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POSTER ABSTRACTS

904.OUTCOMES RESEARCH-NON-MALIGNANT CONDITIONS

A Patient-Centric Approach to Sickle Cell Disease Clinical Trials: Integrating Patient Perspectives in the RISE UP Phase 2/3 Trial of Mitapivat for Informed Protocol Design and Associated Patient Community Benefit

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Background: Sickle cell disease (SCD) is a genetic blood disorder that affects millions of people worldwide. There are currently limited treatment options and a high unmet need; new therapies - and therefore new trials - are essential. Although there is evidence of growing patient (pt) participation in the drug development processes, there is a lingering suspicion among the community that they are not treated as equal partners and too frequently regarded as mere data sources. Involving pts in planning and execution of clinical trials is essential to improve participation and meet the real needs of the patient community. Mitapivat is a first-in-class, oral, allosteric activator of pyruvate kinase (PK), approved by the United States Food and Drug Administration for the treatment of hemolytic anemia in adults with PK deficiency, by the European Union European Medicines Agency, and the Medicines and Healthcare products Regulatory Agency in Great Britain for the treatment of PK deficiency in adults. The RISE UP phase 2/3 trial (NCT05031780) of mitapivat in pts with SCD was therefore devised to use a new approach to clinical trial design and recruitment that considered pt preferences wherever possible.
Objective: Using the RISE UP Phase 2/3 trial, redefine best practices in clinical trial design by asking pts with SCD to describe what matters most to them in a trial setting and by involving them in decision making processes and trial awareness communications.
Methods: Nine SCD pts and advocates (five from the US, one from Bahrain, one from France and two from the UK) took part in a series of clinical trial design workshops. Four remote advisory board interviews were held with pts (>16 years of age) and advocates to consult on the RISE UP Phase 2/3 clinical trial design. The insights gained from these consultations were incorporated into the proposed trial protocol design that was subsequently shared with Health Authorities (HAs) for their comment from a regulatory perspective. Once finalized, feedback from HAs was presented to the steering committee to determine whether changes requested by HAs met the needs and barriers-to-uptake expressed during partner consultations. In addition, a group of seven patients were involved in the development of the RISE UP phase 2/3 clinical trial awareness campaign, which sought to educate the community about the RISE UP clinical trial and value of pt participation.
Results: Pt contributions to the protocol design included modified inclusion/exclusion criteria and the addition of pain (beyond pain crises) and fatigue as study outcomes. An overview of the community feedback is shown in Table 1. In response to pt input, monthly study visits were implemented for seven months, followed by visits every three months. An open label extension period was also added with visits on the second, fourth, eighth, and twelfth weeks of the extension period, followed by every 3 months up to 1.5 years and every six months thereafter.
Taking additional pt input into account, the trial was adjusted to include a recommendation for tailored management of SCD pain crises using a daily diary. Additionally, following patient recommendations, the trial approved reimbursement for study-related travel, lodging, and specific non-study assessments.

The RISE UP communications campaign was effective, with heightened interest in clinical trial participation generated within the community. Strong social media engagement and digital efforts resulted in increased trial website views, and community education and awareness efforts resulted in increased *clinicaltrials.gov* views to an average of 2-3 clicks per day. Approximately 278,000 users visited the RISE UP website and the campaign's YouTube video, which launched on World Sickle Cell Day has attracted 3 million views since Q4 2022.

Conclusion: To meet the needs of the SCD pt and caregiver community and advance clinical trial research, we implemented a patient-centered approach to clinical trial protocol design and trial recruitment. Overall, this patient-centric approach could be useful in improving community engagement, designing trials that better reflect the needs and concerns of the pt population, and ultimately improving pt participation and diverse representation in clinical trials.

Disclosures Jonassaint: *Agios:* Consultancy, Honoraria; *Expressive Painimation:* Current Employment, Current equity holder in private company. **Eppinger:** *Agios:* Consultancy, Honoraria. **Friend:** *Agios:* Consultancy, Honoraria. **Green:** *Agios:* Consultancy, Honoraria. **Robinson:** *Agios:* Consultancy, Honoraria. **Woolford:** *Agios Pharmaceuticals:* Consultancy, Honoraria. **Wyant:** *Agios:* Consultancy, Honoraria. **Davis:** *Agios Pharmaceuticals:* Current Employment, Current equity holder in publicly-traded company. **Oluyadi:** *Agios Pharmaceuticals, Inc.:* Current Employment, Current equity holder in publicly-traded company. **Zaidi:** *Agios Pharmaceuticals:* Current Employment, Current equity holder in publicly-traded company. **John:** *Agios:* Current Employment, Current equity holder in publicly-traded company. **Smith:** *Agios:* Consultancy, Research Funding.

Table 1. RISE UP trial design. Summary of community feedback on different aspects of the study design. Hb=hemoglobin; PROs=patient-reported outcomes.

Study Aspect	Community Feedback
Study duration	• 12-month study duration may hamper participation and/or compromise compliance.
Post-study access	• Important to provide patients access to treatment after completion of the clinical trial.
Study endpoints	• Correlate Hb change with high quality PROs. • Evaluate pain and fatigue. • Provide flexibility with questionnaire and minimize questionnaire burden.
Eligibility criteria	• Demonstrating effect in patients with Hb <8 g/dL could be beneficial. • Prohibiting concomitant therapies (e.g., hydroxyurea or exchange transfusion) may preclude patient participation.

Figure 1

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