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Case Report

Antineoplastic Effect of Trastuzumab Deruxtecan in A Patient with A Previous Allogeneic Hematopoietic Stem Cell Transplantation

Jorge Illarramendi[1], Amaya Zabalza[2], Isabel Blanco[3] and Jose Juan Illarramendi[4]*

[1]Department of Hematology and Cellular Therapy, Hôpital Haut Lévêque, Pessac, France

[2]Department of Hematology, Hospital Universitario de Navarra, Pamplona, Spain

[3]Department of Nuclear Medicine, Hospital Universitario de Navarra, Pamplona, Spain

[4]Department of Medical Oncology, Hospital Universitario de Navarra, Pamplona, Spain

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***Corresponding author:** Jose Juan Illarramendi. Department of Medical Oncology, Hopital Universitario de Navarra, Pamplona, Spain

ABSTRACT

Allogeneic hematopoietic stem cell transplantation is a consolidated therapy for patients with acute leukemia and for other diseases. Second neoplasms and relapses of previously diagnosed malignancies are potential late complications of concern for these patients, but current knowledge on the use of antineoplastic drugs in this setting is scarce. Our case report describes an elderly female patient with a previous history of allogeneic stem cell hematopoietic transplantation that received long-term trastuzumab deruxtecan, a breakthrough antibody-drug conjugate, for the treatment of advanced breast cancer with liver metastases. We are unaware of previous reports on the use of this drug in patients with a previous allogeneic transplant. Tolerance to the treatment has been excellent and a complete response to the therapy is maintained so far. As the starting dose was the lowest registered for breast cancer, we review the published data about starting dose reductions, but current information about this subject is incomplete and further evidence is needed.

Keywords: Trastuzumab deruxtecan; Breast cancer; Acute leukemia; Allogeneic stem cell transplantation

Introduction

The potential appearance of second neoplasms are among the most significant late complications of allogeneic hematopoietic stem cell or bone marrow transplantation for leukemia and other diseases (ASCT)[1]. Current knowledge about the systemic therapy of second neoplasms arising after an ASCT is limited and there is a need to increase the information with reports and studies about the activity and tolerance to new anticancer drug developments, such as antibody drug conjugates, kinase inhibitors and immunotherapies in this setting. We report herein the activity and tolerance to trastuzumab deruxtecan (TDxd), a breakthrough antibody drug conjugate, in a patient with metastatic breast cancer (BC) who had previously undergone an ASCT for acute leukemia.

Case Report

A 63-year woman (born in August 1954) was diagnosed

with BC in Abril 2018. Histopathology disclosed a phenotype Her2/neu grade 2 invasive ductal carcinoma, with negative hormone receptors and overexpression of the human epidermal growth factor receptor-2 (Her2/neu). Liver metastases were found on radiologic staging. She started systemic therapy with the combination of docetaxel plus pertuzumab and trastuzumab in May 2018. Chemotherapy with docetaxel was maintained until December 2018, with imaging findings of complete response at that time. Maintenance therapy with the antiHer2/neu monoclonal antibodies pertuzumab and trastuzumab were continued until October 2020, when the patient was admitted with a diagnosis of mixed-phenotype acute leukemia. BC restaging showed a persisting complete response. Therapy for leukemia was started according to the PETHEMA LAL 2019 protocol, with administration of the FLAG-IDA scheme (fludarabine, cytarabine, granulocyte colony-stimulating factor, idarubicin), with complete response. In March 2021 the patient underwent reduced-intensity allogeneic stem cell transplantation from an HLA-matched sister. Fludarabine plus melphalan were used for conditioning. Prophylaxis of graft versus host disease (GVHD) was done with tacrolimus plus methotrexate. A complete response of acute leukemia has been maintained, with negative minimal residual disease. Ongoing controls have found a complete chimerism and a mild chronic relapsing GVHD, with mainly ocular mucosal and cutaneous involvement. Tacrolimus was stopped in September 2021.

Oncologic evolution was uneventful until February 2023, when a relapse of BC in her right breast was detected by positron emission tomography-computed tomography (PET-CT), without findings of distant metastases. The patient underwent a segmentectomy with axillary lymphadenectomy. Histopathology showed a grade 1 invasive carcinoma of 33 millimeters, with apocrine differentiation, 2/22 involved axillary nodes and a Her2/neu phenotype.

A follow-up PET-CT detected in June 2023 the appearance of multiple liver metastases, involving the segments IVa, III/IVb, V and VI **(Figure 1)**. Systemic therapy was started with TDxd. After taking into consideration the context and the frailty of the patient, treatment was initiated with the lowest registered dose of TDxd, corresponding to 3.2 mg/kg, aiming to a potential increase of dose in case of good tolerance. There were signs of a nearly complete response of liver metastases in the control PET-CT after three months of therapy and of complete response in the control PET-CT studies done afterwards **(Figure 2)**. Tolerance to TDxd has been fair, with a mild hematological toxicity and lack of pulmonary and cardiac complications. The patient underwent surgery for cataracts in June 2025. Therapy with TDxd is ongoing at the time of this report, with the 35th cycle started in September 2025. The dose of 3.2 mg/kg has been maintained, in consideration to her excellent response and tolerance.

