A Phase 2, Multi-Arm Study of Magrolimab Combinations in Patients With Relapsed/Refractory Multiple Myeloma

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Study Design

Patients with R/R MM and ≥3 prior therapies, including an IMiD and a PI

Safety run-in cohorts

n = 6 to 9 (up to 3 dose levels[a])

- Magrolimab + daratumumab
- Magrolimab + pomalidomide + dexamethasone
- Magrolimab + carfilzomib + dexamethasone
- Magrolimab + bortezomib + dexamethasone

Safety evaluation and RP2D

Dose-expansion cohorts

n = 24

- Magrolimab + daratumumab
- Magrolimab + pomalidomide + dexamethasone
- Magrolimab + carfilzomib + dexamethasone
- Magrolimab + bortezomib + dexamethasone

Magrolimab + bortezomib + dexamethasone may be initiated based on preliminary safety and efficacy data in the magrolimab + carfilzomib + dexamethasone cohort, and if initiated, will require only 1 prior line of therapy

[a]Magrolimab 1 mg/kg initial priming dose then 15-30 mg/kg

Primary Objectives

Safety run-in cohorts

- Evaluate safety and tolerability of magrolimab with other therapies
- Determine the RP2D

Dose-expansion cohorts

- Evaluate the efficacy of magrolimab with other therapies, as determined by ORR

Key Inclusion Criteria

- Adults (≥18 years) with previously diagnosed MM currently requiring treatment
- Measurable disease, defined as ≥1 of the following: serum M-protein level ≥0.5 g/dl, urine M-protein level ≥200 mg/24 hours, and/or SFLC level ≥100 mg/l with abnormal SFLC ratio
- At least 3 previous lines of therapy, including an IMiD and a PI
- ECOG PS ≤2
- ANC ≥1000 cells/µl, platelet count ≥75,000 cells/µl, and hemoglobin level ≥9.0 g/dl

Patients who have previously received daratumumab or pomalidomide are eligible for enrollment.

Key Exclusion Criteria

- Known amyloidosis, including myeloma complicated by amyloidosis
- MM of immunoglobulin M subtype
- Waldenström macroglobulinemia or myelodysplastic syndromes
- Plasma cell leukemia
- POEMS syndrome
- Immunotherapy or chemotherapy within 28 days prior to enrollment
- Prior treatment with CD47- or SIRPα-targeting agents

Study End Points

Safety run-in cohorts	Dose-expansion cohorts
Primary • DLTs and AEs • Laboratory abnormalities	**Primary** • ORR **Secondary** • Safety: AEs and laboratory abnormalities • Efficacy: DOR, PFS, OS • PK and ADAs **Exploratory** • MRD negativity rate • Mutational profile of myeloma cells and correlation with clinical response • Changes from baseline in biomarkers of immune cell recruitment • Changes from baseline in known phagocytic regulators in myeloma cells • Change from baseline in FACT-MM questionnaire • TTR

Timeline of Key Assessments for Expansion Cohorts

Cycle 1: 35 days; cycles 2+: 28 days

Screening

30-day window

- Blood phenotyping and screening
- Bone marrow sample
- Imaging (CT ± PET or MRI)
- MM Frailty Index (age >65 years)
- FACT-MM questionnaire

Enrollment

- Magrolimab + daratumumab
- Magrolimab + pomalidomide + dexamethasone
- Magrolimab + carfilzomib + dexamethasone
- Magrolimab + bortezomib + dexamethasone

Magrolimab + bortezomib + dexamethasone may be initiated based on preliminary safety and efficacy data of the magrolimab + carfilzomib + dexamethasone cohort.

Cycle 1

- PK (days 1, 22)
- ADA (day 1)
- Peripheral blood (days 1, 8, 15)

Cycle 2

- PK (day 1)
- IMWG response (day 1)
- Bone marrow sample (day 1)

Cycle 3

- PK (day 1)
- IMWG response (day 1)

Cycles 4+

- PK (day 1)
- Imaging (CT ± PET or MRI) (day 1)
- IMWG response (day 1)
- MRD assessment (at serologic CR)

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ADA, antidrug antibody; AE, adverse event; ANC, absolute neutrophil count; CD, cluster of differentiation; CR, complete response; CT, computed tomography; DLT, dose-limiting toxicity; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; FACT-MM, Functional Assessment of Cancer Therapy – Multiple Myeloma; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; MM, multiple myeloma; MRD, minimal residual disease; MRI, magnetic resonance imaging; ORR, objective response rate; OS, overall survival; PET, positron emission tomography; PFS, progression-free survival; PI, proteasome inhibitor; PK, pharmacokinetics; POEMS, plasma cell dyscrasia with polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes; PS, performance status; RP2D, recommended phase 2 dose; R/R, relapsed/refractory; SFLC, serum free light chain; SIRPα, signal regulatory protein α; TTR, time to response.

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