NIHR | Innovation Observatory

Newcastle University

Health Technology Briefing
March 2025

Mozafancogene autotemcel for treating Fanconi anaemia subtype A in children and adolescents

Company/Developer	Rocket Pharmaceuticals Inc

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 28213	NICE ID: Not available	UKPS ID: N/A

Licensing and Market Availability Plans

Currently in phase II clinical trials.

Summary

Mozafancogene autotemcel is in development for the treatment of Fanconi anaemia subtype A (FA-A) in children. Fanconi anaemia (FA) is a rare genetic condition caused by changes (mutations) in certain genes that help repair deoxyribonucleic acid (DNA). In people with FA-A, the affected gene is called FANCA. When DNA is not properly repaired, it can cause cells to die prematurely or grow in an uncontrolled way. This can lead to physical abnormalities, low numbers of blood cells, and an increased risk of cancer. Over time, FA can cause the bone marrow (the soft, spongy tissue inside bones that makes blood cells) to stop working properly, also known as bone marrow failure. Bone marrow makes stem cells, which produce red blood cells, white blood cells, and platelets, all of which are essential for staying healthy. There are currently limited options for treating FA.

Mozafancogene autotemcel is a type of stem cell therapy that uses the patient's own stem cells and modifies them *ex-vivo* (outside of the body) by adding a working FANCA gene. The corrected cells are then returned to the patient through an infusion into a vein. The goal of this treatment is to address bone marrow failure risk. If licenced, mozafancogene autotemcel could provide a new treatment for patients with FA-A.

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.

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Proposed Indication

Treatment of Fanconi anaemia subtype A (FA-A) in children and adolescents.[1]

Technology

Description

Mozafancogene autotemcel (RP-L102) is an autologous therapy that utilises FA-A CD34+ enriched hematopoietic stem and progenitor cells (HSPCs) that have been transduced *ex-vivo* with a functional Fanconi Anaemia Complementation Group A (*FANCA*) gene. Fanconi anaemia (FA) is associated with progressive bone marrow failure (BMF), which 80% of FA patients develop. In preclinical studies, mozafancogene autotemcel has been shown to provide a survival advantage to the gene-modified stem cells, leading to correction of progressive BMF.[2]

Mozafancogene autotemcel is currently in clinical development for the treatment of FA-A in children and adolescents. In the phase II clinical trials (NCT04069533, NCT04248439), the corrected HSPCs are infused intravenously back to the patient.[1,3] Given the nature of the underlying disease, individual dose may vary per patient.[a]

Key Innovation

Approximately 60-70% of all cases of FA result from mutations in the *FANCA* gene.[4,5] Three out of every four patients develop evidence of at least mild BMF within the first decade of life.[6] About 90% of people with FA have BMF or lack of function. People with BMF can develop blood disorders such as aplastic anaemia and myelodysplastic syndrome (a form of pre-leukaemia).[7] Preclinical studies have shown mozafancogene autotemcel to provide a survival advantage to the stem cells that have been gene-modified *ex vivo*, leading to correction of BMF.[2] A current treatment for FA, allogeneic hematopoietic stem cell transplantation (alloHSCT), offers a haematolymphoid cure. However, it confers significant risk of morbidity and mortality and is thereby indicated only after development of severe BMF or dysplasia. *Ex vivo* HSPC-based gene therapy with mozafancogene autotemcel offers an alternative strategy for earlier and potentially safer intervention with the goal of preventing BMF and the need for alloHSCT.[8] Mozafancogene autotemcel for FA is an advanced therapy medicinal product (ATMP) classification within the definition of a gene therapy medicine. The scientific recommendation for an ATMP classification is issued by the EMA's Committee for Advanced Therapies (CAT).[9] If licenced, mozafancogene autotemcel will provide an additional treatment option for patients with FA-A.

Regulatory & Development Status

Mozafancogene autotemcel does not currently have marketing authorisation in the EU/UK for any indication.

Mozafancogene autotemcel is not in phase II/III clinical development for any other indications.[10]

Mozafancogene autotemcel has the following regulatory designations/awards for Fanconi anaemia:

- a PRIME status by the European Medicines Agency (EMA) in December 2019
- a Regenerative Medicine Advanced Therapy (RMAT) status by the US Food and Drug Administration (FDA) in November 2018
- a Fast Track status by the US FDA in November 2018

[a] Information provided by Rocket Pharmaceuticals Inc

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- an Orphan drug by the EMA in December 2010

