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Previewing at Level 3

Refid: 10, Hu, Y. H. and Ruckenstein, E., Tunable Delocalization of Unpaired Electrons of Nitroxide Radicals for Sickle-Cell Disease Drug Improvements, *J Phys Chem B*, 2007

State: Excluded, Level: 2

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ARTICLE Review Form

Does this article POTENTIALLY apply to any of the Key Questions?

1. **NO, this article DOES NOT apply to any of the Key Questions** (check all of the following reasons that apply):

- [ ] no original data (include ineligible reviews in this category)
- [ ] in vitro only
- [ ] too small-case report or case series of < 20 unless it is PRIMARILY reporting toxicities
- [x] not relevant to key questions
- [ ] other: specify

2. **ARTICLE OF INTEREST (does not apply to key questions)**

- ( ) Pull article for hand searching or reference
- ( ) Not relevant to project but please tag

Clear Selection

This article MAY apply to one or more of the Key Questions, choose all that apply. (identify which key question an article applies to AND the subquestion it applies to)

Key Question 1

What is the evidence regarding efficacy of hydroxyurea treatment for patients with SCD?

Key Question 1	This is a study of patients with **sickle cell anemia**, taking **HU alone or in combination** and is a:
( ) Applies to KQ1 Clear Selection	[ ] Controlled trial or randomized trial of any size [ ] Case series/cohort involving > or = 20 patients [ ] Small Case series involving < 20 patients with sickle cell but leukemia or malignancy is mentioned as an outcome despite this being an effectiveness study [ ] Study of biomarkers in > or = 20 patients on HU

Key Question 2

What is the evidence regarding effectiveness of hydroxyurea treatment for patients with SCD?

Key Question 2	This is a study of patients with **sickle cell anemia**, taking **HU alone or in combination** and is a:
( ) Article applies to KQ2 Clear Selection	[ ] Controlled trial or randomized trial of any size in a community or primary care setting [ ] Case series/cohort involving > or = 20 patients [ ] Small Case series involving < 20 patients with sickle cell but leukemia or malignancy is mentioned as an outcome despite this being an effectiveness study

	☐ Study of biomarkers in > or = 20 patients on HU

Key Question 3

What is the evidence regarding the short- and long-term harms of hydroxyurea treatment?

Key Question 3	This study is:
○ Applies to KQ3 Clear Selection	☐ Any study design, any size, describing toxicities of HU *alone or in combination* in sickle cell anemia ☐ Observational studies (> or = 20) of HU *alone* in CML/ET/PV/HIV/psoriasis/etc. including desription of toxicities ☐ Case report or small case series (<20) ***primarily*** describing toxicities of HU *alone* in these other diseases (CML/ET/PV/HIV/psoriasis/etc) ☐ Controlled trials or randomized trials (two or more arms): in CML/ET/PV/psoriasis where the comparison is HU vs. anything including placebo (must have at least 20 patients in the HU alone arm) ☐ Controlled trials or randomized trials (two or more arms): in HIV where the comparison is: HU vs. HIV drugs; HU vs. HU/HIV drugs; HU vs. no drug (must have at least 20 patients in the HU alone arm)

Key Question 4

What barriers to the use of therapies for treatment of SCD have been investigated and what is the evidence that these purported barriers influence use of these treatments?

Key Question 4	This study is:
○ Applies to KQ4 Clear Selection	☐ Any study design with primary data about the *test of an intervention to overcome barriers to care* that interfere with 1) receipt of medication, 2) receipt of scheduled care, 3) adherence to mediciation ☐ Any study design in which *barriers to care* were investigated as affecting 1) receipt of medication, 2) receipt of scheduled care, 3) adherence to mediciation ☐ Any study design in which patients/providers/family report what they perceive to be barriers to 1) receipt of medication, 2) receipt of scheduled care, 3) adherence to mediciation ☐ Any study design with primary data about the existence of the barriers in our causal diagram*

*we are not collecting studies about the existence of a) cognitive difficulties, b) genotype differences, c) disease severity, d) comorbidities unless these are described specifically as barriers to care

11. **Reviewer Comments**

Enlarge Shrink

Submit Data

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Previewing at Level 9

Refid: 10, Hu, Y. H. and Ruckenstein, E., Tunable Delocalization of Unpaired Electrons of Nitroxide Radicals for Sickle-Cell Disease Drug Improvements, *J Phys Chem B*, 2007

State: Excluded, Level: 2

Submit Data

Key Question 4

What barriers to the use of therapies for treatment of SCD have been investigated and what is the evidence that these purported barriers influence use of these treatments?

This form is to be filled out for ALL studies applying to KQ4

1. Does study provide evidence: (check all that apply)

- ☐ for the existence of putative barrier **(D)**
- ☐ for patients/providers reports of barriers **(C)**
- ☐ that a (putative or other) barrier is a barrier **(B)**
- ☐ for the effectiveness of an intervention to overcome a barrier? **(A)**

2. Study Design

- ○ RCT
- ○ CCT
- ○ Pre-post intervention evaluation
- ○ Descriptive--quantitative
- ○ Descriptive--qualitative
- ○ Descriptive--Mixed

Clear Selection

3. Nurses	4. Physicians	5. Other Health Professionals	6. Patients	7. Family/caregivers
☐ mixed or unspecified	☐ unspecified or mixed	☐ PA	○ check here if this population is providing data	○ specify
☐ inpatient	☐ hematologists	☐ social worker	Clear Selection	Clear Selection
☐ outpatient	☐ ED doctors	☐ other		
☐ ED	☐ internists			
☐ other	☐ pediatricians			
	☐ physiciens-in-training			
	☐ other			

Population characteristics of each category identified above

Population characteristics of PATIENTS only

8. N	9. Age	10. Gender	11. Race	12. Genotype	13. Substance use	14. Socioeconomic status
Enlarge Shrink	Mean	Male, n (%)	White (non-hispanic), n (%)	SS, n (%)	Alcohol user, n (%)	Low, define
	Median	Female, n (%)	Black (non-hispanic), n (%)	SC, n (%)	Smoker, n (%)	n (%)
	Range		White hispanic, n (%)	S ß+ thalassemia, n (%)	Illegal dug user, n (%)	Middle, define
			Black hispanic, n (%)	S ß^0 thalassemia, n (%)		n (%)
			Latino/Hispanic, n (%)	other, define, n (%)		High, define
			Asian/Pacific Islander, n (%)			n (%)
			Other (specify), n (%)			

Population characteristics of NON-PATIENTS only

	describe	n	sex	race
15. Category 1				
16. Category 2				
17. Category 3				
18. Category 4				

Type of Barrier (check all that apply)

System	Patient	Provider	Other
☐ health system organization	☐ age	☐ provider race/ethnicity	specify
			specify

insurance	health beliefs	speciality	
costs	risk tolerance	respect for patients	specify
continuity of care	depression	outcome expectancy	specify
access to providers	distrust	familiarity	
patient-provider communication	self-efficacy	practice Patterns	
quality of pain management	substance abuse	risk tolerance	
	preferences	attitudes	
	genotype	time constraints	
	knowledge	knowledge	
	SES	resources	
	burden	monitoring burden	
	family/social support	training	
	cognitive abilities	self-efficacy	
	disease severity	inertia	
	comorbid conditions		
	pseudoaddiction		

For A, B, and C ONLY

23. Type of outcome measure (check all that apply)

- Attendence at scheduled provider visits
- Receipt of medications
- Adherence to medications

24. If outcome measure is about use of a medication/therapy: (check all that apply)

- hydroxyurea
- folate
- penicillin
- iron chelators
- transplant
- transfusion
- vaccines
- other drugs (arginine,azacitine, sodium butyrate, decitabine)
- dental care
- pain management regimen
- other, specify
- not specified

For A and B ONLY

25. How was the Outcome Measured? (check all that apply)

- Patient report
- Provider report
- Family report
- Administrative data
- Biologic outcome, specify (e.g tooth decay, HgF, etc.)
- Other, specify

For A Only

26. Objective of intervention (concisely write in)

Enlarge Shrink

27. Description of the intervention including a brief description of any control population (concisely write in)

Enlarge Shrink

28. Reviewer interpretation of data from intervention studies:

- [ ] Improvement as a results of the intervention
- [ ] Partial improvement as a results of the intervention
- [ ] No improvement as a results of the intervention
- [ ] Worsening as a results of the intervention

For ALL KQ 4 Studies

29. Main Results (concisely write in)

Enlarge Shrink

30.

