An observational study to evaluate the routine management, healthcare resource use and outcomes for patients with transfusion-dependent β-thalassaemia treated in the United Kingdom: an interim analysis

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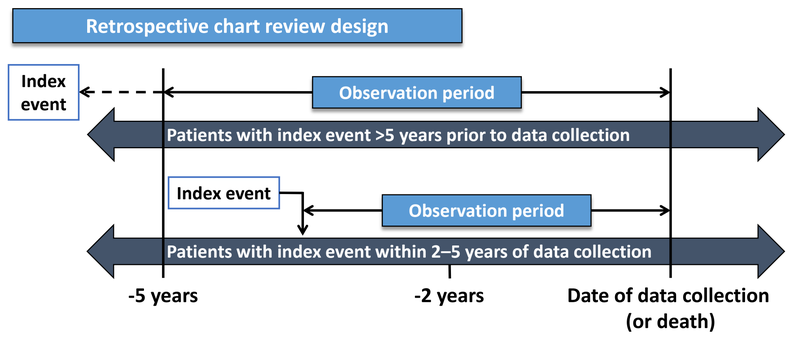
INTRODUCTION

- β-thalassaemias are a group of inherited blood disorders resulting in defects in haemoglobin (Hb) synthesis.[1]
- The most severe forms of β-thalassaemia require chronic transfusion therapy to sustain life (transfusion-dependent thalassaemia [TDT]).[2]
- Long-term blood transfusion therapy causes iron overload; if untreated, this can lead to the development of endocrine disorders, organ damage and premature death.
- Regular monitoring of iron burden and iron chelation are essential to reduce the risk of complications.
- Currently, allogeneic haematopoietic stem cell transplantation (aHSCT) is the only potentially curative treatment available to patients with TDT.[1]
- There is a paucity of real-world data concerning the management of patients with TDT in the United Kingdom (UK).
- As a result, current UK management pathways for TDT and associated National Health Service (NHS) costs are poorly understood.
- This study aims to describe the real-world routine management of patients with TDT in the UK NHS.
- Here we report the results of an interim analysis of 70 patients' retrospective data (target population of 200 patients).

STUDY DESIGN



- A multicentre, observational study ongoing in 9 centres in the UK, involving retrospective data collection and cross-sectional patient reported outcomes.
- The **observation period** was defined as:
  - The five year period prior to the date of data collection/death **or**;
  - For patients with an index event between two to five years prior to the date of data collection/death, the observation period will be from the index event date to the date of data collection.
- **Transfusion dependence** was defined as β-thalassaemia treated with ≥8 transfusions during the first year of chronic transfusion therapy or a history of at least 100 mL/kg/year of packed red blood cells.
- The **index event** was defined as the date on which the decision to commence long-term blood transfusion therapy is documented in the patient's medical record *or* the date of the first transfusion within the first 12 month period where at least 8 transfusions for β-thalassaemia were recorded.
  - The **index event** for patients with disease recurrence post-aHSCT was the date of the first transfusion within the first 12 month period where at least 8 transfusions for β-thalassaemia were recorded after disease recurrence.
- The **baseline** is defined as the start of a patients' observation period.

METHODS

Study patients (retrospective review)

- Inclusion criteria:
  - Patients with a documented diagnosis of TDT (as defined above).
  - Patients with ≥2 years post-index data available prior to data collection.
- Exclusion criteria:
  - Patients who have undergone aHSCT except those with disease recurrence post-transplant receiving transfusion therapy and meeting the definition of TDT.
  - Living patients for whom written informed consent has not been obtained (from either the patient or their parent/carer, as appropriate to their age) for access to their medical records for the purposes of this study.
  - Patients with <2 years of continuous data available prior to the date of data collection.
  - Patients participating in any clinical trial during the study observation period.

Data source

- Data were collected retrospectively from consenting patients' medical records, including demographics, clinical characteristics, TDT treatment, monitoring and iron chelator therapy.

Analysis

- The **primary objective** is the number of blood transfusions per patient per year, according to reason for transfusion.

