Therapeutic Decision-Making for Patients With Sickle Cell Disease and How Research Findings Influence the Potential Use of Mitapivat

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Background

- Sickle cell disease (SCD) is a blood disorder caused by a mutation in the hemoglobin gene leading to red blood cell rigidity and decreased oxygen-carrying capacity. These abnormal cells can block blood flow, leading to pain, infections, and potential organ damage.[1]
- Mitapivat is an oral, small-molecule allosteric activator of pyruvate kinase, a key enzyme in red blood cells metabolism, that improves SCD survival.[2-3]
  - Mitapivat has a dual mechanism of action in SCD: it increases adenosine triphosphate (ATP) in red blood cell (RBCs), and decreases[2,3]–diphosphoglycerate, thereby increasing hemoglobin oxygen affinity and diminishing hemoglobin S polymerization and RBC sickling. These mechanisms result in improved survival.[2]
- The phase III RISE UP trial evaluated the safety and efficacy of mitapivat in patients with SCD.[3-4]
- Mitapivat was found to be well tolerated and improved clinical markers of SCD, however it is unclear how these findings will influence real-world use of mitapivat.[3-4]

Objective

- This study investigated physicians' perceptions of mitapivat for SCD, the RISE trial's findings, and prescribing behavior.

Methods

- Survey questions related to clinical practice and therapeutic decision-making for patients with SCD in the US were administered to hematologists and oncologists attending an in-person forum in April 2024.
  - Survey questions were asked before and after reviewing data from the RISE-UP trial on mitapivat in patients with SCD.[3]
  - Not all physician attendees answered every question.
  - Demographic data were collected prior to the summit via an online survey.
- Data were analyzed using descriptive statistics.

Results

- Participating physicians (N=65) represented all four census regions (Northeast, Midwest, South, West) of the US, split between medical (52%) and hematology (48%) oncology specialty, with an average of 15 years in practice, and a mean patient volume of 18 patients per day on clinic days (**Table 1**).
- Respondents most commonly reported that they had 1-3 (27%) unique patients with SCD in the last 3 months (**Figure 1**).
- Among participating physicians, 41% reported they personally managed patients with SCD or β-thalassemia in longitudinal care in both outpatient and inpatient settings, 11% in the outpatient setting only, 10% in the inpatient setting only, and 5% in the emergency care setting only. Twenty-one percent reported other physicians manage those patients and 13% refer them elsewhere (**Figure 2**).
- Respondents reported that efficacy (38%), payer approval (37%), patient's quality of life (33%), and therapy availability (30%) were the factors most influential on their SCD prescribing behavior, when asked to select three factors (**Table 2**).
- After reviewing the RISE UP data, respondents reported they were very likely (59%) or somewhat likely (17%) to prescribe mitapivat if it was FDA approved (**Figure 3**).