Comments

Enlarge Shrink

Submit Data

Click a link below to review this article at these other levels.

4. TRIAGE
5. GENERAL
6. KQs 1, 2, or 3
7. Additional Arms
8. KQ3 TOX Case Reports
10. QUALITY--observational studies
11. QUALITY--controlled trials
12. QUALITY--qualitative studies
13. QUALITY--surveys
19. Renee data abstraction

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Previewing at Level 11

Refid: 10, Hu, Y. H. and Ruckenstein, E., Tunable Delocalization of Unpaired Electrons of Nitroxide Radicals for Sickle-Cell Disease Drug Improvements, *J Phys Chem B*, 2007

State: Excluded, Level: 2

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QUALITY FORM
JADAD (quality for controlled trials)

1. Was the study described as randomized (this includes the use of words such as randomly, random, and randomization)? *In other words, was the allocation concealed?*

Hint: appropriate methods of randomization are computer-generated random numbers, random number tables (if unspecified, don't give them a +1 or a -1)

- Yes
- No

Clear Selection

2. If the answer to question #1 is "yes," then answer the following:

- Was the method used to generate the sequence of randomization described and it was appropriate? (+1)
- Was the method of randomization was described but it was inappropriate? (-1)
- Neither a nor b

Clear Selection

3. Was the study described as double blind? *In other words, were the outcome assessors blind in addition to the patients?*

- Yes
- No

Clear Selection

4. If the answer to question #3 is "yes," then answer the following:

- the method of double blinding was described and it was appropriate (+1)
- the study was described as being blind but the method of blinding was inappropriate (-1)

Clear Selection

5. Was there a description of withdrawals and dropouts?

- Yes
- No

Clear Selection

Did the study report the number lost to follow-up?

	Yes (enter "n")	No
6. Arm 1		Clear
7. Arm 2		Clear
8. Arm 3		Clear

9. Arm 4 Clear

Submit Data

Click a link below to review this article at these other levels.

4. TRIAGE
5. GENERAL
6. KQs 1, 2, or 3
7. Additional Arms
8. KQ3 TOX Case Reports
9. KQ4 Barriers
10. QUALITY--observational studies
12. QUALITY--qualitative studies
13. QUALITY--surveys
19. Renee data abstraction

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Previewing at Level 12

Refid: 10, Hu, Y. H. and Ruckenstein, E., Tunable Delocalization of Unpaired Electrons of Nitroxide Radicals for Sickle-Cell Disease Drug Improvements, *J Phys Chem B*, 2007

State: Excluded, Level: 2

Submit Data

QUALITY FORM
Qualitative Research

1. How were the data generated? (Check all that apply)

- [ ] Field observation/participant observation
- [ ] In-depth interviews
- [ ] Focus groups
- [ ] Document analysis
- [ ] Other _____

2. Is there a description of the theoretical basis for the study?

- ( ) No
- ( ) To some extent
- ( ) Yes, with description of a named theory or presentation of a causal diagram

Clear Selection

3. Is there description of why these participants were selected?

- ( ) No
- ( ) To some extent
- ( ) Yes, with detailed description: *how these specific people are expected to contribute, conditions which make them eligible for study*

Clear Selection

4. Did the researchers compose the focus groups or interview setting to maximize data gathering (ensuring patient comfort, confidentiality, choice of appropriate interviewer or techniques for data gathering)?

- ( ) No or can't tell
- ( ) To some extent
- ( ) Yes, with detailed description

Clear Selection

5. Do the authors report theme exhaustion (continuing the discussion until no new themes emerge)?

- ( ) NA
- ( ) No
- ( ) To some extent
- ( ) Yes, with detailed description

Clear Selection

6. Has the author rendered transparent the processes by which data have been collected, analyzed and presented? (can be audited, verified)

- ( ) No

- ○ To some extent
- ○ Yes: *detailed description of theoretical, methodological and analytic decisions*

Clear Selection

7. Do the authors describe their own biases? (also called reflexivity)

- ○ No
- ○ To some extent
- ○ Yes, with detailed description

Clear Selection

8. Is there any use of triangulation, i.e. gathering of additional data to provide a more complete picture of the participants' world and experiences? An additional piece of the puzzle?

- ○ No mention
- ○ To some extent
- ○ Yes, with detailed description of the source of additional data and how it corroborates observed results

Clear Selection

9. Do the authors synthesize, interpret, or develop a concept, model, or theory based on the subjective data collected?

- ○ No (just present raw material)
- ○ To some extent (just synthesis of data)
- ○ Yes, well-developed interpretation of how reports support model

Clear Selection

Submit Data

Click a link below to review this article at these other levels.

4. TRIAGE
5. GENERAL
6. KQs 1, 2, or 3
7. Additional Arms
8. KQ3 TOX Case Reports
9. KQ4 Barriers
10. QUALITY--observational studies
11. QUALITY--controlled trials
13. QUALITY--surveys
19. Renee data abstraction

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Previewing at Level 13

Refid: 10, Hu, Y. H. and Ruckenstein, E., Tunable Delocalization of Unpaired Electrons of Nitroxide Radicals for Sickle-Cell Disease Drug Improvements, *J Phys Chem B*, 2007

State: Excluded, Level: 2

Submit Data

QUALITY FORM
Surveys

1.
What data collection methods were used in the study? (Check all that apply)

- [ ] Self-administered questionnaire
- [ ] Mailed questionnaire
- [ ] Group-administered setting
- [ ] Face-to-face interviews
- [ ] Telephone interviews
- [ ] Computer or computer assisted device (CAD)
- [ ] Other/unclear

2. Did the study describe the setting or population from which the study sample was drawn?

- ( ) No
- ( ) To some extent
- ( ) Yes, with detailed description: *setting (e.g., clinic), location, and dates*

Clear Selection

3. Were the inclusion or exclusion criteria described? (just saying “sickle cell disease” is insufficient)

- ( ) No
- ( ) To some extent
- ( ) Yes, with detailed description: *methods for selection of participants, or inclusion/exclusion criteria, or diagnostic criteria for enrollment*

Clear Selection

4. Does the study describe key characteristics of study participants at enrollment/baseline?

- ( ) No
- ( ) To some extent
- ( ) Yes, with detailed description: *ages, sex, genotype, relevant comorbidities which would influence outcomes*

Clear Selection

5. What is the survey completion rate?

- ( ) Can’t calculate
- ( ) n/N
- ( ) %

Clear Selection

6. Is there a statement that the authors used a previously validated instument?

- ( ) No

- To some extent (provides a reference)
- Yes, providees a reference and states that it was validated in the sickle cell population

Clear Selection

7.

Is there any discussion of the **validity** of the survey instrument (any one is sufficient)

- NA--this is NOT an option do not select this answer!
- No
- Yes. Only poor discussion of validity or good discussion with poor validity
- Yes, good definition and high validity

Clear Selection

Face / content validity	Degree to which an instrument accurately represents the skill or characteristic it is designed to measure, based on people's experience and available knowledge
Concurrent criterion validity	Degree to which an instrument produces the same results as another accepted or proven instrument that measures the same variable
Predictive criterion validity	Degree to which a measure accurately predicts expected outcomes
Construct validity	Degree to which a test measures the theoretical construct it intends to measure

8. Is there any discussion of the **reliability** of the survey insturment? (any one is sufficient)

- No
- Yes. Only poor discussion of reliability or good discussion with poor reliability
- Yes, good discussion and high reliability

Clear Selection

Intra-rater reliability	Degree to which measurements are the same when repeated by the same person
Inter-rater reliability	Degree to which measurements are the same when obtained by the different persons
Test-retest reliability	Degree to which the same test produces the same results when repeated under the same conditions
Equivalence reliability	Degree to which alternate forms of the same measurement instrument produce the same results
Internal consistency (inter-item) reliability	How well items reflecting the same construct yield similar results

Submit Data

Click a link below to review this article at these other levels.

