Poster
MM-382

iMMagine-3: A Global Phase 3, Randomized Study to Compare the Efficacy and Safety of Anitocabtagene Autoleucel Versus Standard of Care in Patients With Relapsed/Refractory Multiple Myeloma

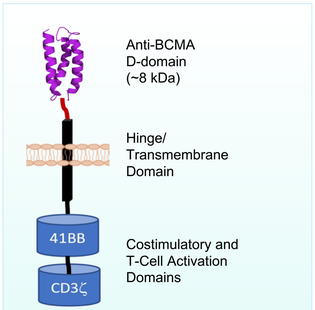
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BACKGROUND

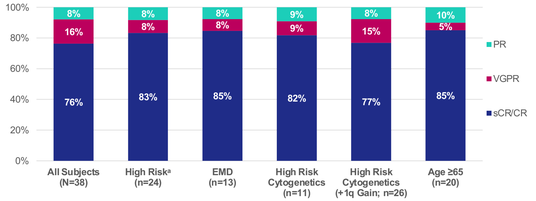
- Despite the addition of new treatment options, relapsed/refractory multiple myeloma (RRMM) remains incurable, and outcomes worsen with subsequent lines of therapy[1]
- Anitocabtagene autoleucel (anito-cel, formerly CART-ddBCMA) is an autologous anti–B-cell maturation antigen (BCMA) chimeric antigen receptor (CAR) T-cell therapy with a small non–antibody-derived synthetic protein D-Domain binder (**Figure 1**)[2]
- The D-Domain's small size (8kDa) facilitates high T-cell transduction and CAR expression, resulting in more CAR positive cells and more CARs expressed per T cell with a low total T-cell dose[2]

Figure 1. Anito-Cel CAR Structure[2,3]



Anito-cel, anitocabtagene autoleucel; BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor.

Figure 2. Best Overall Responses in Phase 1 Study of Anito-cel in Patients With RRMM[3]



Data cut-off: October 15, 2023. [a] High risk defined as a patient with EMD, ISS Stage III (B2M ≥5.5), or BMPC ≥ 60%. Anito-cel, anitocabtagene autoleucel; BMPC, bone marrow plasma-cell; CR, complete response; EMD, extramedullary disease; ISS, international staging system; PR, partial response; RRMM, relapsed/refractory multiple myeloma; sCR, stringent complete response; VGPR, very good partial response.

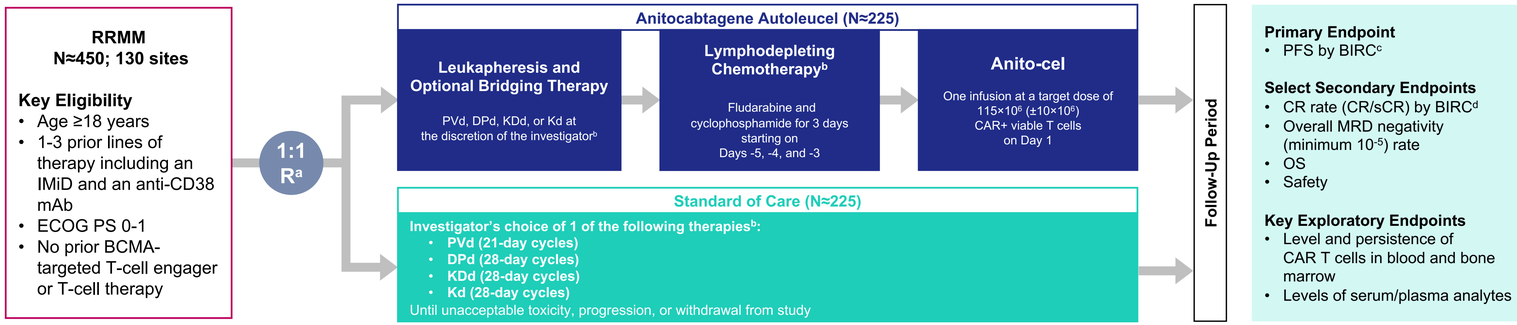
- In a first-in-human, Phase 1 dose escalation and expansion study of anito-cel in 38 patients with RRMM who had ≥3 prior lines of therapy[3,4]
  - The overall response rate (ORR) was 100% including a 76% complete response (CR)/stringent CR (sCR) rate (**Figure 2**)
  - With median follow-up of 26.5 months (range, 14-44), median progression-free survival (PFS) and overall survival (OS) were not reached, and the estimated 24-month PFS rate was 56%
  - At a dose of 100×10^6 CAR+ T cells (n=32), no patient had Grade ≥3 cytokine release syndrome, 1 patient had Grade 3 immune effector cell-associated neurotoxicity syndrome, and there were no delayed neurotoxicities
- An ongoing Phase 2 study, iMMagine-1, is investigating anito-cel (115 [±10] ×10^6 CAR+ cells) in patients with RRMM who had ≥3 prior therapies including a proteasome inhibitor, an immunomodulatory drug (IMiD®), and an anti-CD38 monoclonal antibody (mAb; NCT05396885)
- iMMagine-3 is a global, randomized, open-label, Phase 3 study to compare the efficacy and safety of anito-cel versus standard-of-care (SOC) therapy in patients with RRMM who received 1-3 prior lines of therapy including an IMiD and an anti-CD38 mAb (NCT06413498)

