MM-1157

Trial in progress: QUINTESSENTIAL—a phase 2 study of arlocabtagene autoleucel (arlo-cel) in patients with relapsed and refractory multiple myeloma (RRMM)

Krina Patel,[1] Sarah M Larson,[2] Omar Nadeem,[3] Nikhil Munshi,[3] Shinsuke Iida,[4] Sham Mailankody,[5] Paola Neri,[6,7] Tara Gregory,[8,9] Julia Piasecki,[10] Safiyyah Ziyad,[10] Hongxiang Hu,[10] Svenja Groeneveld,[10] Sarah Johnston,[10] Tim Pulham,[10] Sandy W Wong,[10] Jaclyn Davis,[10] Susan Bal,[11] Anupama Kumar,[12] Ciara L Freeman[13]

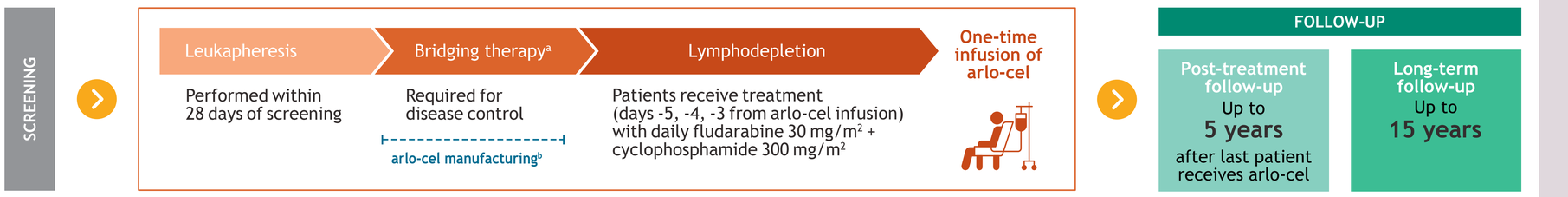
[1]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Division of Hematology-Oncology, UCLA School of Medicine, Los Angeles, CA, USA; [3]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA; [4]Nagoya City University Institute of Medical and Pharmaceutical Sciences, Nagoya, Japan; [5]Myeloma Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [6]Arnie Charbonneau Cancer Research Institute, University of Calgary, Calgary, Alberta, Canada; [7]Arthur J.E. Child Comprehensive Cancer Centre, Department of Hematology and Oncology, Calgary, Alberta, Canada; [8]Colorado Blood Cancer Institute, Denver, CO, USA; [9]Sarah Cannon Transplant and Cellular Therapy Program at Presbyterian/St Luke's Medical Center, Denver, CO, USA; [10]Bristol Myers Squibb, Princeton, NJ, USA; [11]University of Alabama at Birmingham, Birmingham, AL, USA; [12]UCSF Helen Diller Medical Center, San Francisco, CA, USA; [13]Moffitt Cancer Center, Tampa, FL, USA

The QUINTESSENTIAL study (NCT06297226) is investigating efficacy and safety of arlo-cel, a GPRC5D-directed CAR T-cell therapy in RRMM, an approach that offers a novel mechanism of action and requires only 1 infusion

STUDY SNAPSHOT

- **Phase 2** Ongoing trial
- **RRMM** N ~ 175 (planned)
- **Open label, single-arm**
- **Multicenter** ~47 sites in 3 countries

Figure 1. Study design overview



[a]Bridging therapy (mandatory) excludes experimental therapy, GPRC5D-directed agents, or T-cell engagers; treatment must be discontinued ≥ 7 days prior to initiation of lymphodepletion, except corticosteroids (discontinued ≥ 72 hours prior); [b]Once arlo-cel is manufactured and available to the treatment center, the patient will undergo pretreatment evaluation to ensure they remain eligible to receive lymphodepletion and arlo-cel infusion.

arlo-cel, arlocabtagene autoleucel; CAR, chimeric antigen receptor; GPRC5D, G protein-coupled receptor class C group 5 member D; RRMM, relapsed and refractory multiple myeloma.