4. TRIAGE
5. GENERAL
6. KQs 1, 2, or 3
7. Additional Arms
8. KQ3 TOX Case Reports
9. KQ4 Barriers
10. QUALITY--observational studies
11. QUALITY--controlled trials
12. QUALITY--qualitative studies
19. Renee data abstraction

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Previewing at Level 1

Refid: 10, Hu, Y. H. and Ruckenstein, E., Tunable Delocalization of Unpaired Electrons of Nitroxide Radicals for Sickle-Cell Disease Drug Improvements, *J Phys Chem B*, 2007

State: Excluded, Level: 2

Submit Data

1. Does this article POTENTIALLY apply to ANY of the Key Questions

- ○ YES--this article POTENTIALLY applies
- ◉ NO--this article DOES NOT apply

Clear Selection

Submit Data

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Form Last Modified: Not available

Previewing Only: You cannot submit data from this form

Previewing at Level 8

Refid: 10, Hu, Y. H. and Ruckenstein, E., Tunable Delocalization of Unpaired Electrons of Nitroxide Radicals for Sickle-Cell Disease Drug Improvements, *J Phys Chem B*, 2007

State: Excluded, Level: 2

Submit Data

Key Question 3
Causality Form for Toxicity Case Reports

Case 1

1. What is the underlying disease?

- [ ] Sickle cell anemia
- [ ] Thalessemia
- [ ] CML
- [ ] Polycythemia vera
- [ ] Essential thrombocythemia
- [ ] Leukemia
- [ ] Psoriasis
- [ ] Other cancer
- [ ] HIV
- [ ] Other

2. Age

years:

3. Sex:

- ( ) Male
- ( ) Female

Clear Selection

4. Is the treated patient a child (under 18) or an adult?

- ( ) Child
- ( ) Adult

Clear Selection

5. What is the reported event?

- [ ] Leg ulcer
- [ ] Nail change
- [ ] Rash
- [ ] Cytopenia
- [ ] Leukemia
- [ ] Cytogenetic change
- [ ] Other cancer
- [ ] Birth defect
- [ ] Other

Causality assessment

	Yes	No	
6. Is the time relationship from drug administration to the event *plausible* for causality to be established?	( )	( )	Clear
7. Is there an absence of concurrent diseases or other drugs that may have caused the event?	( )	( )	Clear
8. Is there a reasonable response to drug withdrawal?	( )	( )	Clear
9. Is there the existence of a rechallenge in this report or a demonstrated biological/pharmacological explanation?	( )	( )	Clear

10. Duration of Treatment

Enlarge Shrink

11. Time to occurene of toxicity

Enlarge Shrink

Case 2
DO NOT fill in this portion of the form if only 1 case is reported

12. What is the underlying disease?

- [ ] Sickle cell anemia
- [ ] Thalessemia
- [ ] CML
- [ ] Polycythemia vera
- [ ] Essential thrombocythemia
- [ ] Leukemia
- [ ] Psoriasis
- [ ] Other cancer
- [ ] HIV
- [ ] Other

13. Age

years:

14. Sex:

- ◯ Male
- ◯ Female

Clear Selection

15. Is the treated patient a child (under 18) or an adult?

- ◯ Child
- ◯ Adult

Clear Selection

16. What is the reported event?

- [ ] Leg ulcer
- [ ] Nail change
- [ ] Rash
- [ ] Cytopenia
- [ ] Leukemia
- [ ] Cytogenetic change
- [ ] Other cancer
- [ ] Birth defect
- [ ] Other

Causality assessment

	Yes	No	
17. Is the time relationship from drug administration to the event *plausible* for causality to be established?	◯	◯	Clear
18. Is there an absence of concurrent diseases or other drugs that may have caused the event?	◯	◯	Clear
19. Is there a reasonable response to drug withdrawal?	◯	◯	Clear
20. Is there the existence of a rechallenge in this report or a demonstrated biological/pharmacological explanation?	◯	◯	Clear

21. Duration of Treatment

Enlarge Shrink

22. Time to occurene of toxicity

Enlarge Shrink

Case 3
DO NOT fill in this portion of the form if only 1 case is reported

23. What is the underlying disease?

- [ ] Sickle cell anemia
- [ ] Thalessemia
- [ ] CML
- [ ] Polycythemia vera
- [ ] Essential thrombocythemia
- [ ] Leukemia
- [ ] Psoriasis
- [ ] Other cancer
- [ ] HIV
- [ ] Other

24. Age

years:

25. Sex:

- ( ) Male
- ( ) Female

Clear Selection

26. Is the treated patient a child (under 18) or an adult?

- ( ) Child
- ( ) Adult

Clear Selection

27. What is the reported event?

- [ ] Leg ulcer
- [ ] Nail change
- [ ] Rash
- [ ] Cytopenia
- [ ] Leukemia
- [ ] Cytogenetic change
- [ ] Other cancer
- [ ] Birth defect
- [ ] Other

Causality assessment

	Yes	No	
28. Is the time relationship from drug administration to the event *plausible* for causality to be established?	( )	( )	Clear
29. Is there an absence of concurrent diseases or other drugs that may have caused the event?	( )	( )	Clear
30. Is there a reasonable response to drug withdrawal?	( )	( )	Clear
31. Is there the existence of a rechallenge in this report or a demonstrated biological/pharmacological explanation?	( )	( )	Clear

32. Duration of Treatment

Enlarge Shrink

33. Time to occurene of toxicity

Enlarge Shrink

Case 4
DO NOT fill in this portion of the form if only 1 case is reported

34. What is the underlying disease?

- [ ] Sickle cell anemia
- [ ] Thalessemia
- [ ] CML
- [ ] Polycythemia vera
- [ ] Essential thrombocythemia
- [ ] Leukemia
- [ ] Psoriasis
- [ ] Other cancer
- [ ] HIV
- [ ] Other

35. Age

years:

36. Sex:

- ◯ Male
- ◯ Female

Clear Selection

37. Is the treated patient a child (under 18) or an adult?

- ◯ Child
- ◯ Adult

Clear Selection

38. What is the reported event?

- [ ] Leg ulcer
- [ ] Nail change
- [ ] Rash
- [ ] Cytopenia
- [ ] Leukemia
- [ ] Cytogenetic change
- [ ] Other cancer
- [ ] Birth defect
- [ ] Other

Causality assessment

	Yes	No	
39. Is the time relationship from drug administration to the event *plausible* for causality to be established?	◯	◯	Clear
40. Is there an absence of concurrent diseases or other drugs that may have caused the event?	◯	◯	Clear
41. Is there a reasonable response to drug withdrawal?	◯	◯	Clear
42. Is there the existence of a rechallenge in this report or a demonstrated biological/pharmacological explanation?	◯	◯	Clear

43. Duration of Treatment

Enlarge Shrink

44. Time to occurene of toxicity

Enlarge Shrink

Case 5

DO NOT fill in this portion of the form if only 1 case is reported

45. What is the underlying disease?

- [ ] Sickle cell anemia
- [ ] Thalessemia
- [ ] CML
- [ ] Polycythemia vera
- [ ] Essential thrombocythemia
- [ ] Leukemia
- [ ] Psoriasis
- [ ] Other cancer
- [ ] HIV
- [ ] Other

46. Age

years:

47. Sex:

- ◯ Male
- ◯ Female

Clear Selection

48. Is the treated patient a child (under 18) or an adult?

- ◯ Child
- ◯ Adult

Clear Selection

49. What is the reported event?

- [ ] Leg ulcer
- [ ] Nail change
- [ ] Rash
- [ ] Cytopenia
- [ ] Leukemia
- [ ] Cytogenetic change
- [ ] Other cancer
- [ ] Birth defect
- [ ] Other

Causality assessment

	Yes	No	
50. Is the time relationship from drug administration to the event *plausible* for causality to be established?	◯	◯	Clear
51. Is there an absence of concurrent diseases or other drugs that may have caused the event?	◯	◯	Clear
52. Is there a reasonable response to drug withdrawal?	◯	◯	Clear
53. Is there the existence of a rechallenge in this report or a demonstrated biological/pharmacological explanation?	◯	◯	Clear

54. Duration of Treatment

Enlarge Shrink

55. Time to occurene of toxicity

Enlarge Shrink

Case 6

DO NOT fill in this portion of the form if only 1 case is reported

56. What is the underlying disease?

- [ ] Sickle cell anemia
- [ ] Thalessemia
- [ ] CML
- [ ] Polycythemia vera
- [ ] Essential thrombocythemia
- [ ] Leukemia
- [ ] Psoriasis
- [ ] Other cancer
- [ ] HIV
- [ ] Other

