ELSEVIER

Blood 142 (2023) 3871–3873

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

114.SICKLE CELL DISEASE, SICKLE CELL TRAIT AND OTHER HEMOGLOBINOPATHIES, EXCLUDING THALASSEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Transcranial Doppler Screening of Children with Sickle Cell Disease for a Large, Multinational Interventional Study: Experience from the Phase 3 HOPE-Kids 2 Trial Investigating the Effect of Voxelotor Treatment on Transcranial Doppler Flow Velocity

Halima Bello-Manga, MBBS, MPH[1], *Videlis Nduba*[2], *Shehu Umar Abdullahi, MD*[3], *Jessie Githanga*[4], *Bernhards Ogutu*[2], *Amal M. El-Beshlawy, MD*[5], *Hoda MA Hassab, MD*[6], *Mohamed Badr, MD*[7], *Azza Tantawy*[8], *Biobele J Brown, MBBS, FWACP*[9], *Vivian Paintsil*[10], *Adeseye Michael Akinsete, MBBS*[11], *Catherine I. Segbefia, MBChB*[12], *Iheanyi Okpala, FRCPath*[13], *Yasser Wali*[14], *Mohammed Essa*[15], *Jason Farthing*[16], *Jennifer Doss*[16], *Sandy Dixon*[16], *Clark Brown, MDPhD*[17], *Fenella Kirkham, MD*[18]

[1] Barau Dikko Teaching Hospital, Kaduna State University, Kaduna, Nigeria
[2] Kenya Medical Research Institute (KEMRI), Nairobi, Kenya
[3] Department of Pediatrics, Bayero University/Aminu Kano Teaching Hospital, Kano, Nigeria
[4] University of Nairobi, Nairobi, Kenya
[5] Cairo University, Giza, Egypt
[6] Alexandria University, Alexandria, Egypt
[7] Fayoum University, Faiyum, Egypt
[8] Ain Shams University, Cairo, Egypt
[9] College of Medicine, Department of Paediatrics, University of Ibadan, Ibadan, Nigeria
[10] Kwame Nkrumah University of Science and Technology, Kumasi, Ghana
[11] College of Medicine, University of Lagos, Idi-Araba, Lagos, Nigeria
[12] Department of Child Health, University of Ghana Medical School, Accra, Ghana
[13] College of Medicine, University of Nigeria, Enugu, Nigeria
[14] Sultan Qaboos University, Muscat, Oman
[15] King Abdullah Specialist Children's Hospital, Ministry of National Guard, Riyadh, Saudi Arabia
[16] Pfizer Inc, South San Francisco, CA
[17] Pfizer Inc, Norcross, GA
[18] University College London, London, United Kingdom

Introduction: Transcranial Doppler (TCD) ultrasound is an effective screening tool for identifying children with sickle cell disease (SCD) who are at high risk of stroke. Implementing TCD screening, along with appropriate therapies, for the purpose of primary stroke prevention in resource-constrained settings remains challenging. HOPE-KIDS 2 (NCT04218084) is an ongoing, phase 3, multicenter, double-blind, placebo-controlled trial of voxelotor in children with SCD and elevated arterial cerebral blood flow (measured by time-averaged maximum of the mean velocity [TAMMV]). Our aim is to describe the findings from successful implementation of a standardized TCD screening protocol that was conducted in a multinational setting.
Methods: The purpose of HOPE-KIDS 2 is to evaluate the effect of voxelotor treatment on reducing the risk of stroke in participants aged 2 to <15 years with SCD who have conditional TAMMV (170 to <200 cm/s) at baseline. Children aged 2 to <15 years with SCD (HbSS/HbSβ^0) were screened after local sonographers were trained and certified on standardized TCD examination protocol, using the same model of Multi-Dop T digital machine (Compumedics DWL, Germany). TCD assessments were sent for central quality review and interpretation by 2 independent reviewers. STOP criteria were used to classify stroke risk: normal, <170 cm/s; conditional, 170 to <200 cm/s; or abnormal, ≥200 cm/s. Patient baseline characteristics, including clinical measurements of markers of anemia and hemolysis, were measured during study screening. The reasons for patient screen failure were summarized.
Results: Between Nov 2020 and Feb 2023, 708 participants consented at 29 sites in Nigeria (n=250; 5 sites), Kenya (n=241; 4 sites), Egypt (n=145; 4 sites), Ghana (n=28; 2 sites), the US (n=17; 8 sites), Italy (n=9; 3 sites), Oman (n=9; 1 site), Saudi Arabia (n=8; 1 site), and the UK (n=1; 1 site). Of these patients, 92.1% (652/708) completed TCD screening examinations (mean