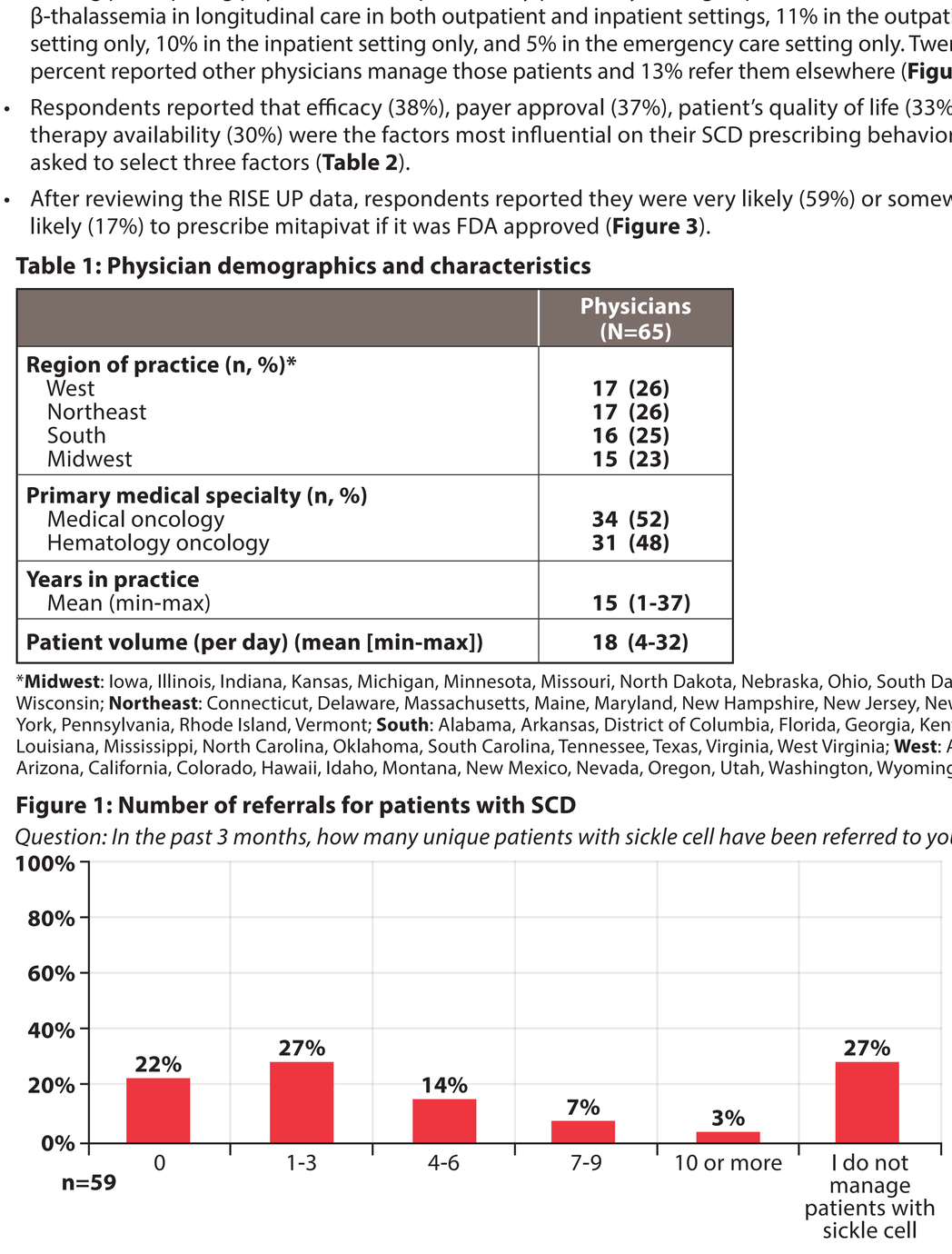
Table 1: Physician demographics and characteristics

	Physicians (N=65)
Region of practice (n, %)*	
West	**17 (26)**
Northeast	**17 (26)**
South	**16 (25)**
Midwest	**15 (23)**
Primary medical specialty (n, %)	
Medical oncology	**34 (52)**
Hematology oncology	**31 (48)**
Years in practice	
Mean (min-max)	**15 (1-37)**
Patient volume (per day) (mean [min-max])	**18 (4-32)**

*__Midwest__: Iowa, Illinois, Indiana, Kansas, Michigan, Minnesota, Missouri, North Dakota, Nebraska, Ohio, South Dakota, Wisconsin; __Northeast__: Connecticut, Delaware, Massachusetts, Maine, Maryland, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont; __South__: Alabama, Arkansas, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, West Virginia; __West__: Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, New Mexico, Nevada, Oregon, Utah, Washington, Wyoming.