57. Age

years:

58. Sex:

- ◯ Male
- ◯ Female

Clear Selection

59. Is the treated patient a child (under 18) or an adult?

- ◯ Child
- ◯ Adult

Clear Selection

60. What is the reported event?

- [ ] Leg ulcer
- [ ] Nail change
- [ ] Rash
- [ ] Cytopenia
- [ ] Leukemia
- [ ] Cytogenetic change
- [ ] Other cancer
- [ ] Birth defect
- [ ] Other

Causality assessment

	Yes	No	
61. Is the time relationship from drug administration to the event *plausible* for causality to be established?	◯	◯	Clear
62. Is there an absence of concurrent diseases or other drugs that may have caused the event?	◯	◯	Clear
63. Is there a reasonable response to drug withdrawal?	◯	◯	Clear
64. Is there the existence of a rechallenge in this report or a demonstrated biological/pharmacological explanation?	◯	◯	Clear

65. Duration of Treatment

Enlarge Shrink

66. Time to occurene of toxicity

Enlarge Shrink

Case 7

DO NOT fill in this portion of the form if only 1 case is reported

67. What is the underlying disease?

- [ ] Sickle cell anemia

- [ ] Thalessemia
- [ ] CML
- [ ] Polycythemia vera
- [ ] Essential thrombocythemia
- [ ] Leukemia
- [ ] Psoriasis
- [ ] Other cancer
- [ ] HIV
- [ ] Other

68. Age

years:

69. Sex:

- ( ) Male
- ( ) Female

Clear Selection

70. Is the treated patient a child (under 18) or an adult?

- ( ) Child
- ( ) Adult

Clear Selection

71. What is the reported event?

- [ ] Leg ulcer
- [ ] Nail change
- [ ] Rash
- [ ] Cytopenia
- [ ] Leukemia
- [ ] Cytogenetic change
- [ ] Other cancer
- [ ] Birth defect
- [ ] Other

Causality assessment

	Yes	No	
72. Is the time relationship from drug administration to the event *plausible* for causality to be established?	( )	( )	Clear
73. Is there an absence of concurrent diseases or other drugs that may have caused the event?	( )	( )	Clear
74. Is there a reasonable response to drug withdrawal?	( )	( )	Clear
75. Is there the existence of a rechallenge in this report or a demonstrated biological/pharmacological explanation?	( )	( )	Clear

76. Duration of Treatment

Enlarge Shrink

77. Time to occurene of toxicity

Enlarge Shrink

Case 8

DO NOT fill in this portion of the form if only 1 case is reported

78. What is the underlying disease?

- [ ] Sickle cell anemia
- [ ] Thalessemia
- [ ] CML

- [ ] Polycythemia vera
- [ ] Essential thrombocythemia
- [ ] Leukemia
- [ ] Psoriasis
- [ ] Other cancer
- [ ] HIV
- [ ] Other

79. Age

years:

80. Sex:

- ( ) Male
- ( ) Female

Clear Selection

81. Is the treated patient a child (under 18) or an adult?

- ( ) Child
- ( ) Adult

Clear Selection

82. What is the reported event?

- [ ] Leg ulcer
- [ ] Nail change
- [ ] Rash
- [ ] Cytopenia
- [ ] Leukemia
- [ ] Cytogenetic change
- [ ] Other cancer
- [ ] Birth defect
- [ ] Other

Causality assessment

	Yes	No	
83. Is the time relationship from drug administration to the event *plausible* for causality to be established?	( )	( )	Clear
84. Is there an absence of concurrent diseases or other drugs that may have caused the event?	( )	( )	Clear
85. Is there a reasonable response to drug withdrawal?	( )	( )	Clear
86. Is there the existence of a rechallenge in this report or a demonstrated biological/pharmacological explanation?	( )	( )	Clear

87. Duration of Treatment

Enlarge Shrink

88. Time to occurene of toxicity

Enlarge Shrink

Case 9

DO NOT fill in this portion of the form if only 1 case is reported

89. What is the underlying disease?

- [ ] Sickle cell anemia
- [ ] Thalessemia
- [ ] CML
- [ ] Polycythemia vera
- [ ] Essential thrombocythemia

- [ ] Leukemia
- [ ] Psoriasis
- [ ] Other cancer
- [ ] HIV
- [ ] Other

90. Age

years:

91. Sex:

- ◯ Male
- ◯ Female

Clear Selection

92. Is the treated patient a child (under 18) or an adult?

- ◯ Child
- ◯ Adult

Clear Selection

93. What is the reported event?

- [ ] Leg ulcer
- [ ] Nail change
- [ ] Rash
- [ ] Cytopenia
- [ ] Leukemia
- [ ] Cytogenetic change
- [ ] Other cancer
- [ ] Birth defect
- [ ] Other

Causality assessment

	Yes	No	
94. Is the time relationship from drug administration to the event *plausible* for causality to be established?	◯	◯	Clear
95. Is there an absence of concurrent diseases or other drugs that may have caused the event?	◯	◯	Clear
96. Is there a reasonable response to drug withdrawal?	◯	◯	Clear
97. Is there the existence of a rechallenge in this report or a demonstrated biological/pharmacological explanation?	◯	◯	Clear

98. Duration of Treatment

Enlarge Shrink

99. Time to occurene of toxicity

Enlarge Shrink

Case 10

DO NOT fill in this portion of the form if only 1 case is reported

100. What is the underlying disease?

- [ ] Sickle cell anemia
- [ ] Thalessemia
- [ ] CML
- [ ] Polycythemia vera
- [ ] Essential thrombocythemia
- [ ] Leukemia
- [ ] Psoriasis

- [ ] Other cancer
- [ ] HIV
- [ ] Other

101. Age

years:

102. Sex:

- ( ) Male
- ( ) Female

Clear Selection

103. Is the treated patient a child (under 18) or an adult?

- ( ) Child
- ( ) Adult

Clear Selection

104. What is the reported event?

- [ ] Leg ulcer
- [ ] Nail change
- [ ] Rash
- [ ] Cytopenia
- [ ] Leukemia
- [ ] Cytogenetic change
- [ ] Other cancer
- [ ] Birth defect
- [ ] Other

Causality assessment

	Yes	No	
105. Is the time relationship from drug administration to the event *plausible* for causality to be established?	( )	( )	Clear
106. Is there an absence of concurrent diseases or other drugs that may have caused the event?	( )	( )	Clear
107. Is there a reasonable response to drug withdrawal?	( )	( )	Clear
108. Is there the existence of a rechallenge in this report or a demonstrated biological/pharmacological explanation?	( )	( )	Clear

109. Duration of Treatment

Enlarge Shrink

110. Time to occurene of toxicity

Enlarge Shrink

Case 11

DO NOT fill in this portion of the form if only 1 case is reported

111. What is the underlying disease?

- [ ] Sickle cell anemia
- [ ] Thalessemia
- [ ] CML
- [ ] Polycythemia vera
- [ ] Essential thrombocythemia
- [ ] Leukemia
- [ ] Psoriasis
- [ ] Other cancer
- [ ] HIV

Other

112. Age

years:

113. Sex:

Male

Female

Clear Selection

114. Is the treated patient a child (under 18) or an adult?

Child

Adult

Clear Selection

115. What is the reported event?

Leg ulcer

Nail change

Rash

Cytopenia

Leukemia

Cytogenetic change

Other cancer

Birth defect

Other

Causality assessment

	Yes	No	
116. Is the time relationship from drug administration to the event *plausible* for causality to be established?			Clear
117. Is there an absence of concurrent diseases or other drugs that may have caused the event?			Clear
118. Is there a reasonable response to drug withdrawal?			Clear
119. Is there the existence of a rechallenge in this report or a demonstrated biological/pharmacological explanation?			Clear

120. Duration of Treatment

Enlarge Shrink

121. Time to occurene of toxicity

Enlarge Shrink

Case 12

DO NOT fill in this portion of the form if only 1 case is reported

122. What is the underlying disease?

Sickle cell anemia

Thalessemia

CML

Polycythemia vera

Essential thrombocythemia

Leukemia

Psoriasis

Other cancer

HIV

Other

123. Age

years:

