# Spinal Muscular Atrophy: New Treatments for Better Outcomes

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## What is SMA?

Spinal muscular atrophy (SMA) is a genetic disorder caused by defective copies of SMN1 gene. The disease affects the nerve cells of the spinal cord. The damage to the nerve cells leads to weakness of muscles of all limbs and trunk of the body.

It is one of the rare disorders where new treatment options are changing the paradigm of outcome. Most of the cases of SMA are due to defect in the both copies of SMN1 gene in the patient and cause death during infancy or lifelong disability. The novel treatments have shown opportunity of improving longevity and quality of life for patients with SMN1 related SMA.

## What are the types of SMA?

Depending on the severity the disease is classified into main 4 types.SMA type I manifest before 6 months of age with floppiness and weakness leading to lack of limb movements and death before two years due to respiratory failure without treatment. The children manifesting between 6 month to 2 years of life, grouped as SMA type II, are able to sit on their own but are wheel chair bound and usually develop spinal deformities after teenage. Some cases manifesting during later childhood and adulthood may remain mobile for long time.

## How is SMA inherited?

In patients with SMA, both the copies of the SMN1 gene are defective, one defective copy inherited from the parents. It means that the parents are carriers of the disease and have one normal and one defective copy of SMN1 gene. There can be more than one affected offspring in a family. Frequency of SMN1 mutation carriers in Indian population is reported to be around 3%.

## About parents –DON'T KNOW WHAT IT MEANS?

## What are the currently available treatments for SMA?

There are three therapies approved by FDA for SMA due to SMN1 defects at present. The available information about the therapies is given below.

| Therapy | Type of drug and action | Mode of delivery | Eligibility of patients | Reported outcomes |
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| Nusinersen (Spinraza from Biogen ) | Antisense Oligo | Regular intrathecal (by lumbar puncture) Continued therapy every 4 months | At least two copies of SMN2 should be present Any age | Motor milestones improve including sitting and walking. |
| Risdiplam (Roche) | Antisense Oligo | Orally per day continued therapy | | |

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| Zolgensma (Novartis) | Gene therapy (AAV based) | Intravenous one time infusion | Approved for children less than 2 years of age | Gain of motor milestones like sitting without support.<br>Improvement of lungfunction in patients with SMA type I<br>Shows the promise of cure |

**Efficacy of the therapies**

Severe forms of SMAmanifesting with marked limpness of body and weakness of all muscles including the muscles of respiration during the first year of life usually die by 2 years of life. This is the natural outcome of most of the cases. The supportive treatments including lifelong artificial respiration mostly are not feasible and acceptable and are associated with morbidity and excessive burden on the family.

The novel therapies of 21$^{st}$ century have shown dramatic change in the outcome during short term follow ups. **The children with SMA type I who could not even hold the heads and survive beyond have been walking if the treatment is started at the earliest**. Making the new therapies available in India is a major ray of hope for the parents of infants and children with such serious but now treatable disorder.

**What is the approximate cost of therapy?**

The approximate costs of the treatments are as following.

Zolgensma – One time about Rs 16 crore

Risdiplam – About Rs one to 2 crore per year

Nusinersane – About Rs 3 to 5 crore per year