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Targeted Therapies in ROS1-Mutated NSCLC: Long-Term Efficacy and Renal Cyst Formation with Crizotinib and Entrectinib

Clinical solid tumor oncology
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Background and Objective

Managing advanced lung adenocarcinoma remains challenging, but new treatments like immunotherapy and targeted therapies have improved long-term outcomes. The ROS1 mutation, seen in 1-2% of cases, is a key target for these therapies. While Crizotinib has been effective as the first ROS1-directed treatment, it can cause significant side effects, notably renal impairment, which requires careful clinical assessment and management.

Methods

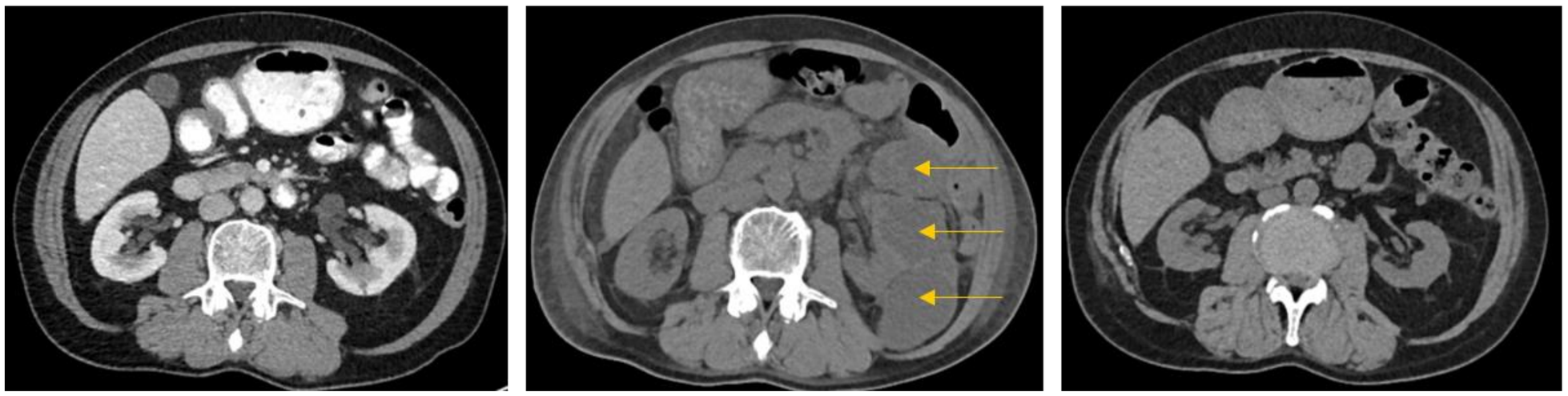
We report the case of a 73-year-old patient with a central lung tumour harbouring a ROS1 mutation. The patient developed progressive renal cysts during Crizotinib therapy. Suspected malignancy prompted two biopsies, both of which were negative, indicating a drug-related effect. The treatment was subsequently switched to Entrectinib, resulting in resolution of most cysts, though one persistent lesion remained. Renal function declined with both therapies, necessitating dose adjustments. The patient's long-term response was monitored, and possible co-mutations contributing to sustained efficacy were explored.

Results

Crizotinib-associated renal cysts (CARCs) exhibited radiological features mimicking malignancy and abscess formation, underscoring the importance of pathological confirmation to prevent misdiagnosis. The cysts appeared linked to the MET pathway, as Crizotinib targets both ROS1 and c-MET proto-oncogenes. Switching to Entrectinib is advised when cysts form and malignancy is excluded, given its different mechanism of action. The patient's response to Crizotinib significantly exceeded the median duration of 17.6 months, lasting over 55 months and persisting after the switch to Entrectinib. Co-mutations are hypothesised to contribute to this prolonged response, though further molecular studies are needed.

Conclusion

Renal cyst formation is a rare but known adverse event of crizotinib. This patient also had renal fibrosis, which reversed after switching to entrectinib, suggesting it may have less renal toxicity. The molecular mechanisms of crizotinib-induced toxicity remain unclear but may involve MET and MATE-1 inhibition. This case highlights the potential impact of co-mutations on prolonged treatment response, warranting further research into the molecular mechanisms that influence therapeutic outcomes.



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