Poster CML-541

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Real-World Evaluation of First-Line and Second-Line Tyrosine Kinase Inhibitors in Chronic Myelogenous Leukemia in Chronic Phase: The Phase 4 ASC4REAL-2 Study

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EXPECTED IMPACT

- ASC4REAL-2 is a large, prospective, US-based real-world registry designed to generate comprehensive long-term data on tolerability, safety, effectiveness, and PROs associated with approved 1L and 2L TKIs, including asciminib, in patients with Ph+CML-CP
- Findings from this registry are expected to enhance understanding of real-world treatment patterns and outcomes, support patient-centered clinical decision-making, and inform optimization of long-term management strategies for CML in routine clinical practice

As of June 2026, 41 patients have been enrolled in 8 active sites

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INTRODUCTION

- Chronic myelogenous leukemia in chronic phase (CML-CP) is a myeloproliferative neoplasm driven by the Philadelphia chromosome, resulting from the reciprocal translocation between chromosomes 9 and 22 and formation of the constitutively active BCR::ABL1 tyrosine kinase that promotes uncontrolled proliferation and survival of leukemic cells[1,2]
- Tyrosine kinase inhibitors (TKIs) have transformed CML into a chronic disease with near-normal life expectancy, shifting treatment goals toward treatment-free remission (TFR) and improved quality of life; achieving sustained deep molecular responses with effective and well-tolerated therapy is central to these goals[3]
- Unlike other ATP-competitive TKIs (imatinib, nilotinib, dasatinib, and bosutinib), asciminib inhibits the ABL kinase activity of the BCR::ABL1 fusion protein by binding to the ABL myristoyl pocket and prevents unregulated cell proliferation[4-7]
- Long-term real-world data (RWD) on first-line (1L) and second-line (2L) CML treatments, including, asciminib, remain limited beyond clinical trial settings; furthermore, RWD reflects broader population in the US and outcomes, but patient reported outcomes (PROs) across CML treatments remains limited

AIM

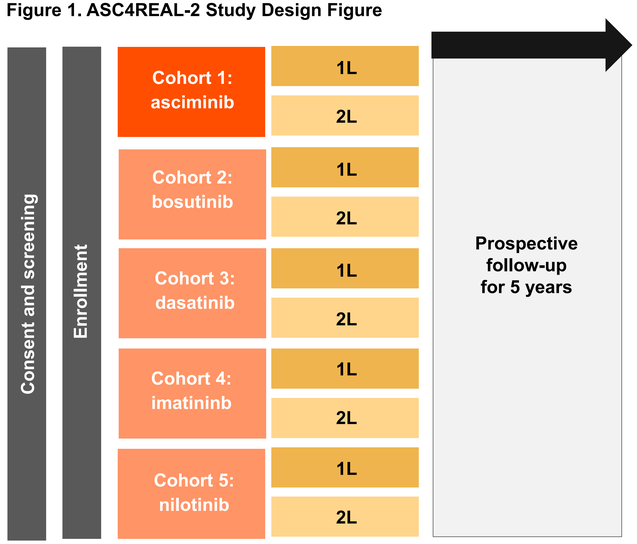
- To obtain real-word evidence on tolerability, safety, effectiveness, TFR, and PROs in patients with Philadelphia chromosome-positive (Ph+) CML-CP receiving 1L or 2L TKIs, including a 5-year prospective follow-up to identify and describe long-term treatment outcomes

METHODS

Trial Design

- ASC4REAL-2 (NCT07091019) is an ongoing, phase 4, US, multicenter, observational CML disease registry enrolling patients with Ph+ CML-CP who are receiving 1L or 2L TKI therapy **(Figure 1)**
  - 5 patient cohorts will be included based on patient TKI treatment in routine medical practice at enrollment and each cohort will include subpopulations for 1L and 2L therapy at enrollment
- Patients aged ≥18 years at the time of diagnosis who received TKI treatment (asciminib, bosutinib, dasatinib, imatinib, or nilotinib) either as initial therapy or after 1 prior TKI therapy are eligible for inclusion **(Table 1)**
- Enrollment will be ongoing for ~2.5 years
- Patients will be followed for 5 years or until loss to follow-up, death, or the end of the study, whichever comes first

Figure 1. ASC4REAL-2 Study Design Figure



1L, first-line; 2L, second-line.