METHODS CONTINUED

Analysis continued

- Secondary objectives include:
  - Patients' transfusion requirements.
  - Hb assessments during the observation period (e.g. number of Hb assessments per year).
  - Iron chelation treatments (types and formulations).
  - Assessment of body iron stores during the observation period (e.g. serum ferritin/liver iron/cardiac iron).

Statistics

- Distributions and descriptive statistics of central tendency (mean or median) and dispersion (standard deviation [SD] or interquartile range [IQR]) were calculated for quantitative variables.
- Nominal variables were described with frequencies and percentages.
- If data were unavailable for some patients the total n is reported in brackets.

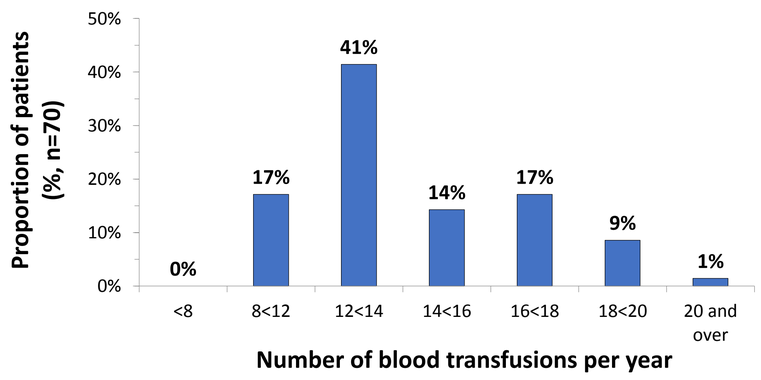
RESULTS

- The median observation period was 5.0 (IQR 5.0–5.0) years.
- Patient demographic characteristics are shown in **Table 1**.
- One patient was deceased at data collection.

Table 1. Patient demographics

Characteristic	Group	
Age distribution (years)	**n**	**%**
>12<18	7	10%
18<30	30	43%
30<40	18	26%
40<50	6	9%
50<60	6	9%
60 and over	3	4%
Total	70	
Age (years)		
Median (IQR)	28.5 (23.9 to 37.3)	
Range	12.1 to 67.4	
Female, n (%)	34 (49%)	
Disease duration at data collection/death (years)		
Mean (SD)	19.2 (10.7)	
Median (IQR)	17.7 (11.1 to 24.6)	

Figure 1. Number of blood transfusions per year during observation period



- Patients had a median of 13.2 (IQR 12.2–16.2) transfusion episodes per year (n=70).
- Patients received a median of 33.8 (IQR 30.5–39.1) units of blood per patient per year (n=44).
- >99% of transfusion episodes (4855/4858) were for routine management of TDT.
- Pre-transfusion Hb test results are shown in **Table 2**.
  - There were 3146 pre-transfusion tests recorded for 62 patients.

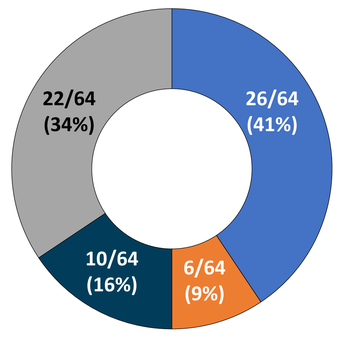
Table 2. Pre-transfusion Hb test results

Pre-transfusion Hb (g/L)	n results	% (n=3146)
<95	1100	35%
≥95	2046	65%
Total	3146	
Mean (SD)	97.8 (9.7)	
Median	98.0 (92.0 to 104.0)	
Range	60.0 to 140.0	
Number of pre-transfusion Hb test results (per patient per year)		
Total patients with results	62	
Mean (SD) results	10.4 (5.4)	
Median (IQR) results	12.1 (7.7 to 13.6)	
Range	0.2 to 25.6	

RESULTS CONTINUED

- All patients received ≥1 chelation therapy during the observation period.
- 91% (64/70) were receiving iron chelators at data collection, summarised in **Figure 2**.

