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Poster# **EE590**

Modelling Treatment-Free Remission Outcomes for Asciminib in Newly Diagnosed Chronic Myeloid Leukaemia: Assumptions, Methodology, and Projections

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KEY FINDINGS & CONCLUSIONS

- The proposed model shows that asciminib can noticeably improve the number of patients eligible for TFR.
- Given that TFR reduces medication burden and eliminates tolerability issues, significantly improving quality of life while offering substantial cost savings from discontinued TKI therapy.
- Mature data would help provide additional evidence to better describe the clinical value of asciminib

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INTRODUCTION

- Asciminib, a first-in-class BCR::ABL1 inhibitor, demonstrated superior outcomes in the ASC4FIRST trial (NCT04971226) compared to investigator-selected tyrosine kinase inhibitors (IS-TKIs), achieving notably:
  - higher major molecular response (MMR) rates at 96 weeks (74.1% vs. 52.0%, p < .001),
  - improved MR4.5 rates (30.8% vs. 17.6%, p < .005).
- Sustaining patients on first-line therapy without progression is a key goal in the management of CML, as achieving MMR is associated with a low risk of disease progression and near-zero CML-specific mortality according to the European Leukemia Network (ELN) guidelines.
- Treatment-free remission (TFR) is one of the key therapeutic goals in chronic myeloid leukaemia (CML), achievable in patients who sustain a deep molecular response (DMR).
- **The objective of this study is to present a methodology to model TFR outcomes for Asciminib and IS-TKIs in the long-term using a Markov-based model.**

METHODS

Methodology to model TFR

Model structure: patient pathway to response

- A Markov-based model was developed using a 40 year time horizon and monthly cycles to project long-term outcomes of asciminib versus IS-TKIs, including eligibility for TFR (**Figure 1**).
- Health states of the model include:
  - **Frontline Chronic Phase (CP) Treated** → patients who are diagnosed with CML in its chronic phase and undergoing their first round of treatment with TKIs.
  - **MMR** → BCR-ABL1 IS <=0.1% (e.g. >=3 log reduction from the IRIS standardised baseline).
  - **MR4.5** → BCR-ABL1 IS ≤0.0032% or undetectable disease in cDNA with >32,000 control transcripts. (e.g. >=4.5 log reduction from the IRIS standardised baseline)
  - **TFR** → This state represents patients who safely discontinued their treatment given they entered a remission phase.
  - **non-CML related death**.

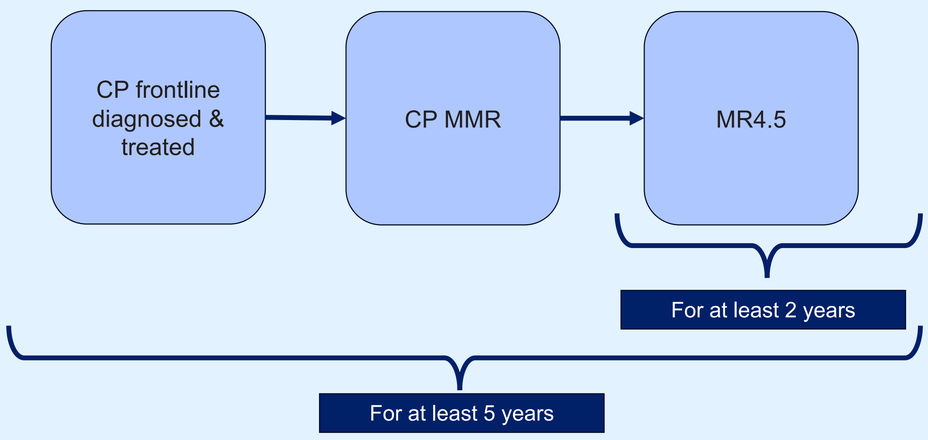
Figure 1. Model structure illustrating patients' pathway to response

- Patients enter the model at the CP Frontline state, where they are diagnosed and treated. At each cycle, patients may remain in their current state, transition to another state upon achieving a response, or die from non-CML causes.
- Model estimates also 1L treatment after 36 months will transition to 2L.
- Those who do not respond to treatment transition to second-line and later therapies, even though these are not explicitly presented here. Patients responding to treatment transition through MMR and MR4.5 health states to a dedicated TFR health state.

TFR modelling using the above model structure

- Modelling of TFR eligibility focused on patients with Chronic Phase CML who had received first-line TKI therapy for at least five years and achieved sustained MR4.5 for a minimum of two years, aligning with optimal definition described in the European LeukemiaNet guidelines for TFR (**Figure 2**).[1]
- The eligibility thresholds of five-year treatment duration and two year sustained MR4.5 were considered conservative assumptions compared to real-world clinical practice in CML treatment, according to a panel of experts.
- Tunnel-state approach ensures patients remain on 1L TKI for at least 60 months with ≥24 months in DMR (MR4.5) before entering TFR
- Transition probabilities were primarily informed by ASC4FIRST data at 96 weeks.
- The duration of TFR was assumed to be equal across treatment arms, meaning the benefit of TFR was driven by the proportion of patients entering the TFR state rather than the length of time spent in TFR.
- If patients lose response while in the TFR state, they will return to their initial 1L treatment in the CP Long term DMR state. These patients will not be eligible for a subsequent attempt at TFR.

