população. **Conclusão:** Notou-se que o IMC foi significativamente menor nos pacientes com genótipo HbSS, indicando um impacto considerável deste genótipo no estado nutricional. A avaliação da função renal revelou níveis elevados de taxa de filtração glomerular (TFG), possivelmente devido à hipostenúria característica da DF. A microalbuminúria se mostrou um marcador precoce e sensível de comprometimento renal, sugerindo a necessidade de sua inclusão nas avaliações rotineiras desses pacientes para permitir intervenções mais precoces e melhorar os desfechos renais. Estes achados reforçam a importância de um acompanhamento multidisciplinar e personalizado para os pacientes com DF, considerando as variações genotípicas e suas implicações clínicas.

https://doi.org/10.1016/j.htct.2024.09.050

PRELIMINARY RESULTS FROM A MULTICENTER PHASE 2/3 STUDY OF NEXT-GENERATION SICKLE HEMOGLOBIN POLYMERIZATION INHIBITOR OSIVELOTOR (GBT021601) FOR THE TREATMENT OF PATIENTS WITH SICKLE CELL DISEASE

SL Saraf [a], SU Abdullahi [b], AM Akinsete [c], FA Fasola [d], M Idowu [e], S Pennington [f], WB Ershler [g], MP Stagg [h], EA Lisbon [i], F Montealegre-Golcher [i]

[a] *University of Illinois College of Medicine, Chicago, United States*
[b] *Bayero University/Aminu Kano Teaching Hospital, Kano, Nigeria*
[c] *College of Medicine, University of Lagos, Idi-Araba, Lagos, Nigeria*
[d] *College of Medicine, University of Ibadan/ University College Hospital, Ibadan, Nigeria*
[e] *University of Texas Health McGovern Medical School, Houston, United States*
[f] *Mississippi Center for Advanced Medicine, Madison, United States*
[g] *Inova Adult Sickle Center, Schar Cancer Institute, Fairfax, United States*
[h] *Our Lady of the Lake Cancer Institute, Baton Rouge, United States*
[i] *Pfizer Inc, New York, United States*

Objectives: Osivelotor (previously GBT021601) is a next-generation sickle hemoglobin (HbS) polymerization inhibitor in development for sickle cell disease (SCD). Compared with the first-in-class HbS polymerization inhibitor voxelotor, osivelotor has improved pharmacokinetic properties, which may enable higher Hb occupancy at lower doses to potentially reduce treatment burden and improve clinical outcomes. We report preliminary phase 2 data from an ongoing phase 2/3 study of osivelotor in SCD. **Methods:** Preliminary data are reported from Part A of a 3-part, multicenter phase 2/3 study (NCT05431088). Part A is a randomized (1:1), open-label, 12-week, dose-finding study of oral osivelotor in patients with SCD (HbSS/HbSβ^0 genotype) aged 18–65 y and Hb 5.5–10.5 g/dL. Patients received a loading dose twice-daily for 4 days then once-daily maintenance doses (100 or 150 mg) through Week 12. The primary endpoint was change from baseline in Hb at Week 12. Secondary endpoints included ektacytometry (Oxygenscan) to assess red blood cell (RBC) deformability as a function of the partial pressure of oxygen, expressed as elongation index (EI). **Results:** At cutoff date (June 20, 2023), 35 patients had been treated (osivelotor 100 mg, n = 17; 150 mg, n = 18); 28 had completed 12 weeks' treatment. Mean (range) age was 29.7 (18–59) y, 32/35 patients were HbSS, and 16/35 were on stable hydroxyurea at baseline. Increases in Hb from baseline were seen from Week 1 and sustained to Week 12. At Week 12, for the 100-mg (n = 13) and 150-mg (n = 12) groups, respectively, mean (SD) increases from baseline in Hb (g/dL) were 2.63 (1.42) and 3.27 (1.70) and in hematocrit (%) were 7.83 (4.06) and 9.73 (4.26); mean (SD) changes in erythropoietin (IU/L) were −121.7 (346.3) (n = 13) and −89.9 (243.4) (n = 11). Indirect bilirubin and reticulocytes also showed reductions from baseline. Ektacytometry showed EI increased and point of sickling (PoS) during deoxygenation decreased from baseline to Week 12. For 27 patients with ≥1 vaso-occlusive crisis (VOC) at baseline, the annualized VOC rate (95% CI) was 2.30 (1.85–2.86) at baseline and 1.20 (0.58–2.48) on-study, with median (range) on-study duration 0.4 (0.03–0.41) y. Treatment-emergent adverse events (TEAEs) were reported for 20 patients (57.1%). Treatment-related TEAEs, reported for 6/35 patients (17.1%), were headache (n = 4), diarrhea (n = 2), and abdominal discomfort, nausea, upper abdominal pain, and urticaria (n = 1 each). One death, deemed unrelated to osivelotor, was due to a cerebrovascular accident (CVA) in a patient with a history of CVA and seizures, after new-onset high fever and no change from baseline in Hb (8.0 g/dL). **Discussion:** In preliminary results from Part A of this phase 2/3 study, loading and daily doses of osivelotor for 12 weeks were well tolerated in adults with SCD. Results to date show large increases in mean Hb accompanied by improvements in markers of hemolysis. Although oxygen delivery was not directly measured, no impairment was suggested by indicators of oxygen delivery (ie no increases in erythropoietin levels or VOCs). Ektacytometry results suggested improvement in RBC deformability and delayed HbS polymerization. **Conclusions:** These results support ongoing clinical development of osivelotor as a potential SCD therapy.
Funding: This study was sponsored by Pfizer.

https://doi.org/10.1016/j.htct.2024.09.051

DOENÇA HEMOLÍTICA DO FETO E DO RECÉM-NASCIDO POR ALOIMUNIZAÇÃO RH - INQUIRIÇÃO NARRATIVA

LBS Paiva [a], ILS Dantas [a], APBP Silva [b], WS Teles [b], FECD Carmo [b], JS Nascimento [b], FKF Oliveira [b]

[a] *Universidade Tiradentes (UNIT), Aracaju, SE, Brasil*
[b] *Centro de Hemoterapia de Sergipe (HEMOSE), Aracaju, SE, Brasil*