Trial in progress: QUINTESSENTIAL-2—a phase 3 study of arlocabtagene autoleucel versus standard of care in adult patients with relapsed and refractory multiple myeloma (RRMM) exposed to lenalidomide

2302

Eyal Lebel,[1] Ahmed Abdulgawad,[2] Stefania Bramanti,[3] Gonzalo Garate,[4] Phoebe Joy Ho,[5] Mikko Keränen,[6] Yael Cohen,[7] Maja Vase,[8] Amit Khot,[9] Ida Bruun Kristensen,[10] Richard LeBlanc,[11] Cindy Lee,[12] Wojciech Legiec,[13] Hila Magen,[14] María-Victoria Mateos,[15] Danielle Oh,[16] Ludek Pour,[17] Natalia Schutz,[18] Alexandros Spyridonidis,[19] Katja Weisel,[20] Jan Zaucha,[21] Sarah Larson,[22] Asya Varshavsky-Yanovsky,[23] Kimberly Grazioli,[24] Debashree Basudhar,[24] Hongxiang Hu,[24] Ya Meng,[24] Lamis Eldjerou,[24] Susan Bal,[25] Simon Harrison,[9] Rakesh Popat,[26] Marc Raab,[27] Paula Rodriguez-Otero[28]

[1]Hadassah Medical Center, Jerusalem, Israel; [2]Christie NHS Foundation Trust, Manchester, United Kingdom; [3]IRCCS Istituto Clinico Hummanitas, Rozzano, Italy; [4]Hospital Aleman, Buenos Aires, Argentina; [5]Royal Prince Alfred Hospital and University of Sydney, Camperdown, NSW, Australia; [6]Helsinki University Hospital, Helsinki, Finland; [7]Tel Aviv Sourasky Medical Center & Gary Faculty of Medical and Health Sciences, Tel Aviv, Israel; [8]Aarhus Universitetshospital, Midtjylland, Denmark; [9]Peter MacCallum Cancer Centre and Royal Melbourne Hospital, University of Melbourne, Melbourne, VIC, Australia; [10]Odense Universitetshospital, Syddanmark, Odense, Denmark; [11]Hematology-Oncology and Cell Therapy University Institute, Hôpital Maisonneuve-Rosemont Research Center, Université de Montréal, Montreal, QC, Canada; [12]Royal Adelaide Hospital, Adelaide, SA, Australia; [13]St. John of Dukla Oncology Center of Lublin Land, Lublin, Poland; [14]Department of Hematology Chaim Sheba Medical Center, Ramat-Gan, Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; [15]Hospital Universitario de Salamanca, Salamanca, Spain; [16]Monash Health and Monash University, Clayton, VIC, Australia; [17]Masaryk University and University Hospital Brno, Brno, Czech Republic; [18]Hospital Italiano de Buenos Aires, Buenos Aires, Argentina; [19]University Hospital of Patras, Rio-Patras, Greece; [20]University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [21]Medical University of Gdańsk and University Clinical Center, Gdansk, Poland; [22]UCLA Medical Center, Los Angeles, CA, United States; [23]Fox Chase Cancer Center Temple Health, Philadelphia, PA, United States; [24]Bristol Myers Squibb, Princeton, NJ, United States; [25]University of Alabama at Birmingham, Birmingham, AL, United States; [26]University College London Hospital, London, United Kingdom; [27]Universitaetsklinikum Heidelberg, Heidelberg, Germany; [28]Clinica Universidad de Navarra, Pamplona, Spain

Introduction

- Despite advances in the management of multiple myeloma (MM), most patients relapse,[1] highlighting the need for new drug classes to improve outcomes in relapsed and refractory (RR) MM
- Further, RRMM exposed to lenalidomide poses an additional challenge as the disease is less likely to respond to subsequent treatment[1,2]
- G protein-coupled receptor class C group 5 member D (GPRC5D) is a promising therapeutic target for MM as it is highly expressed on malignant plasma cells. Although also present on normal plasma cells and epithelial tissues (skin, hair follicles, tongue), GPRC5D shows minimal to no expression in other immune cells, bone marrow progenitors, and other healthy tissues. This restricted expression profile supports its potential for selective targeting in MM[3]
- Arlocabtagene autoleucel (arlo-cel; BMS-986393) is a GPRC5D-directed autologous chimeric antigen receptor (CAR) T-cell therapy that has been granted FDA Regenerative Medicine Advanced Therapy Designation for RRMM[4] (**Figure 1**)
- Arlo-cel has demonstrated safety and efficacy in patients with RRMM in a first-in-human phase 1 study[4,5]
  - Following a single infusion of arlo-cel (150 × 10^6 CAR T-cells) in those with 1-3 prior lines of therapy (LOT), overall response rate (ORR) and complete response rate (CRR) were 94% and 71%, respectively[6]
  - Among patients with ≥ 3 prior LOT treated with arlo-cel at doses of 75 x 10^6 and 150 x 10^6, ORR were 92% and 91%, respectively; CRR were 58% and 44%, respectively[7]
  - Based on the observed efficacy comparability and with the intent of optimizing benefit-risk for an early RRMM population, the dose on the phase 3 study was reduced to 75 x 10^6 CAR T-cells[7]