OBJECTIVES

- The primary objective is to compare the efficacy of anito-cel versus SOC therapy in patients with RRMM as measured by PFS per blinded independent review committee

STUDY DESIGN AND ENDPOINTS

Figure 3. Global Phase 3 iMMagine-3 Study Design



Primary Endpoint
- PFS by BIRC[c]

Select Secondary Endpoints
- CR rate (CR/sCR) by BIRC[d]
- Overall MRD negativity (minimum 10^{-5}) rate
- OS
- Safety

Key Exploratory Endpoints
- Level and persistence of CAR T cells in blood and bone marrow
- Levels of serum/plasma analytes

[a] Prior to randomization, the investigator will select one SOC regimen that will be used as treatment if the patient is randomized to the SOC arm or may be used as optional bridging therapy if the patient is randomized to the anito-cel arm. [b] Lymphodepleting therapy to include fludarabine (30 mg/m^2/day) and cyclophosphamide (300 mg/m^2/day) for 3 days starting on Days -5, -4, and -3. [c] Defined as the time from randomization to disease progression per the 2016 IMWG criteria, or death due to any cause, whichever occurs first.[5,c] Per the 2016 IMWG criteria.[5]
Anito-cel, anitocabtagene autoleucel; BCMA, B-cell maturation antigen; BIRC, blinded independent review committee; CAR, chimeric antigen receptor; CR, complete response; DPd, daratumumab, pomalidomide, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; Kd, carfilzomib and dexamethasone; KDd, carfilzomib, daratumumab, and dexamethasone; mAb, monoclonal antibody; MRD, minimal residual disease; OS, overall survival; PVd, pomalidomide, bortezomib, and dexamethasone; R, randomized; RRMM, relapsed/refractory multiple myeloma; sCR, stringent CR; SOC, standard of care.

PATIENT ELIGIBILITY

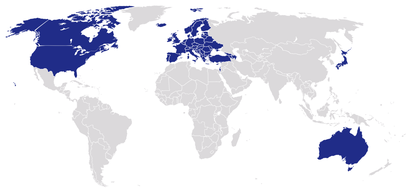
Table 1. iMMagine-3 Key Inclusion and Exclusion Criteria

Key Inclusion Criteria	Key Exclusion Criteria
• Age ≥18 years • MM with documented PD per IMWG criteria[5] on or within 12 months of the last dose of the last regimen • Received 1-3 prior lines of therapy, including an IMiD and an anti-CD38 mAb (≥2 cycles each)[a] • Measurable disease at screening per IMWG[4b] • Candidate to receive at least 1 of the 4 SOC therapy regimens (PVd, DPd, KDd, or Kd) as determined by the investigator	• Prior BCMA-targeted therapy, T-cell engager therapy, CAR T-cell therapy or other genetically modified T-cell therapy • Prior allogeneic SCT at anytime or prior autologous SCT within 12 weeks before randomization • Active or prior history of CNS or meningeal involvement of MM • Active non-MM malignancy requiring treatment within last 24 months • MDS even without ongoing treatment is not permitted

[a] Including an IMiD and an anti-CD38 mAb (≥ 2 cycles of each in any prior line is required; the IMiD and anti-CD38 mAb do not need to be from the same regimen). [b] Measurable disease defined as serum M-protein level ≥0.5 g/dL or urine M-protein level ≥200 mg/24 hours; or light chain MM without measurable disease in the serum or urine: serum-free light chain ≥10 mg/dL and abnormal serum-free light chain ratio.
BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; CNS, central nervous system; DPd, daratumumab, pomalidomide, and dexamethasone; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; Kd, carfilzomib and dexamethasone; KDd, carfilzomib, daratumumab, and dexamethasone; mAb, monoclonal antibody; MDS, myelodysplastic syndrome; MM, multiple myeloma; PD, progressive disease; PVd, pomalidomide, bortezomib, and dexamethasone; SCT, stem cell transplantation.

STATUS

Figure 4. Map of Global iMMagine-3 Clinical Trial Sites



- The iMMagine-3 study start is expected in 2024 at ~130 study sites across North America, Europe, and rest of world

REGISTRATION

- This study is registered at ClinicalTrials.gov (NCT06413498)

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- This trial-in-progress abstract was previously accepted for publication only at the 2024 European Hematology Association Annual Meeting[6]

DISCLOSURES

- **TM:** consulting for Pfizer and GlaxoSmithKline and research funding from Bristol Myers Squibb, Janssen and Sanofi
- Full author disclosure information is available through the Quick Response (QR) code

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