Base genetic editing

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In news– A 13 year old patient named Alyssa become the first person in the world to benefit from base editing, the experimental cancer treatment.

Blood cancer-

- Alyssa was diagnosed with a kind of **blood cancer known as T-cell acute lymphoblastic leukaemia (T-ALL)**.
- **T-ALL affects the stem cells in the bone marrow** that produce a particular kind of white blood cells (WBC) called T lymphocytes (T cells). These cells provide a person immunity by killing cells carrying infections, activating other immune cells, and regulating the immune response.
- At least 20% of these WBC are atypical– as they accumulate in the bone marrow, they crowd out "good" WBCs and hence weaken the immune system. These unhealthy cells can also accumulate in other parts of the body like the liver, spleen and lymph nodes.

- **While found in both children and adults, T-ALL's incidence decreases with age.**

How is T-ALL typically treated?

- Typical treatment for T-ALL is **similar to that of any leukaemia– chemotherapy and stem cell/bone marrow transplant.**
- Doctors will first administer **multiple rounds of chemotherapy.** This either kills the cancerous cells or stops them from further dividing. The exact schedule is guided by an individual's age and general health.
- If this fails, and the individual is suitable, doctors will conduct bone marrow transplant.
- First the patient will undergo radiation therapy and/or chemotherapy that will kill the cancerous cells but also

wreck an individual's immunity system along with it.

- Thus, patients receive an infusion of healthy bone marrow cells that will hopefully multiply and restore immunity.
- Overall treatment for T-ALL is pretty effective– children have a survival rate of over 85 per cent after five years of receiving this treatment.
- Unfortunately, Alyssa lay in the unlucky 15 per cent of children where the treatment just did not work.

The Experimental treatment received by Alyssa-

- Alyssa, from Leicester in UK, began a trial where she received a dose of healthy T-cells from a donor that would hopefully attack her cancerous cells without destroying each other.
- Known as CAR-T therapy, this principle has been around for a while, but Alyssa's case was different.
- **Traditionally, CAR-T therapy involves adding a gene to T-cells that causes them to seek out and destroy cancerous cells.**
- The **modified cells are known as CAR-T cells.** First, an individual's own T-cells are removed, which are then modified and reintroduced to the individual.
- The problem with such an approach (besides the expense) is that very often, when an individual is really sick, it is simply impossible to obtain enough healthy T-cells to create CAR-T cells.
- While donors can provide healthy T-cells to an individual, these T-cells from a foreign body are going to attack every single cell in that patient's body, making the treatment counterproductive.
- Thus, s**cientists have resorted to what is known as base editing– through this technique of genetic editing, they make it possible for one donor to supply T-cells to multiple recipients**, without the traditional risks associated with it.

- Thus, Alyssa received genetically **modified cells that were programmed to specifically attack** her **cancer** while leaving the rest of her body alone.

What is base editing?

- According to a BBC report, "**Bases are the language of life. Just as letters in the alphabet spell out words** that **carry meaning, the billions of bases in our DNA spell** out the instruction manual for our body."
- **With advances in genetic technology, scientists have been able to zoom into a precise part of the genetic code to alter the molecular structure of just one base,** effectively changing its genetic instructions.
- A team at the Great Ormond Street Hospital managed to use base-editing to create a new type of T-cell from a healthy donor that would not attack other cells in Alyssa's body, not kill each other, survive chemotherapy and finally, hunt down all other T-cells in Alyssa's body (healthy and cancerous).
- After this therapy worked in its initial stages, Alyssa was given another bone marrow transplant to restore her immunity.
- As of today, Alyssa is 6 months into remission. While doctors are still monitoring her and will do so for the foreseeable future, currently the cancer cells have disappeared with no signs of reappearing just yet.
- Prof Waseem Qasim, consultant immunologist and the doctor at the forefront of Alyssa's treatment, told the BBC that genetic manipulation is a "very fast-moving area of science" with "enormous potential" across a range of diseases. Success in Alyssa's case will have a positive impact on the research that is conducted and ultimately benefit many patients.
- "Base editing is particularly promising, not just in this case but for genetic disorders," Robin Lovell-Badge of the Francis Crick Institute in London told the

NewScientist.

- Currently, three more trials that use this technique are underway.