[SD] age 7.6 [3.24] years; range 2.0-14.0 years; 50.8% male; 23.0% receiving hydroxyurea). Of the patients who completed TCD screening, the mean (SD) TAMMV was 163.0 (31.26) cm/s, and 47.1% (307/652) had conditional TCD at baseline (29.0% low conditional, 18.1% high conditional). The main reason for screen failure was index TAMMV outside of conditional range (abnormal, n=39 [6.0%]; normal, n=306 [46.9%]). Elevated TAMMV on screening TCD was more common in younger children (2 to ≤8 years vs >8 to <15 years); patients aged 2-8 years comprised 66.8% and 82.1% of the conditional and abnormal TCD categories, respectively. There were 39 assessments that required adjudication, but only 9 were deemed unreadable. Of all patients screened, 36.2% (236/652) fulfilled eligibility criteria for randomization; the characteristics at screening of these patients are summarized (Table). The mean (SD) Hb level and TAMMV at screening for randomly assigned patients was 7.7 (1.06) g/dL and 182.7 (7.53) cm/s, respectively.

Conclusions: Clinical sites for the HOPE-KIDS 2 study successfully implemented a standardized, local TCD screening protocol supported by central quality review. For a large interventional trial aimed at reducing the risk of stroke in children with SCD, African and Middle Eastern sites presented relatively few limitations with respect to participant screening.

Disclosures Bello-Manga: *Global Blood Therapeutics/Pfizer:* Consultancy; *Forma Therapeutics/Novo Nordisk:* Other: Clinical trial activity; *National Institutes of Health Fogarty International Center (K43TW011583):* Research Funding. **El-Beshlawy:** *Global Blood Therapeutics:* Research Funding. **Hassab:** *Global Blood Therapeutics:* Research Funding. **Wali:** *Global Blood Therapeutics:* Honoraria, Research Funding. **Farthing:** *Pfizer Inc:* Current Employment, Current holder of *stock options* in a privately-held company; *Global Blood Therapeutics:* Ended employment in the past 24 months. **Doss:** *Pfizer Inc:* Current Employment, Current holder of *stock options* in a privately-held company; *Global Blood Therapeutics:* Ended employment in the past 24 months. **Dixon:** *Pfizer Inc:* Current Employment, Current holder of *stock options* in a privately-held company; *Global Blood Therapeutics:* Ended employment in the past 24 months. **Brown:** *Pfizer Inc:* Current Employment, Current holder of *stock options* in a privately-held company, Research Funding; *Global Blood Therapeutics:* Consultancy, Ended employment in the past 24 months, Research Funding; *Imara:* Consultancy, Research Funding; *Novartis:* Consultancy, Research Funding; *Forma Therapeutics:* Research Funding. **Kirkham:** *Global Blood Therapeutics/Pfizer:* Other: Clinical trial activity.

Table. Characteristics at Screening of Randomly Assigned Patients (n=236)

Characteristic at Screening	Randomly Assigned Patients n=236
Age, years	
Mean (SD)	7.2 (3.15)
Range	2.0–14.0
Median (range) weight, kg	19.0 (11–54)
Sex, n (%)	
Female	122 (51.7)
Male	114 (48.3)
Race or ethnic origin, n (%)	
African	149 (63.1)
Arab	23 (9.7)
Black or African American	10 (4.2)
White	2 (0.8)
Multiracial[a]	52 (22.0)
SCD genotype, n (%)	
HbSS	224 (94.9)
HbSβ^0	12 (5.1)
Hb, g/dL[b]	
Mean (SD)	7.7 (1.06)
Range	5–10
HbF, %[c]	
Mean (SD)	11.6 (6.64)
Range	2–30
Reticulocyte count, %[b]	
Mean (SD)	7.3 (5.95)
Range	0–24
Current hydroxyurea/hydroxycarbamide use, n (%)[d]	
Yes	75 (31.8)
No	161 (68.2)
Current malaria chemoprophylaxis use, n (%)	
Yes	105 (44.5)
No	131 (55.5)
Number of VOCs in the previous 12 months, n (%)	
0	128 (54.2)
≥1	108 (45.8)
TCD velocity, cm/s[e]	
Mean (SD)	182.7 (7.53)
Median	182.0
Range	170–199

[a] Patients could be in multiple race/ethnic origin categories. [b] Value is the average of all values before the randomization date up to Day −35. [c] Value is defined as the average of all values before or on the randomization date. [d] Concomitant hydroxyurea was permitted provided that the dose was stable for ≥90 days. [e] Baseline is defined as a value from the screening visit.

Hb=hemoglobin; HbF=fetal hemoglobin; HbSβ^0=sickle beta zero thalassemia; HbSS=homozygous for hemoglobin S; SCD=sickle cell disease; TCD=transcranial Doppler; VOC=vaso-occlusive crisis.

Figure 1

https://doi.org/10.1182/blood-2023-188677