Talquetamab in multiple myeloma

by Lawrence Liu and Amrita Krishnan

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Talquetamab in multiple myeloma

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Author Contributions: LL: Performed data search, literature review, and manuscript writing. AK: Supervision and manuscript writing and editing.


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Abstract

Initial results of the Phase 1 trial of talquetamab, a bispecific antibody targeting GPRC5D and CD3, were reported in December of 2022 for the treatment of relapsed or refractory multiple myeloma in the fourth line or later setting. It demonstrated a similar efficacy profile and durability of response to teclistamab, the first bispecific antibody therapy to be approved in multiple myeloma. Additionally, it has less infections than teclistamab but demonstrates unique class specific side effects including skin, oral, and nail-related adverse events. Despite this, it is still a highly efficacious and well-tolerated therapy that will add to the armamentarium of therapeutics against heavily pretreated multiple myeloma.

Background

Historically, relapsed or refractory multiple myeloma (RRMM) has been associated with a median overall survival of 6.6 - 8 months in penta-refractory or penta-exposed patients. The arsenal of T cell redirecting therapies like CAR T cells and bispecific antibodies represent a step forward in improving outcomes. BCMA targeting agents were the first approved including idecabtagene vilocileucel demonstrating a 73% overall response rate (ORR) and complete response (CR) or better rate of 33% and median progression free survival (mPFS) of 8.8 months in a heavily pretreated population in the original report. This was followed by ciltacabtagene autoleucel which demonstrated an impressive ORR of 97%, CR/stringent CR (sCR) rate of 67%, and mPFS that was not reached (12-month PFS was 77%) in a very similar patient population in August of 2022, the results of teclistamab trial came out demonstrating an ORR of 63% with CR/sCR of 39.4% and mPFS of 11.3 months transforming the landscape of relapsed and refractory disease. However, as we recognize that patients relapse post CART and Teclistamab with different mechanisms including mutations and deletions in the BCMA target there remains a need for new targets and new drugs.

Talquetamab is an IgG4 bispecific antibody binding to G-protein-coupled receptor class 5 member D (GPRC5D) and CD3 to recruit and activate T cells to target myeloma cells. GPRC5D is cell surface receptor that was initially discovered in highly keratinized tissue like nails and hair. Gene expression studies of MM bone marrow samples have demonstrated high levels of GPRC5D in plasma cells and the levels correspond to MM disease burden. It has been demonstrated to have low RNA expression in other tissue, like lung and inferior olivary nucleus neurons. However, actual GPRC5D protein expression in lung and inferior olivary nucleus neurons was not identified. Although a preclinical study noted low level GPRC5D RNA expression in the cerebellum, neither RNA transcript or protein expression was noted in the translational studies of the trial. Following these findings, GPRC5D has become a therapeutic target for MM via CAR T cell and bispecific antibody therapy. An initial CART targeting GPRC5D demonstrated activity in MM resistant to BCMA CART in studies of xenografts in mice. In preclinical studies, talquetamab demonstrated high cytotoxicity in bone marrow samples with MM. As such, this therapy was an ideal candidate to move forward to clinical studies.

Efficacy

Talquetamab was initially studied in the Phase I open-label MonumenTAL-1 Trial demonstrating high efficacy in a heavily pre-treated population with a median of 6 previous lines of therapy. Especially notable was that 79% of the patients were triple-class refractory and 30% were penta-refractory. In the group treated with subcutaneous talquetamab, almost a third had extramedullary disease, seventeen percent had high disease burden (60% or more bone marrow plasma cells), and sixteen percent had
high-risk cytogenetic abnormalities. This is similar to the study population for teclistamab, the first approved bispecific antibody in RRMM targeting B-cell maturation antigen (BCMA), with the exception of talquetamab having had more MM with extramedullary disease (32% versus 17%) and teclistamab with slightly more high-risk cytogenetics (25.7% versus 16%). Additionally, the talquetamab trial had higher percentage of International Staging System (ISS) class II (45% versus 35.2%) and III (19% versus 12.3%).

