## Abstract 2231

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# Low Sickle Cell Disease Mortality In Belgium and Benefit From Hydroxyurea Therapy

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In Western countries, mortality among patients with sickle cell disease (SCD) has decreased in the last decades by means of neonatal screening (NS), infectious prophylaxis and care improvements. The major causes of death in children include acute chest syndrome, sepsis, splenic sequestration, stroke, aplastic crisis while in adults end-stage organ failure contributes also to premature death. Hydroxyurea (HU) and stem cell transplantation (SCT) are used in Belgium for more than 20 years but their possible influences on survival have not been yet analyzed.

The Belgian SCD Registry was created in 2008 including patients of 8 centres. All available data in 2008 were retrospectively encoded in the database. After 2008 and until 2012, all data were recorded prospectively for already registered patients as well as newly diagnosed subjects. Data were registered from NS or from diagnosis (first contact) until last follow up (FU) visit, SCT or death. Data included diagnosis, demography and outcome data. After SCT, only vital status and cause of death were recorded.

Up to date, data from 470 pts are recorded (224 males), 412 are HbSS, 14 HbS$\beta^0$, 7 HbS$\beta^+$ and 37 HbSC. The median age at diagnosis and at last FU was respectively 0.7 year (y) and 9.9 y. The FU for the whole cohort was 3810 patient-years (PY) and with 136 patients aged over 18y, their FU during adulthood accounted for 520 PY. Thirteen patients died (2.8%). The mortality per 100-PY was 0.34 and the median

age at death was 14.5 y (range, 1.5-23.7 y). All deaths occurred in HbSS patients, 5 after SCT and 8 due to an acute event. Complete data set is missing for 3 of the 8 patients. For the 5 well documented SCD related deaths, causes were: hemorrhagic stroke (2), sepsis due to *S. pneumoniae* (1), aplastic crisis (1) and infection during stay in homeland (1).

At last FU, 91 patients were transplanted, 182 were on HU, 7 on HU + chronic transfusion (CT), 19 on CT (4 after HU treatment). The remaining 171 patients never had disease modifying therapy (DMT). Compared with the latter, mortality rate for those on HU was significantly reduced (0.1 vs 0.5/100-PY) while patients on HU have longer FU and are older at last FU (Table 1).

Among 91 patients transplanted at a median age 6.9 y, 5 died: 3 from acute transplant related toxicity, 1 from secondary acute myeloblastic leukemia after cGVHD, and 1 is unexplained more than 7 years post SCT.

The data issued from the most recent NS cohorts report a low death rate during childhood ranging from 0.13 to 0.52. Even if our Belgian cohort is not exclusively issued from neonatal diagnosis, the observed death rate is low (0.34/100-PY). Several methodological biases are present in this partially retrospective study (incomplete or unavailable data, lost of FU, no information if death occurred before the first contact in a center, …). Nevertheless our low mortality is not underestimated since 1) most patients were followed since infancy and during a long period (3810 PY); 2) the FU during adulthood (period of increased mortality) accounted for 520 PY; 3) our cohort represents a very large part of the Belgian SCD population since a national inquiry performed in 2007 estimated the whole SCD population to 500. The effect of HU on mortality has been reported in adults and more recently in children. Despite longer FU and older age at last FU, our data confirms those previously results.

With only one case, death by infection is rare while SCT complications contributed to about 40 % of deaths. Even if SCT is the only curative option for SCD, it encompasses a risk of mortality. As life expectancy of SCD patients has been extended which is confirmed by our results (especially for patients on HU), SCT should be reserved for clinically severe cases. Population-based prospective studies evaluating the survival in transplanted and non transplanted patients are needed.

**Table 1. Data on follow-up and mortality according to last treatment**

| | All cohort | No DMT | CT | HU only | SCT | P** |
|---|---|---|---|---|---|---|
| Number of patients | 470 | 171 | 26 | 182 | 81 | |
| Median age at diagnosis, years (range) | 0.7 (0-34.6) | 0 (0-34.6) | 0.6 (0-19.3) | 1.2 (0-27.6) | 1.8 (0-14.5) | 0.0003 |

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|---|---|---|---|---|---|---|
| Median FU, years (range) | 6.7 (0-48.7) | 5.6 (0-48.7) | 10.5 (0.1-21.8) | 9.9 (0.1-32.8) | 3.4(0.1-13.1)* | <0.0001 |
| Median age at last FU, years (range) | 9.9 (0-52.7) | 7.2 (0-52.7) | 11.8 (0.9-27.8) | 12.9 (2.1-39.6) | 6.9(1-19)* | <0.0001 |
| Total patient-years FU | 3810 | 1184 | 176 | 1970 | 480* | |
| Deaths | 13 | 6 | 0 | 2 | 5 | ns |
| Death-rate/100 patient-years | 0.34 | 0.5 | 0 | 0.1 | NA | 0.014 |
| * Until date of SCT | | | | | | |
| ** Comparison between HU and No DMT | | | | | | |