124. Sex:

- Male
- Female

Clear Selection

125. Is the treated patient a child (under 18) or an adult?

- Child
- Adult

Clear Selection

126. What is the reported event?

- Leg ulcer
- Nail change
- Rash
- Cytopenia
- Leukemia
- Cytogenetic change
- Other cancer
- Birth defect
- Other

Causality assessment

	Yes	No	
127. Is the time relationship from drug administration to the event *plausible* for causality to be established?	◯	◯	Clear
128. Is there an absence of concurrent diseases or other drugs that may have caused the event?	◯	◯	Clear
129. Is there a reasonable response to drug withdrawal?	◯	◯	Clear
130. Is there the existence of a rechallenge in this report or a demonstrated biological/pharmacological explanation?	◯	◯	Clear

131. Duration of Treatment

Enlarge Shrink

132. Time to occurene of toxicity

Enlarge Shrink

Case 13

DO NOT fill in this portion of the form if only 1 case is reported

133. What is the underlying disease?

- Sickle cell anemia
- Thalessemia
- CML
- Polycythemia vera
- Essential thrombocythemia
- Leukemia
- Psoriasis
- Other cancer
- HIV
- Other

134. Age

years:

135. Sex:

Male

Female

Clear Selection

136. Is the treated patient a child (under 18) or an adult?

Child

Adult

Clear Selection

137. What is the reported event?

Leg ulcer

Nail change

Rash

Cytopenia

Leukemia

Cytogenetic change

Other cancer

Birth defect

Other

Causality assessment

	Yes	No	
138. Is the time relationship from drug administration to the event *plausible* for causality to be established?			Clear
139. Is there an absence of concurrent diseases or other drugs that may have caused the event?			Clear
140. Is there a reasonable response to drug withdrawal?			Clear
141. Is there the existence of a rechallenge in this report or a demonstrated biological/pharmacological explanation?			Clear

142. Duration of Treatment

Enlarge Shrink

143. Time to occurene of toxicity

Enlarge Shrink

Case 14

DO NOT fill in this portion of the form if only 1 case is reported

144. What is the underlying disease?

Sickle cell anemia

Thalessemia

CML

Polycythemia vera

Essential thrombocythemia

Leukemia

Psoriasis

Other cancer

HIV

Other

145. Age

years:

146. Sex:

Male

Female

Clear Selection
147. Is the treated patient a child (under 18) or an adult?

- ◯ Child
- ◯ Adult

Clear Selection
148. What is the reported event?

- ☐ Leg ulcer
- ☐ Nail change
- ☐ Rash
- ☐ Cytopenia
- ☐ Leukemia
- ☐ Cytogenetic change
- ☐ Other cancer
- ☐ Birth defect
- ☐ Other

Causality assessment

	Yes	No	
149. Is the time relationship from drug administration to the event *plausible* for causality to be established?	◯	◯	Clear
150. Is there an absence of concurrent diseases or other drugs that may have caused the event?	◯	◯	Clear
151. Is there a reasonable response to drug withdrawal?	◯	◯	Clear
152. Is there the existence of a rechallenge in this report or a demonstrated biological/pharmacological explanation?	◯	◯	Clear

153. Duration of Treatment

Enlarge Shrink
154. Time to occurene of toxicity

Enlarge Shrink

Case 15
DO NOT fill in this portion of the form if only 1 case is reported

155. What is the underlying disease?

- ☐ Sickle cell anemia
- ☐ Thalessemia
- ☐ CML
- ☐ Polycythemia vera
- ☐ Essential thrombocythemia
- ☐ Leukemia
- ☐ Psoriasis
- ☐ Other cancer
- ☐ HIV
- ☐ Other

156. Age

years:

157. Sex:

- ◯ Male
- ◯ Female

Clear Selection
158. Is the treated patient a child (under 18) or an adult?

- ◯ Child

Adult

Clear Selection

159. What is the reported event?

- Leg ulcer
- Nail change
- Rash
- Cytopenia
- Leukemia
- Cytogenetic change
- Other cancer
- Birth defect
- Other

Causality assessment

	Yes	No	
160. Is the time relationship from drug administration to the event *plausible* for causality to be established?			Clear
161. Is there an absence of concurrent diseases or other drugs that may have caused the event?			Clear
162. Is there a reasonable response to drug withdrawal?			Clear
163. Is there the existence of a rechallenge in this report or a demonstrated biological/pharmacological explanation?			Clear

164. Duration of Treatment

Enlarge Shrink

165. Time to occurene of toxicity

Enlarge Shrink

Case 16

DO NOT fill in this portion of the form if only 1 case is reported

166. What is the underlying disease?

- Sickle cell anemia
- Thalessemia
- CML
- Polycythemia vera
- Essential thrombocythemia
- Leukemia
- Psoriasis
- Other cancer
- HIV
- Other

167. Age

years:

168. Sex:

- Male
- Female

Clear Selection

169. Is the treated patient a child (under 18) or an adult?

- Child
- Adult

Clear Selection

170. What is the reported event?

- [ ] Leg ulcer
- [ ] Nail change
- [ ] Rash
- [ ] Cytopenia
- [ ] Leukemia
- [ ] Cytogenetic change
- [ ] Other cancer
- [ ] Birth defect
- [ ] Other

Causality assessment

	Yes	No	
171. Is the time relationship from drug administration to the event *plausible* for causality to be established?	◯	◯	Clear
172. Is there an absence of concurrent diseases or other drugs that may have caused the event?	◯	◯	Clear
173. Is there a reasonable response to drug withdrawal?	◯	◯	Clear
174. Is there the existence of a rechallenge in this report or a demonstrated biological/pharmacological explanation?	◯	◯	Clear

175. Duration of Treatment

Enlarge Shrink

176. Time to occurene of toxicity

Enlarge Shrink

Case 17

DO NOT fill in this portion of the form if only 1 case is reported

177. What is the underlying disease?

- [ ] Sickle cell anemia
- [ ] Thalessemia
- [ ] CML
- [ ] Polycythemia vera
- [ ] Essential thrombocythemia
- [ ] Leukemia
- [ ] Psoriasis
- [ ] Other cancer
- [ ] HIV
- [ ] Other

178. Age

years:

179. Sex:

- ◯ Male
- ◯ Female

Clear Selection

180. Is the treated patient a child (under 18) or an adult?

- ◯ Child
- ◯ Adult

Clear Selection

181. What is the reported event?

- [ ] Leg ulcer

- [ ] Nail change
- [ ] Rash
- [ ] Cytopenia
- [ ] Leukemia
- [ ] Cytogenetic change
- [ ] Other cancer
- [ ] Birth defect
- [ ] Other

Causality assessment

	Yes	No	
182. Is the time relationship from drug administration to the event *plausible* for causality to be established?	◯	◯	Clear
183. Is there an absence of concurrent diseases or other drugs that may have caused the event?	◯	◯	Clear
184. Is there a reasonable response to drug withdrawal?	◯	◯	Clear
185. Is there the existence of a rechallenge in this report or a demonstrated biological/pharmacological explanation?	◯	◯	Clear

186. Duration of Treatment

Enlarge Shrink

187. Time to occurene of toxicity

Enlarge Shrink

Submit Data

Click a link below to review this article at these other levels.

4. TRIAGE
5. GENERAL
6. KQs 1, 2, or 3
7. Additional Arms
9. KQ4 Barriers
10. QUALITY--observational studies
11. QUALITY--controlled trials
12. QUALITY--qualitative studies
13. QUALITY--surveys
19. Renee data abstraction

Form took 1.0625 seconds to render
Form Creation Date: Not available
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Previewing Only: You cannot submit data from this form

Previewing at Level 2

Refid: 10, Hu, Y. H. and Ruckenstein, E., Tunable Delocalization of Unpaired Electrons of Nitroxide Radicals for Sickle-Cell Disease Drug Improvements, *J Phys Chem B*, 2007

State: Excluded, Level: 2

Keywords:
No keywords available

Increase Font Size
Decrease Font Size

Abstract:
Hydroxyurea is a drug recently approved to treat sickle cell diseases. Hydroxyurea benefits the patients by increasing the level of fetal hemoglobin via a nitroxide radical pathway. Here, we report an unpaired-electron-delocalization approach to tune the stability of nitroxide radicals. In this approach, the substitution by an unsaturated alkyl group containing conjugated C=C double bonds for the hydrogen on the nitrogen atom attached to the hydroxyl of hydroxyurea can significantly increase its ability to generate nitroxide radical. Furthermore, the increase can be remarkably enhanced by increasing the number of conjugated C=C double bonds. For a hydroxyurea derivative that contains two conjugated C=C double bonds, the reaction rate to generate its radical is 118 times faster than that of hydroxyurea, and for a hydroxyurea derivative containing 20 conjugated C=C double bonds, the reaction rate to form its radical is 238 times faster than that of hydroxyurea. For this reason, hydroxyurea derivatives with conjugated C=C double bonds may constitute new potential drugs for the treatment of sickle-cell diseases.

