

# Appropriately De-Escalating Talquetamab to Monthly Dosing in Multiple Myeloma



**Joseph Mikhael, MD**  
Translational Genomics  
Research Institute;  
City of Hope



**Samer Al Hadidi, MD**  
University of Arkansas for  
Medical Sciences



**Muhamed Baljevic, MD**  
Vanderbilt University Medical Center



**Tara Gregory, MD**  
Colorado Blood  
Cancer Institute



**Omar Nadeem, MD**  
Dana-Farber Cancer Institute



**Hashim Mann, MD**  
VCU Health



**Shambavi Richard, MD**  
Mount Sinai



**Ajay K. Nooka,  
MD, MPH, FACP**  
Emory Winship  
Cancer Institute

**A**n unusual patient case was presented during a *Frontline Forum* where experts worked through how to appropriately treat a patient who was having consistent fevers and pain. The panel spoke about the de-escalation of treatment and when clinicians should consider doing so.

The patient case highlighted relapse along with responses, and adverse effects (AEs) that left the treating physician puzzled about how to proceed with subsequent lines of therapy. Read on to see how the panel discussed the next best approach and what to do for this patient.

## PATIENT CASE

- A 63-year-old man was diagnosed with Revised International Staging System II immunoglobulin G (IgG)  $\lambda$  multiple myeloma symptomatic with bone lesions, renal failure, and anemia.
- Laboratory results:
  - IgG: 7630  $\mu$ mol/L;  $\lambda$  free light chain: 113.85 mg/L;  $\kappa$  free light chain: 5.86 mg/L
  - Albumin: 2.8 g/dL;  $\beta$ 2 microglobulin: 6.02 mg/L; lactate dehydrogenase: 216 IU/L
  - Creatinine: 1.68 mg/dL; hemoglobin: 8.4 g/dL; calcium: 8 mg/dL
  - Urine protein electrophoresis with M spike of 30 mg/24 hours

## PATIENT CASE, CONTINUED

- Bone marrow biopsy at Good Samaritan Hospital with 80% cellularity, and 90% plasma cells.  $\lambda$  monocytic plasma cells noted by flow (16%). Karyotype 46XY, only 2 cells resulted. FISH gain of 1q and del13
- PET/CT: Multiple lytic lesions involving right scapula, L4, uptake in the fractured coracoid process
- MRI of T and L spine. Acute compression deformity of the T12 vertebral body. Acute or unhealed presumed pathologic compression deformity of the T9 vertebral body
- Treatment:
  - First-line therapy:
    - Bortezomib plus dexamethasone for 1 cycle then bortezomib, lenalidomide, and dexamethasone for 3 cycles. A very good partial response (VGPR) occurred
    - Hemodialysis with melphalan at 200 mg/m<sup>2</sup> with autologous stem cell transplant
    - Maintenance therapy on single-agent daratumumab study
    - The best response continued VGPR
    - Progressive disease after 10 months
  - Second-line therapy:
    - Daratumumab, pomalidomide, and dexamethasone
  - Third-line therapy:
    - Daratumumab, carfilzomib, and dexamethasone
  - Fourth-line therapy:
    - Pomalidomide plus dexamethasone to qualify for chimeric antigen receptor (CAR) T-cell therapy
  - Fifth-line therapy:
    - CAR T-cell therapy in the study and given CT053
    - A complete response occurred
    - Progressive disease occurred within 9 months
    - Penta-refractory disease and progressive disease post anti-BMCA
  - Sixth-line therapy:
    - Talquetamab was given
    - M spike: 5.2 g/dL; IgG: 6771  $\mu$ mol/L;  $\lambda$  free light chain: 254 mg/L; circulating plasma cells were noted
    - After cycle 4, VGPR by labs with an M spike of 0.3 g/dL;  $\lambda$  free light chain: 1.6 mg/L
    - Bone marrow and PET were negative
    - Persistent fevers and bone pain after each talquetamab infusion on days 2-6
    - Cycle 5: M spike up to 0.4 g/dL;  $\lambda$  free light chain: 2.1 mg/L
    - Pomalidomide given 2 mg on days 1 to 21, every 28 days added
    - Worsening fevers and severe bone pain/neuropathy post each infusion
    - Resolved with prednisone premedication

As the case was being presented, Mikhael questioned whether bridging occurred during the 6 lines of treatment outlined. Gregory noted that she was only able to go back to using pomalidomide (Pomalyst) plus dexamethasone. She did highlight that she had never had a patient hit a complete response and then continue to progression 9 months later, which was “unusual” to her.

The case was also unusual in that once the patient received talquetamab-tgvs (Talvey), he began to have severe fevers, which were similar to grade 1 cytokine release syndrome (CRS), and continued bone pain after every dose of talquetamab. Gregory found out that a predose of 40 mg of prednisone before talquetamab helped to mitigate those severe AEs.

Gregory asked her colleagues at what point she should de-escalate treatment to once a month, and whether she

should continue premedicating him. She hypothesized he may experience immune fatigue.

Richard has had patients who have this CRS-like response from pomalidomide treatment. Even though this occurred before she began pomalidomide, she still believes it could be an instigator. In those situations, she began to give pomalidomide at 1 mg 3 times a week to lessen these AEs.

Gregory asked what to do about steroid use and whether Richard had acquired a “sweet spot” for dosing.

“There’s just no specific way. What I do sometimes is just give a tiny dose of dexamethasone, for day 2 and day 3. Everybody’s different, right? Sometimes I’ve just tried maybe 4 mg [twice a day] of dexamethasone or a onetime [dose of] 8 mg. I have to say I don’t have a particular standard. If they have a big tumor flare each time, I might do a 10-mg onetime dose and that seems to take away the fever and the bone flare,” Richard said.

Al Hadidi asked whether Gregory’s patient was experiencing any other AEs like taste issues or skin toxicities related to CRS. Gregory responded that his skin had been fine and around cycle 4 his taste began to improve, which is typical. Of note, he has more of an appetite and is no longer losing weight.

Al Hadidi did sympathize with Gregory but noted that a once-a-month dose may help to decrease these AEs. He noted that patients who do tend to relapse on talquetamab do it regardless of the dosing frequency. He would recommend going down to once a month since there is a partial response and it could help with the low-grade CRS.

At Vanderbilt, Baljevic will try to de-escalate talquetamab and other bispecific antibodies as soon as possible. With data to back it up, he believes the patient should be switched to monthly talquetamab. He suggested exploring the use of dexamethasone to become more liberal with the premedication management.

As the case discussion concluded, Mikhael let Gregory ponder whether pomalidomide should be the correct treatment option for this patient. He did highlight there were many options in the space to choose from that might not be so impactful regarding AEs.

“In summary, this is helping us understand that although CRS in the vast majority of our patients is not something we have to think about after a few cycles, there are people, and we’ve seen this all along the way—for those of you who have enough gray hair, in the early days of rituximab [Rituxan], daratumumab [Darzalex], and others. There are some patients who continue to have that. I’m just glad you’ve been able to wean him off the tocilizumab,” Mikhael concluded. ■



**ONCOLOGY<sup>®</sup>**  
is the top-  
tier journal  
committed to  
publishing high-  
quality research  
and promoting  
the latest  
advancements  
in the field.

*Submission of  
manuscripts are free  
to anyone interested in  
being published. Submit  
your research today.*



**Submission  
Guidelines**

**Submission  
Types**



**ONCOLOGY<sup>®</sup>**  
cancer**network<sup>®</sup>**