Fig 1. The morphology of sickle cells that were incubated under hypoxic conditions in the absence or presence of various concentrations of Sailin-HbS after 4hrs observed under 40x magnification.

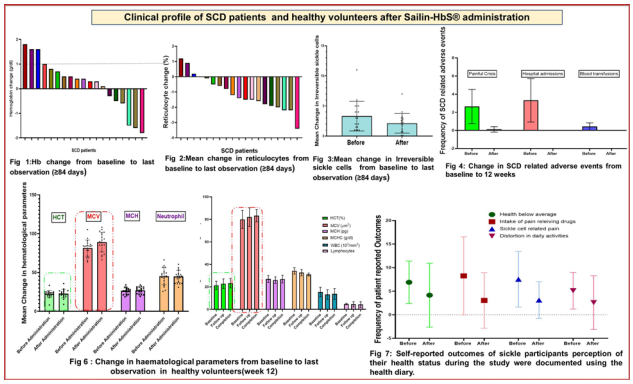

Fig 2. Clinical profile of sickle cell patients administered with Sailin-HbS.
The authors do not declare any conflict of interest

P-090 IS A DEDICATED MARKETING APPROVAL OF HYDROXYUREA IN SICKLE CELL DISEASE MAY INCREASE THE CLINICAL BENEFIT OF THE DRUG?

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Purpose: The first marketing approval of hydroxyurea in SCD was granted in US in 1998 in adults. 10 years after EMA gave a marketing approval in SCD in children from 2 years old. In 2017 in US HU was approved in children. However, in the majority of African countries, in Brazil or in India where the SCD population is important hydroxyurea is not approved in SCD, but only in myeloproliferative disorders and in adults only. Is there an interest in patients and clinicians to have hydroxyurea products dedicated to the SCD?
Materials and methods: Escort HU (European Sickle Cell Disease Cohort – Hydroxyurea) is a non-interventional prospective cohort study conducted in patients treated with HU according to current clinical practice with SCD. The main objective was to refine the safety profile of hydroxycarbamide, but clinical effectiveness were evaluated by recording painful crises lasting more than 48 hours, episodes of ACS, number of hospitalisations related to SCD, and biological parameters were also regularly recorded according to the frequency of the hospital visits.
Results: At inclusion, 926 (48.7%) patients had been previously treated off the label with HU (as HU was only approved for myeloproliferative disorders at the time), with mean duration of HU treatment of 5.74 ± 4.98 years. The mean age of this subgroup was 27.60 ± 14.81 years compared to 19.75 ± 15.79 years of the patients never been treated with HU before enrolment
As showed in the Table 1, hemoglobin level remains unchanged during the first two years but the HbF% increased in the HU-pretreated subgroup. In the "HU-naïve group", despite lower baseline Hb level et HbF% at baseline, similar outcome were obtained after 12 or 24 months. In terms of clinical outcomes, after 1 year of treatment the number of vaso-occlusive crises (VOC), acute chest syndrome (ACS) or hospitalizations decreased dramatically (Table 2) in both group. The median duration of follow-up in the cohort was 45 months (0-128). 123.7 ± 62.7 months. In term of safety, neutropenia, thrombocytopenia and dry skin were the most frequent HU-related adverse events reported but with comparable cumulated incidence between the HU-pretreated subgroup and HU-naïve subgroup (Table 3).
Conclusion: In real life setting, a significant improvement of the vaso-occlusive symptoms was observed even in patients previously treated with HU for a long time. It was observed an improvement of compliance and consequently of effectiveness as suggested by the lower MCV than expected, at baseline in patients previously treated with HU. Paule and al (2011) demonstrated that daily regimen of HU could be superior in term of efficacy to weekly regimen. The fine tuning of the daily dose possible with HU tablets might be another reason of clinical optimization. Even hydroxyurea is available for SCD patients, dedicated marketing approvals of the drug for SCD patients seem support the compliance of the patients materialized by better clinical benefits. These data may encourage Health authorities and pharmaceutical companies to develop and to approve drugs in the indication and so to avoid off-label uses.

