Treatment with epidermal growth factor receptor tyrosine kinase inhibitors in a patient on peritoneal dialysis with non–small cell lung cancer: a case report

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This article was published on 10 Apr 2026 at www.hkmj.org.

This version may differ from the print version.

Hong Kong Med J 2026;32:Epub
https://doi.org/10.12809/hkmj2513424

Case presentation

A 61-year-old female with lupus nephritis on peritoneal dialysis presented to our institution in May 2018 with an incidental finding of a right lung nodule on chest X-ray. Subsequent computed tomography of the thorax and positron emission tomography–computed tomography (PET-CT) showed a right lower lobe nodule and two right pleural nodules. Wedge resection of the three lesions confirmed epidermal growth factor receptor (EGFR) exon 19 deletion–positive metastatic adenocarcinoma of the lung with pleural metastases. She had baseline Eastern Cooperative Oncology Group performance status score of 1 and had been on continuous ambulatory peritoneal dialysis for 10 months prior to the cancer diagnosis due to end-stage renal failure secondary to lupus nephritis, with baseline estimated glomerular filtration rate below 5 mL/min/1.73 m^2 and normal albumin level. Concomitant medications included hydroxychloroquine and prednisolone for lupus.

The patient started on erlotinib 150 mg daily in December 2018 with close monitoring of renal function. Disease control was sustained with best response of stable disease confirmed by serial PET-CT scans performed approximately every 6 months. Erlotinib was well tolerated except for a CTCAE (Common Terminology Criteria for Adverse Events) grade 1 skin reaction manifesting as skin dryness and pruritic maculopapular rash, managed with topical emollients. Nonetheless, after 15 months of treatment, her skin reaction progressed to grade 2, with development of paronychia, blepharitis and increased pruritus. Erlotinib was suspended for 3 weeks. She also experienced grade 2 mucositis with recurrent epistaxis, treated with topical emollients, topical steroids and nasal ointment. Erlotinib was resumed at 100 mg daily after resolution of toxicities and was subsequently well tolerated. Renal function remained stable on continuous ambulatory peritoneal dialysis throughout erlotinib treatment.

In May 2020, following 18 months of erlotinib treatment, PET-CT of the patient revealed disease progression in the pleura, liver, and lymph nodes as well as bone metastases. She was switched to osimertinib 80 mg daily in June 2020 after plasma EGFR mutational analysis revealed a T790M mutation. Treatment was well tolerated with only a grade 1 skin reaction controlled by oral doxycycline and topical emollients. There was an initial biochemical response with carcinoembryonic antigen level decreasing from 246 ng/mL to a nadir of 83.1 ng/mL after 3 months of treatment, but only a mixed response on PET-CT, evidenced by responding lymph node metastases and existing liver metastases, alongside the development of new liver metastases and new collapse of the T4 vertebra with narrowing of the spinal canal. Magnetic resonance imaging showed severe spinal stenosis with radiological cord compression at T4. The orthopaedic team was consulted but the patient declined surgical intervention and was managed conservatively with thoracolumbar orthoses. She had previously received palliative radiotherapy to the same site for pain control. Clinically, she had no limb weakness, sensory changes or sphincter disturbance. With limited options for next-line treatment due to end-stage renal failure, she opted to continue osimertinib.

After a further 9 months of osimertinib treatment, the patient was hospitalised in March 2021 with epigastric pain and newly deranged liver function. She had previously tested negative for hepatitis B surface antigen, with positive anti–hepatitis B antigen, positive anti-hepatitis B antibody, and undetectable hepatitis B virus DNA. The PET-CT confirmed further disease progression with extensive liver metastases, described in the report as almost entirely involving the liver with new hepatomegaly of up to 17 cm. Osimertinib was stopped and the patient succumbed 1 week later to liver failure secondary to liver metastases.

Discussion

Lung cancer is the most common cancer and the leading cause of cancer-related mortality in

Hong Kong.[1] Genetic profiling has revolutionised treatment. In Hong Kong, EGFR mutation represents the most common driver mutation, occurring in up to 50% of lung adenocarcinomas among Asians.[2] Treatment with *EGFR* tyrosine kinase inhibitors (TKIs) has demonstrated excellent efficacy and tolerability, extending median survival in patients with metastatic disease to more than 3 years.[3] In general, systemic treatment for cancer patients with end-stage renal failure poses particular concerns as renal impairment affects drug excretion as well as absorption and protein binding. Clinical data on the use of EGFR TKIs in patients on dialysis are scarce and largely limited to those on haemodialysis. Hong Kong has adopted a Peritoneal Dialysis First policy since 1985 and has the highest peritoneal dialysis-to-haemodialysis ratio globally.[4] This raises specific challenges, as drug elimination by peritoneal dialysis differs from that by haemodialysis. Our case report represents the first in the literature to demonstrate the efficacy and safety of erlotinib and osimertinib in a patient on peritoneal dialysis.

There are no recommendations for dose adjustment when prescribing erlotinib in the presence of renal impairment. Erlotinib is mainly metabolised in the liver by the cytochrome P450 system, primarily CYP3A4 (80%). Renal excretion plays a minor role in its elimination (around 9%).[5] Pharmacokinetic analysis in lung cancer patients with chronic renal failure undergoing haemodialysis showed that erlotinib plasma levels were similar before and after dialysis, possibly due to its high protein binding of up to 95%.[5] There are no pharmacokinetic data for erlotinib in patients undergoing peritoneal dialysis.

For osimertinib, no dosage adjustment is necessary in mild-to-moderate renal impairment, but it is not recommended for patients with creatinine clearance below 15 mL/min according to the United States Food and Drug Administration labelling.[6] Osimertinib is mainly eliminated by hepatic metabolism (68%), with 14% undergoing renal excretion.[7] In a pharmacokinetic study of osimertinib in renally impaired patients, parameters were similar between the control group, comprising patients with normal renal function, and two groups stratified by severity of renal impairment (estimated glomerular filtration rates 30-50 mL/min/1.73 m^2 and <30 mL/min/1.73 m^2).[7] Nonetheless, a higher incidence and severity of toxicities were observed in the two groups with renally impaired patients.[7] For patients on haemodialysis, safety data and clinical outcomes with osimertinib are limited to case reports and small pharmacokinetic studies, which suggest that it can be administered safely. One case report demonstrated that therapeutic drug monitoring may be useful: osimertinib 80 mg daily resulted in grade 3 fatigue in a patient on haemodialysis, but dose adjustment guided by periodic plasma concentration monitoring achieved sustained stable disease for more than a year without recurrence of toxicities.[8] Although therapeutic drug monitoring may not be routinely available, careful clinical monitoring for adverse effects during administration of EGFR TKIs in patients with renal impairment is warranted. Drug suspension and dosage adjustments may be undertaken at the clinician's discretion.

In conclusion, there remains room for exploration regarding the use of EGFR TKIs in patients with end-stage renal failure on peritoneal dialysis. This case demonstrates that both erlotinib and osimertinib exhibited a tolerable safety profile and reasonable treatment efficacy in patients on peritoneal dialysis and may be administered by clinicians with close monitoring.

Author contributions

Both authors contributed to the concept or design, acquisition of data, analysis or interpretation of data, drafting of the manuscript, and critical revision of the manuscript for important intellectual content. Both authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

Both authors have disclosed no conflicts of interest.

Acknowledgement

The authors are grateful to the patient and their family for their support.

Funding/support

This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethics approval

The patient was treated in accordance with the Declaration of Helsinki. As the patient is deceased, her elder sister, as next of kin, provided written consent for publication of the case report.

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