Talquetamab administered subcutaneously at 800 mcg/kg every two weeks (Q2W) or 405 mcg/kg weekly (QW) with step up doses demonstrated similar efficacy across both levels. At a median follow up of 12.7 months, the 0.8 mg/kg dose level had an overall response rate (ORR) 71.7% and VGPR or better rate of 60.7%: 9% with CR and 29.7% with sCR with a median duration of response of 7.8 months. At a median follow up of 18.8 months, the 0.4 mg/kg dose level achieved an ORR of 74.1% and 59.4% VGPR or better: 9.8% CR and 23.8% sCR with a median duration of response of 10.2 months. These results in patients with heavily pre-treated and very refractory disease led to the U.S. Food and Drug Administration (FDA) granting Breakthrough Therapy Designation (BTD) for talquetamab on June 29, 2022. The updated Phase 2 results reported at ASCO 2023 are very similar. Additional benefits of talquetamab were high efficacy in high risk MM and extramedullary disease which had ORR/CR/sCR of 55.6/33.3/11.1 and 40/6.7/6.7 for the 800 mcg/kg Q2W dosing respectively. These results are similar to those of teclistamab and offers another therapeutic targeting option for patients.

Of special interest is the efficacy in patients who have had prior T-cell redirection therapy such as CAR T cell therapy or other bispecific antibody (BsAb) therapy due to concern for T cell fatigue or exhaustion. The MonumenTAL-1 Phase 2 results were recently presented at ASCO 2023 demonstrating an ORR 63%, 53% with VGPR or better at median follow up of 11.8 months in patients with prior BsAb or CAR T. In this cohort, 71% had prior CAR T, 35% had prior BsAb, and 6% had both. The median progression free survival (mPFS) was 5.1 months. The results demonstrate that talquetamab retains efficacy in a population with prior T cell redirection therapies. Combination therapies with talquetamab could address this area of T cell exhaustion/fatigue. Of particular interest is whether daratumumab can help overcome T cell fatigue/exhaustion since it has demonstrated the ability to alter T cell subsets to promote expansion of effector T cells and deplete regulatory T cells. Initial results of the TRIMM-2 Phase 1b study with correlatives showing that the combination increased proinflammatory cytokines and levels of effector T cells supporting the ability of a daratumumab to overcome T cell exhaustion/fatigue when administered with a BsAb.

Talquetamab is also being studied in combination with daratumumab in the TRIMM-2 trial in patients with 3 or more prior lines of therapy, including a proteasome inhibitor (PI) and immunomodulatory drug (IMiD). The Phase 2 trial recently reported results at ASCO 2023 in a population that had a median 5 prior lines of therapy, 18% with high-risk cytogenetics, 25% with extramedullary disease, and 58% triple-class refractory (77% were refractory to anti-CD38 therapy). With a median follow up of 11.5 months, the ORR was 78% in the whole cohort (100% in patients without prior anti-CD38 therapy) with 45% CR/sCR and 66% VGPR or greater. The mPFS was 19.4 months and 12-month overall survival (OS) was 93%. Even in patients refractory to anti-CD38, anti-BCMA, and BsAb therapy, the ORR was 76%, 64%, and 75% respectively.

Beyond talquetamab, the GPRC5D target has been studied as a CART construct. Based on preclinical data from Smith et al. of a GPRC5D CART with high efficacy in BCMA CART resistant MM, Mailankody et al.
studied this CART in a Phase 1 trial and found that in patients receiving the MTD of 150x10^6 cells or lower, the response rate was 58% with a median duration of response of 7.8 months.\textsuperscript{22} Of note, this trial had a broader inclusion criteria recruiting patients suffering from MM with: history of allogeneic stem cell transplantation (18%), extramedullary disease (47%), prior BCMA-directed therapy (59%), triple class refractory status (94%), high-risk cytogenetic abnormalities (76%). Other GPRC5D CART constructs have been studied with ORR ranging from 86-100% and 60-64% CR/sCR rates.\textsuperscript{23-25} Another bispecific antibody with a two GPRC5D binding sites, RG6234, is undergoing investigation and reported ORR of 71.4% and 60.4% with CR/sCR rates of 28.5% and 18.8% for intravenous and subcutaneous administration respectively.\textsuperscript{26}

