

# Dramatic Response to Elranatamab in a Patient with Large Plasmacytomas

## Büyük Plazmositomları Olan Bir Hastada Elranatamab'a Dramatik Yanıt

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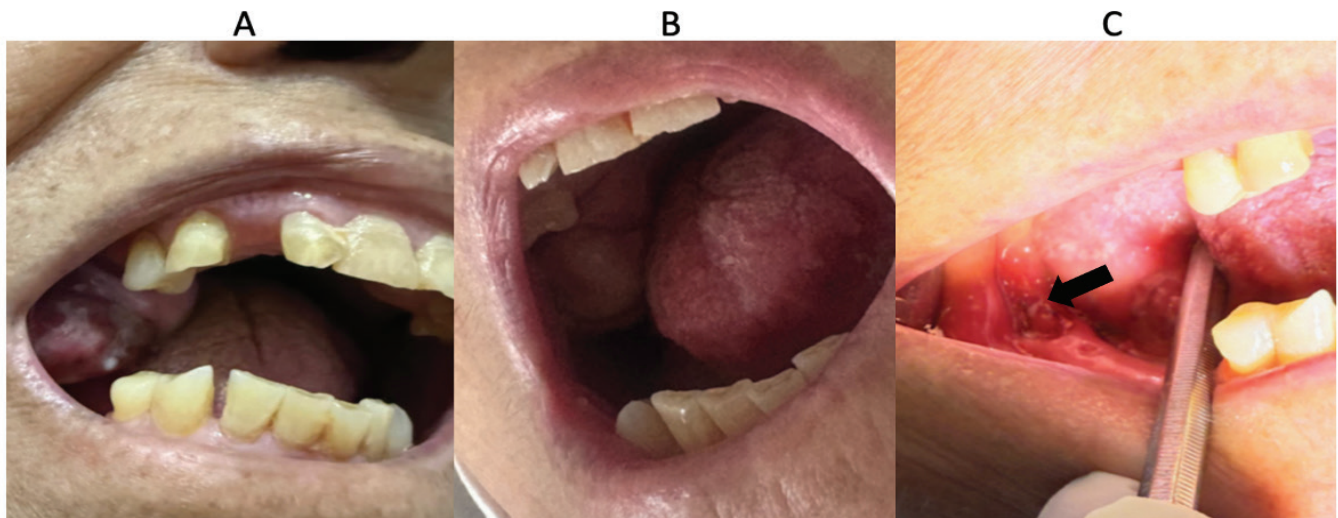
### To the Editor,

Despite significant advances, including proteasome inhibitors, immunomodulatory drugs, and monoclonal antibodies, treatment outcomes remain unsatisfactory in patients with relapsed/refractory multiple myeloma (RRMM) presenting with extramedullary (EMD) disease [1,2]. Elranatamab is a bispecific antibody developed for the treatment of multiple myeloma (MM) [2,3,4]. It has been approved as monotherapy for RRMM based on the phase II MagnetisMM-3 study [3].

