A Phase 2, Open Label Study to Evaluate Vimseltinib in Adults with Active Chronic Graft-Versus-Host Disease after Failure of Prior Systemic Therapies

Poster: 385

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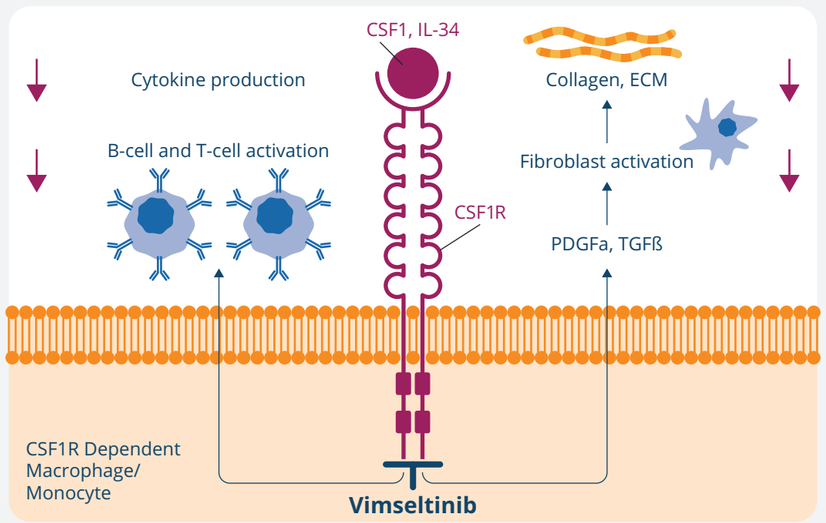
Introduction

- Colony-stimulating factor 1 receptor (CSF1R) signaling is a key pathway involved in the expansion and infiltration of donor-derived macrophages that mediate chronic graft-versus-host disease (cGVHD)[1,2]
  - cGVHD and its treatment typically require the prolonged use (2–3.5 years) of immunosuppressants
  - Both cGVHD and its treatment are associated with high morbidity and late mortality, with 5-year and 12-year cumulative incidence estimates of non-relapse mortality being 23% and 40%, respectively
  - Thus, there is an unmet need for novel therapies that can improve patient quality of life and long-term mortality rates
- Vimseltinib, an oral, selective small molecule inhibitor of CSF1R (**Figure 1**), has recently received US Food and Drug Administration and European Medicines Agency approval as a safe and effective systemic treatment for adult patients with tenosynovial giant cell tumor (TGCT)[3–5]
  - In the US, vimseltinib is indicated for treatment of adult patients with symptomatic TGCT for which surgical resection will potentially cause worsening functional limitation or severe morbidity
- Based on the manageable safety profile, vimseltinib is currently being investigated for treatment of cGVHD
- As an oral agent targeting this key inflammatory and fibrotic pathway that characterizes cGVHD, vimseltinib may offer an advantage over other therapies

Figure 1. Vimseltinib mechanism of action



CSF1R is a receptor for CSF1, a cytokine that promotes the differentiation and survival of macrophages.[6] In cGVHD, CSF1R signaling is upregulated in donor-derived macrophages, which are believed to be a major source of fibrotic damage.[7] Blocking CSF1R signaling can lead to a reduction in cGVHD, particularly the fibrotic manifestations in the skin and lungs. CSF1R inhibitions depletes monocytes and macrophages, thereby interfering with the activation of fibroblasts.[8]

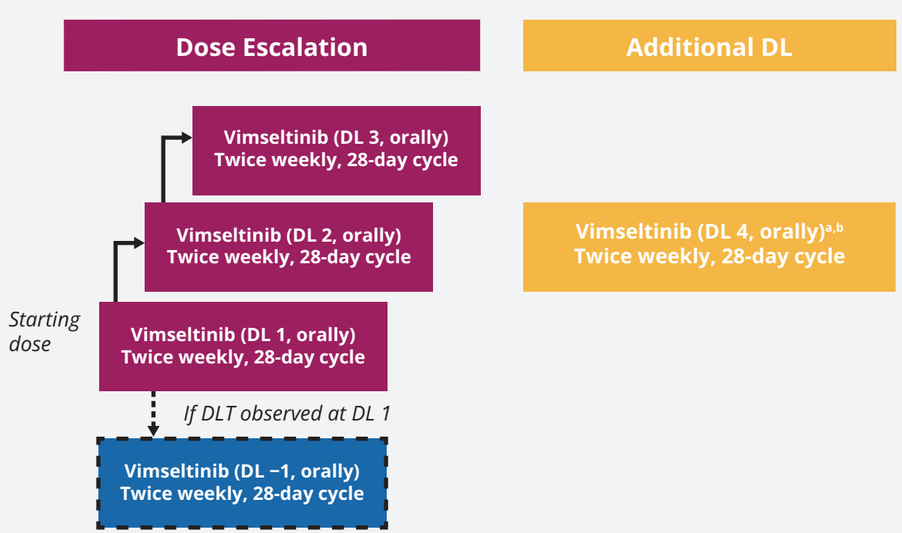
cGVHD, chronic graft versus host disease; CSF1R, colony stimulating factor 1 receptor; ECM, extracellular matrix; PDGFa, platelet-derived growth factor subunit a; TGFβ, transforming growth factor beta.