parameters		Mean ± SD	HU previously treated (N=926)	HU Naive (N=976)
Hb (g/dL)		Baseline	9.01 ± 1.47	8.63 ± 1.60
		12 months	9.01 ± 1.56	9.01 ± 1.41
		24 months	9.04 ± 1.48	9.01 ± 1.46
Hb F (%)		Baseline	13.58 ± 9.44	7.12 ± 5.94
		12 months	16.24 ± 10.08	15.50 ± 9.67
		24 months	16.20 ± 9.80	15.34 ± 9.15
MCV (fL)		Baseline	86.15 ± 14.37	85.07 ± 12.34
		12 months	94.72 ± 16.39	89.55 ± 13.44
		24 months	95.31 ± 15.05	89.45 ± 12.91
Neutrophils count (10(9)/L)		Baseline	4.78 ± 2.44	5.54 ± 3.06
		12 months	4.41 ± 2.51	4.61 ± 2.98
		24 months	4.07 ± 2.01	4.23 ± 2.49

pre-treated with another HU		Yes N=926		No N=976	
		in the previous year	within the 12 months after initiation of Siklos	in the previous year	within the 12 months after initiation of Siklos
Nb of VOC	Mean ± SD	2.79 ± 2.66	0.77 ± 1.37	2.96 ± 2.69	0.79 ± 1.94
	95% CI	2,68;2,89	0.68 ; 0.86	2,79;3,12	0.66 ; 0.92
Nb of ACS	Mean ± SD	1.20 ± 0.53	0.11 ± 0.38	1.30 ± 0.81	0.07 ± 0.27
	95% CI	0,85;1,54	0.08 ; 0.13	0,79;1,8	0.05 ; 0.09
Nb of Hospitalizations	Mean ± SD	2.36 ± 1.85	0.73 ± 1.26	2.51 ± 1.63	0.67 ± 1.33
	95% CI	2,27;2,44	0.64 ; 0.81	2,40;2,61	0.58 ; 0.75

Table 1 Biological parameters in the subgroups after 12 and 24 months
Table 2. Number of VOC, ACS and hospitalizations after 1 year of HU treatment in the cohort compared to the previous year before enrolment

pre-treated with another HU	Yes (N=926)	No (N=976)	RR [CI 95%]
Neutropenia	50 (5.4%)	62 (6.4%)	0.85 [0.59 , 1.22]
Thrombocytopenia	50 (5.4%)	50 (5.1%)	1.05 [0.72 , 1.54]
Dry skin	59 (6.4%)	61 (6.3%)	1.02 [0.72 , 1.44]
Anaemia	33 (3.6%)	22 (2.3%)	1.58 [0.93 , 2.69]
Skin ulcer	21 (2.3%)	12 (1.2%)	1.84 [0.91 , 3.73]
Alopecia	20 (2.2%)	19 (1.9%)	1.11 [0.60 , 2.07]
Headache	20 (2.2%)	14 (1.4%)	1.51 [0.77 , 2.96]
Nail pigmentation	12 (1.3%)	15 (1.5%)	0.84 [0.40 , 1.79]
Weight increased	13 (1.4%)	15 (1.5%)	0.91 [0.44 , 1.91]
Dizziness	10 (1.1%)	14 (1.4%)	0.75 [0.34 , 1.69]

Table 3. Most Frequent Adverse Events Sorted by Relative Risk by Previous HU Treatment Other Than HU tablets
E. VOSKARIDOU declares a conflict of interest:
Consultancy, Expert: Addmedica: Consultancy
Invitation to national or international congresses: NO
Patent or product inventor: NO
Research support/Scientific studies: PARTICIPATION OF THE SITE IN HU-ESCORT STUDY AND HU ESCORT STUDY EXTENTION
Stock shareholder: NO
Trainings, Teaching: NO

