The Impact of Adjuvant EGFR-TKIs and 14-gene Molecular Assay on Stage I Non–Small Cell Lung Cancer with Sensitive EGFR Mutations

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Background

- Currently, the role of EGFR-TKIs as adjuvant therapy for stage I, especially IA NSCLC, after surgical resection remains unclear.
- We aimed to compare the effect of EGFR-TKIs versus observation on survival in such patients by incorporating an established 14-gene molecular assay for risk stratification.

Method

- From March 2013 to February 2019, completely resected stage I non-squamous NSCLC (8th TNM staging) patients with sensitive EGFR mutation, who were followed up for at least five years, were included.
- Patients with eligible samples for molecular risk stratification were subjected to the 14-gene prognostic assay.
- The 5-year disease-free survival (DFS) and overall survival (OS) rates between EGFR-TKI and observation groups were compared using Kaplan-Meier analysis and Cox regression with propensity score matching (PSM).
- The 14-gene assay was performed in 71 patients; 16 (22.5%), 21 (29.6%) and 34 (47.9%) were considered at high, intermediate and low risk, respectively. In the observation group, patients in the high-risk group had inferior DFS compared to the intermediate (HR=3.48, P=0.192) and low-risk groups (HR=12.50, P=0.024).

Result

- A total of 227 stage I NSCLC patients were enrolled, with 55 in EGFR-TKI group and 172 in the observation group. After PSM, a matched cohort of 96 (48:48) patients was generated. The median follow-up was 81.2 months.
- The 5-year DFS rates (97.9% vs. 81.3%; P=0.008) and OS rates (100.0% vs. 87.5%; P=0.011) of the EGFR-TKI group were significantly better than the observation group.
- The 14-gene assay was performed in 71 patients; 16 (22.5%), 21 (29.6%) and 34 (47.9%) were considered at high, intermediate and low risk, respectively. In the observation group, patients in the high-risk group had inferior DFS compared to the intermediate (HR=3.48, P=0.192) and low-risk groups (HR=12.50, P=0.024).
- Among intermediate-high-risk patients, EGFR-TKIs were associated with a significant improvement in 5-year DFS rates compared to observation (95.2% vs. 68.8%; P=0.030), while no difference was found in low-risk patients (100.0% vs. 89.5%; P=0.200).

Discussion

- This study figured out the dominant population that may benefit from adjuvant EGFR-TKIs that has previously been overlooked.
- The waning treatment effect was not observed in stage IA patients in the current study. It raises questions regarding the impact of adjuvant EGFR-TKIs on the natural progression of the disease, specifically whether they improve cure rates or merely delay relapse.

Conclusion

- Our study suggested that adjuvant EGFR-TKI might improve DFS and OS of stage IA and IB EGFR-mutated NSCLC, and the 14-gene molecular assay could help enrich those benefits from treatment. This modality merits prospective interventional trials in the future.