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Safety and efficacy of trastuzumab emtansine (TDM-1) in a patient on hemodialysis for renal failure

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ABSTRACT

HER2-positive metastatic breast cancer is an aggressive disease with a limited number of treatment options. In the last 15 years, new drugs such as trastuzumab, pertuzumab, lapatinib or trastuzumab emtansine (TDM-1) have sprouted for these patients. There is a huge lack of evidence on the use of some of these drugs in patients with chronic renal failure, who need hemodialysis. We have reviewed the use of TDM-1 in these type of patients in the literature with unsuccessful results.

In this article we want to present a case report to illustrate the safety and efficacy of TDM-1 in a patient on hemodialysis.

Introduction

TDM-1 is an antibody-drug conjugate approved for the treatment of advanced HER2-positive breast cancer. It is also approved for adjuvant treatment when not achieving complete pathological response after neoadjuvant treatment [1,2].

Trastuzumab has become one of the most important drugs since its approval. It has been used in patients on dialysis with good results [3].

Emtansine (DM1) is an antimicrotubular agent that does not seem to have a widely renal excretion. Other antimicrotubulars agents such as paclitaxel have been extensively used in a patient with hemodialysis [4].

TDM-1 binds to HER2 receptor of the surface tumor cell and by the mechanism of endocytosis it enters into the cell. DM1 release occurs after a proteolytic degradation of the antibody part in the lysosome.

In preliminary studies with pharmacokinetic results, it seems that TDM-1 has a mainly hepatic elimination with a minimum urine presence of TDM-1 metabolites. Some patients with mild or moderate renal impairment who have been treated with TDM-1 have exhibited a similar behavior than normal renal function patients [5].

TDM-1 has a half-life of 3.5 days, and systemic clearance is faster than clearance of total trastuzumab [6].

The safety of TDM-1 on hemodialysis patients has been suggested to some authors [7].

Sometimes the summary of product characteristics does not state or assure if the use of some antineoplastic drugs is safe in patients with renal replacement therapies.

Case report

In this brief article, we present the case of a 73-year-old female patient with several comorbidities.

The patient presented with a remarkable medical history of hypertension for more than 20 years of evolution, diabetes mellitus type 2 of 12 years of evolution, including treatment with oral anti-diabetic drugs, and hyperlipidemia.

She also had a history of multivessel ischemic cardiopathy 9 years ago with the need for coronary artery revascularization.

Lastly, we need to mention that the patient presented with chronic renal impairment in the predialysis stage because of multifactorial reasons (vascular/diabetic).

This woman was diagnosed with hormonal receptor-negative, HER2-positive early breast cancer in May 2013 after mammography screening. Breast conservative surgery plus axillary dissection were done in June 2013. The decision on primary or adjuvant chemotherapy the same as trastuzumab use was refused because of high comorbidities and the patient received only radiotherapy in July 2013. After that, the patient went for follow ups.

In October 2014, the CT scan showed a sternum osteolytic lesion that is associated with a soft tissue mass. Biopsy was performed some months later, which confirmed the histology of HER2-positive breast cancer.

In February 2015, the patient started on trastuzumab alone as a first line of metastatic disease. She neither experienced side effects during the treatment nor any cardiac adverse event. She completed 31 cycles of

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trastuzumab with stable disease as best response.

In January 2017, axillary and cutaneous progression were confirmed.

One month later, after discussions with the tumor board and an agreed decision, the patient was started with TDM-1 at 3.6 mg per kg of body weight intravenously every 21 days, always the day prior to the hemodialysis session. She used to receive TDM-1 on Friday and hemodialysis program was carried out on Tuesdays, Thursdays and Saturdays. Early clinical response was observed after the first cycle, besides the CT scan showed almost complete response in the axilla and skin (Fig. 1).

As main toxicities, the patient presented with continuous asthenia grade 1, which increased to grade 2 after 4 cycles. She also developed anemia grade 2. We decided to modify the dose to 3.0 mg per kg before the fifth cycle.

This dose level was well tolerated and after 12 cycles of TDM-1, the patient maintained partial response. After a mutual agreement, we decided to stop the treatment because she was tired of several hospital visits. Unfortunately, two months later, new cutaneous disease progression was observed, and the patient presented with a poor performance status to propose active treatment. She was referred to the palliative care unit.

The patient finally died in June 2018.

Conclusion

We summarized that TDM-1 is an effective and safe drug for patients with HER2-positive breast cancer who are on hemodialysis treatment. Although a pharmacokinetic study has not been performed, we think that dose adjustment is not needed as TDM-1 has mainly hepatic metabolization and renal excretion is minimal.

Besides the lack of pharmacokinetics samples, the use of TDM-1 should be considered in patients with HER2-positive breast cancer on hemodialysis based on these data.

Ethics approval

After bibliography review, an internal committee was formed and the treatment was approved. The patient signed informed consent for TDM-1 administration and gave us full approval for both the case and image publication.

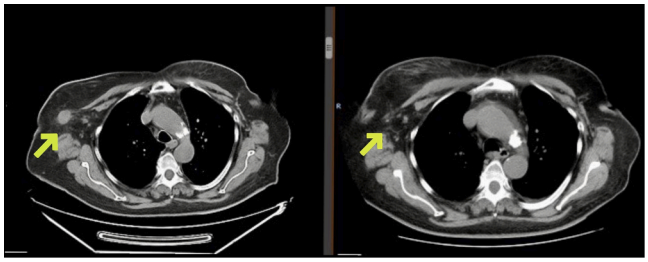

Fig. 1.

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Declaration of Competing Interest

Falcón González A: Advisory board: Roche; Speech fee: Roche, Novartis, Pfizer, Lilly and Grünenthal. Travel expenses: Roche and Novartis.

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