P-091 EFFECTS OF CARICA PAPAYA LEAF EXTRACTS IN TRANSCRIPTIONAL REGULATION OF FETAL HEMOGLOBIN

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Purpose: Sickle cell disease (SCD) is one of the most common human genetic disorders, which is caused by a single point mutation (Glu6Val) on the HBB gene. Currently, one of the treatments for this global health problem involves induction of fetal hemoglobin (HbF). There are some drugs on the market that pharmacologically induce HbF, namely Hydroxyurea (HU), however, their safety concerns and the expensive cost in low- and middle-income countries limit their use. In this context, it is essential to study novel fetal hemoglobin-inducing compounds that have fewer adverse effects and are widely available, such as natural compounds. Therefore, the main aim of this work was to evaluate the effects of Carica Papaya methanolic leaf extracts (CPMLE) in HbF reactivation.
Materials and methods: In order to achieve these goals, gene expression studies on globin and HbF regulators/silencers genes were performed

using three biological replicates in K562 cells. The cells were exposed for 24 hours to three concentrations of CPMLE (0,5; 50 and 100 µg/ml), and to 25 µg/ml of HU, which was used as a positive control. Exposed cells and controls were harvested, and parameters such as cell proliferation and cell viability were microscopically evaluated. Variation in gene expression after CPMLE exposition was quantified from total RNA by quantitative Real Time PCR. The studied genes were α, β and γ-globin genes, as well as the HbF regulators genes MYB, KLF1, BCL11A and BGLT3, and GAPDH was used as a reference gene.
Results: The proliferation rates were calculated as the ratio between the value at 24h and the initial number of cells (1X105 cells/well). The results for the CPMLE concentrations of 0,5; 50 and 100 µg/ml were of 2,12; 2,48 and 2,15, respectively, while for control (cells non-treated) the value was 2,35. The percentages obtained for the viability, as assessed by trypan blue staining, were of 90,02% in control cells, 94,33%; 89,22% and 84,42% for the CPMLE concentrations of 0,5; 50 and 100 µg/ml, respectively. Altogether, these results indicate that some concentrations of CPMLE affect the proliferation and viability of K562 cells, although no cytotoxic effects were observed. Transcriptional analysis demonstrated that all CPMLE concentrations repress BCL11A expression and increase expression of HBA, HBB, MYB and KLF1, relative to control cells, which is in line with the HU results observed for each gene. Additionally, an overexpression of γ-globin and BGLT3 genes was observed upon incubation with 0,5 µg/ml of CPMLE. Thus, the results observed for the BGLT3 gene where distinct between CPMLE and HU. For the other CPMLE concentrations, there was a reduction in the expression of the same genes.
Conclusion: Overall, this preliminary study suggests that CPMLE can modulate the expression of HbF and regulator genes, thus potentially constituting an effective approach for treatment of SCD.
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The authors do not declare any conflict of interest