**Table 1**

**Safety and Tolerability**

All patients had AEs and Grade 3 or 4 AEs were 78%. However, there were no deaths related to talquetamab use as compared to teclistamab with 5 deaths (3%).\textsuperscript{4,16} CRS was experienced in 78% with a median duration of 2 days. None of the CRS events were Grade 3 or greater. Other common AEs were hypogammaglobulinemia, oral AEs, infections, anemia, asthenia, and skin exfoliation (all greater than 40%). Of the 63% with infections, 22% were grade 3 or 4; however, there were 2 patients (3%) with grade 5 (pneumonia) possibly related to the therapy. Neutropenia was noted in 38% with 26% reaching grade 3 or 4. Hypogammaglobulinemia was noted in 85% of patients; however, intravenous immunoglobulin supplementation was only utilized in 32% of patients.

The initial Monumental-1 Phase 1 study reported four dose-limiting toxicities: one was pancreatitis related to extramedullary disease in the pancreas and the other three were grade three rashes that resolved on stopping therapy with two of those patients able to resume therapy without recurrence of the rash. Skin AEs (largely xeroderma, pruritis, and peeling), taste issues, cytopenias, fatigue, rashes, nail issues, dry mouth, dysphagia, weight loss, fevers, diarrhea, and decreased appetite were the most common AEs across all dose levels.

Cytokine-release syndrome (CRS) was noted in around 80% of the patients receiving subcutaneous talquetamab with a median duration of 2 days. However, Grade 3 or greater CRS was rare (3% in the 405-mcg dose level and none in the 800-mcg dose level). Most of the CRS events (81.7%) occurred during the step-up doses. Recurrent CRS episodes with the step up and target doses occurred in around 30% of patients for both subcutaneous dose levels. 63% of patients in 405 mcg dose level and 54% in the 800-mcg dose level received tocilizumab. Corticosteroid administration for CRS was relatively minimal (3% at the 405-mcg dose and 7% at the 800-mcg dose). Vasopressor use occurred in one patient at the 405-mcg dose level (3.3%). One patient (3.3%) in the 405-mcg dose level and two patients (4.5%) in the 800-mcg dose level required supplemental oxygen. Overall, around half of patients in both subcutaneous dose levels required other supportive care measures for CRS including intravenous fluids and anti-pyretics.

Neurotoxicity was noted in 10% of patients receiving the 405-mcg dose and 5% of patients receiving the 800-mcg dose and were grade 1 or two and resolved. In each subcutaneous dose level, there was one event of encephalopathy occurring during the step-up doses and target dose. In the group receiving intravenous talquetamab, 3% experienced grade 3 ICANS. As such, the intravenous dose level was not pursued for the Phase 2 trial. In the phase 2 trial results, ICANS was reported at a rate of 10.7% and 11% for the 0.4 mg/kg and 0.8 mg/kg groups respectively.
Nail issues and taste changes were frequent and likely related to the expression of GPRC5D in these tissue.\textsuperscript{5,10} Nail AEs tended to occur at a median of 50.5 days with a wide range. These AEs can range from nail thinning to complete separation of the nail plate from the matrix due to disruption of growth, onychomadesis, as noted in an early case report.\textsuperscript{27} In this report, topical corticosteroids were heavily applied to the hands, feet, and skin in general due to the patient’s diffuse xerosis and pruritus but only the pruritus and xerosis resolved with the topical corticosteroids. Despite the potential for severe nail-related AEs, no discontinuations resulted from them.\textsuperscript{16} In another study, nail and skin AEs were managed with ammonium lactate cream, triamcinolone cream, and Vaseline applied twice a day.\textsuperscript{28} Grade 3 rashes resolved with oral and topical corticosteroids and treatment resumption was possible afterwards in most patients.\textsuperscript{28} Oral antihistamines can also be employed to reduce associated pruritus.\textsuperscript{29} The median time to skin toxicities was 24 days in the subcutaneous dosing group with close to half resolving at a median duration was 39 days.

