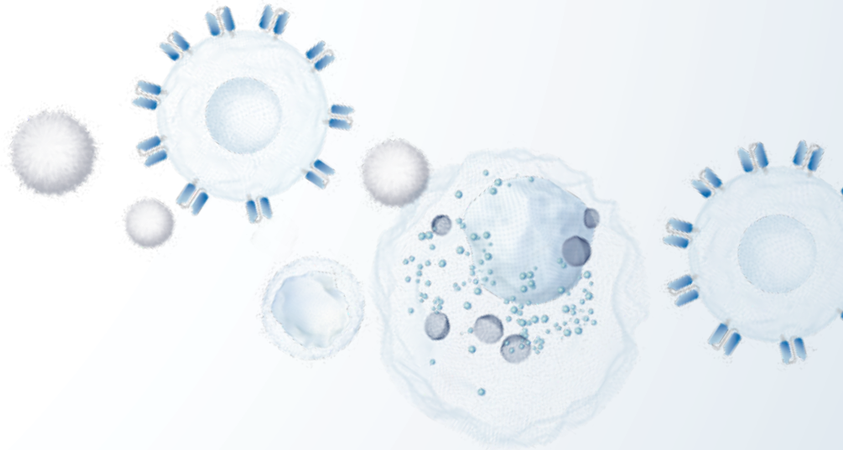
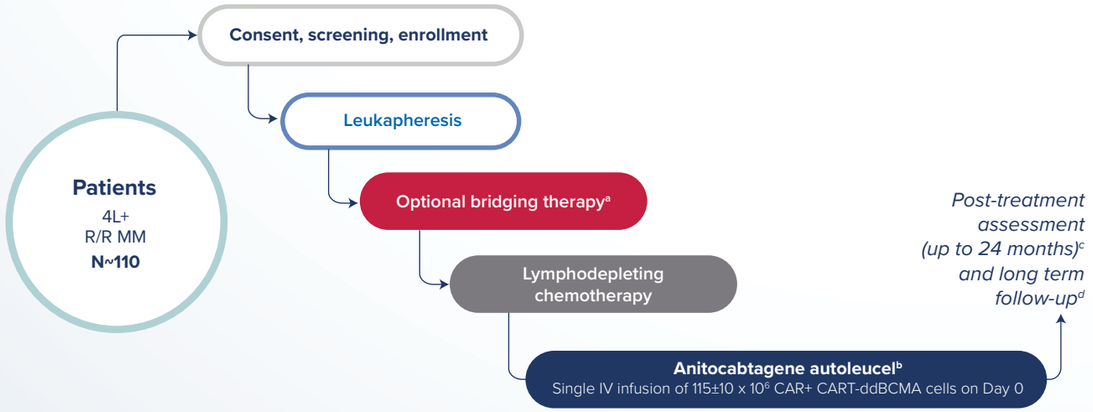
ClinicalTrials.gov Identifier: NCT05396885

iMMagine-1: A Phase 2, Multicenter Study Evaluating the Safety and Efficacy of Anitocabtagene Autoleucel (CART-ddBCMA) in Participants with Relapsed or Refractory Multiple Myeloma



Study Design[1,2]



[a]If necessary, bridging therapy is allowed to control growth of MM disease while CART-ddBCMA is being manufactured.
[b]CART-ddBCMA drug product consists of autologous T cells that have been genetically modified ex vivo to express a D-domain Chimeric Antigen Receptor (CAR), followed by a cluster of differentiation 8 (CD8) hinge and transmembrane region that is fused to the intracellular signaling domains for 4-1BB and CD3ξ, that specifically recognizes B-cell maturation antigen (BCMA). The active substance of CART-ddBCMA is CAR+ CD3+ T cells that have undergone ex vivo T-cell activation, gene transfer by replication-deficient lentiviral vector, and expansion.
[c]Following a single infusion of CART-ddBCMA both safety and efficacy data will be assessed. Efficacy will be assessed monthly for the first 6 months, then quarterly up to study completion, or upon patient relapse.
[d]Long-term safety data will be collected under a separate long-term follow up study for up to 15 years per health authority guidelines.

4L, fourth line; BCMA, B cell maturation antigen; CAR, chimeric antigen receptor; IV, intravenous; MM, mulitple myeloma; R/R, relapsed or refractory.

Endpoints[1,2]

Primary Endpoint

- ORR, per IMWG criteria as assessed by IRC

Secondary Endpoints

- sCR or CR rate, per IMWG criteria as assessed by IRC
- ORR in patients limited to 3 prior LOT, per IMWG criteria as assessed by IRC
- Duration of response
- VGPR and PR rate
- Time to initial response
- PFS
- OS
- Safety profile of anitocabtagene autoleucel
- PK of anitocabtagene autoleucel
- HRQoL
- Anti-CART-ddBCMA antibodies
- MRD negativity
- Time to progression

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CR, complete response; HRQoL, health-related quality of life; IMWG, International Myeloma Working Group; IRC, independent review committee; LOT, line of therapy; MRD, minimal residual disease; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.