Patient Group

Disease Area and Clinical Need

FA is a rare genetic disorder, in the category of inherited BMF syndromes. The chromosomes within the cells of individuals with FA are unable to repair deoxyribonucleic acid (DNA) damage, and thus break and rearrange easily (chromosome instability). This occurs due to certain gene mutations that encode proteins that are involved in the FA pathway. The FA pathway brings DNA repair proteins to the area of DNA damage. Disruption of this pathway results in a build-up of DNA damage that can lead to premature cell death or abnormal cell growth. The death of cells results in a decrease in blood cells and physical abnormalities associated with FA. Uncontrolled cell growth can lead to the development of acute myeloid leukaemia or other cancers. Half of FA patients are diagnosed prior to age 10, while about 10% are diagnosed as adults. At least 60% of individuals affected with FA are born with at least one physical anomaly, such as small size, abnormal thumbs and/or radial bones, skin pigmentation, small heads, small eyes, abnormal kidney structures, and cardiac and skeletal anomalies. The disorder is often associated with a progressive deficiency of all bone marrow production of blood cells, red blood cells, white blood cells, and platelets. Affected individuals have an increased risk of developing a cancer of blood-forming cells in the bone marrow called acute myeloid leukaemia (AML), or tumours of the head, neck, skin, gastrointestinal system, or genital tract.[11] Fifteen genetic subtypes of FA have been distinguished. The majority of patients (≈60%) belong to the subtype A, which is caused by a mutation in the *FANCA* gene.[11,12]

The incidence of FA in Europe and America is estimated at 1:360,000 births, based on a carrier frequency of 1 in 300 and an autosomal recessive model in Europe and USA.[13] FA is the most common genetic cause of aplastic anaemia.[14] In England, 2023-24, there were 2,464 finished consultant episodes (FCEs) and 2,425 admissions for constitutional aplastic anaemia (ICD-10 code D61.0), of which FA makes up a large subset of the population, which resulted in 1,578 FCE bed days and 2,135 day cases.[15]

Recommended Treatment Options

There is no treatment option recommended by NICE for FA.[16]

There are currently no approved pharmacological treatment options for FA, however, non-approved management of FA may include androgen administration, hematopoietic growth factors, AlloHSCT, cancer treatment, and surgery to correct skeletal malformations and gastrointestinal abnormalities.[11]

Clinical Trial Information

Trial	NCT04069533; **EudraCT-** 2018-002502-31; A Phase II Clinical Trial to Evaluate the Efficacy of the Infusion of Autologous CD34+ Cells Transduced With a Lentiviral Vector Carrying the FANCA Gene (Orphan Drug) in Patients With Fanconi Anemia Subtype A **Phase II** – Active, not recruiting **Locations:** UK and one other EU country **Primary completion date (estimated):** February 2025
Trial Design	Single group assignment, open label
Population	N=7; aged 1 to 17 years with FA-A.

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Intervention(s)	Mozafancogene autotemcel: CD34+ enriched cells from subjects with FA-A transduced *ex vivo* with lentiviral vector carrying the FANCA gene.
Comparator(s)	No comparator
Outcome(s)	Primary outcome: Phenotypic correction of bone marrow colony forming units after infusion of Mozafancogene autotemcel. During months 12-36 post-infusion, the survival of bone marrow colony forming units to 10nM mitomycin C (MMC) increases to over or equal to 10% with respect to values determined at baseline (pretreatment evaluation) [Time frame: 3 years] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Trial	NCT04248439; A Phase 2 Clinical Trial to Evaluate the Efficacy of the Infusion of Autologous CD34+ Cells Transduced With a Lentiviral Vector Carrying the FANCA Gene in Pediatric Subjects With Fanconi Anemia Subtype A **Phase II** – Active, not recruiting **Locations:** USA **Primary completion date (estimated):** May 2026
Trial Design	Single group assignment, open label
Population	N=5; aged 1 year and older with FA-A.
Intervention(s)	Mozafancogene autotemcel: CD34+ enriched cells from subjects with FA-A transduced *ex vivo* with lentiviral vector carrying the FANCA gene.
Comparator(s)	No comparator
Outcome(s)	Primary outcome: Bone Marrow colony-forming cell mitomycin-C (MMC) resistance ≥20% at 12 months post-infusion with a confirmatory result at 18 or 21 months (MMC at 10 nM concentration) [Time frame: 21 months] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of mozafancogene autotemcel is not yet known.

Relevant Guidance

NICE Guidance

There are currently no NICE guidelines available for FA.

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NHS England (Policy/Commissioning) Guidance

- NHS England. Clinical Commissioning Policy: Haematopoietic Stem Cell Transplantation (HSCT) (All Ages): Revised Reference. B04/P/a. July 2021.
- NHS England. NHS Standard Contract Paediatric Medicine: Haematology. E03/S/f. 2013.
- NHS England. NHS Standard Contract for Haematopoietic Stem Cell Transplantation (Children). B04/S/b. 2013.

Other Guidance

- Fanconi Cancer Foundation. Clinical Care of Fanconi Anemia: Hematologic Issues. 2023.[6]
- Fanconi Anemia Research Fund. Fanconi Anemia Clinical Care Guidelines: Fifth Edition. 2020.[17]
- UK & Ireland Fanconi Anaemia Clinical Network, Fanconi Hope Charitable Trust, and Paediatric Forum of British Society of Haematology. Standards of Care for Fanconi Anaemia Affected Individuals and their Families. 2009.[18]

Additional Information

Rocket Pharmaceuticals Inc did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources.

UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit.

We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

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