Figure 1. Mechanism of action of arlo-cel, a CAR T-cell therapy targeting GPRC5D[8,9]

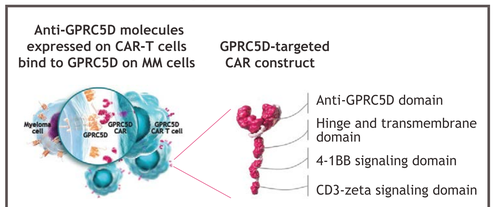
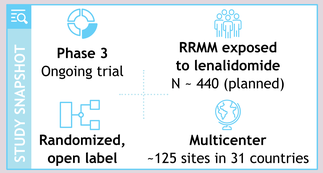
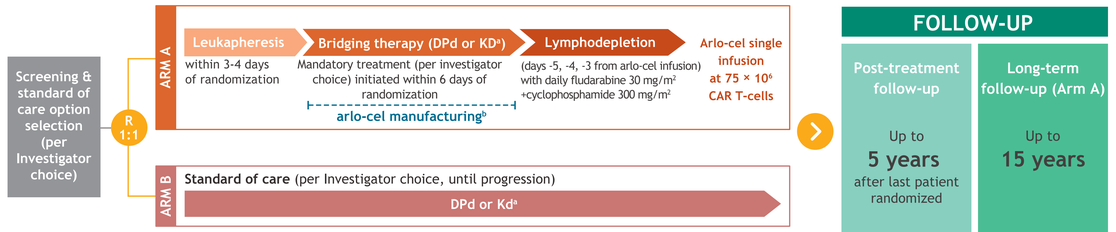


Figure previously presented by Bal S, et al 2023 ASH Annual Meeting.[8]
arlo-cel, arlocabtagene autoleucel; CAR, chimeric antigen receptor; GPRC5D, G protein-coupled receptor class C group 5 member D; MM, multiple myeloma.

Study design: QUINTESSENTIAL-2 (NCT06615479) is a randomized, open-label, multicenter, phase 3 confirmatory study comparing the efficacy and safety of arlo-cel vs standard of care (SOC) in adults with RRMM and prior lenalidomide exposure





[a]DPd or Kd dosed per labeling; [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; DPd, daratumumab, pomalidomide, and dexamethasone; GPRC5D, G protein-coupled receptor class C group 5 member D; Kd, carfilzomib and dexamethasone; R, randomization; RRMM, relapsed and refractory multiple myeloma.

- In patients with RRMM after 1-3 prior LOT treated with arlo-cel (N=31)[6]:
  - Treatment-emergent adverse events (TEAEs) were predominantly hematologic. No grade ≥ 3 infections were reported
  - Treatment-related AEs (TRAEs):
    - Cytokine-release syndrome (CRS) was the most common TRAE; all events of CRS and immune effector cell-associated neurotoxicity (ICANS) were grade ≤ 2 and resolved
    - Other select neurotoxicities occurred in 2 patients: one experienced grade 2 ataxia and gait disturbance (ongoing), and one patient had grade 1 gait disturbance (resolved) and grade 1 dysarthria (ongoing)
    - On-target/off-tumor toxicities (skin, oral/dysgeusia, and nail disorders) were observed in 55% of patients; all events were grade ≤ 2 and did not require intervention in most cases
    - One patient experienced grade 1 weight loss that resolved without intervention
- Here, we present the design of the phase 3 QUINTESSENTIAL-2 study

Population

- Adult patients who have received 1-3 prior LOT and have been exposed to lenalidomide (**Figure 2**)
  - Prior B-cell maturation antigen-directed therapy is permitted in a limited number of patients

Figure 2. Key eligibility criteria

INCLUSION CRITERIA
- Men and women ≥ 18 years of age
- Documented diagnosis of MM per IMWG criteria
- Received 1-3 prior LOT[a] including prior exposure to lenalidomide with ≥ 2 consecutive cycles, unless PD was the best response to lenalidomide-containing treatment or if there was lenalidomide intolerance or unacceptable toxicity
- Measurable disease
- ECOG performance status 0 or 1
- Documented disease progression during or after their last anti-myeloma regimen