Taste AEs tended to occur at a median of 13.5 days. This and other oral AEs including dysphagia, appetite loss, dry mouth can lead to significant malnutrition and weight loss. Many clinicians recommend extra vigilance for oral and esophageal candidiasis and early treatment if suspected. Other management strategies include biotin sprays and mouthwashes geared towards managing mucositis and the incorporation of thin liquids and nutritional supplement shakes to improve nutrition and caloric intake.\textsuperscript{29} Artificial saliva has been tried with limited success. Early dose and schedule adjustments seem the optimal management strategy.\textsuperscript{28}

\textbf{[Table 2]}

Infections occurred in 58.7% at the 0.4 mg/kg dose (Grade 3 or 4 in 19.6%) and 66.2% at the 0.8 mg/kg dose (Grade 3 or greater in 14.5%).\textsuperscript{16} Opportunistic infections were noted at 3.5% and 5.5% in the 0.4 mg/kg and 0.8 mg/kg dose groups respectively. Overall, the most common infections noted in real world studies were viral and bacterial.\textsuperscript{30,31} COVID-19 infection occurred in 13% at the 405 mcg dose and 2% at the 800 mcg dose. However, there were no fatalities related to COVID-19 infection with talquetamab use as compared to teclistamab use (7.3%). A recent pooled analysis demonstrated that in patients treated with BsAb, around half developed an infection and BCMA-targeting BsAbs had almost 3 times more Grade 3 or 4 infections compared to non-BCMA targeting BsAbs. Additionally, neutropenia was lower in non-BCMA BsAbs. COVID-19 infections were common although more frequent and more likely to be fatal in the BCMA-targeting BsAbs.\textsuperscript{32} Furthermore, a quarter of the deaths were attributed to infections, including COVID-19, Streptococcus pneumoniae, and influenza which further supports the need for vaccination counseling.\textsuperscript{32} Opportunistic infections like cytomegalovirus (CMV), Pneumocystis jirovecii, herpes simplex virus (HSV), varicella-zoster virus (VZV) were also reported. As such, prophylaxis with acyclovir or valacyclovir, shingles vaccination, and Bactrim is routinely employed at our institution for patients receiving bispecific antibody therapy. Hypogammaglobulinemia was reported in 87% at the 405 mcg dose and 71% at the 800 mcg dose.\textsuperscript{5} Our institution employed the practice of aggressive repletion with intravenous immunoglobulins if patients have recurrent infections or immunoglobulin levels under 400 mg/dL.

\textbf{[Table 3]}

Serious AEs (SAEs) occurred in 43% of patients receiving the 405 mcg dose and 34% of patients receiving the 800 mcg dose per the original report by Chari et al.\textsuperscript{5} In the Phase 2 update, 14.7% and 8.3% of patients had dose reductions and 4.9% and 8.3% of patients had dose discontinuations in the 0.4 mg/kg
QW and 0.8 mg/kg Q2W groups respectively.\textsuperscript{16} Despite the potential for extensive skin AEs and oral AEs, there were only five discontinuations for these events across the combined cohort including 288 patients.

**Initiation of Therapy**

Talquetamab offers the advantage of subcutaneous administration with a QW and Q2W dosing schedule depending on patient preference. At our institution, patients are admitted for the step up dosing to monitor for CRS or other complications. The 405 mcg QW dosing strategy offers the advantage of quicker arrival at target dose since it only requires two step up doses (10 and 60 mcg per kg). The 800 mcg Q2W dose requires three step up doses (10, 60, and 300 mcg) which means a longer admission to reach the target dose but with the benefit of less frequent administration and visits for the patient. Side effects, as mentioned above, are similar between both dosing strategies with the 805 mcg Q2W dosing strategy having less infections, hypogammaglobulinemia, and neurotoxicity but with slightly increased incidence of grade 3 or greater rashes.

