Letter to the Editor

rare tumors

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"A beacon of hope for relapsed multiple myeloma patients: TALVEY™"

Nawal Khaliq[1], Rumaisa Riaz[1], Aleeza Hasan[2] and Sara Alauddin[2]

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Dear Editor,

Multiple myeloma, a significant hematological malignancy affecting about 10% of such cases globally, presents a substantial health challenge.[1] Despite medical advancements, most patients eventually face relapse and resistance to treatment. Particularly, patients with triple-class exposed relapsed/refractory multiple myeloma (RRMM), pretreated with immunomodulatory drugs, proteasome inhibitors, and anti-CD38 monoclonal antibodies, have poor overall survival rates.[2] Recent breakthroughs in immunotherapy, including CAR T-cell therapy and bispecific antibodies (BispAbs), offer promising options for RRMM management. CAR T-cell therapy is effective but has a time-consuming manufacturing process. On the other hand, BispAbs are readily available and show remarkable efficacy in RRMM treatment.[2] Recognizing this, the Food and Drug Administration (FDA) has recently given accelerated approval to Talquetamab, a pioneering second bispecific antibody that targets GPRC5D and CD3 receptors. This off-the-shelf therapy shows remarkable therapeutic achievement for heavily pretreated RRMM patients.[3]

Multiple myeloma (MM), the second most prevalent hematologic cancer after non-Hodgkin lymphoma, predominantly affects high-income countries. It is defined by the infiltration of bone marrow with monoclonal plasma cells, producing monoclonal immunoglobulins detectable in the blood or urine. The buildup of these immunoglobulins can result in organ dysfunction, commonly referred to as CRAB symptoms (hypercalcemia, kidney problems, anemia, and bone abnormalities), which signify the onset of symptomatic disease.[4] TALVEY™ (talquetamab-tgvs), a GPRC5D-targeted therapeutic bispecific antibody, effectively engages T-cells and demonstrates the capacity to attach to both the CD3 receptor situated on T-cells and the G protein-coupled receptor class C group 5 member D (GPRC5D), which is present on the surfaces of both multiple myeloma cells and non-cancerous plasma cells. Furthermore, it also interacts with normal tissues such as epithelial cells in keratinized regions of the skin and tongue. In experimental settings, talquetamab-tgvs prompted the activation of T-cells, resulting in the emission of inflammatory signaling molecules and leading to the elimination of multiple myeloma cells.[5]

The effectiveness of TALVEY as a standalone treatment was assessed in patients with relapsed or refractory multiple myeloma. This evaluation took place in a study called MMY1001 (MonumenTAL-1) (NCT03399799, NCT4634552), involving 187 patients who had received at least four previous systemic treatments. Patients were given either talquetamab-tgvs 0.4 mg/kg subcutaneously weekly after initial step-up doses, or talquetamab-tgvs 0.8 mg/kg subcutaneously every 2 weeks following initial step-up doses. Treatment will be administered until either the disease advances or intolerable side effects occur. The main group under analysis consisted of patients who had undergone at least four prior therapies, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody. In the group receiving 0.4 mg/kg weekly, the overall response rate (ORR) was 73%, with a median duration of response (DOR) of 9.5 months. In the 0.8 mg/kg biweekly group, the ORR was 73.6%, and the median DOR was not estimable. About 85% of those who

[1]Department of Internal Medicine, Dow University of Health Sciences, Karachi, Pakistan
[2]Department of Internal Medicine, Karachi Medical and Dental College, Karachi, Pakistan

Corresponding author:
Rumaisa Riaz, Department of Internal Medicine, Dow University of Health Sciences, Mission Rd, New Labour Colony Nanakwara, Karachi 74200, Pakistan.
Email: riazrumaisa@gmail.com

responded to treatment maintained their response for a minimum of 9 months.[3]

TALVEY™ presents a comprehensive safety profile that demands attention from both healthcare professionals and patients alike. Notably, it bears a Boxed Warning, emphasizing the potential risks associated with cytokine release syndrome (CRS) and neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS). In addition, it comes with vital Warnings and Precautions encompassing oral toxicity, weight loss, infections, cytopenias, skin toxicity, hepatoxicity, and embryo-fetal toxicity. When considering adverse reactions, some affecting more than 20% of patients include fever, CRS, taste disturbances (dysgeusia), nail issues, musculoskeletal pain, skin problems, rashes, fatigue, weight loss, dry mouth, dry skin (xerosis), difficulty swallowing (dysphagia), upper respiratory tract infections, diarrhea, hypotension, and headaches. Furthermore, it's noteworthy that Grade 3 or 4 laboratory abnormalities, occurring in over 30% of cases, involve decreased lymphocyte count, neutrophil count, white blood cell count, and hemoglobin levels. Given these safety considerations, patients and healthcare providers should exercise caution and vigilance when utilizing TALVEY™ in the treatment of multiple myeloma.[5]

In conclusion, the FDA approval of TALVEY™ (Talquetamab-tgvs) represents a significant breakthrough in the treatment of relapsed or refractory multiple myeloma. This innovative therapy provides a valuable option for patients who have exhausted standard treatments. Talquetamab-tgvs, with its dual targeting approach involving CD3 and GPRC5D, holds promise in tackling the patient's immune system to effectively combat myeloma. Preliminary research has shown its potential efficacy and safety. Ongoing studies aim to refine its use and explore potential combinations with other treatments to improve outcomes for patients with relapsed or refractory multiple myeloma.

Author Contributions

Nawal Khaliq researched the literature. Rumaisa Riaz, Aleeza Hasan and Sara Alauddin drafted the manuscript. NK revised it critically for important intellectual content. All authors approved the final version of article to be published.

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ORCID iD

Rumaisa Riaz https://orcid.org/0000-0002-2277-0183

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