Figure 2. Distribution of iron chelators at data collection

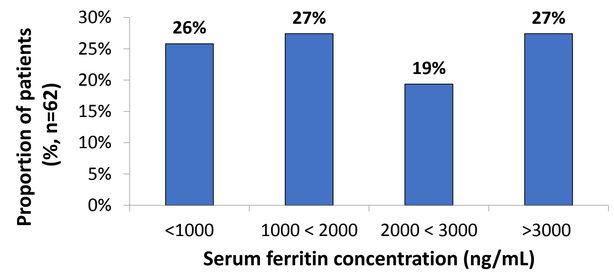


*5 Patients were not receiving an iron chelator at data collection; one patient was deceased.

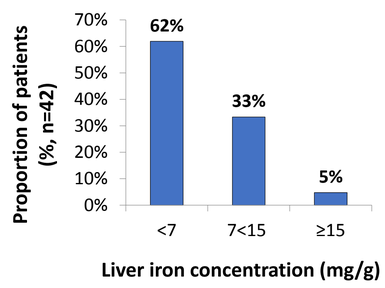
- The results of patients' iron concentration tests (serum ferritin, liver iron and cardiac iron) are shown in **Figure 3**.
  - The median serum ferritin concentration closest to data collection (n=62) was 1852.0 (IQR 985.3–3346.5) ng/mL.
  - In the 42 patients with liver iron concentration (LIC) measured by magnetic resonance (MR) R2, the median LIC closest to data collection (n=42) was 5.3 (IQR 2.5–9.8) mg/g.
  - The median cardiac MR T2* value closest to data collection (n=62) was 29.8 (IQR 18.1–35.6) ms.

Figure 3. Results of patients' iron concentration tests

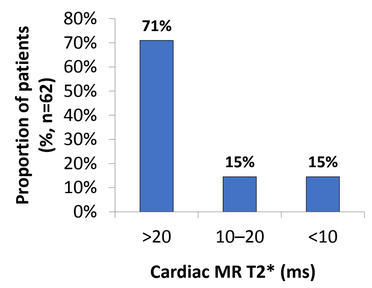
(A) Serum ferritin concentration



(B) Liver iron concentration (LIC) measured by MR R2 test



(C) Cardiac iron measured by MR T2* test



- There was a median interval of 2.5 (IQR 1.4–2.5) years between LIC measurements (all protocols, including biopsy, T2* or R2).
  - There were no LIC measurements recorded for 4/70 (6%) of patients.
- There was a median interval of 2.5 (IQR 1.7–5.0) years between cardiac iron measurements.
  - There were no cardiac iron measurements recorded for 6/70 (9%) of patients.

CONCLUSIONS

- These interim results provide insight into real-world management and iron loading of patients with TDT treated in the UK NHS.
- The majority of patients had ≥12 blood transfusions per year.
- The data suggest a subset of TDT patients have iron levels above recommended thresholds, and monitoring may be less frequent than recommended (UK Thalassaemia Society 2016 standards).[3]
- Data collection is ongoing. The final analysis is expected to provide a more complete description of treatment patterns, clinical outcomes, healthcare resource use and patient reported outcomes associated with the management of TDT in UK routine clinical practice.
- This analysis does not include patents aged ≤12 years, and therefore the demographics of this analysis group may not be representative of all TDT patients across the UK.

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DISCLOSURES

KR states nothing to declare; SP states nothing to declare; PT declares advisory committee (Global Blood Therapeutics, Novartis, bluebird bio), data monitoring committee (Pfizer), clinical trial activity (Apopharma, Celgene, Global Blood Therapeutics, Novartis, Napp Pharma), investigator led funding (Kyowa Kirin Limited, bluebird bio) and speaker activity (Apopharma, Terumo plc); FS declares advisory board (silence therapeutics, Roche, Novartis) and Steering committee for trial (Celgene) involvement; JK declares advisory boards with Jazz and Novartis; SP declares Novartis support to attend educational meetings; RW states nothing to declare; MV states advisory board for bluebird bio; EC declares consultancy fees from Novartis; JH is an employee of pH Associates; CP and MJ are employees of bluebird bio and own stock in the company.

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