Discussion

BC relapses after ASCT for therapy-related myeloid neoplasms are uncommon. In a retrospective study by the Chronic Malignancies Working party of the European Society for Blood and Marrow Transplantation (EMBT), only 17 out of 252 patients with a previous history of BC before ASCT had BC relapses, after a median follow-up of 20 months[2].

Some reported cases on the use of the antiHer2/neu antibody trastuzumab for BC therapy in women or men after ASCT have been published in the context of localized[3,4] or metastatic disease[5], in monotherapy or in combination with paclitaxel, carboplatin or pertuzumab, without any specific concern about the tolerance to these drugs in such context.

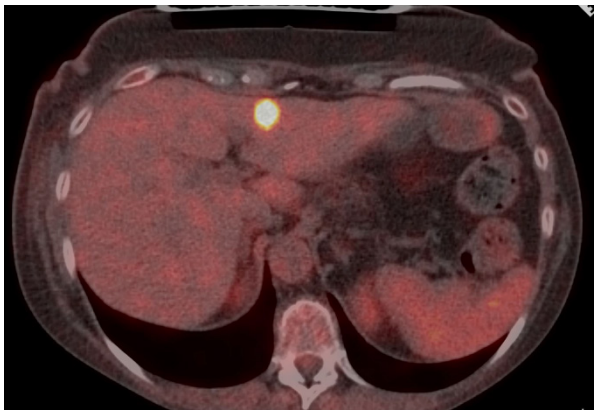

Figure 1: PET-CT imaging at the start of therapy with TDxd, showing one of the liver metastases.

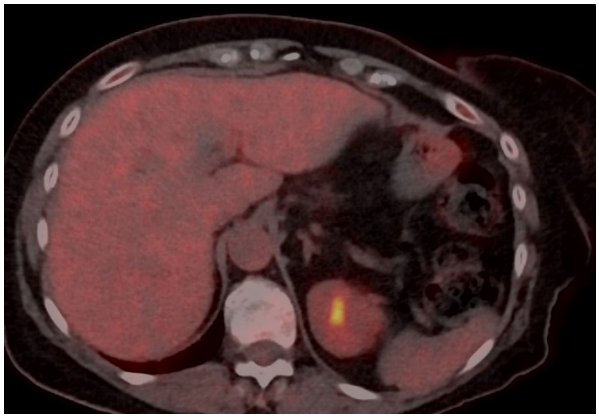

Figure 2: Follow-up PET-CT during the treatment with TDxd, showing complete disappearance of the liver lesion, the other liver lesions were also disappeared.

We are unaware of any previous communication on the use of TDxd after an ASCT. There is one published report on the use of TDxd in a BC patient with a previous history of autologous (not allogeneic) bone marrow transplant for Hodgkin lymphoma[6]. Of note, this patient also received a reduced dose of TDxd of 3.2 mg/kg, with good tolerance.

The pulmonary toxicity of TDxd may be regarded as a potential concern for the use of this drug after ASCT, but there were no significant clinical, imaging or functional signs of lung complications with the long-term use of this conjugated antibody in our patient. Authors from Slovenia have reported some worries about the use of immune checkpoint inhibitors in this setting, not only for pulmonary risk, but also for a potential aggravation of GVHD[7]. Furthermore, a case of irinotecan-induced interstitial lung disease has been reported in a patient with colorectal cancer and a previous history of ASCT[8].

The use of a reduced starting dose is obviously absent in the pivotal trials done for the regulatory approval of TDxd and is uncommon in most observational reports performed on this drug, not including those conducted in patients with severe liver impairment. However, the Italian DE-REAL study concluded that the real-world progressive-free and overall survivals were not affected by dose reductions[9]. A retrospective observational

report from Florida described a 29% of patients with starting dose reductions[10]. Data from the European multicenter TREX-old registry reported a similar starting dose reduction in 30% of the 158 patients included in this series of elderly BC women[11]. A higher percentage of nearly or even more than 90% of patients with starting dose reduction of TDxd have been described in two recently published Chinese observational studies, but was influenced by economic reasons in at least one of these reports[12] and resulted in a significantly negative impact of dose reduction on the efficacy of TDxd in the other study[13]. On the other hand, another observational study in an Asian population from Singapore reported no significant impact on progression-free survival for a reduced dose of TDxd resulting in <85% of relative dose intensity in a cohort of 87 patients, with 47% of them starting with a reduced dose of this drug[14].

Finally, the large cohort of real-life data from the temporary use authorization program of TDxd in France reported a starting reduced dose of 4.4 mg/kg for one woman with BC and chronic myeloid leukemia among the 459 registered patients[15]. Data about the treatment of the chronic myeloid leukemia is not available from this report, but is described that the old age of that patient was another reason for considering a starting dose reduction in this setting, as was also addressed for our patient.

Conclusion

Our case report describes the use of TDxd in an elderly patient with a previous ASCT that developed liver metastases from BC. There has been an excellent response and tolerance to a starting reduced dose of TDxd, that is ongoing during a long follow-up. Further knowledge about dose management and other aspects of therapy in this setting and for other patients with frailty is needed, as current data is incomplete and with some conflicting results.

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Conflicts of Interest

Jose Juan Illarramendi received honorary fees from Daiichi-Sankyo.

Ethical Approval

Comité de Etica de Investigación con Medicamentos de Navarra.

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