The safety and efficacy of these investigational agents have not been established, and they have not received marketing authorization in this setting. There is no guarantee that these investigational agents and/or uses will receive Health Authority approval and/or become commercially available.

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Key Eligibility Criteria[1,2,a]

Key Inclusion Criteria

- 18 years and older
- Relapsed or refractory multiple myeloma with ≥3 prior regimens of systemic therapy including a PI, iMiD®, and anti-CD38 antibody refractory to last line of therapy. For each line, 2 consecutive cycles are required unless best response after 1 cycle was PD
  - Note: IMWG criteria define refractory disease as disease progression on or within 60 days of a therapy
  - Note: Induction treatment with or without hematopoietic stem cell transplant and with or without maintenance is considered a single regimen
- Documented measurable disease including at least one or more of the following criteria:
  - Serum M-protein ≥1 g/dL
  - Urine M-protein ≥200 mg/24 hours
  - Involved serum free light chain ≥10 mg/dL with abnormal κ/λ ratio (ie, >4:1 or <1:2)
- ECOG PS 0-1
- Adequate bone marrow, renal, hepatic, pulmonary, and cardiac function
- Resolution of AEs from any prior systemic anticancer therapy, radiotherapy, or surgery to grade 1 or baseline (except grade 2 alopecia and grade 2 sensory neuropathy)
- Life expectancy >12 weeks
- Male and female participants of childbearing potential must agree to use highly effective methods of birth control through 12 months after the dose of study treatment
- Willing to comply with and able to tolerate study procedures, including consent to participate in separate Long-term Safety Follow-up lasting up to 15 years per FDA guidance
- Subject's leukapheresis product from non-mobilized cells is received and accepted for cell processing by manufacturing site.
  - NOTE: Leukapheresis will be performed only after all other eligibility criteria are confirmed

[a]Other protocol defined Inclusion/Exclusion criteria may apply.

AE, adverse event; CD, cluster of differentiation; ECOG PS, Eastern Cooperative Oncology Group performance status; FDA, The Food and Drug Administration; IMiD®, immunomodulatory drug; IMWG, International Myeloma Working Group; PD, progressive disease; PI, proteasome inhibitor.

Key Eligibility Criteria (cont'd)

Key Exclusion Criteria

- Plasma cell leukemia or history of plasma cell leukemia
- Any of the following prior therapies:
  - Systemic treatment for multiple myeloma or high-dose systemic steroid therapy within the 14 days prior to leukapheresis
  - Gene therapy or gene-modified cellular immune therapy
  - BCMA-directed therapy
  - Autologous stem cell transplant within 3 months prior to leukapheresis
  - Allogeneic stem cell transplant
- Solitary plasmacytomas without evidence of other measurable disease
- Active CNS involvement by malignancy or any sign of active or prior CNS pathology[a]
- History of allergy or hypersensitivity to study drug components
- Contraindication to fludarabine or cyclophosphamide
- Active malignancy not related to myeloma that has required therapy in the last 3 years or is not in complete remission[b]
- Active hepatitis B or C infection at the time of screening,[c] or HIV seropositive
- Severe or uncontrolled intercurrent illness or laboratory abnormalities[d]
- Any significant medical condition, laboratory abnormality, or psychiatric illness that would prevent the subject from participating in study (or full access to medical records) as written including follow-up, the interpretation of data, or place the subject at unacceptable risk
- Any vaccine ≤6 weeks before leukapheresis and/or anticipation of the need for such a vaccine during subject's participation in the study

[a]Including but not limited to history of epilepsy, seizure, paresis, aphasia, stroke, subarachnoid hemorrhage or CNS bleed, severe brain injury, dementia, cerebellar disease, Parkinson's disease, organic brain syndrome or psychosis. [b]Exceptions to this criterion include successfully treated nonmetastatic basal cell or squamous cell skin carcinoma, or prostate cancer that does not require therapy. [c]Subjects with history of treated hepatitis B or C and have nondetectable viral DNA are eligible. [d]Including but not limited to active infection, symptomatic CHF, other cardiac disease (unstable angina, arrhythmia, or MI within 6 months prior to screening), significant pulmonary dysfunction, uncontrolled thromboembolic events or recent severe hemorrhage within 1 year, PE within 12 months or DVT within 3 months of enrollment, autoimmune disease requiring immunosuppressive therapy within the last 24 months.

BCMA, B-cell maturation antigen; CHF, congestive heart failure; CNS, central nervous system; DNA, deoxyribonucleic acid; DVT, deep vein thrombosis; HIV, human immunodeficiency virus; MI, myocardial infarction; PE, pulmonary embolism.

References

1. Clinicaltrials.gov website. Accessed February 27, 2024. https://www.clinicaltrials.gov/ct2/show/NCT05396885
2. Data on file. Gilead Sciences, Inc.; 2022.

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