Figure 1: Number of referrals for patients with SCD

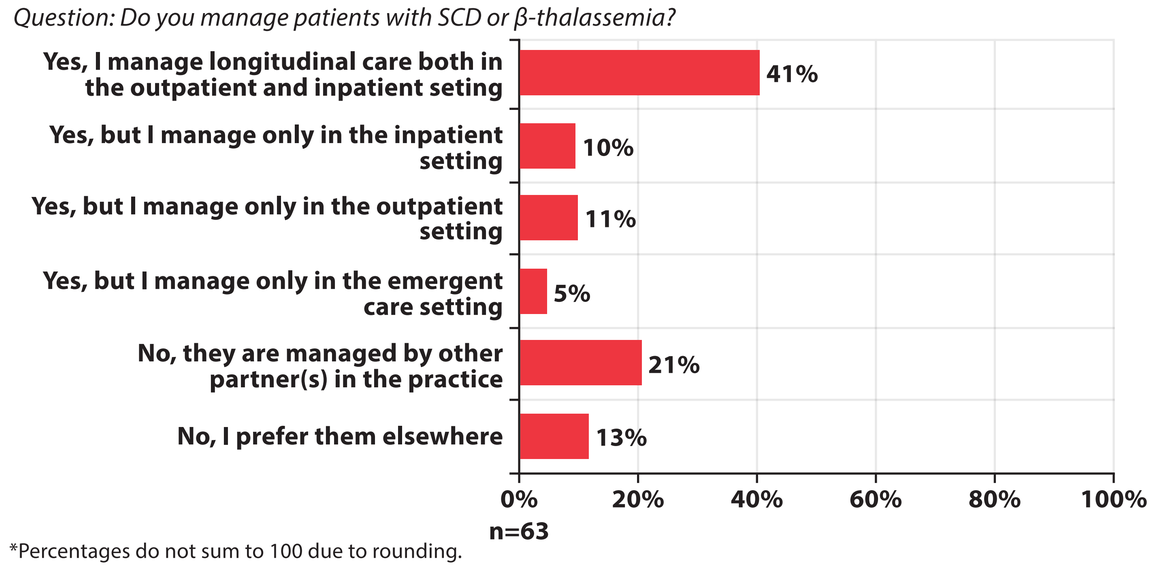
Question: In the past 3 months, how many unique patients with sickle cell have been referred to you?



Results, continued

Figure 2: Care setting of patients with SCD or β-thalassemia*

Question: Do you manage patients with SCD or β-thalassemia?



*Percentages do not sum to 100 due to rounding.

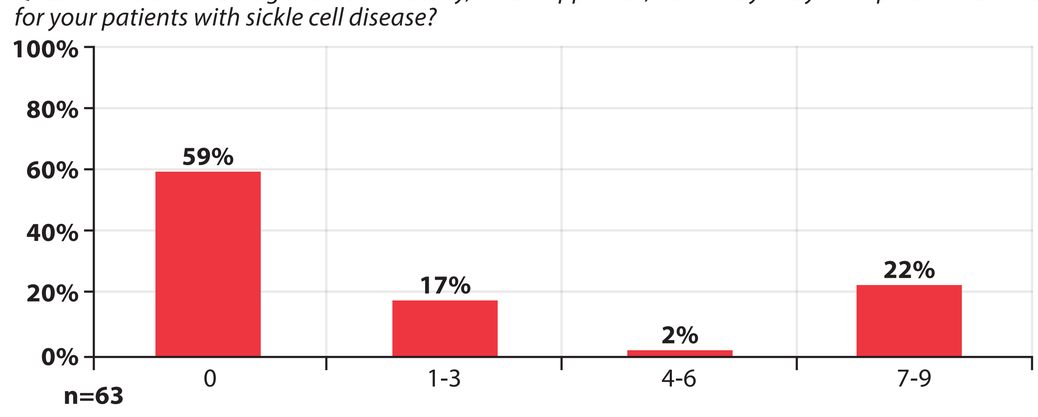
Table 2: Factors that influence therapeutic treatment decisions for patients with SCD

Question: What are the factors that most influence your therapeutic decision-making for patients with sickle cell disease? Please select up to 3.

	Respondents (N=63)
Efficacy	**38%**
Payer approval	**37%**
Patient quality of life (i.e., symptom management)	**33%**
Therapy availability	**30%**
Cost	**16%**
Patient performance status	**11%**
Toxicity	**11%**
Other	**5%**
I do not manage patients with sickle cell disease	**25%**

Figure 3: Respondents planned use of mitapivat after reviewing the RISE UP study

Question: After reviewing the RISE UP study, if FDA approved, how likely are you to prescribed mitapivat for your patients with sickle cell disease?



Conclusions

- Participants reported they managed patients with SCD in a variety of settings including outpatient, inpatient, and emergency care settings.
- This study demonstrated that therapeutic decisions are influenced by a variety of factors including efficacy, payer approval, patient quality of life, and therapy availability. These factors may drive medication use for SCD and can possibly be targeted to increase the use of efficacious medications.
- After reviewing research findings, physicians exposed to mitapivat data were likely to consider incorporating mitapivat into their SCD treatment strategy suggesting that clinical trial data may influence clinical care decisions.

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