Clinical Commissioning Policy Statement
Allogenic Mesenchymal Stromal Cell Infusion Therapy for Children with Severe Generalised Recessive Dystrophic Epidermolysis Bullosa (1805)

Commissioning Position

Summary

Allogenic mesenchymal stromal cell therapy is not recommended to be available as a treatment through routine commissioning in children with severe generalised recessive dystrophic epidermolysis.

Information about allogenic mesenchymal stromal cells

The intervention

Mesenchymal stem cells (MSCs) are a type of cell derived from the bone marrow of humans and have the ability to help heal damaged tissues of the body. The exact mechanism of action of MSCs is unknown but they are thought to modify the inflammatory response thereby encouraging tissue repair and regeneration. More research is being undertaken into how they work and whether they can help treat certain diseases that have an inflammatory component. Allogenic refers to the source of MSCs originating from a donor rather than the person affected by the disease.

Committee discussion

The condition

Epidermolysis Bullosa (EB) covers a group of rare genetic skin conditions that affect the outer layers of the skin: the epidermis and its anchoring to the layer beneath. The genetic abnormalities result in the abnormal formation of, or a reduction in, the number of proteins that maintain the structural integrity of these layers. The skin is very fragile and unable to withstand damage from minimal mechanical forces. As a result, patients are susceptible to recurrent infections and have chronic inflammation.

Epidermolysis Bullosa is a rare disease that is estimated to affect 1 in 17,000 live births and there are around 5,000 people living with EB in the UK. Recessive dystrophic EB (RDEB) is a severe form of dystrophic EB affecting approximately 5% of the cases of EB. The cause of RDEB is a mutation in the *COL7A1* gene which leads to reduced or absent production of type VII collagen (C7). C7 is integral in anchoring the epidermis to its underlying layer, the dermis.

The most severe form of RDEB is severe generalised RDEB (SG-RDEB). SG-RDEB is a life-limiting multi-system disease, starting at birth, resulting in chronic and extensive skin blistering, scarring and contractures. This can lead to profound physical disabilities with significant difficulties in doing activities of daily living such as feeding, bathing, going to the toilet and walking. The mucosal surfaces of the eyes and gastro-intestinal tract can be affected causing impaired vision and nutrition. Other complications of SG-RDEB include osteoporosis, anaemia and a higher risk of developing certain aggressive types of skin cancer.

Current treatments

Available treatment for SG-RDEB aims to look after the skin and blisters using protective dressings, ensuring a healthy diet and preventing and treating infections. It is also important to provide regular follow up so that possible complications, including certain types of aggressive skin cancers, can be detected early. The provision of psychosocial support to the patient and their family is also important. There is no cure at present.

Comparators

There have been no studies with treatment comparators.

Clinical trial evidence

The evidence submitted consisted of one single centre, non-randomised, open-label phase I/II clinical trial. This evaluated the use of intravenous allogenic MSCs in ten children (5 males, 5 females) aged between 1 and 11 years old with a genetically confirmed diagnosis of RDEB. The trial was conducted at Great Ormond Street Hospital for Children, London, England. Each child received three intravenous infusions of MSCs. The primary outcome of the trial was to evaluate safety and a range of secondary outcomes were assessed.

The Clinical Panel determined that the paper was a limited series of an early use of the intervention but there was no clear clinical benefit at this stage.

Paper. Petrof, G. *et al.,* 2015. Potential of Systemic Allogeneic Mesenchymal Stromal Cell Therapy for Children with Recessive Dystrophic Epidermolysis Bullosa. *The Journal of Investigative Dermatology*, 135(9), pp.2319–2321.

Secondary outcomes included assessment of severity, levels of pain, fatigue and pruritus. Quality of life and qualitative data from semi-structured interviews was also assessed. Secondary clinical outcomes included assessment of the skin (median blister count and suction blister time) and blood samples to assess renal, liver and bone marrow function.

The Birmingham Epidermolysis Bullosa Severity (BEBS) score demonstrated a reduction in severity at day 180 (mean difference -6.9, 95% CI: -12.7, -1.1) compared with baseline (defined as up to 120 days prior to starting the first infusion of MSCs). The Global Severity Score (GSS) demonstrated a reduction in severity at day 60 (mean difference -2.4, 95% CI: -3.4, -1.4) and reduced further at day 180 (mean difference -1.6, 95% CI: -2.96, -0.24) compared with baseline. Results reported for pain, fatigue and pruritus did not show any statistically significant difference at either day 60 or day 180 compared with baseline. The Paediatric Quality of Life score (Parent version) demonstrated an improvement at day 60 (mean difference -4.4, 95% CI: -8.1, -0.7).

Blood samples taken during the course of the trial did not identify any impact on kidney, liver or bone marrow function. The median blister count at baseline was 5.5 (interquartile range (IQR) 2.0, 6.0). The median blister count was lower at day 60 (median 3.5, IQR 1.0, 7.0) and 180 (median 3.5, IQR 3.0, 7.0). The suction blister time was also measured. This is a measure of the time taken for a blister to form by the application of suction (negative pressure) to an area of the skin. There was an improvement in the suction blister time at day 100 (mean difference 1.7 minutes, 95% CI: -0.5, 3.9) compared to baseline but this was not statistically significant.

Qualitative data from semi-structured interviews undertaken 9 months after the last infusion reported a range of positive experiences by parents. This included an improved rate of wound healing, a reduction in pain and analgesia requirement, a reduction in time required for skin care and the number of dressings used and an improvement in family quality of life.

Adverse events

Adverse events were categorised according to their relationship to the MSC infusion ranging from definitely to not related. A total of 163 adverse events were experienced in the study (n=10). None of these were serious and the majority (65%, 107) did not require any action.

Thirty-two adverse events were recorded as being directly attributable to the administration of MSCs and included: dimethyl sulfoxide (DMSO, a preservative used in MSCs) odour, abdominal pain, bradycardia and nausea. These adverse events did not require any alteration to the dose or discontinuation of the infusions.

Policy review date

This is a policy statement, which means that the full process of policy production has been abridged: a full independent evidence review has not been conducted; and public consultation has not been undertaken. If a review is needed due to a new evidence base then a new Provisional Policy Proposal needs to be submitted by contacting england.CET@nhs.net.

Links to other Policies

Not applicable.

Equality Statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and

- Given regard to the need to reduce inequalities between patients in access to and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities