MM-1162

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

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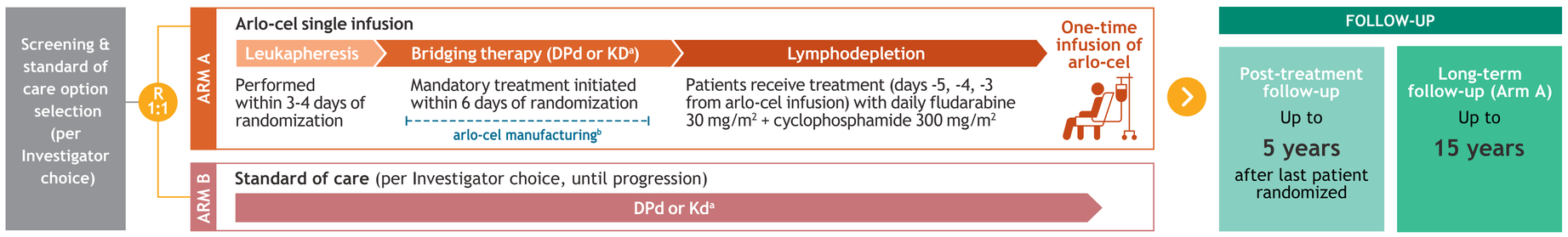
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The QUINTESSENTIAL-2 study (NCT06615479) is investigating the efficacy and safety of arlo-cel (a GPRC5D-directed CAR T-cell therapy requiring only 1 infusion) vs standard of care in adults with RRMM exposed to lenalidomide

STUDY SNAPSHOT

- **Phase 3** Ongoing trial
- **RRMM exposed to lenalidomide** N ~ 440 (planned)
- **Randomized, open label**
- **Multicenter** ~126 sites in 31 countries

Figure 1. Study design overview



[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.

Background

- 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 (an immunomodulatory drug used in frontline and maintenance therapies) 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 the receptor is highly expressed on malignant plasma cells; it has little to no expression on non-plasma immune cells and limited expression in healthy tissues[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 2**)
- 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), overall response rate (ORR) was 96% (23/24) and 91% (21/23) in those with 1-3 and ≥ 3 prior lines of therapy (LOT), respectively
- Here, we present the design of the phase 3 QUINTESSENTIAL-2 study

Figure 2. Mechanism of action of arlo-cel, a CAR T-cell therapy targeting GPRC5D[6,7]

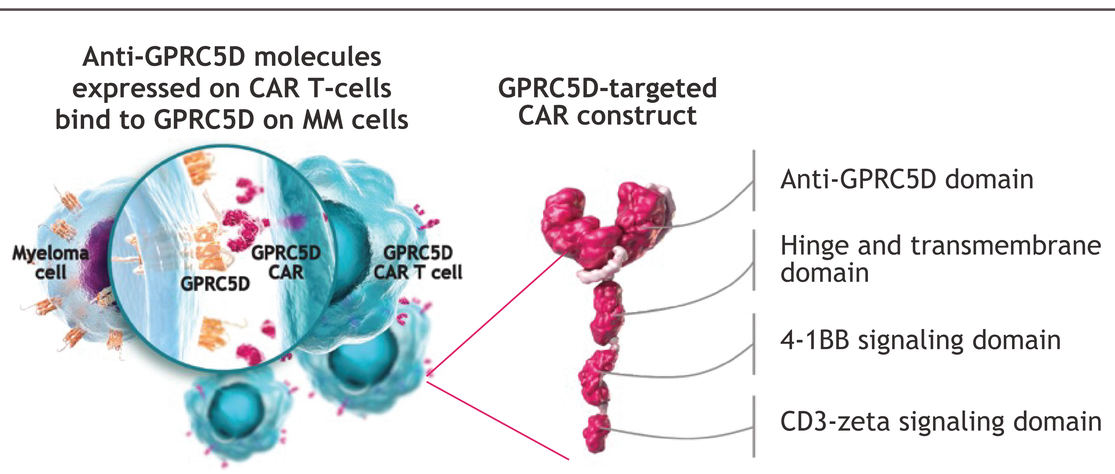


Figure previously presented by Bal S, et al 2023 ASH Annual Meeting.[6]
arlo-cel, arlocabtagene autoleucel; CAR, chimeric antigen receptor; GPRC5D, G protein-coupled receptor class C group 5 member D; MM, multiple myeloma.

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
- Eligible patients will be randomized 1:1 to 1 of 2 treatment arms (**Figure 1**)
  - Arm A: one-time infusion of arlo-cel, with leukapheresis, mandatory bridging therapy per Investigator choice, and lymphodepletion prior to arlo-cel infusion
  - Arm B: SOC with DPd or Kd per Investigator choice
- Patients will be followed for ≤ 5 years after the last patient is randomized, with a subsequent long-term follow-up study (≤ 15 years after infusion) for patients receiving arlo-cel (**Figure 1**)

Population

- Adult patients must have received 1-3 prior LOT and be exposed to lenalidomide (**Figure 3**)
  - Prior B-cell maturation antigen–directed therapy is permitted

Figure 3. 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 during screening
- 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, and anti-CD38 monoclonal antibody; 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 4**

Figure 4. 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

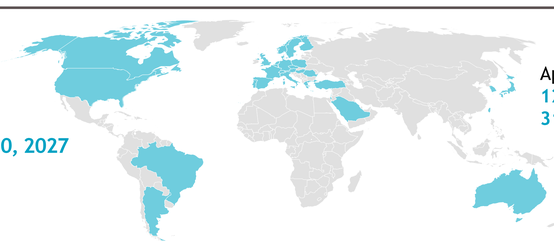
- The study is currently recruiting and is expected to enroll 440 patients across ~126 sites (**Figure 5**)

Figure 5. 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**

Study information as of July 2025.



Approximately **126** sites in **31** countries

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. Oral presentation at the American Society of Hematology (ASH) Annual Meeting; December 9-12, 2023; San Diego, CA. Abstract 219.
7. Smith EL, et al. *Sci Transl Med*. 2019;11(485):eaau7746.

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