In countries where income per capita is not a problem hydroxyurea is used routinely to circumvent the risk of serious vaso-occlusive complications in patients with sickle cell disease (SCD). Unfortunately to-date, its use in sub-Saharan Africa has been limited due to concerns regarding its cost and the potential clinical impact in a population group with a much higher overall incidence of comorbidities (increased mortality rates, e.g.’s: from malaria and other serious infections in Africa).

Other important barriers in the use of hydroxyurea are the large absolute numbers of individuals with SCD; the lack of clinicians trained in its use; the uncertainty regarding the benefits and lastly the overall risks in resource-poor settings. An example is in the lack of availability of routine monitoring of full blood counts (FBC’s). And the high costs of visits for important follow-up and laboratory monitoring may be just too exorbitant per capita income.

An intensive study in 2018 has now demonstrated that hydroxyurea can be administered safely to children with SCD. The REACH (Realising Effectiveness Across Continents with Hydroxyurea) study enrolled 635 children with SCD in four sub-Saharan African countries (Angola, Democratic Republic of Congo, Kenya and Uganda). Hydroxyurea’s ability to improve numerous outcomes including survival; vaso-occlusive pain; and rates of malaria and other life-threatening infections was proved beyond doubt.¹

At a follow-up of three years, over 90% of the 635 children were still participating in the study. Laboratory confirmative data included a mean increase in the haemoglobin (Hb) of 1g/dL and a mean increase in foetal haemoglobin (HbF) of 12.5%. The most striking feature however, was that transfusions were reduced from 43 to 14 per 100-patient years. Hydroxyurea is now used where possible in sub-Saharan Africa, especially for children with a history of stroke or a high risk of stroke based on elevated transcranial Doppler measurements. Foetal haemoglobin (Hb F) has a higher oxygen affinity, than hemoglobin S or A, due to its lower affinity for 2, 3 DPG, and hence alters the shape of the oxygen dissociation curve moving it towards the left, hence increasing oxygen saturation. Results show that hydroxyurea increases oxygen saturation in children with SCD. The increase in saturation was strongly correlated with increase in Hb F. (See Figure).

### Summary and Recommendations

The majority of the over 300,000 babies born annually with SCD arise in sub-Saharan Africa.

- The diagnosis of SCD early in life improves survival. Screening of the newborn is vital in order to identify affected individuals before the development of complications is the ideal. Unfortunately, most individuals in sub-Saharan Africa are diagnosed when they present with symptoms during childhood at a mean age of ±2-years.

- The risk of bacterial infections is dramatically increased in SCD, particularly in children less than 5-years of age. Two major prophylactic interventions are recommended—vaccinations, especially against encapsulated organisms and daily oral penicillin.

- Although the sickle mutation is somewhat protective against malaria, infection still occurs and may be catastrophic. Various strategies for the control and prevention of malaria include mosquito control; personal protection and antimalarial prophylaxis.

- Vaso-occlusive events (e.g. stroke, pain episodes, acute chest syndrome) are significant cause of morbidity and mortality. Hydroxyurea therapy can be used in children with a history of stroke or elevated transcranial Doppler (TCD) velocities.

### REFERENCES