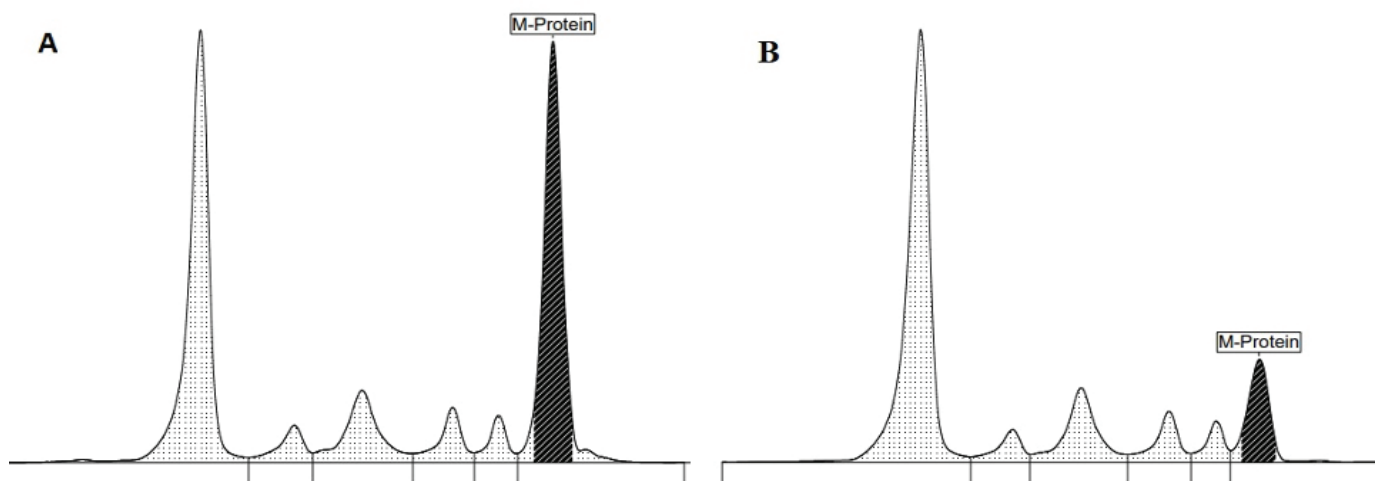
A 71-year-old female patient had been previously diagnosed with MM and plasmacytoma in September 2015 at the age of 62. Her Revised International Staging System (R-ISS) stage was II and no myeloma-specific molecular abnormalities were detected. She received four cycles of bortezomib, cyclophosphamide, and dexamethasone together with radiotherapy, followed by autologous stem cell transplantation with 200 mg of melphalan as conditioning. In the third month after the transplant, a complete medullary and partial EMD response was achieved. She subsequently received six cycles of bortezomib, lenalidomide, and dexamethasone, followed by lenalidomide maintenance therapy. In May 2023, positron emission tomography/computed tomography (PET/CT) revealed a recurrent expansile mass in the sacrum. Treatment was switched to carfilzomib, lenalidomide, and dexamethasone. After six cycles, a partial response was achieved; however, in the 16th cycle, disease progression was detected with a new 6-cm mass in the sacrum. The lesion was treated with involved-field radiation therapy. Subsequently, daratumumab, pomalidomide, and dexamethasone were initiated. After two cycles, serum protein electrophoresis (SPEP) showed a significant increase in M-protein (from 1.1 g/dL to 2.9 g/dL), and the serum free light chain (FLC) ratio was 36 with serum free lambda level of 132 mg/dL and kappa level of 3.67 mg/dL. PET/CT revealed multiple lesions in the axial and

appendicular skeleton, in both scapulae, and the largest one, measuring 5.8x4.5 cm, was located at the anterior end of the second rib, extending toward the pleura and lung parenchyma, with an associated soft-tissue component. One was visibly located in the oral cavity (Figure 1A). As biochemical progression was evident, a bone marrow biopsy was not performed; however, a tru-cut biopsy taken from the oral lesion was consistent with lambda-positive plasma cell infiltration. As fifth-line therapy, elranatamab monotherapy was started. The patient developed grade 1 cytokine release syndrome, grade 2 thrombocytopenia, grade 3 neutropenia during treatment, and grade 5 infection; however, no immune effector cell-associated neurotoxicity syndrome was observed. The oral mass (Figure 1A) showed marked regression by day 10 of treatment (Figure 1B) and had completely disappeared by the first month (Figure 1C). After two cycles of treatment, the M-protein level on SPEP decreased to 0.68 g/dL (Figure 2) and the FLC ratio declined to 12 (serum free lambda level of 2.02 mg/dL and free kappa level of 0.17 mg/dL). Unfortunately, while the third cycle of treatment was ongoing, the patient developed cytomegalovirus (CMV) reactivation and coronavirus disease-2019 (COVID-19) infection and died due to respiratory failure requiring intensive care unit admission. Therefore, long-term follow-up outcomes cannot be presented.

