ELSEVIER

Blood 142 (2023) 1125–1127

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

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

Duffy-Null Patients with Sickle Cell Disease Are at Risk for Low Neutrophil Counts with HU Treatment

Yan Zheng, MD PhD[1], *Pei-Lin Chen, MPH*[2], *Jeffery Gossett*[3], *Guolian Kang, PhDMS*[4], *Clifford M Takemoto, MD*[5]

[1] Pathology, St. Jude Children's Research Hospital, Memphis, TN
[2] St. Jude Children's Research Hospital, Memphis, TN
[3] Department of Biostatistics, St. Jude Children's Research Hospital, Memphis
[4] Department of Biostatistics, St. Jude Children's Research Hospital, Memphis, TN
[5] Department of Hematology, St. Jude Children's Research Hospital, Memphis, TN

Introduction

The Duffy blood group consists of two main antigens, Fya and Fyb, and is encoded by the atypical chemokine receptor 1 (*ACKR1)* gene. About 60% of Black individuals have the Duffy null phenotype, Fy(a-b-) characterized by absence of expression of the Fya and Fyb antigens on red cells. The Duffy null phenotype in Black individuals is caused by homozygosity for a SNP (rs2814778; T>C; CC) in the *ACKR1* gene promoter. This polymorphism results in the disruption of a binding site for the GATA1 erythroid transcription factor and silences expression of the Duffy antigens. There is a strong correlation between the Duffy null phenotype and the lower range of absolute neutrophil counts (ANC) observed in some Black individuals. The impact of Fy(a-b-) status on clinical outcomes in individuals with sickle cell disease (SCD) is not well studied. Neutropenia is a common toxicity with hydroxyurea (HU) in the treatment for SCD. We hypothesized that SCD patients with the Duffy null phenotype are at risk for lower ANCs with HU treatment, and potentially have different clinical outcomes compared to Duffy-positive patients.

Methods

Pediatric patients with SCD (HbSS and HbSβ^0-thalassemia) treated with HU and enrolled in the St. Jude Children's Research Hospital observational cohort study, the Sickle Cell Clinical Research and Intervention Program (SCCRIP) were eligible. Patients who had available Duffy genotype and reached a maximal tolerated dose (MTD) of HU before 12/31/2021 were included. The MTD based on neutrophil counts was considered to be achieved at a dose when the ANC was between 1000 and 3000 /mm ^{3}. Multivariate generalized linear regression model was used for association analysis after adjusting for age at HU initiation, sex, and 5 principal components. Mediation analysis was conducted to evaluate indirect effect of the Duffy null phenotype on time to MTD via baseline ANCs.

Results

A total of 250 patients met the inclusion criteria. One hundred eighty (72%) patients were Duffy null, and 70 (28%) patients were positive for at least one of Duffy antigen. The average patient age at starting HU was 5.9 ± 4 years old. Female patients accounted for 44.8% (n= 112) of the study population. The mean MTD of HU was 28.0 ± 5.5 mg/kg/day, the time to MTD was 2.3 ± 2.7 years, and there was no significant difference between Duffy-null and Duffy-positive patients. The Duffy null phenotype was associated with a significantly lower baseline ANCs (Duffy-null: 3800 ± 2684 /mm ^{3} vs. Duffy-positive: 4702 ± 3015 /mm ^{3}; p = 0.005; Figure A), and more frequent episodes of ANC <1500 /mm ^{3} in the first two years after starting HU (Duffy-null: 1.2 ± 2.3 times/patent vs. Duffy-positive: 0.5 ± 1.2 times/patient; p = 0.006; Figure B). Although the Duffy null phenotype did not have a direct effect on the time to MTD, it affected the time to MTD indirectly via baseline ANC (mediation indirect effect test p = 0.01) since the higher the baseline ANCs were, the longer it took to reach MTD (p = 0.0002). We did not find the Duffy null phenotype associated with Hgb, MCV and HbF at base line, one or two years after starting HU. In addition, there was no association of Duffy status on frequencies of vaso-occlusive crisis and acute chest syndrome within 2 years after HU initiation. Notably, MCV increased significantly after HU initiation (Baseline: 83.5 ± 7.6 fl; two-year post HU: 99.0 ± 12.0 fl; p <0.00001), the increases were similar between Duffy-null and Duffy-positive patients (p = 0.36), suggesting similar HU adherence.