Figure 2. TFR Eligibility



DATA INPUTS AND RESULTS

Transition probabilities to inform the TFR eligibility

- All patients entered the model in the CP Frontline state (diagnosed and treated). At 96 weeks, 81.09% of patients in the Asciminib arm achieved MMR compared with 61.27% in the All Comparators arm (**Table 1**).
- Among patients achieving MMR, 44.79% in the Asciminib arm and 35.20% in the All Comparators arm achieved MR4.5 at 96 weeks (**Table 1**).

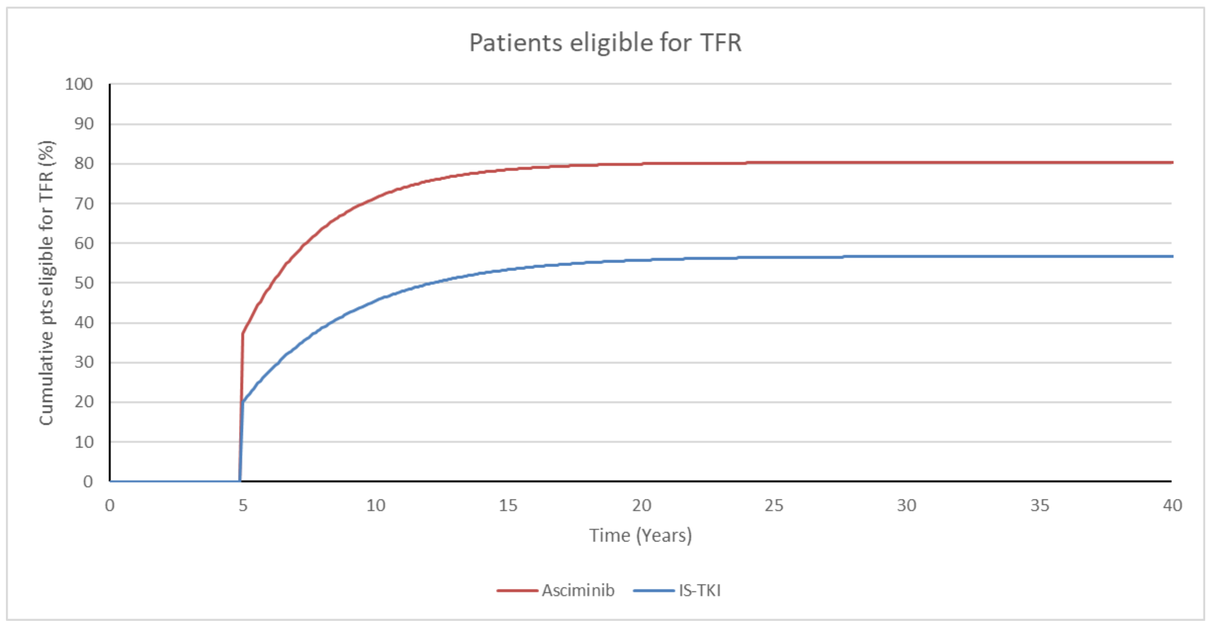
Table 1. ASC4FIRST MMR at 96 weeks

	All Patients (IS-TKI)	
Outcome	Asciminib	All Comparators
Number of subjects (n)	201	204
MMR at 96 weeks (n)	163	125
MMR Rate at 96 weeks (%)	81.09%	61.27%
MR4.5 at 96 weeks (n)	73	44
MR4.5 rate at 96 weeks (%)	44.79%	35.20%

TFR eligibility

- At the first eligibility point (5 years), 37.2% of asciminib-treated patients were projected to qualify for TFR, compared to 19.9% for IS-TKIs. Over a 40-year horizon, asciminib increased the probability of achieving TFR by 23.6 percentage points. The projections for IS-TKIs align with TKI long-term clinical trial data (**Figure 3**).

Figure 3. Patients eligible for TFR



Time in TFR

- Given TFR data was not available from the ASC4FIRST trial, a targeted literature search was conducted focusing on studies in first line CML reporting TFR outcomes.[2]
- Based on an analysis of IPD from the ENESTFreedom trial with a follow-up of 5 years, the mean time in TFR was estimated to be 30 months.[3] Time in TFR was assumed to be equal for both treatment arms, which was considered a conservative assumption.
- As longer-term follow-up becomes available, the estimated mean time in TFR is expected to increase, reflecting the tail-end plateau of the ENESTFreedom time-to-event curve

Discussion

- Based on the definition of TFR eligibility, it is anticipated that asciminib-treated patients will, on average, spend more time on DMR (MR4.5) before attempting TFR. This could potentially lead to a longer TFR duration compared to other treatment options. [4]

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Disclosures

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