Background

- Despite advances in the management of multiple myeloma (MM), most patients relapse and become refractory to available treatments and continue to progress[1]
- Limited treatment options exist for patients with relapsed and refractory (RR) MM who have been exposed to 3 or more drug classes, including immunomodulatory drugs (IMiDs), proteasome inhibitors (PIs), anti-CD38 monoclonal antibodies, and B-cell maturation antigen (BCMA)-targeted therapy[2,3]
- To address this unmet therapeutic need, new treatment options with alternative targets and mechanisms of actions are needed for late-line populations, which are growing as more patients become quadruple-class exposed (QCEx) following the use of anti-BCMA therapy in earlier lines[4,5]
- G protein-coupled receptor class C group 5 member D (GPRC5D) is an orphan receptor expressed on plasma cells, with limited expression in healthy tissues, making it a promising therapeutic target for MM[6]
- Arlocabtagene autoleucel (arlo-cel; BMS-986393) is a potential first-in-class autologous chimeric antigen receptor (CAR) T-cell therapy targeting GPRC5D (**Figure 2**)
- Data from an ongoing phase 1 first-in-human study (NCT04674813) suggested that arlo-cel is safe and efficacious in patients with heavily pretreated RRMM, including patients who received prior BCMA-targeted therapy[7]
  - Overall response rate (ORR) was 91% (21/23) and complete response rate (CRR) was 48% (11/23) following a single infusion of arlo-cel (150 × 10^6 CAR T-cells)
  - Median progression-free survival (PFS) was 18.3 months (95% CI, 11.8–21.9) for efficacy-evaluable patients treated with arlo-cel (n = 79)
- Here, we present the design of the phase 2 QUINTESSENTIAL study

Figure 2. Mechanism of action of arlo-cel, a CAR T-cell therapy targeting GPRC5D[8,9]

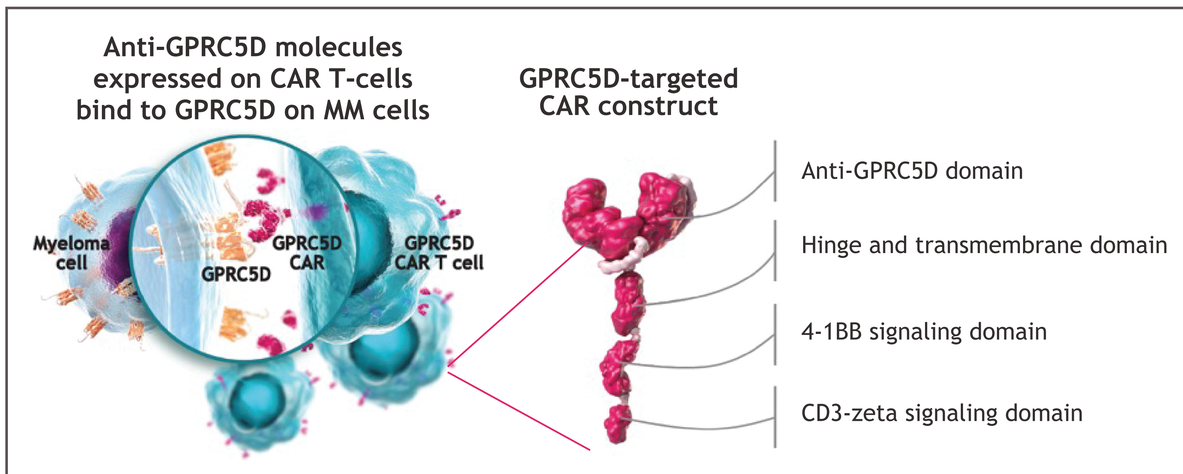


Figure previously presented by Bal S, et al 2023 ASH Annual Meeting.[8]
arlo-cel, arlocabtagene autoleucel; CAR, chimeric antigen receptor; GPRC5D, G protein-coupled receptor class C group 5 member D; MM, multiple myeloma.

Study design

- QUINTESSENTIAL (NCT06297226) is an open-label, single-arm, multicenter, phase 2 study evaluating efficacy and safety of arlo-cel in patients with RRMM
- Following screening, eligible patients will undergo leukapheresis, mandatory bridging therapy during arlo-cel manufacturing, and lymphodepletion prior to the one-time infusion of arlo-cel (**Figure 1**)
- Patients will be followed for ≤ 5 years after the last patient receives arlo-cel, with a subsequent long-term follow-up study (≤ 15 years after infusion; **Figure 1**)

Population

- Adult patients with ≥ 3 classes of MM treatment (including IMiDs, PIs, and anti-CD38 antibody) and ≥ 3 prior lines of therapy are eligible for the study (**Figure 3**)

Figure 3. Key eligibility criteria

INCLUSION CRITERIA
- Men and women ≥ 18 years of age
- Documented diagnosis of MM per IMWG criteria
- Received ≥ 3 classes of MM treatment, including IMiD, PI, and anti-CD38 antibody
- Received ≥ 3 prior lines of therapy
- Documented disease progression during or after their last anti-myeloma regimen, per IMWG criteria
- Measurable disease during screening
- ECOG performance status 0 or 1

EXCLUSION CRITERIA
- Active or history of central nervous system involvement with MM
- Active systemic fungal, bacterial, viral, or other infection despite appropriate anti-infective treatment at the time of leukapheresis
- Received any prior GPRC5D-directed therapy or other prior MM treatment without the required washout prior to leukapheresis

ECOG, Eastern Cooperative Oncology Group; GPRC5D; G protein-coupled receptor class C group 5 member D; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; MM, multiple myeloma; PI, proteasome inhibitor.