Increase Font Size
Decrease Font Size

Submit Data

ABSTRACT Review Form

Does this article POTENTIALLY apply to any of the Key Questions?

1. **NO, this article DOES NOT apply to any of the Key Questions** (check all of the following reasons that apply):

- [ ] not English
- [ ] no original data (include ineligible reviews in this category)
- [ ] animals only
- [ ] in vitro only
- [ ] case report or case series of less than 10 unless it is PRIMARILY reporting toxicities **{see below for details}**
- [x] not relevant to key questions
- [ ] other: specify

2. **ARTICLE OF INTEREST (does not apply to key questions)**

- ( ) Pull article for hand searching
- ( ) Not relevant to project but please tag

Clear Selection

3. **UNCLEAR**

- ( ) can not determine from abstract alone OR no abstract available

Clear Selection

4. **This article MAY apply to one or more of the Key Questions** (choose all that apply, ONLY if you have not marked any of the options above)

- [ ] Key Question 1: What is the evidence regarding efficacy of hydroxyurea treatment for patients with SCD?
- [ ] Key Question 2: What is the evidence regarding effectiveness of hydroxyurea treatment for patients with SCD?
- [ ] Key Question 3: What is the evidence regarding the short- and

long-term harms of hydroxyurea treatment?

☐ Key Question 4: What barriers to the use of therapies for treatment of SCD have been investigated and what is the evidence that these purported barriers influence use of these treatments? Specifically, what are barriers to use of treatments to increase hemoglobin F (hydroxyurea, sodium phenylbutyrate, arginine butyrate, decitibine, and 5-azacytidine); barriers to established therapies for disease-management (penicillin, folate, vaccinations, iron chelation, nutrition counseling, pain management, dental care, and chronic transfusions); and barriers to bone marrow transplantation?

Notes on Key Question 4

We think that we will have evidence in the following three evidence subgroups. These are ordered by what we consider to be the strength of this evidence for answering the question.

1. Evidence to support interventions for overcoming barriers to treatments.
2. Evidence about how named barriers are associated with 1) use of therapies, 2) biological outcomes, or 3) access to therapies
3. Evidence which describes the existence of the purported barriers. This will include:
    a. Description of the existence of elements from our causal diagram (whether described in the article as a "barrier" or not)
    b. Description of barriers where the respondent states that something is a barrier in that it interferes with receipt of care or interferes with optimal health

CASE SERIES RULES
1. Include biomarker studies ONLY IF IN 10 OR MORE.
2. Include effiicay studies ONLY IF IN 10 OR MORE
3. Efficacy study exception: can include if there are LESS THAN 10 if the abstract specifically states they observed LEUKEMIA OR OTHER MALIGNANCY
4. Include studies of less than 10 if they are PRIMARILY describing toxicities (skin rashes, leg ulcers, leukemia)

5. **Comments:**

Enlarge Shrink

Submit Data

Form took 0.671875 seconds to render
Form Creation Date: Not available
Form Last Modified: Not available

Previewing Only: You cannot submit data from this form

Previewing at Level 5

Refid: 10, Hu, Y. H. and Ruckenstein, E., Tunable Delocalization of Unpaired Electrons of Nitroxide Radicals for Sickle-Cell Disease Drug Improvements, *J Phys Chem B*, 2007

State: Excluded, Level: 2

Submit Data

HYDROXYUREA TREATMENT FOR SICKLE CELL DISEASE

GENERAL FORM
Complete this form for all key questions.

1. This study is best described as (check all that apply):

- ☐ efficacy study: is in a controlled setting
- ☐ effectiveness study: is in a primary care setting, has less stringent eligibility criteria, reports on health outcomes rather than surrogate measures, describes how the drug is used in practice
- ☐ toxicity study

Study Characteristics

2. Study design

- ○ RCT
- ○ Cohort with a comparison arm
- ○ Case series
- ○ Case-control
- ○ Case report--individually describes patients **do not continue filling out this form**
- ○ Other

Clear Selection

3. Study location

- ☐ United States/Canada
- ☐ Europe
- ☐ Central/South America/Mexico
- ☐ Carribean
- ☐ Middle East
- ☐ Southeast Asia
- ☐ Africa
- ☐ Other (specify)

4. Disease (check all that apply)

- ☐ Sickle cell anemia
- ☐ CML
- ☐ AML
- ☐ Polycythemis vera
- ☐ Essential thronbocytosis
- ☐ Psoriasis
- ☐ Solid tumors
- ☐ Thalasssemia
- ☐ HIV
- ☐ Other

5. Study Duration

- ☐ NA

Planned duration of treatment (include units)

6. Recruitment Period

Start date (mm/dd/yyyy)

End date (mm/dd/yyyy)

Duration (include units)

STUDY inclusion/exclusion criteria

	Inclusion	Exclusion	Specify
7. Age (specify)	☐	☐	
8. Race (specify)	☐	☐	
9. Sickle Cell Anemia	☐	☐	
10. Sickle ß+ thalassemia	☐	☐	
11. Sickle ß° thalassemia	☐	☐	
12. Sickle α+ thalassemia	☐	☐	
13. SC genotype	☐	☐	
14. Splenomegaly	☐	☐	
15. Neutropenia	☐	☐	
16. Leukopenia	☐	☐	
17. Transfusion dependant	☐	☐	
18. Pregnancy	☐	☐	
19. Opiod Use	☐	☐	

20. Substance abuse	☐	☐	
21. Concurrent treatment with an antisickling agent	☐	☐	
22. Pain episodes (include number and time period)	☐	☐	
23. Cardiovascular event including stroke (define)	☐	☐	
24. Renal failure	☐	☐	
25. Liver failure	☐	☐	
26. Sepsis	☐	☐	
27. Acute chest syndrome (include n if available)	☐	☐	
28. HIV+	☐	☐	
29. Current medication use that can increase the toxicity of HU	☐	☐	
30. Prior hydroxyurea treatment	☐	☐	
31. Other (specify)	☐	☐	
32. Other (specify)	☐	☐	
33. Other (specify)	☐	☐	
34. Other (specify)	☐	☐	
35. Other (specify)	☐	☐	
36. Other (specify)	☐	☐	
37. Other (specify)	☐	☐	
38. Other (specify)	☐	☐	

39. Does this study contain more than 1 arm?

○ Yes define arms (including control) below

○ No proceed to patient characteristics--ONLY fill in ARM 1 information

Clear Selection

	Define (i.e., low dose HU, high dose HU, etc.)	Total N	Drug	Starting dose	Titration regimen
40. ARM 1 (HU or single arm)					
41. ARM 2					
42. ARM 3					
43. ARM 4					

Description of administered therapies:

ARM 1

ALWAYS use for HU

Use when only one set of data is available for study population

44. drugs(s)	45. # on MTD	46. Duration of therapy	47. concomittant therapy recieved	48. duration of observation	49. Indicator of adherence	50. denominator for outcomes (ITT if available)	51. frequency of monitoring labs (write in)
Enlarge Shrink	Enlarge Shrink	Months mean ☐ median	Enlarge Shrink	Months mean median	Please Select	Enlarge Shrink	Enlarge Shrink

ARM 2

52. drugs(s)	53. # on MTD	54. Duration of therapy	55. concomittant therapy recieved	56. duration of observation	57. Indicator of adherence	58. denominator for outcomes (ITT if available)	59. frequency of monitoring labs (write in)
Enlarge Shrink	Enlarge Shrink	Months mean ☐ median	Enlarge Shrink	Months mean median	Please Select	Enlarge Shrink	Enlarge Shrink

ARM 3

60. drugs(s)	61. # on MTD	62. Duration of therapy	63. concomittant therapy recieved	64. duration of observation	65. Indicator of adherence	66. denominator for outcomes (ITT if available)	67. frequency of monitoring labs (write in)
Enlarge Shrink	Enlarge Shrink	Months mean ☐ median	Enlarge Shrink	Months mean median	Please Select	Enlarge Shrink	Enlarge Shrink

ARM 4

68. drugs(s)	69. # on MTD	70. Duration of therapy	71. concomittant therapy recieved	72. duration of observation	73. Indicator of adherence	74. denominator for outcomes (ITT if available)	75. frequency of monitoring labs (write in)
Enlarge Shrink	Enlarge Shrink	Months mean ☐ median	Enlarge Shrink	Months mean median	Please Select	Enlarge Shrink	Enlarge Shrink

Patient Population Characteristics

Fill out PATIENT characteristics for each arm. If the study is a TRIAL, ALWAYS use arm 1 for data on the HU group. If the study is not a trial use arm 1 ONLY for data abstraction

ARM 1
ALWAYS use for HU group
Use when only one set of data is available for study population

DATA ENTRY INSTRUCTIONS: for ALL ARMS, report percentages in ( ), do not use the % within the ( ); report ranges in (-).