**Managing Toxicities**

First, and foremost, talquetamab should be initiated with close monitoring in a setting with direct access to tocilizumab, critical care facilities, and capacity of neurologic evaluation and treatment.

Adverse events related to the nails can be managed with ammonium lactate cream, Vaseline, and various topical steroid ointments. Skin changes like xerosis and pruritus can be managed similarly with topical steroids and oral antihistamines for itchiness. Grade 3 rashes in the original study resolved after oral or topical corticosteroid use and talquetamab was able to be restarted in most patients with this issue.

Taste and other oral adverse events can lead to significant malnourishment and weight loss and need extra vigilance. Artificial saliva, biotin sprays and anesthetic mouthwashes can improve dry mouth, mucositis, oral cavity pain. Close monitoring for candidiasis and early treatment is necessary. It can be helpful to encourage softer diets and nutritional supplements in the form of shakes.

Infections remain a significant challenge in the field of MM immunotherapies. At our institution, acyclovir/valacyclovir and Bactrim for prophylaxis is regularly employed. Patients are encouraged to get shingles, COVID, and influenza vaccination and any other vaccines that are indicated. We regularly check immunoglobulin levels and our institution recommends intravenous immunoglobulin repletion for recurrent infections or levels below 400 mg/dL.

**Sequencing of Therapy**

The ideal time to use talquetamab in MM is a challenging question to answer. It can depend on many factors including, but not limited to, prior therapies (especially BCMA-directed ones), speed of progression, and institutional time from leukapheresis to CART administration. It has utility in post-BCMA CART relapse as a quick off-the-shelf option to get disease control while using a different target. Additionally, it could be utilized as a bridge to BCMA CART in rapid progressors or MM with high disease burden. In patients with frequent or chronic infections, this may present a therapeutic option with less suppression of humoral immunity compared to the BCMA-directed therapies. A major consideration is
the potential for T cell fatigue related to chronic antigenic stimulation from bispecific antibody therapies which can provide a rationale not to use it before CAR T cell therapy leukapheresis.

**Combination therapies with talquetamab**

Furthermore, preclinical studies have demonstrated mechanisms of antigen escape from BCMA and GPRC5D directed immunotherapy involving mutational changes in the proteins leading to disruption of bispecific or CART binding to the epitope. Preclinical studies of bispecific CART constructs targeting BCMA and GPRC5D demonstrated higher survival than CARTs directed to either target alone. This suggests that the simultaneous targeting of BCMA and GPRC5D or other targets may lead to improved efficacy whether it be via immunotherapies with two targets or combination therapies.

In addition to the previously mentioned TRIMM-2 study evaluating the daratumumab/teclistamab and daratumumab/talquetamab combinations in RRMM, there are many other studies evaluating combination therapies to improve on the efficacy of talquetamab. These combinations span the range of different lines of therapy to elucidate the best combination with talquetamab and inform the sequencing of therapy.

**[Table 4]**

**Conclusion**

Talquetamab represents yet another T cell redirection option for patients with RRMM. Future trials are ongoing to answer the question of optimal sequencing of these T cell redirecting therapies as well as optimal combinations.
References