EXCLUSION CRITERIA
- Active or history of central nervous system involvement with MM
- Solitary plasmacytomas or non-secretory myeloma without other evidence of measurable disease
- Need for urgent treatment due to rapidly progressing MM
- Active systemic fungal, bacterial, viral, or other infection despite appropriate anti-infective treatment at time of leukapheresis
- Received any prior GPRC5D-directed therapy or other prior MM treatment without the required washout prior to leukapheresis

[a]May include a proteasome inhibitor, immunomodulatory drug, anti-CD38 monoclonal antibody, and in a limited number of patients, B-cell maturation antigen-directed therapy; must have undergone ≥ 2 consecutive cycles of treatment for each LOT (except for CAR T-cell therapy), unless PD was the best response to the regimen or in the event of unacceptable toxicity. CAR, chimeric antigen receptor; ECOG, Eastern Cooperative Oncology Group; GPRC5D, G protein-coupled receptor class C group 5 member D; IMWG, International Myeloma Working Group; LOT, lines of therapy; MM, multiple myeloma; PD, progressive disease.

Study endpoints

- Study endpoints are detailed in **Figure 3**

Figure 3. Study endpoints

DUAL PRIMARY ENDPOINTS
- **Progression-free survival (PFS)[a]**
- **Minimal residual disease (MRD) negativity in complete response (CR)[b]**

SECONDARY ENDPOINTS

KEY
- Overall survival (OS)
- Overall response rate (ORR)[a]

OTHER
- Safety and tolerability[c]
- CR rate[a]
- Time to response (TTR)[a,d]
- Duration of response (DOR)[e]
- MRD-negative status
- Pharmacokinetics
- Patient-reported quality of life outcomes (EORTC QLQ-C30 and -MY20)

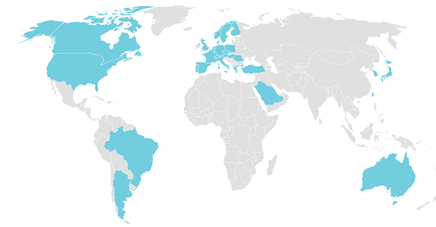
[a]Based on the IMWG Uniform Response Criteria for MM as assessed by an IRC (or death due to any cause for PFS); [b]Defined as MRD negativity at 10^{-5} sensitivity level and with CR/stringent CR, per IMWG criteria as assessed by IRC; [c]Based on incidence and severity of AEs, AEs of special interest, serious AEs, and laboratory results; [d]Defined as time from randomization to first documentation of partial response or better; [e]Defined as time from first documentation of partial response or better to first documentation of progressive disease or death from any cause, whichever occurs first.
AE, adverse event; 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; MM, multiple myeloma; MY20, multiple myeloma module.

Enrollment

- The study is currently recruiting and is expected to enroll 440 patients across ~125 sites (**Figure 4**)

Figure 4. Planned enrollment

QUINTESSENTIAL-2
- **Study start date (first patient first visit):** March 12, 2025
- **Estimated primary analysis completion date:** December 30, 2027
- **Estimated study completion date:** June 22, 2032
- **Estimated enrollment:** 440



Approximately 125 sites in 31 countries

Study information as of October 2025.

References

1. Rajkumar SV. *Am J Hematol*. 2024;99(9):1802-1824.
2. Lecat CSY, et al. *Front Oncol*. 2021;11:703233.
3. Rodriguez-Otero P, et al. *Blood Cancer J*. 2024;14(1):24.
4. Bal S, et al. Poster presentation at the American Society of Hematology (ASH) Annual Meeting; December 7–10, 2024; San Diego, CA. Abstract 2069.
5. Bal S, et al. Oral presentation at the American Society of Hematology (ASH) Annual Meeting; December 7–10, 2024; San Diego, CA. Abstract 922.
6. Bal S, et al. Poster presentation at the International Myeloma Society (IMS) Annual Meeting; September 17-20, 2025; Toronto, Canada. PA-080.
7. Bal S, et al. Poster presentation at the International Myeloma Society (IMS) Annual Meeting; September 17-20, 2025; Toronto, Canada. PA-076.
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 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 Jacqueline Benjamin, 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 QR code via a barcode reader application
QR codes are valid for 30 days after the congress presentation date.

Copies of this poster obtained through QR (Quick Response) and/or text key codes are for personal use only and may not be reproduced without written permission of the authors.