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SPECIFIC COMMENTS TO AUTHORS

The authors reviewed all previous case reports about EGFR-Tkis in NSCLC patients Undergoing HD $_{\circ}$ It was mentioned that since the main metabolic pathway of EGFR-Tkis is through the liver, and the plasma protein binding rate of EGFR-Tkis is very high, there is no need to adjust the dose after HD. Therefore, EGFR-Tkis are effective and well tolerated in HD patients. It provides a good direction for the selection of clinical medication, and I suggest that this article can be accepted. However, I am not an expert in pharmacokinetics, please refer to the opinions of other experts for relevant content. Thank you for inviting !

Answer: Thank you for your comments. We did our best to describe the clinical significance and pharmacokinetics of TKIs in patients undergoing hemodialysis. We plotted the figures of pharmacokinetics of these TKIs to give readers a clear understanding of the pharmacokinetics of TKIs in patients undergoing hemodialysis.



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This well written and extensive narrative review of case reports on hemodialysis patients with metastatic lung cancer in most treated by the different oral Epidermal Growth Factor receptor (EGFR)-Tyrosine Kinase inhibitors (TKIs) is of high interest owing to the lack of clinical trial of EGFR-TKIs in end-stage kidney disease (ESKD). It shows in details the efficiency of these molecules together with their good tolerance in ESKD. This review is in the scope of the Journal and of high scientific interest owing the the usual contraindication of classical chemotherapy in dialysis setting. Two specific comments: in the introduction paragraph, I would add that cancer frequency "in general" (not only lung cancer) is highly increased in dialysis patients. Concerning Cisplatin, I would also add that there is an important risk of bone marrow aplasia in ESKD.

Answer: Thank you for your comments.

- We changed the description about the higher incidence of cancers, not only lung cancer in CRF patients undergoing HD.
- 2. We added the description "Cisplatin is one of the most widely used chemotherapeutic agent for cancers. However, its clinical application is limited by its adverse effects, such as bone marrow suppression leading to hematopoietic abnormalities. An increased incidence of adverse reactions to cisplatin has been reported in patients with renal insufficiency.

References:

- World J Gastroenterol. 2011 Aug 14;17(30):3510-7 Prediction of nephrotoxicity induced by cisplatin combination chemotherapy in gastric cancer patients. Hyung Hwan Moon 1, Kyung Won Seo, Ki Young Yoon, Yeon Myung Shin, Kyung Hyun Choi, Sang Ho Lee)
- Aldossary SA, Review on Pharmacology of Cisplatin: Clinical Use, Toxicity and Mechanism of Resistance of Cisplatin. Biomed Pharmacol J 2019;12(1):7-15)"