Table 1. Key Inclusion and Exclusion Criteria

Key inclusion
• Patients ≥18 years at the time of Ph+ CML-CP diagnosis
• Patients receiving bosutinib, dasatinib, imatinib, or nilotinib in routine medical practice on or after October 2021
• Patients receiving asciminib include those who:
– Completed or discontinued 1L asciminib study and are continuing asciminib in routine medical practice on or after October 2021
– Started 1L/2L asciminib on or after FDA approval in October 2024
• Patients receiving treatment at US and US territories medical practice (eg, community-based, office-based, hospital-based, academic)
• Signed informed consent form prior to participation in the study including agreement to be tokenized so that the patient's anonymized RWD (EMRs and/or claims data) can be accessed
Key exclusion
• Currently being treated with a CML TKI in 3L or beyond
• Known presence of T315I mutation
• Currently in TFR phase and are not on active CML TKI therapy
• Previously received treatment with a prior stem cell transplant
• Pregnant or nursing (lactating) female

1L, first-line; 2L, second-line; 3L, third-line; CML, chronic myelogenous leukemia; CML-CP, CML in chronic phase; EMR, electronic medical record; FDA, US Food and Drug Administration; Ph+ CML-CP, Philadelphia chromosome–positive CML-CP; RWD, real-word data; TFR, treatment-free remission; TKI, tyrosine kinase inhibitor.

Data Collection and Planned Sample Size

- Data collection is expected from September 2025 to March 2033; data will be collected retrospectively and prospectively from the index visit, i.e., the date of signed study consent
- At the time of enrollment, retrospective data of patient's medical history will be collected from an RWD electronic medical record or medical and pharmacy claims data source(s)
- Then, over a period of 5 years, the study will prospectively collect data from patient medical records and medical claims data and directly from the patient
- All data will be collected and captured into an electronic case report form using a fully validated software
- The study population will include approximately 1000 patients; enrollment is expected to occur across up to 200 sites, with an estimated 200 patients per TKI cohort and a roughly equal representation of 1L and 2L treatment

Key Real-World Outcomes

- ASC4REAL-2 will evaluate the long-term tolerability of approved CML TKIs, including asciminib, for Ph+ CML-CP patients in the US; effectiveness, TFR, safety, and QoL based on PROs will also be analyzed **(Table 2)**
- All the primary, secondary, and exploratory analyses will be performed descriptively by the TKI cohort and by line-therapy subgroups (1L and 2L)

Table 2. Objectives and Related Endpoints

Objectives	Endpoints
Primary	
To describe the tolerability of CML TKIs	The rate of discontinuation of index TKI due to AEs
Secondary	
To describe additional tolerability and safety parameters	Overview of AEs (including type, frequency, severity, AEs leading to dose reduction/interruption, and duration of AEs), rate and time to switches in TKI, time to discontinuation of TKI, and reasons for TKI treatment discontinuation
To describe tolerability based on PROs	PRO-CTCAE and FACIT-GP5
To describe quality of life based on PROs	PROMIS-GH-10
To describe adherence to TKIs based on PROs	MARS-10
To describe TKI effectiveness based on molecular responses and hematologic responses	Rates of molecular and complete hematologic response at or by specified timepoints; duration of molecular response
To describe additional parameters of effectiveness	FFS, PFS, OS
Key exploratory	
To describe TFR eligibility for all patients	Proportion of patients who meet TFR eligibility as per investigator or designee assessment irrespective of entry into the TFR period
To describe sequence of therapy from initial TKI and throughout study duration and its impact on tolerability, safety, and effectiveness	For patients who enter TFR period: for each attempt at TFR: TFR success rate at 6 months, 1 year, and every 6 months until study discontinuation/completion or TFR failure
To explore impact of mutations in the BCR::ABL1 gene and other cancer associated genes on treatment outcomes and failure rates	Descriptive assessment of BCR::ABL1 mutations and mutations in AGAs in the patient population in correlation with the impact on clinical outcome
To evaluate a new patient CML symptom assessment tool for TKI intolerance and its clinical relevance	• Clinical outcomes: evaluate the impact of using the tool on patient outcomes, such as symptom improvement or treatment adjustments or discontinuation • Reliability: assess the consistency of the tool's results over repeated applications • Usability: determine the ease of use and integration of the tool into clinical workflows

AE, adverse event; AGA, additional genetic abbreviation; CML, chronic myelogenous leukemia; FACIT-GP5, functional assessment of chronic illness therapy – item-GP5; FFS, failure-free survival; MARS-10, medication adherence report scale-10; OS, overall survival; PFS, progression-free survival; PRO, patient-reported outcome; PRO-CTCAE, PROs version of the common terminology criteria for AEs; PROMIS-GH-10, PROs measurement information system-global health-10; TFR, treatment-free remission; TKI, tyrosine kinase inhibitor.

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