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Teclistamab: A Novel Therapeutic Drug for Multiple Myeloma Patients with Limited Treatment Options: Case Report

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Abstract

Although treatment for multiple myeloma (MM) has expanded substantially in recent years, it remains an incurable disease with inevitable cycles of remission and relapse. In each one, the disease becomes refractory to previous treatments and requires the use of a new strategy based on drugs with novel targets.

Teclistamab is a T-cell–redirecting bispecific antibody that binds B-cell maturation antigen (BCMA), a member of the tumor necrosis factor family of receptors highly expressed on MM cells, and CD3, expressed on the surface of T cells.

Here, we present a case of a 65-year-old male with MM who was heavily pre-treated. He has progressed to 3 previous lines of therapy and is currently being treated with this new drug, teclistamab. He has achieved a complete response (CR) and is still under treatment with no clinically relevant adverse effects. This is a case report in an unrestricted real-world context, which provides information on efficacy and safety of this anti-myeloma new drug.

Keywords: Teclistamab; Multiple myeloma; Treatment; Relapsed

Abbreviations: MM: multiple Myeloma; ASCT: Autologous Stem Cell Transplantation; IMiDs: Inmunomodulatory Drugs; VRd: Bortezomib, Lenalidomide, Dexamethasone; VTd: Bortezomib, Thalidomide, Dexaethasone; PIs: Proteasome Inhibitors; BCMA: B-Cell Maturation Antigen; EMA: European Medicines Agency; ISS-R: Revised International Staging System; AE: Adverse Effects; CR: Complete Response; MRD: Minimal Residual Disease; VTD-PACE: Cisplatin, Doxorrubicine, Cyclophosphamide, Etoposide

Introduction

Multiple myeloma (MM) is an age-associated disease that occurs when plasma cells of the bone marrow suffer a malignant proliferation [1]. Therapeutic landscape in MM has witnessed significant advances over the last years with the progress of high-dose therapy with autologous stem cell transplantation (ASCT), the approval of proteasome inhibitors, immunomodulatory drugs (IMiDs), monoclonal antibodies, and the combination of these therapies. Although these new strategies improve patients´s survival, MM remains an incurable disease with inevitable cycles of remission and relapse in the majority of patients [1].

Treatment of MM patients depends on the risk stratification and transplant eligibility. Based on that, patients who are considered fit for transplant usually receive induction treatment over 3 or 4 months to reduce tumor burden prior to ASCT [2]. This induction treatment normally involves 4 cycles of bortezomib, lenalidomide, and dexamethasone (VRd) or of bortezomib, thalidomide, and dexamethasone (VTd) followed by melphalan for transplant conditioning. After ASCT, lenalidomide is the most common maintenance therapy, administered until disease progression. Options for relapsed MM include combinations of drugs with different targets, such as antibodies anti CD38,

daratumumab or isatuximab, proteasome inhibitors (PIs), carfilzomib or bortezomib, and IMiDs, pomalidamide, thalidomide or lenalidomide [3]. Selecting among all these therapeutic options depends on prior drug exposure and/or resistance to previous treatment [4].

In this context, teclistamab is a new drug that has recently been approved for the treatment of adult patients with relapsed and refractory MM, who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody, and whose cancer has worsened since receiving the last treatment.

Teclistamab is a bispecific antibody that binds B-cell maturation antigen (BCMA), a member of the tumor necrosis factor family of receptors highly expressed on MM cells, and CD3, expressed on the surface of T cells, recruiting and activating these T cells to kill BCMA-expressing MM cells [5]. On July 2022, based on a phase 1/2, multicentre, open label, single-arm clinical trial, European Medicines Agency (EMA) recommended a conditional marketing authorisation in the European Union (EU). This report describes the case of a 65-year-old male with MM who was heavily pretreated and is currently being treated with teclistamab.

Clinical Case

This case concerns a 65-year-old male for whom the disease was characterized by extramedullary disease and treatment with teclistamab was started after three previus lines of treatment. He was diagnosed in May 2020 with IgA lambda MM on a Revised International Staging System (ISS-R) stage II.

When diagnosed he suffered from Bence Jones proteinuria and renal failure, requiring hemodialysis. He was considered fit for trasplant and started induction chemotherapy with VTd. As complications he presented bacteremia due to methicillin-resistant S. Aureus secondary to central venous catheter treated with Cloxacillin, febrile peaks for over 1 month without clear focus requiring different antiobiotics (ceftriaxone, levofloxacin, ciprofloxacin and levofloxacin) and pruritic skin rash probably because of toxicoderma secondary to thalidomide. Due to this last adverse effect, thalidomide was suspended and changed to cyclophosphamide until desensitization in allergy Department. He received a total of 6 cycles of VTd, presenting peripheral neuropathy and astenia as main adverse effects (AE). After CR with negative minimal residual disease (MRD -), an ASCT was performed (after conditioning with melphalan). He started maintenance with lenalidomide, receiving a total of 6 cycles, with significant neuropathy and clinical progression. He started rescue treatment with DVd (daratumumab, bortezomib, dexamethasone), with adjusted doses of bortezomib (administered at 50%) due to previous neuropathy. He experimented with febrile neutropenia during the first DVd cycle.

A new early relapse was observed after 3 cycles of DVd, with the need to start a new rescue chemotherapy protocol, VTD-PACE (cisplatin + doxorrubicine + cyclophosphamide + etoposide), adjusted to 50% doxorrubicine and etoposide for hypertransaminemia with good tolerance. As complications, he presented thrombophlebitis, treated with amoxicillin/clavulanic acid and an isolation of Clostridium in stool culture that required vancomycin. Due to a new early relapse, teclistamab was initiated as 4th line therapy. After 2 months, treatment is still ongoing with patient in CR, and no relevant adverse effects.

Discussion and Conclusions

In the phase I-II study (MajesTEC-1) [6], teclistamab as monotherapy demonstrated important antimyeloma activity in patients with relapsed or refractory MM heavily pretreated. Despite the lack of a solid phase III clinical trials, teclistamab was recently granted a conditional marketing authorisation, one of the EU regulatory mechanisms to promote early access to medicines that fulfil an unmet medical need, where the benefit of immediate availability of the medicine outweighs the risk inherent in the fact that additional data are still required [7]. Information derived from routinely collected real-world data is also a valuable tool to increase the knowledge and management of these drugs.

This is a case report on real-life clinical use of teclistamab outside of controlled clinical trials. This bispecific antibody is indicated to treat MM patients that have received previous lines of treatment that contain at least three drugs with different targets [8]. In this context, isatuximab is another therapeutic alternative, associated with carfilzomib and dexamethasone -Isa-Kd- or pomalidomide and dexamethasone -IsaPd-. In this patient, the use of teclistamab was preferred over isatuximab because there is no solid data on rescue treatment with an antiCD38 drug (isatuximab) in patients previously treated with another antiCD38 (daratumumab). In fact, in isatuximab´s clinical trials, ICARIA [9] and IKEMA 7[10], patients previously treated with daratumumab were excluded, as in the case of this patient.

Treatment is still ongoing with 14 cycles completed so far, and the patient has obtained a complete response. Treatment is being very well tolerated, without any relevant AE. The patient did not require any discontinuation or dose reductions and he did not present cytokine release syndrome or cytopenias, which are the most frequently reported AE in clinical trials. The major limitation of our work is the fact that it is a single patient case report, with limited follow-up. We therefore suggest, in addition to clinical trials, real life studies including as many patients as possible in order to increase the knowledge of teclistamab in relapsed and refractory MM patients.

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