AML-399

A Phase 2, Open-Label, Multiarm, Multicenter Study to Evaluate Magrolimab Combined With Antileukemia Therapies for First-Line, Relapsed/Refractory, or Maintenance Treatment of Acute Myeloid Leukemia

Paresh Vyas[1], Naval G. Daver[2], Mark P. Chao[3], Guan Xing[3], Camille Renard[3], Giri Ramsingh[3], Andrew H. Wei[4], David A. Sallman[5]

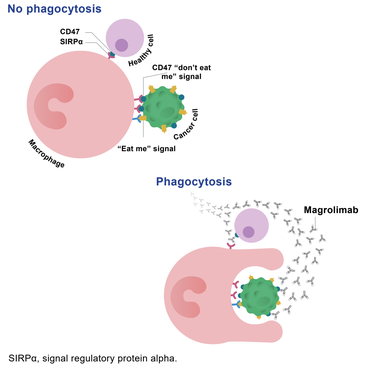
[1]University of Oxford, Oxford, United Kingdom; [2]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [3]Gilead Sciences, Inc., Foster City, CA, USA; [4]Alfred Hospital and Monash University, Melbourne, Australia; [5]Moffitt Cancer Center, Tampa, FL, USA

An online version of this poster can be found through this QR code.

Background

- Magrolimab is a monoclonal antibody that blocks the macrophage-inhibitory immune checkpoint cluster of differentiation 47 (CD47), a "do not eat me" signal overexpressed on tumor cells that prevents phagocytosis of tumor cells[1,2]
- Chemotherapy and hypomethylating agents synergize with magrolimab by inducing "eat me" signals on leukemic blasts, thereby enhancing phagocytosis[2]
- Magrolimab + azacitidine (AZA) has shown encouraging clinical efficacy with an objective response rate (ORR) of 49% and a complete remission (CR) or CR with incomplete hematologic recovery (CRi) rate of 42% in untreated *TP53*-mutated acute myeloid leukemia (AML)[3]
- Patients with newly diagnosed AML who are ineligible for intensive chemotherapy (IC) have limited response duration and survival despite the progress made with AZA + venetoclax (VEN).[4,5] In addition, patients with relapsed/refractory (R/R) AML after intensive regimens have a dismal prognosis[6,7]
- For patients in remission, maintenance therapy with oral AZA has improved overall survival (OS) and reduced relapse risk, although relapse rates remain high
- This phase 2 study (NCT04778410) evaluates the efficacy, safety, and tolerability of magrolimab in combination with different antileukemia therapies in patients with newly diagnosed or R/R AML or in maintenance post-intensive chemotherapy

Magrolimab Mechanism of Action



SIRPα, signal regulatory protein alpha.

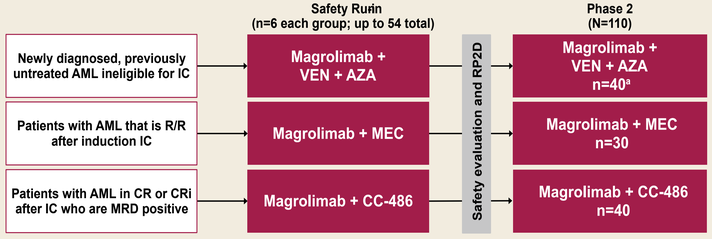
Objectives

- To evaluate the efficacy, safety, and tolerability of magrolimab in combination with VEN + AZA in patients with previously untreated AML and who are ineligible for IC
- To evaluate the efficacy, safety, and tolerability of magrolimab in combination with mitoxantrone, etoposide, and cytarabine (MEC) in patients with AML that is R/R after induction IC
- To evaluate the efficacy, safety, and tolerability of magrolimab in combination with CC-486 in patients with AML in CR or CRi and with minimal residual disease (MRD) after IC

Methods Summary

- Open-label, multiarm, multicenter study, including 3 safety run-ins with corresponding phase 2 cohorts
- Each cohort will enroll patients 6 by 6 to assess dose-limiting toxicities (DLTs) for 1 cycle (28 days) and determine the recommended phase 2 dose (RP2D)
- After completion of the safety run-in, additional patients will be enrolled in cohorts 1, 2, and 3 for phase 2. In phase 2, patients in cohorts 1 and 3 will receive study treatments at RP2D until progressive disease (PD), unacceptable toxicity, or loss of clinical benefit. Patients in cohort 2 will receive 2 to 3 cycles of MEC and up to 12 months of magrolimab

Study Design



[a] Patient enrollment in cohort 1 (magrolimab + VEN + AZA) is closed.