- Here, we describe an ongoing Phase 2 study evaluating vimseltinib for the treatment of adults with active moderate-to-severe cGVHD after failure of prior systemic therapy

Study Design

- This is a Phase 2, open-label, dose-finding, multicenter study to evaluate the safety, tolerability, pharmacokinetics (PK), and efficacy of twice weekly vimseltinib in adults with active cGVHD after prior systemic therapy failure (NCT06619561)
- Enrolled patients across dose escalation cohorts will receive vimseltinib orally in 28-day cycles (**Figure 2**)
  - Based on a 3+3 design, all 3 dose levels have been successfully cleared to date
  - An additional dose level between dose level 1 and 2 has been incorporated, although is separate from the 3+3 design

Figure 2. Phase 2, open-label, dose-finding, multicenter study (NCT06619561)



[a]Additional patients may be enrolled at dose levels with 0 DLTs out of 3 DLT-evaluable patients or ≤1 DLT out of 6 DLT-evaluable patients to better characterize the safety, PK, and PD. Up to 12 DLT evaluable patients per dose level may be enrolled. [b]This dose has been incorporated between dose level 1 and 2 but is separate from the 3+3 design.

AE, adverse event; C, cycle; cGVHD, chronic graft versus host disease; CSF1Ri, colony stimulating factor 1 receptor inhibitor; D, day; DL, dose level; DLT, dose-limiting toxicity; DoR, duration of response; HSCT, hematopoietic stem cell transplantation; ORR, objective response rate.

Key Eligibility Criteria

KEY INCLUSION CRITERIA

Adults aged ≥18 years

Must be hematopoietic stem cell transplant (HSCT) recipients with moderate-to-severe cGVHD requiring systemic immune suppression

Patients may have persistent active acute GVHD and cGVHD manifestations (ie, overlap syndrome), per 2014 NIH cGVHD Criteria

Have failed ≥2 prior lines of systemic therapy

KEY EXCLUSION CRITERIA

Prior use of a CSF1R inhibitor

History or other evidence of severe illness, uncontrolled infection, and/or malignancy (except for the underlying malignancy for which HSCT was performed

Key Outcome Measures

Primary outcome measures

- Frequency and severity of dose-limiting toxicities
- Adverse events [AEs], and serious AEs

Secondary outcome measures

- Objective response rate (from baseline up to Cycle 7, Day 1), duration of response, and organ-specific response
- Failure-free survival
- PK (C_{max})

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REFERENCES

1. Malard F, Mohty M. *Am J Hematol*. 2023;98(10):1637-1644.
2. DeFilipp Z, et al. *Blood Adv*. 2021;5(20):4278-4284.
3. ROMVIMZA (vimseltinib) capsules, for oral use. [highlights of prescribing information]. Deciphera Pharmaceuticals; 2025.
4. European Medicines Agency (EMA). (2025, September 22). Romvimza (vimseltinib) EPAR - Public assessment report (EMA/CHMP/139482/2025). Retrieved from https://www.ema.europa.eu/en/documents/assessment-report/romvimza-epar-public-assessment-report_en.pdf.
5. Palmerini E, et al. *Curr Oncol Rep*. 2025;27(7):844-855.
6. Stanley ER, et al. *Mol Reprod Dev*. 1997;46(1):4-10.
7. Alexander KA, et al. *J Clin Invest*. 2014;124(10):4266-4280.
8. Lee S, Zeiser R. *Blood*. 2025;145(8):795-800.

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