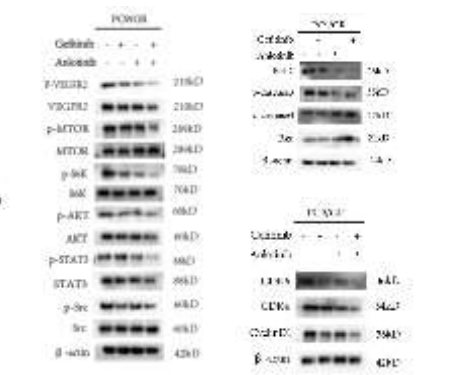


Figure4. Combined gefitinib and anlotinib downregulates cell cycle proteins, induces apoptosis, and suppresses phosphorylation of VEGFR2/AKT/mTOR/STAT3/Src signaling proteins in PC9/GR cells.

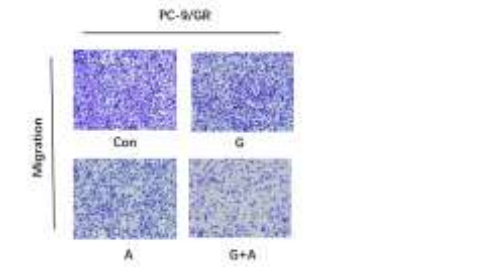


Figure 2. Combination treatment with gefitinib and anlotinib exerts an inhibitory effect on the migration of PC-9/GR cells.

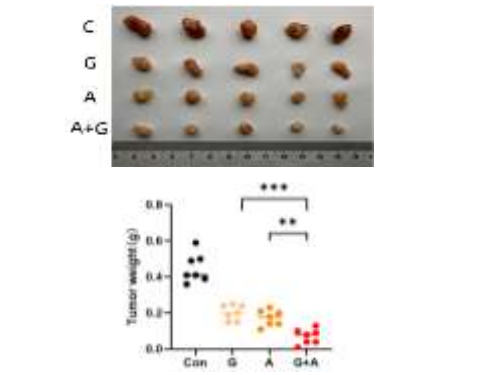


Figure 5.shows the tumor images of PC-9/GR xenografts under different treatment regimens