Patient Eligibility

Key inclusion criteria

- All patients
  - WBC count ≤20×10^3/μL and hemoglobin level≥9 g/dL prior to first dose
  - Adequate liver and renal functions
  - Pretreatment blood crossmatch completed
- Cohort 1: AML unfit for IC
  - Patients with previously untreated AML, ineligible for standard IC due to age ≥75 years or ≥1 of the following: ECOG PS 2-3, lung carbon monoxide–diffusing capacity ≤65% or FEV_1 ≤65%, LVEF ≤50%, ClCr <45 mL/min
  - Age ≥75 years and ECOG PS 0-2 or 18-74 years and ECOG PS 0-3
- Cohort 2: R/R AML
  - Patients with AML that is R/R to initial induction IC ± consolidation
  - At least 2 weeks since any prior systemic/ targeted antileukemia drug
  - ECOG PS 0-2 and LVEF ≥50%, lack of symptomatic congestive heart failure or clinically significant cardiac arrhythmias
- Cohort 3: post-chemotherapy maintenance
  - AML in CR or CRi with MRD positivity by flow cytometry after induction IC ± consolidation with ECOG PS 0-2

Key exclusion criteria

- Prior treatment with CD47 or SIRPα-targeting agents
- Clinical suspicion of active CNS involvement with AML
- Acute promyelocytic leukemia
- Significant disease or medical conditions, as assessed by the investigator and sponsor, that would substantially increase the risk-benefit ratio of participating in the study
- Second malignancy, except MDS, treated basal cell or localized squamous skin carcinomas, localized prostate cancer, or other malignancies for which patients are not on active anti-AML therapies and who are in CR for >1 year

ClCr, creatinine clearance; CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group performance status; FEV_1, forced expiratory volume in the first second of expiration; LVEF, left ventricular ejection fraction; MDS, myelodysplastic syndromes; SCT, stem cell transplant; WBC, white blood cell.

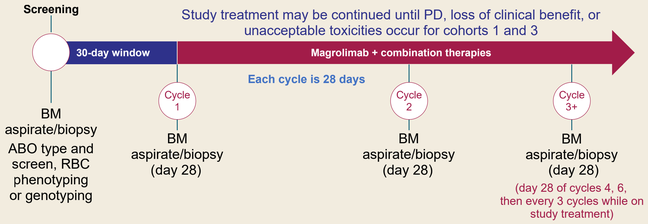
Treatment

Cohort	Combination treatment	Cycle 1	Cycle 2+[a]
1	AZA 75 mg/m² SC or IV	Days 1-7	Days 1-7
	VEN PO	100 mg on day 1, 200 mg on day 2, 400 mg on days 3-28	400 mg on days 1-28
2	Mitoxantrone 8 mg/m² IV Etoposide 100 mg/m² IV Cytarabine 1000 mg/m² IV	Days 1-5	Days 1-5
3	CC-486 300 mg PO	Days 1-14	Days 1-14

Cohort	Magrolimab	
All	1 mg/kg IV	Days 1 and 4
	15 mg/kg IV	Day 8
	30 mg/kg IV	Days 11 and 15, then QW × 5 doses
	30 mg/kg IV	Q2W beginning 1 week after the 5th weekly 30-mg/kg dose[a]

Dose de-escalation may be conducted per protocol for DLTs.
IV, intravenous; PO, orally; QW, every 2 weeks; QW, once weekly; SC, subcutaneous.
[a] In cohort 2, 2 to 3 cycles of MEC and up to 12 months of total magrolimab treatment.

Key Assessments and Timing



BM, bone marrow; RBC, red blood cell.

Endpoints

Primary Endpoints

Safety run-ins

- Percent of patients with DLTs[a]
- Safety
- Tolerability

Unfit, R/R cohorts

- CR rate

Maintenance cohort

- MRD-negative CR rate

Secondary Endpoints

Secondary endpoints: all cohorts

- OS
- RBC transfusion independence rate
- Platelet transfusion independence rate
- Safety, tolerability, PK, immunogenicity

Unfit, R/R cohorts (including safety run-ins)

- ORR
- DCR
- CR_{MRD-} rate
- CR/CRh rate, duration of CR/CRh
- CR/CRi rate, duration of CR/CRi
- EFS, DOR

Maintenance cohort (including safety run-ins)

- RFS
- MRD-negative CR/CRi rate, duration of MRD-negative CR and CR/CRi

Dose de-escalation may be conducted per protocol for DLTs
CRh, complete remission with partial hematologic recovery; DCR, duration of complete remission; DOR, duration of remission; EFS, event-free survival; PK, pharmacokinetics; RFS, relapse-free survival
[a] In cohort 2, 2 to 3 cycles of MEC and up to 12 months of total magrolimab treatment.