### Table 1

<table>
<thead>
<tr>
<th>BsAb</th>
<th>Phase</th>
<th>Acronym (NCT number)</th>
<th>Target</th>
<th>Minimum prior lines of therapy (median)</th>
<th>Median follow up time (months)</th>
<th>Administration</th>
<th>ORR (%)</th>
<th>CR/sCR rate (%)</th>
<th>mDOR</th>
<th>mPFS</th>
<th>mOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Talquetamab (SC: 405 mcg QW)(^{16})</td>
<td>2</td>
<td>MonumenTAL-1 (NCT03399799)</td>
<td>GPR C5D</td>
<td>2 (6)</td>
<td>18.8</td>
<td>SC</td>
<td>74</td>
<td>33.6</td>
<td>9.5</td>
<td>7.5</td>
<td>76.4%</td>
</tr>
<tr>
<td>Talquetamab (SC: 800 mcg Q2W)(^{16})</td>
<td></td>
<td></td>
<td></td>
<td>2 (5)</td>
<td>12.7</td>
<td>SC</td>
<td>73</td>
<td>38.7</td>
<td>NR</td>
<td>11.9</td>
<td>77.4%</td>
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<td></td>
<td></td>
<td>2 (6)</td>
<td>10.2</td>
<td>IV</td>
<td>72</td>
<td>72.2</td>
<td>27.8</td>
<td></td>
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<td>Tecristamab(^{4})</td>
<td>1-2</td>
<td>MajesTEC-1 (NCT03145181 / NCT04557098)</td>
<td>BCM A</td>
<td>4 (5)</td>
<td>14.1</td>
<td>SC</td>
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<td>65</td>
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<td>11.3</td>
<td>18.3</td>
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<td>MagnetisMM (NCT03269136 / NCT04649359 / NCT05014412)</td>
<td>BCM A</td>
<td>2 (7)</td>
<td>10.3</td>
<td>SC</td>
<td>45</td>
<td>17.4</td>
<td>NR</td>
<td>18.4</td>
<td>NR</td>
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<td>NCT03275103</td>
<td>FcRH 5</td>
<td>2 (6)</td>
<td>6.1</td>
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<td>100</td>
<td>62.5</td>
<td>50% had DOR ≥ 6 months</td>
<td>NA</td>
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*These results were from the pooled results of MM-1, MM-3, and MM-9 which included patients in the initial dose finding and safety study and later patients who received the subcutaneous 76 mg weekly dose. Additionally, all patients had prior BCMA-targeting therapy.\(^{36}\)

Abbreviations: BsAb, bispecific antibody; NCT, national clinical trial; ORR, overall response rate; CR, complete response; sCR, stringent complete response; mDOR, median duration of response; mPFS, median progression free survival; mOS, median overall survival; SC, subcutaneous; GPRC5D, G-protein coupled receptor, class C, group 5 member D; BCMA, B-cell maturation antigen; FcRH5, Fc receptor-homolog-5; QW, weekly; Q2W, every 2 weeks; NR, not reached; NA, not available.
### Table 2

<table>
<thead>
<tr>
<th>BsAb</th>
<th>Grade 3 or 4 AE (%)</th>
<th>Anemia Grade ≥ 3 (%)</th>
<th>Neutropenia Grade ≥ 3 (%)</th>
<th>Lymphopenia Grade ≥ 3 (%)</th>
<th>Thrombocytopenia Grade ≥ 3 (%)</th>
<th>CRS Any Grade ≥ 3 (%)</th>
<th>ICA NS Any Grade ≥ 3 (%)</th>
<th>Grade 5 AE (%)</th>
<th>Dysgeusia (%)</th>
<th>Skin-related (%)</th>
<th>Nail-related (%)</th>
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<td>87</td>
<td>30</td>
<td>60</td>
<td>40</td>
<td>23</td>
<td>77</td>
<td>3</td>
<td>10*</td>
<td>0</td>
<td>63</td>
<td>67</td>
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<tr>
<td>Talquetamab 800 µg</td>
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<td>23</td>
<td>32</td>
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<td>5*</td>
<td>0</td>
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<td>80</td>
<td>1.3</td>
<td>13</td>
<td>15</td>
<td>15 (0.6)</td>
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*In the Phase 2 trial update at ASCO, these were reported at 10.7% and 11% for the 0.4 mg/kg SQ QW and 0.8 mg/kg SQ Q2W dosing respectively.*

