NHS ENGLAND SPECIALISED SERVICES

CLINICAL PANEL REPORT

Date: April 2022

Intervention: Allogeneic Haematopoietic Stem Cell Transplantation (Allo HSCT)

Indication: Transfusion dependent thalassaemia (adult)

URN: 2120

Gateway: 2, Round 1

Programme: Blood and Infection

CRG: Haemoglobinopathies

Information provided to the Panel

Evidence Review undertaken by NICE

Evidence to Decision Making Report

Clinical Priorities Advisory Group (CPAG) Summary Report

Policy Proposition

Blueteq™ Form

Equalities and Health Inequalities Assessment (EHIA)

Patient Impact Assessment (PIA)

Policy Working Group (PWG) Appendix

This policy proposition recommends allogenic haematopoietic stem cell transplantation (allo-HSCT) as a curative treatment option for adults with transfusion dependent thalassaemia (TDT). TDT is a complex multi-system disease and cardiac, liver and bone disease are significant problems. Iron overload can cause tissue damage and impaired function of affected organs. Allo-HSCT is already commissioned for a number of disorders including children aged up to 18 years old with TDT. Current management of adult patients with TDT is complex and generally involves supportive care.

Clinical Panel were presented with the evidence base which consisted of four studies. These studies included both adults and children but reported subgroup analysis of adults only. They were: a retrospective case control study comparing allo-HSCT with standard treatment; a retrospective cross-sectional study comparing allo-HSCT with standard treatment; two no-comparative retrospective case series.

Overall survival - one case series (n=82) provided very low certainty evidence that that 80% of adults who had HSCT survived after 2 years and the other (n=33) provided very low certainty evidence that 63% survived after 5 years.

Event free survival - the case control study (n=97) and two case series (n=82 and n=33) provided very low certainty evidence that 63% to 76% of adults who had HSCT survived free of thalassaemia for between 2 and 23 years. Panel members considered the presentation of this in the study was unclear in absolute meaning.

The cross sectional study provided very low certainty evidence that adults with TDT who had HSCT at least 2 years previously (n=9), using a quality of life questionnaire, rated their overall health (80.6 vs 60.4, p=0.034), physical health (79.7 vs 66.6, p=0.041), sleep (86.1 vs 68.8, p=0.023) and 'drug independence for a functional life' (91.7 vs 31.3, p=0.001) statistically significantly better than adults who had standard treatment (n=12). However, there was no significant difference between the groups for other quality of life outcomes. Sample sizes are very small and so not considered reliable for decision making.

No cost effectiveness studies were identified.

Panel members discussed what was meant by Event Free Survival as it was not clear to them if this meant no extra treatment required during this period.

The proposition states a cut off age of 45 years old. The member debated this as there needs to be very specific reasons for a definite cut off else this could be a potential area for future challenge, such as a clear clinical evidence base for this.

Panel members raised that various sections within the proposition require some further work.

EHIA – no further comments received.

PIA – no further comments received.

Recommendation

Clinical Panel recommends that the proposition returns to a future Panel meeting.

Why the panel made these recommendations

Clinical Panel members considered that further work and amendments were required to the proposition.

Documentation amendments required

Evidence Review:

- Event Free Survival – it was not clear to members of the meaning of event free survival, did this mean no requirement for transfusion. Needs clarifying.

Policy Proposition:

- Definition of HSCT – this needs to be worded more clearly as doesn't give a sense of the breadth of conditions it is used at treatment for.
- Definition of iron overload chelation therapy - this needs clarification as not clear. Cross check with paediatric policy to ensure alignment.
- Remove age cut off – this will enable the MDT to determine benefits and risk of the individual patient and what is appropriate.
- Exclusion criteria – established renal failure. This requires defining to provide clarity of meaning.
- Exclusion criteria – liver cirrhosis. This requires further defining as to broad a term.
- Flow diagram – check if there is a need to include the wording regarding migration to England. If so, then possibly change to 'adults identified through new-born screening' instead?
- Provide clarity on the impact on the need for future transfusions by introducing this policy.
- By using HSCT, confirm impact on related drugs that are used for this condition.

Post-panel amendments

- The PWG submits the following statement to clarify the definition of event-free survival: *Allo-HSCT is a curative intervention for patients with transfusion dependent thalassaemia and patients who undergo HSCT will have no ongoing transfusion requirement. Indeed failure of the transplant results in a recurrence of transfusion dependence. In the evidence review, event-free survival is defined as, 'how long people live after transplant until either death or thalassaemia recurrence'. The PWG confirm that in this patient cohort, thalassaemia recurrence equates to a recurrence in transfusion dependence.*
- The definition of HSCT was discussed with the PWG. The definition used in this policy is the standard NHS England definition used in previous policies. The PWG confirm this is how HSCT should be defined and requested no change be made to the definition.
- The definition of iron overload chelation therapy was discussed with the PWG. It is the standard NHS England definition used in previous policies. The PWG confirm that this is the correct definition for iron chelation therapy.
- The age cut off has been removed from the policy proposition document.
- The exclusion criteria of established renal failure was discussed with the PWG and further defined as an exclusion criteria of: Glomerular Filtration Rate < 40 ml/min/1.73m^2.
- The exclusion criteria of liver cirrhosis was discussed with the PWG and was removed from the policy proposition document as there is no arbitrary cut off defined in either the literature or PWG consensus. Liver assessment is included in the inclusion criteria as part of the comprehensive organ assessment that involves a liver ultrasound.
- The wording in the flow diagram was revised and newly states, 'adult patient identified as having thalassaemia'. This was rather than the suggested statement above of 'adults identified through new-born screening' as adult patients are identified through two routes including adults who were identified through newborn screening in the UK who did not have parental consent for HSCT as well as adults who migrate to the UK who did not have the option of HSCT in their country of origin.
- The impact of allo-HSCT on the need for transfusions was discussed with the PWG. Allo-HSCT is a curative intervention for patients with transfusion dependent thalassaemia and patients who undergo HSCT will have no ongoing transfusion requirement. Indeed failure of the transplant results in a recurrence of transfusion dependence.
- The impact of allo-HSCT on related drugs used in transfusion dependent thalassaemia was discussed with the PWG and they confirm that iron chelation agents are required by patients undergoing blood transfusions. Patients who have had a HSCT will have no ongoing transfusion requirement and therefore no need for iron chelation agents.

Declarations of Interest of Panel Members: None

Panel Chair: James Palmer, National Director, Specialised Services