Enrollment

- The study opened to accrual on June 28, 2021, and is currently recruiting participants
- Estimated enrollment is approximately 128 patients
- Additional information is available at ClinicalTrials.gov: https://clinicaltrials.gov/ct2/show/NCT04778410

References

1. Liu J, et al. *PLoS One*. 2015;10(9):e0137345. 2. Chao MP, et al. *Front Oncol*. 2019;9:1380. 3. Daver N, et al. Presented at: European Hematology Association 2022; June 2022; Vienna, Austria. Abstract S132. 4. DiNardo CD, et al. *Blood*. 2019;133(1):7-17. 5. Wei AH, et al. *Blood*. 2020;383(7):617-629. 7. Venclexta (venetoclax tablets). Prescribing information. AbbVie Inc; 2020. 8. Platzbecker U, et al. *Leukemia*. 2012;26(3):381-389. 9. Pan J, et al. *Front Oncol*. 2020;10:576924.

Acknowledgements

We extend our thanks to the patients, family, friends, and caregivers as well as to the study staff. This study was funded by Gilead Sciences, Inc. Medical writing support was provided by Jackie Stone, of SciMentum, Inc, a Nucleus Holdings Ltd company, Hamilton, NJ, and funded by Gilead Sciences, Inc.

Disclosures

PV reports consulting fees from AbbVie, Astellas, and Bristol Myers Squibb; honoraria from AbbVie, Astellas, Bristol Myers Squibb, Gilead Sciences, Inc., Jazz Pharmaceuticals, Daiichi Sankyo, Janssen, Takeda, Pfizer, and Novartis; and research funding from Bristol Myers Squibb. **NGD** reports consulting fees from AbbVie, Agios Pharmaceuticals, Amgen, Astellas, Bristol Myers Squibb, Celgene, Daiichi Sankyo, Gilead Sciences, Inc., ImmunoGen, Jazz Pharmaceuticals, Novartis, Pfizer, Servier, Genentech, Trillium, Syndax, Shattuck Labs, and Arog; and research funding from AbbVie, Amgen, Astellas, Bristol Myers Squibb, Daiichi Sankyo, Gilead Sciences, Inc., Pfizer, Servier, Genentech, Hanmi, Trovagene, Fate Therapeutics, Novimmune, Glycomimetics, Trillium, and Arog. **MPC** reports current employment by and equity in Gilead Sciences, Inc.; consulting fees from IconOVir Bio; stock options in IconOVir Bio and TigaTx; stock in HepaTx; membership on the board of directors or advisory committees for TigaTx, HepaTx, and Leukemia and Lymphoma Society; and patent fees and royalties from Gilead Sciences, Inc. and HepaTx. **GX** reports current employment by Gilead Sciences, Inc. and Alphabet; stock in Gilead Sciences, Inc.; and equity in Alphabet. **GR** reports current employment by and stock in Gilead Sciences, Inc. **AHW** reports consulting fees from Servier; honoraria from and membership on the board of directors or advisory committees for AbbVie, Amgen, AstraZeneca, Celgene/BMS, Novartis, Servier, Astellas, Genentech, Janssen, and MacroGenics; research funding from AbbVie, Amgen, AstraZeneca, Celgene/BMS, Novartis, Servier, and F. Hoffmann-La Roche AG; participation in a speakers bureau for AbbVie, Celgene/BMS, and Novartis; and previous employment by and patent fees and royalties from Walter and Eliza Hall Institute. **DAS** reports consulting fees from Magenta, Novartis, and Takeda; research funding from Aprea; membership on the board of directors or advisory committees for AbbVie, Agios, Aprea, Bristol Myers Squibb, Intellia, Kite, Novartis, Syndax, and Shattuck Labs; and participation in speakers bureaus for Bristol Myers Squibb and Incyte.

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

Presented at the Society of Hematologic Oncology 2022 Annual Meeting, September 28 to October 1, 2022; Houston, TX.

© 2022 Gilead Sciences, Inc. All rights reserved.