EMD involvement in MM is usually associated with an aggressive clinical course [1,2,5]. Penta-refractory patients typically have poor treatment responses [6]. Our patient was penta-refractory and presented with multiple EMD plasmacytomas. B-cell maturation antigen (BCMA) is highly expressed on malignant plasma cells and plays a critical role in their survival and proliferation, making it an attractive therapeutic target in MM. Elranatamab is a bispecific antibody that targets BCMA on myeloma cells [3,4]. In the pivotal trial that led to its approval, 31% of patients had EMD disease and 42% were penta-refractory.



**Figure 1.** Clinical photographs showing a large oral plasmacytoma before and after elranatamab treatment. A) Day 1, prior to therapy, demonstrating a prominent plasmacytoma lesion (5x4.5 cm) in the oral cavity. B) Day 10, marked reduction in tumor size (3x2 cm). C) One month after initiation of treatment, complete resolution of the lesion was observed.



**Figure 2.** Serum protein electrophoresis profiles. A) At the initiation of elranatamab therapy, the M-protein level was 2.9 g/dL. B) By the second month of therapy, a marked reduction was observed, with the M-protein level decreasing to 0.69 g/dL.

The overall response rate was 61%, with a complete response achieved in 35% of responders. However, patients with adverse prognostic features such as EMD disease, penta-refractory status, or R-ISS stage III disease had shorter median durations of response [3]. In a French real-world study in which 36% of the included patients had EMD disease and 76% had penta-refractory status, the overall response rate was 51.5%. Again, responses were lower among patients with EMD disease and poor Eastern Cooperative Oncology Group (ECOG) performance status [7]. Teclistamab is another BCMA-targeted bispecific antibody. The phase 1-2 MajesTEC-1 trial was conducted in patients with RRMM. In this study, 30.3% of the patients were penta-refractory and 17% had EMD disease; the overall response rate was 63% and the complete response rate was 39.4% [8]. These results are similar to those of the MagentisMM-3 trial.

Despite being penta-refractory and presenting with multiple plasmacytomas, our patient had a good ECOG performance status. Remarkably, a visible clinical response was observed even after the first cycle of treatment, despite the patient belonging to a group typically expected to have poor outcomes. Despite a marked response after the second cycle, the patient developed CMV reactivation during the third cycle and subsequently died due to COVID-19 infection and respiratory failure. In the pivotal trial leading to the approval of elranatamab, COVID-19 infection was reported in 29.3% of patients, with 1.6% being grade 5 events, and the rate of CMV reactivation was 5.7% [3]. In the phase 1-2 MajesTEC-1 trial of teclistamab, COVID-19 infection was reported in 17.6% of patients. During follow-up, 68 of 168 patients were reported to have died, predominantly due to disease relapse; among these 68 patients, 12 deaths were

attributed to COVID-19 infection [8]. Because our patient had RRMM and preexisting secondary immunodeficiency, routine antiviral (acyclovir), antifungal (fluconazole), anti-*Pneumocystis jirovecii* (co-trimoxazole), and antibacterial (levofloxacin) prophylaxis was administered. Filgrastim was given during episodes of neutropenia and immunoglobulin replacement therapy was provided. Unfortunately, the patient died due to COVID-19 infection. Elranatamab may be an effective treatment option for RRMM patients who have received multiple prior lines of therapy and present with plasmacytomas. However, patients should be regularly monitored for viral reactivation and should be thoroughly counseled on the importance of adhering to routine preventive measures and prophylactic therapies due to the high risk of infection.

**Keywords:** Plasmacytoma, BCMA, Elranatamab

**Anahtar Sözcükler:** Plazmositom, BCMA, Elranatamab

### Ethics

**Informed Consent:** Informed consent was obtained.

### Footnotes

**Conflict of Interest:** No conflict of interest was declared by the author.

**Financial Disclosure:** The author declared that this study received no financial support.

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