P-092 RED BLOOD CELL GLUCOSE CONSUMPTION AND METABOLISM IN SICKLE CELL DISEASE

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Purpose: Glucose is the single most essential component of the red blood cells (RBCs), being its sole energy provider and therefore is implicated in the energy metabolomics of the RBCs. This in turn play a crucial role in RBC lifespan, which in Sickle Cell Disease (SCD) patients is reduced to about 20 days from the usual average 120 days. This motivated us to investigate the process of glucose consumption and metabolism in red blood cells of Sickle Cell Patient of Odisha.
Materials and methods: Blood samples of homozygous SCD patients (HbSS) were collected randomly with informed consent from different parts of Odisha state depending on the availability and accessibility of the subjects. The samples were studied for their hematological and biochemical parameters including levels of glucose. The red blood cells of SCD patients aged and sex matched normal (HbAA) as well as sickle cell traits (HbAS) were separated and incubated for different time intervals to measure the glucose consumption and Pyruvate and Lactate formation. Along with this the membrane stability of the cells were estimated and time dependent glucose uptake was also carried out. Identification of the haemoglobin variant was done by performing sickling test, haemoglobin electrophoresis and HPLC Hb. Variant analysis. All the biochemical estimations were done following the standard methods.
Results: In the red blood cells of SCD cases (HbSS), the levels of glucose consumption were noted to be the higher than the sickle cell trait (HbAS) cases and control/normal (HbAA) samples. Concurrently, formation of blood Pyruvate and Lactate showed higher rate in comparison to HBAA and HbAS red cells indicating raised metabolic turnover in the sickle RBCs. In the time dependent study, the red cells of HbSS patients showed higher rate of glucose consumption compared to trait and normal cells. This data also correlates with the higher hemolytic features of the RBCs showing lower membrane stability with increased metabolism.
Conclusion: The sickle cell mutation causes much more damage to the life of RBCs than mere morphological sickling of cells. The energy consumption plays a vital role in the life span, shape, stability and overall biochemistry of the RBCs, thus being a critical factor of RBC metabolism, which in turn determines the overall blood-based health of the SCD patients. Understanding and pin-pointing the key factors of energy metabolism thus holds many potential and promising factors in controlling the sickling, and indeed overall health of patients in case of sickle cell disease.
The authors do not declare any conflict of interest

P-093 PREVALENCE, KNOWLEDGE AND CLINICAL FEATURES OF PRIAPISM IN SICKLE CELL DISEASE IN SENEGAL

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Purpose: The frequency of priapism is very high in adult sickle cell patients. In Africa, the assessment of the level of knowledge of priapism in sickle cell patients showed that priapism was poorly known. The objective of this study was to assess the knowledge, prevalence and clinical features of priapism in adult sickle cell patients in Senegal.
Materials and methods: This was a seven-month descriptive study of 219 male patients with sickle cell disease (SS, SC, S-beta-thalassemia). SS sickle cell patients were in the majority. A questionnaire was drawn up with a 20-minute interview with each patient to assess his or her knowledge and the clinical features of priapism.
Results: The mean age of the patients was 27.1 years (18-54) (SD=7.1). Twenty-three patients (10.5%) were aware of priapism (p=0.004). The prevalence of priapism in sickle cell patients was 41.5%. SS sickle cell patients were at higher risk (91.2%). Eighty-five patients (93.4%) had at least one episode of intermittent priapism and 24 patients (26.4%) had acute priapism. The mean age of onset of the first episode of priapism was 20.4 years +/- 6.1 years. The majority of patients (62.5%) had consulted within the first 24 hours. The last episode of priapism in 50.5% of patients was more than 6 months ago. Priapism occurred at night during sleep in 92.3% of patients. Fifty-eight patients (63.7%) did not have any factors favouring the occurrence of priapism.
Conclusion: Priapism is a frequent serious vaso-occlusive complication in sickle cell disease. We show in this study, a high prevalence, the lack of knowledge of priapism and the clinical particularities of priapism in sickle cell disease in Senegal.
The authors do not declare any conflict of interest

P-094 EXPLORING SCHOOL LIVED EXPERIENCES OF SECONDARY STUDENTS WITH SICKLE CELL DISEASE THROUGH THEIR PARENTS' LENS

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Purpose: The purpose of this qualitative study was to explore the academic and emotion of secondary students with sickle cell disease school experiences as their parents recalled them. Educators are responsible for ensuring access to quality education for all students. Students with disabilities have a legal right to a free appropriate public education under Section 504 and the Individualized Education Program (IEP).
The chronic illness this research will focus on is children living with sickle cell disease. Sickle cell disease is an inherited blood disorder that causes severe pain episodes when sickled blood cells get stuck in blood vessels. To explore these experiences, the researcher employed a qualitative phenomenological approach to inquiry. The researcher also employed a social constructivism approach.
Materials and methods: The study purpose was to investigate students' academic and emotional school lived experiences through interviews and a focus group. The research method involved using the data from interviews, artifacts, and the focus group to analyze the parents' experiences, background stories, and perspectives.