Abbreviations: BsAb, bispecific antibody; CRS, cytokine release syndrome; ICANS, immune effector cell associated neurotoxicity syndrome; IV, intravenous, NA, not available.
<table>
<thead>
<tr>
<th>BsAb</th>
<th>Infections (%)</th>
<th>Infections Grade ≥ 3 (%)</th>
<th>Hypogammaglobulinemia (%)</th>
<th>COVID-19 (%)</th>
<th>CMV (%)</th>
<th>PJP (%)</th>
<th>PML (%)</th>
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<td>71</td>
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<td>0</td>
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Abbreviations: CMV, cytomegalovirus; PJP, Pneumocystis jirovecii; PML, progressive multifocal leukoencephalopathy; IV, intravenous; NA, not available.
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<thead>
<tr>
<th>Clinical Trial Identifier (phase)</th>
<th>Acronym</th>
<th>Combination</th>
<th>Minimum prior lines of therapy</th>
<th>Primary Outcome</th>
<th>Start Date</th>
<th>Primary Completion Date</th>
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</thead>
<tbody>
<tr>
<td>NCT05455320</td>
<td>MonumentAL-3</td>
<td>Talq/Dara vs Talq/Dara/Pom vs DPd</td>
<td>1</td>
<td>PFS</td>
<td>10/13/2022</td>
<td>2/6/2026</td>
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<tr>
<td>NCT04586426</td>
<td>RedirectT-1</td>
<td>Talq/Tec with or without Dara</td>
<td>Triple class exposed</td>
<td>Toxicity</td>
<td>12/15/2020</td>
<td>6/27/2025</td>
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<tr>
<td>NCT05050097</td>
<td>MonumentAL-2</td>
<td>Combination with Talq, CFZ, Dara, Len, Pom</td>
<td>Not specified</td>
<td>Toxicity</td>
<td>9/22/2021</td>
<td>9/30/2024</td>
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<tr>
<td>NCT05552222</td>
<td>MajesTEC-7</td>
<td>Tec/Dara/Len vs Talq/Dara/Len vs DRd</td>
<td>NDMM</td>
<td>PFS and sustained MRD-negative CR</td>
<td>10/25/2022</td>
<td>5/25/2029</td>
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<tr>
<td>NCT05338775</td>
<td>TRIMM-3</td>
<td>Talq or Tec with PD-1 inhibitor</td>
<td>RRMM*</td>
<td>Toxicity</td>
<td>5/25/2022</td>
<td>9/21/2024</td>
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<tr>
<td>NCT05849610</td>
<td>GEM-TECTAL</td>
<td>DararVRd followed by Tec/Dara or Talq/Dara***</td>
<td>NDMM*</td>
<td>MRD negative CR rate</td>
<td>5/2023</td>
<td>1/2025</td>
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<tr>
<td>NCT04108195</td>
<td>NA</td>
<td>Dara/Talq/Tec/Pom</td>
<td>3</td>
<td>Toxicity</td>
<td>2/21/2020</td>
<td>9/9/2024</td>
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</tbody>
</table>

*Cannot be a candidate for an available therapy.
**High risk MM only.
***After DararVRd, patients will receive intensification with Tec/Dara. If MRD negative after, patients will receive Tec/Dara for 2 years. MRD positive patients or those who become MRD positive or relapse in the Tec/Dara arm will receive Talq/Dara for 6 cycles. If MRD negative after, patients will receive Talq/Dara for 2 years as maintenance and if MRD positive, they will receive salvage therapy per investigator choice.

Abbreviations: NCT, national clinical trial; Talq, talquetamab; Dara, daratumumab; Pom, pomalidomide; DPd, daratumumab/pomalidomide/dexamethasone; PFS, progression free survival; CFZ, carfilzomib; Len, lenalidomide; DRd, daratumumab/lenalidomide/dexamethasone; NDMM, newly diagnosed multiple myeloma; RRMM, relapsed/refractory multiple myeloma; DararVRd, daratumumab/bortezomib/lenalidomide/dexamethasone; MRD, measurable residual disease; CR, complete response; Tec, teclistamab; NA, not available.