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

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Introduction

- 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/refractory (RR) MM who have been exposed to 4 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 action 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]
  - Patients with QCEx RRMM have poor survival outcomes; median event-free survival was 4.6 months (95% CI, 3.9-5.8) and overall survival was 15.6 months (95% CI, 11.5-24.5) in a retrospective study using the Flatiron Health database[6]
- 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 validated therapeutic target for MM[7]
- Arlocabtagene autoleucel (arlo-cel; BMS-986393) is a potential first-in-class autologous chimeric antigen receptor (CAR) T-cell therapy targeting GPRC5D (**Figure 1**)

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

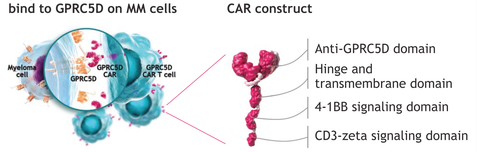
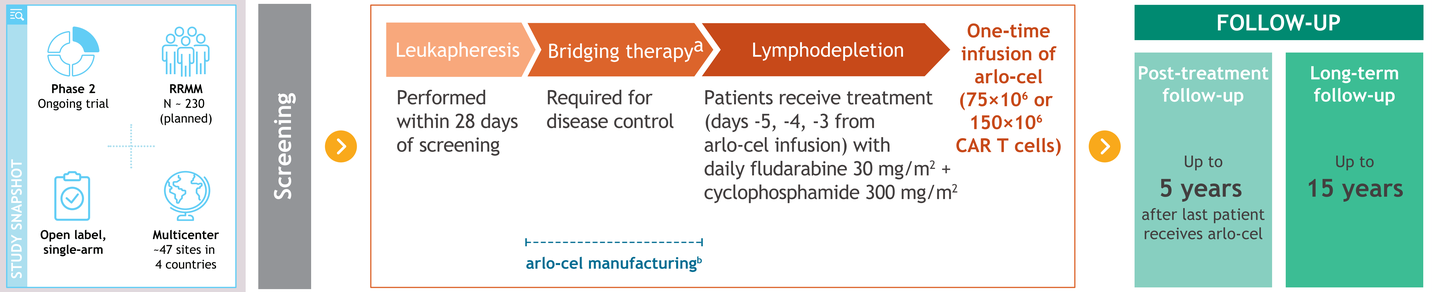


Figure previously presented by Bal S, et al 2023 ASH Annual Meeting.[8]
arlo-cel, arlocabtagene autoleucel; CAR, chimeric antigen receptor; GPRC5D, G protein-coupled receptor class C group 5 member D; MM, multiple myeloma.

- 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 (≥ 3 prior lines of therapy), including patients who received prior BCMA-targeted therapy
  - Findings were comparable between doses of 75×10^6 or 150×10^6 CAR T-cells for overall response rate (ORR; 92% [22/24] and 91% [21/23], respectively) and complete response rate (CRR; 58% [14/24] and 44% [10/23], respectively)[10]
  - Median progression-free survival (PFS) was 18.3 months (95% CI, 11.8-21.9) for all efficacy-evaluable patients treated with arlo-cel (n = 79)[11]
- Here, we present the design of the phase 2 QUINTESSENTIAL study

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

Figure 2. 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/refractory 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 2**)
- 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 2**)

Population

- Adult patients with ≥ 4 classes of MM treatment (including IMiDs, PIs, anti-CD38 antibody, and anti-BCMA therapy) 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 ≥ 4 classes of MM treatment, including IMiD, PI, anti-CD38 antibody, and anti-BCMA therapy
- 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

BCMA, B-cell maturation antigen; 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 QCEx patients with ≥ 3 prior lines of therapy
- BOR of complete response (CR)[b] in 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; MY20, multiple myeloma module; PD, progressive disease; QCEx, quad-class exposed; TCEx, triple-class exposed.

Enrollment

- The study is currently recruiting, with an estimated enrollment of 230 patients
- This study will recruit at ~47 centers across the USA, Canada, Japan, and Australia (**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:** 230

Approximately 47 sites in 4 countries

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