76. Age	77. Gender	78. Race	79. Genotype	80. Haplotype	81. Substance use	82. Socioeconomic status	83. Blood	84. Crises
Mean	Male, n (%)	White (non-hispanic), n (%)	SS, n (%)	Benin, n (%)	Alcohol user, n (%)	Low, define	Total Hg (g/dl), mean or median	Pain crises
Median	Female, n (%)	Black (non-hispanic), n (%)	SC, n (%)	Indian/Arab, n (%)	Smoker, n (%)	n (%)	% Hemoglobin F, mean or median	mean or median
Range		White hispanic, n (%)	S &+ thalassemia, n (%)	Senegal, n (%)	Illegal dug user, n (%)	Middle, define	White count (cells/µl), mean or median	Stroke
		Black hispanic, n (%)	S &º thalassemia, n (%)	CAR, n (%)		n (%)	Platelet count (k/mm^3), mean or median	mean or median
		Asian/Pacific Islander, n (%)	other, define, n (%)			High, define	Absolute neutrophil count (cells/µl), mean or median	Transfusions (per year or total)--specify
		Other (specify), n (%)				n (%)		mean or median
								Chest syndrome
								mean or median
								Ulcer
								mean or median

ARM 2

DATA ENTRY INSTRUCTIONS: for ALL ARMS, report percentages in ( ), do not use the % within the ( ); report ranges in (-).

88. Age	89. Gender	90. Race	91. Genotype	92. Haplotype	93. Substance use	94. Socioeconomic status	95. Blood	96. Crises
Mean	Male, n (%)	White (non-hispanic), n (%)	SS, n (%)	Benin, n (%)	Alcohol user, n (%)	Low, define	Total Hg (g/dl), mean or median	Pain crises
Median	Female, n (%)	Black (non-hispanic), n (%)	SC, n (%)	Indian/Arab, n (%)	Smoker, n (%)	n (%)	% Hemoglobin F, mean or median	mean or median
Range		White hispanic, n (%)	S &+ thalassemia, n (%)	Senegal, n (%)	Illegal dug user, n (%)	Middle, define	White count (cells/µl), mean or median	Stroke
		Black hispanic, n (%)	S &º thalassemia, n (%)	CAR, n (%)		n (%)	Platelet count (k/mm^3), mean or median	mean or median
		Asian/Pacific Islander, n (%)	other, define, n (%)			High, define	Absolute neutrophil count (cells/µl), mean or median	Transfusions (per year or total)--specify
		Other (specify), n (%)				n (%)		mean or median
								Chest syndrome
								mean or median
								Ulcer
								mean or median

ARM 3

DATA ENTRY INSTRUCTIONS: for ALL ARMS, report percentages in ( ), do not use the % within the ( ); report ranges in (-).

100. Age	101. Gender	102. Race	103. Genotype	104. Haplotype	105. Substance use	106. Socioeconomic status	107. Blood	108. Crises
Mean	Male, n (%)	White (non-hispanic), n (%)	SS, n (%)	Benin, n (%)	Alcohol user, n (%)	Low, define	Total Hg (g/dl), mean or median	Pain crises
Median	Female, n (%)	Black (non-hispanic), n (%)	SC, n (%)	Indian/Arab, n (%)	Smoker, n (%)	n (%)	% Hemoglobin F, mean or median	mean or median
Range		White hispanic, n (%)	S &+ thalassemia, n (%)	Senegal, n (%)	Illegal dug user, n (%)	Middle, define	White count (cells/µl), mean or median	Stroke
		Black hispanic, n (%)	S &º thalassemia, n (%)	CAR, n (%)		n (%)	Platelet count (k/mm^3), mean or median	mean or median
		Asian/Pacific Islander, n (%)	other, define, n (%)			High, define	Absolute neutrophil count (cells/µl), mean or median	Transfusions (per year or total)--specify
		Other (specify), n (%)				n (%)		mean or median
								Chest syndrome
								mean or median
								Ulcer
								mean or median

ARM 4

DATA ENTRY INSTRUCTIONS: for ALL ARMS, report percentages in ( ), do not use the % within the ( ); report ranges in (-).

112. Age	113. Gender	114. Race	115. Genotype	116. Haplotype	117. Substance use	118. Socioeconomic status	119. Blood	120. Crises
Mean	Male, n (%)	White (non-hispanic), n (%)	SS, n (%)	Benin, n (%)	Alcohol user, n (%)	Low, define	Total Hg (g/dl), mean or median	Pain crises
Median	Female, n (%)	Black (non-hispanic), n (%)	SC, n (%)	Indian/Arab, n (%)	Smoker, n (%)	n (%)	% Hemoglobin F, mean or median	mean or median
Range		White hispanic, n (%)	S &+ thalassemia, n (%)	Senegal, n (%)	Illegal dug user, n (%)	Middle, define	White count (cells/µl), mean or median	Stroke
		Black hispanic, n (%)	S &º thalassemia, n (%)	CAR, n (%)		n (%)	Platelet count	mean or median
		Asian/Pacific	other, define, n (%)			High, define		Transfusions (per year or total)--specify
						n (%)		mean or

		Islander, n (%) Other (specify), n (%)					(k/mm^3), mean or median Absolute neutrophil count (cells/ul), mean or median	median Chest syndrome mean or median Ulcer mean or median

124. Comments

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4. TRIAGE
6. KQs 1, 2, or 3
7. Additional Arms
8. KQ3 TOX Case Reports
9. KQ4 Barriers
10. QUALITY--observational studies
11. QUALITY--controlled trials
12. QUALITY--qualitative studies
13. QUALITY--surveys
19. Renee data abstraction

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Refid: 10, Hu, Y. H. and Ruckenstein, E., Tunable Delocalization of Unpaired Electrons of Nitroxide Radicals for Sickle-Cell Disease Drug Improvements, *J Phys Chem B*, 2007

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Efficacy/Effectiveness AND Toxicity

Complete this form for Key Questions 1, 2 and 3 where applicable.