Conclusion

Patients with SCD and the Duffy null phenotype have more frequent episodes of lower ANC with HU treatment. However, Duffy status was not associated with risks for other adverse clinical outcomes.

Disclosures No relevant conflicts of interest to declare.

https://doi.org/10.1182/blood-2023-182459

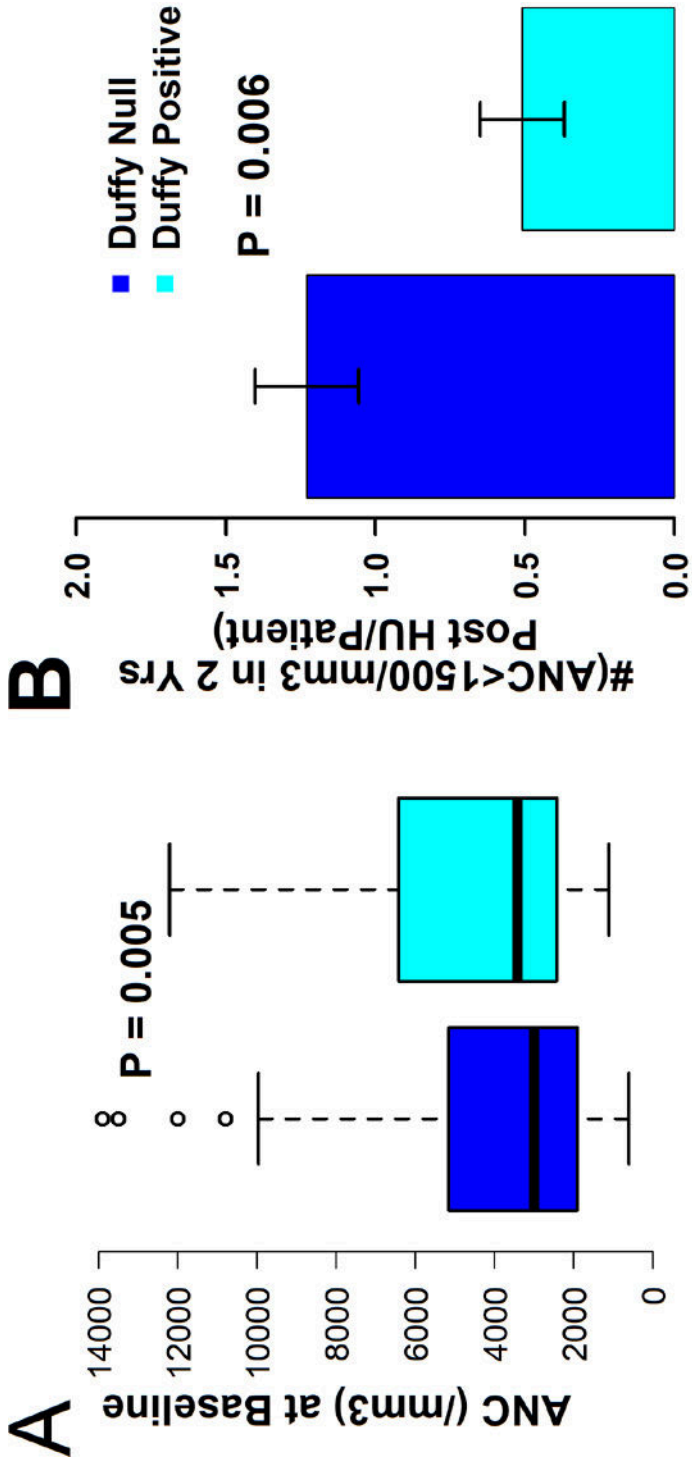

Figure 1