Study endpoints

- Study endpoints are detailed in **Figure 4**

Figure 4. Study endpoints

PRIMARY ENDPOINT
Best overall response (BOR) of partial response (PR) or better[a] in QCEx patients with≥ 4 prior lines of therapy

SECONDARY ENDPOINTS

KEY
- BOR of PR or better[a] in TCEx patients with ≥ 3 prior lines of therapy
- BOR of complete response (CR)[b] in TCEx and QCEx patients with ≥ 3 prior lines of therapy

OTHER
- Minimal residual disease (MRD)-negative status at any time regardless of response
- Time to response (TTR)[a,c,d]
- Duration of response (DOR)[a,c,e]
- Progression-free survival (PFS)[a,c,f]
- Overall response rate (ORR)[c]
- CR rate[c]
- Overall survival (OS)[g]
- Pharmacokinetics
- Patient-reported quality of life outcomes (EORTC QLQ-C30 and -MY20)
- Healthcare resource utilization (HCRU)[h]

[a]According to IMWG Response Criteria as assessed by an IRC; [b]Including stringent CR; [c]According to IMWG Response Criteria as assessed by the Investigator; [d]Defined as time from arlo-cel infusion to first documentation of response of PR or better; [e]Defined as time from first documentation of response of PR or better to first documentation of disease progression or death due to any cause, whichever occurs first; [f]Defined as time from arlo-cel infusion to first documentation of PD or death due to any cause, whichever occurs first; [g]Defined as time from arlo-cel infusion to time of death due to any cause; [h]Frequency of events from enrollment through treatment and posttreatment follow-up, including any non-protocol doctor's office visit, emergency room visit, hospitalization, etc for study drug-related toxicities or disease-related events.
C30, Core30; EORTC QLQ, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; IMWG, International Myeloma Working Group; IRC, independent review committee; PD, progressive disease; MY20, multiple myeloma module; TCEx, triple-class exposed; QCEx, quad-class exposed.

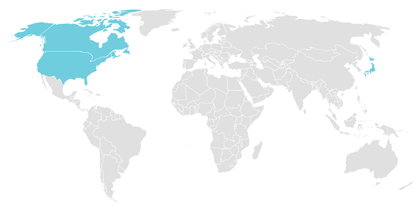
Enrollment

- The study is currently recruiting, with an estimated enrollment of 175 patients
- This study will recruit at ~47 centers across the USA, Canada, and Japan (**Figure 5**)

Figure 5. Planned enrollment

QUINTESSENTIAL

Study start date (first patient first visit): March 21, 2024
Estimated primary analysis completion date: Q1 2027
Estimated study completion date: June 30, 2032
Estimated enrollment:175



Approximately 47 sites in 3 countries

References

1. Rajkumar SV. *Am J Hematol*. 2024;99(9):1802-1824.
2. Dhanasiri S, et al. *Clin Ther*. 2021;43(11):1983-1996.e3.
3. Mailankody S, et al. *N Engl J Med*. 2022;387(13):1196-1206.
4. Kumar SK, et al. *J Natl Compr Canc Netw*. 2023;21(12):1281-1301.
5. Ahmed A, Killeen RB. *StatPearls: Relapsed and Refractory Multiple Myeloma*. 2025.
6. Rodriguez-Otero P, et al. *Blood Cancer J*. 2024;14(1):24.
7. Bal S, et al. Oral presentation at the American Society of Hematology (ASH) Annual Meeting; December 7-10, 2024; San Diego, CA. Abstract 922.
8. Bal S, et al. Oral presentation at the American Society of Hematology (ASH) Annual Meeting; December 9-12, 2023; San Diego, CA. Abstract 219.
9. Smith EL, et al. *Sci Transl Med*. 2019;11(485):eaau7746.

Acknowledgments

- We would like to thank the patients, their families, and the clinical study teams who will participate in the study
- This study is sponsored by Bristol Myers Squibb
- All authors contributed to and approved the presentation; medical writing support was provided by Alexandra L. Thomas, PhD, from Citrus Health Group, Inc. (Chicago, Illinois) and was funded by Bristol Myers Squibb

Scientific Content on Demand

To request a copy of this poster:

SCAN ME

QR codes are valid for 90 days after the congress presentation date.

Presented at the 2025 Society of Hematologic Oncology (SOHO) Annual Meeting; September 3-6; Houston, Texas

Email: KPatel1@mdanderson.org

Copies of this poster obtained through Quick Response (QR) Code are for personal use only and may not be reproduced without permission from the author of this poster.