Categorical Outcomes

Efficacy/effectiveness outcomes:	**Toxicities**
1 any acute chest	**11** neutropenia
2 any acute painful event	**12** thrombocytopenia
3 death	**13** reticulocytopenia
4 symptomatic stroke	**14** anemia
5 definitive new changes on MRI	**15** leukemia
6 transfusion	**16** other neoplasm
7 crisis requiring hosp	**17** leg ulcer
	18 skin rash/nail alterations
	19 hair loss
	20 gastrointestinal upset
	21 cytogenetic or oncogenic abnormalities
	22 fetal abnormalities
	23 spontaneous abortion
8 other	**24** other
9 other	**25** other
10 other	**26** other

3.
Outcome (select number from list above)
Please Select

	n (with outcome)	%	effect estimate relative to	CI	n per year (if applicable)	p-vaule	denominator for this outcome (if different)
4. ARM 1 arm identification should be identical to that in the GENERAL form							
5. ARM 2							
6. ARM 3							
7. ARM 4							

8.
Outcome (select number from list above)
Please Select

	n (with outcome)	%	effect estimate relative to	CI	n per year (if applicable)	p-vaule	denominator for this outcome (if different)
9. ARM 1 arm identification should be identical to that in the GENERAL form							
10. ARM 2							
11. ARM 3							
12. ARM 4							

13.
Outcome (select number from list above)
Please Select

	n (with outcome)	%	effect estimate relative to	CI	n per year (if applicable)	p-vaule	denominator for this outcome (if different)
14. ARM 1 arm identification should be identical to that in the GENERAL form							
15. ARM 2							
16. ARM 3							
17. ARM 4							

18.
Outcome (select number from list above)
Please Select

	n (with outcome)	%	effect estimate relative to	CI	n per year (if applicable)	p-vaule	denominator for this outcome (if different)
19. ARM 1 arm identification should be identical to that in the GENERAL form							

20. ARM 2							
21. ARM 3							
22. ARM 4							

23.
Outcome (select number from list above)
Please Select

	n (with outcome)	%	effect estimate relative to	CI	n per year (if applicable)	p-vaule	denominator for this outcome (if different)
24. ARM 1 arm identification should be identical to that in the GENERAL form							
25. ARM 2							
26. ARM 3							
27. ARM 4							

28.
Outcome (select number from list above)
Please Select

	n (with outcome)	%	effect estimate relative to	CI	n per year (if applicable)	p-vaule	denominator for this outcome (if different)
29. ARM 1 arm identification should be identical to that in the GENERAL form							
30. ARM 2							
31. ARM 3							
32. ARM 4							

33.
Outcome (select number from list above)
Please Select

	n (with outcome)	%	effect estimate relative to	CI	n per year (if applicable)	p-vaule	denominator for this outcome (if different)
34. ARM 1 arm identification should be identical to that in the GENERAL form							
35. ARM 2							
36. ARM 3							
37. ARM 4							

38.
Outcome (select number from list above)
Please Select

	n (with outcome)	%	effect estimate relative to	CI	n per year (if applicable)	p-vaule	denominator for this outcome (if different)
39. ARM 1 arm identification should be identical to that in the GENERAL form							
40. ARM 2							
41. ARM 3							
42. ARM 4							

43.
Continuous Outcomes at last observation

time point of last ovbservation

Efficacy/effectiveness	**Toxicities**
27 Hb F % **28** % F cells **29** hemoglobin **30** MCV **31** reticulocyte count **32** white blood cell count **33** transcranial doppler velocity **34** height **35** weight **36** head circumference **37** Total days in hosp **38** Time to first crisis **39** Time to first acute chest **40** Time to neoplasm **41** Daily pain severity **42** Number of transfusions	**47** platelet count **48** neutrophil count(ANC) **49** sperm count **50** sperm motility

43 Units (RBC) transfused	
44.	45.
44 other	**51** other
45 other	**52** other
46 other	**53** other

46.
Outcome (select number from list above)
Please Select

	units	mean	SD	median	range	Estimate of effect (diff, RR, HR, OR); relative to arm2	Signficance
47. ARM 1 arm identification should be identical to that in the GENERAL form							
48. ARM 2							
49. ARM 3							
50. ARM 4							

51.
Outcome (select number from list above)
Please Select

	units	mean	SD	median	range	Estimate of effect (diff, RR, HR, OR); relative to arm2	Signficance
52. ARM 1 arm identification should be identical to that in the GENERAL form							
53. ARM 2							
54. ARM 3							
55. ARM 4							

56.
Outcome (select number from list above)
Please Select

	units	mean	SD	median	range	Estimate of effect (diff, RR, HR, OR); relative to arm2	Signficance
57. ARM 1 arm identification should be identical to that in the GENERAL form							
58. ARM 2							
59. ARM 3							
60. ARM 4							

61.
Outcome (select number from list above)
Please Select

	units	mean	SD	median	range	Estimate of effect (diff, RR, HR, OR); relative to arm2	Signficance
62. ARM 1 arm identification should be identical to that in the GENERAL form							
63. ARM 2							
64. ARM 3							
65. ARM 4							

66.
Outcome (select number from list above)
Please Select

	units	mean	SD	median	range	Estimate of effect (diff, RR, HR, OR); relative to arm2	Signficance
67. ARM 1 arm identification should be identical to that in the GENERAL form							
68. ARM 2							
69. ARM 3							
70. ARM 4							

71.
Outcome (select number from list above)
Please Select

	units	mean	SD	median	range	Estimate of effect (diff, RR, HR, OR); relative to arm2	Signficance
72. ARM 1 arm identification should be identical to that in the GENERAL form							
73. ARM 2							
74. ARM 3							
75. ARM 4							

76.
Outcome (select number from list above)
Please Select

	units	mean	SD	median	range	Estimate of effect (diff, RR, HR, OR); relative to arm2	Signficance
77. ARM 1 arm identification should be identical to that in the GENERAL form							
78. ARM 2							
79. ARM 3							
80. ARM 4							

81.
Outcome (select number from list above)
Please Select

	units	mean	SD	median	range	Estimate of effect (diff, RR, HR, OR); relative to arm2	Signficance
82. ARM 1 arm identification should be identical to that in the GENERAL form							
83. ARM 2							
84. ARM 3							
85. ARM 4							

86.
What characteristics predict benefit?

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87.
What characteristics predict toxicity?

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88.

The article reports the outcomes by the following groups.

- age
- genotype
- ethnicity/race
- disease
- resource-poor

89.

Comments:

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Click a link below to review this article at these other levels.
4. TRIAGE
5. GENERAL
7. Additional Arms
8. KQ3 TOX Case Reports

9. KQ4 Barriers
10. QUALITY--observational studies
11. QUALITY--controlled trials
12. QUALITY--qualitative studies
13. QUALITY--surveys
19. Renee data abstraction

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QUALITY FORM
Observational Studies

1. Did the study describe the setting or population from which the study sample was drawn?

- No
- To some extent
- Yes, with detailed description: *setting (e.g., clinic), location, and dates*

Clear Selection

2. Were the inclusion or exclusion criteria described? (just saying “sickle cell disease” is insufficient)

- No
- To some extent
- Yes, with detailed description: *methods for selection of participants, or inclusion/exclusion criteria, or diagnostic criteria for enrollment*

Clear Selection

3. Does the study describe the key characteristics of study participants at enrollment/baseline?

- No
- To some extent
- Yes, with detailed description: *age, sex, genotype, relevant comorbidities which can influence outcomes*

Clear Selection

4. Was the intervention described? (intervention may be a drug or an intervention to overcome a barrier)

- NA
- No
- To some extent
- Yes, with detailed description:*how intervention was administered (does, titration schedule), who does intervention, instructions for patients*

Clear Selection

5. Was there a description of adherence to the drug or the completeness of the intervention?

- No
- To some extent
- Yes, with description of method of assessment, *number completing intervention, and how adherence was measured*
- NA

Clear Selection

6. Do the authors report an adjusted or stratified estimate of the treatment effect *if* this study compared two or more groups

- NA
- No

- To some extenrt
- Yes:*multivariate analyses accounting for all potential confounders*

Clear Selection

7. Do the authors report at least one objective outcome from the intervention?

- No
- To some extent
- Yes: *method of assessment is objective, replicable, relevant to the intervention*
- NA

Clear Selection

8. Did the study report the number of participants lost to follow-up?

- No
- To some extent (number only)
- Yes, with description of reasons for loss: *number lost and reason for loss*
- NA

Clear Selection

9. What was the percentage of participants who were lost to follow-up?

- Not reported
- n/N
- %
- NA

Clear Selection

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12. QUALITY--qualitative studies
13. QUALITY--surveys
19. Renee data abstraction

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TRIAGE FORM

Use this form ONLY:

1. If you have reviewed an article for data abstraction and have found that the article SHOULD NOT be reviewed {choose the appropriate reason below}, or

2. If article requires group discussion before data abstraction.

1. This article should NOT be reviewed at this time ofr the following reason(s):

- ○ insufficient data to address question, or very minimal description of study population (e.g. provides no relevant outcome data or no details about the included patients or no description about the intervention except that it was hydroxyurea)
- ○ study is a case series <100 patients
- ○ study is a case report but there is no description of duration of use of hydroxyruea OR no description of dose
- ○ study addresses pregnancy
- ○ triage for group discussion about relevance

Clear Selection

2.

Comment: please write a sentence about the article if it may be a useful article for the discussion

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