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Short Communication

Antisense Therapy at-a- Glance

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There is no doubt that the world is witnessing an unprecedented progress in the field of scientific research. One of the most crucial achievements that are noticed nowadays is the discovery of antisense oligonucleotides (ASOs) therapy.

It is known that the genetic material carried on DNA is transcribed into mRNA that travels to the cytoplasm where proteins can be built by the help of ribosomes in a process called translation.

Antisense therapy aims at the synthesis of single-stranded complementary oligonucleotide sequence that can bind to mRNA to inhibit the translation step and modify protein expression. In this case, mRNA is considered a sense gene that acts as a target for the antisense drug [1].

Clinical application of ASOs has revolutionized the management of several conditions. For instance, Fomivirsen was the first antisense drug approved by the Food and Drug Administration (FDA) in 1998 for treatment of cytomegalovirus (CMV) retinitis in HIV-infected patients. By inhibiting mRNA translation that codes for proteins of cytomegalovirus, Fomivirsen can limit viral replication. Fomivirsen succeeded in ameliorating symptoms and signs of retinitis. Coinciding with the discovery of anti-HIV drugs, marketing of Fomivirsen was ceased in the United States in 2006. The drug was administered by intraocular injection and was associated with ocular inflammation [2].

In 2013, Mipomersen was approved by the FDA for management of homozygous familial hypercholesterolemia (HoFH) when dietary restrictions, high dose statin therapy fail to lower the abnormally elevated cholesterol levels. HoFH is characterized by high LDL cholesterol levels due to genetic mutations that code for abnormal LDL receptors.

Mipomersen inhibits the synthesis of apolipoprotein B (apo B) in the liver (apo B is the main structural lipoprotein in LDL particles). The drug is administered by Subcutaneous injection, achieves peak plasma concentration within 3 - 4 hours, metabolized in tissues, eliminated in urine, is not a substrate for cytochrome p 450 enzymes and is associated with Injection site reactions and flu-like symptoms. Although Mipomersen represents a forwarding step in the era of gene therapy, it carries a black box warning of hepatotoxicity and can be used only through risk evaluation and mitigation strategy (REMS) program [3].

In 2016, the FDA approved Nusinersen, another antisense drug that is injected intrathecally to increase CNS levels of survival motor neuron (SMN) protein in infants who have genetic mutation in SMN gene and suffer from progressive muscle wasting in spinal muscular atrophy [4]. In addition to respiratory tract infection and constipation, Nusinersen carries a risk of renal toxicity and thrombocytopenia.

Duchenne muscular dystrophy is another genetic disorder characterized by progressive muscle weakness due to low dystrophin levels (dystrophin is a protein essential for the strength of muscle fibers). By an exon-skipping mechanism, both Eteplirsen and Golodirsen help the production of dystrophin that stabilizes the muscle [5].

In 2016, Eteplirsen was approved, generally, it was well tolerated but headache, vomiting and balance disorder were reported [6]. Recently, Golodirsen is approved on December 12, 2019, for treatment of Duchenne muscular dystrophy. Regular kidney function tests should be performed in patients taking Golodirsen [5].

At present, ongoing clinical trials are applied to confirm the rationale of antisense therapy in management of cancer, inflammatory bowel diseases and various neurological disorders.

Finally, Antisense drugs reflect the prosperous role of gene therapy in improving human health.

Bibliography

1. Scoles Daniel R and Stefan M Pulst. "Antisense therapies for movement disorders". *Movement Disorders* 34.8 (2019): 1112-1119.

2. Chen Changmai., *et al*. "Chemical modifications of nucleic acid drugs and their delivery systems for gene-based therapy". *Medicinal Research Reviews* 38.3 (2018): 829-869.

3. Fogacci Federica., *et al*. "Efficacy and safety of mipomersen: a systematic review and meta-analysis of randomized clinical trials". *Drugs* 79.7 (2019): 751-766.

4. Gidaro Teresa and Laurent Servais. "Nusinersen treatment of spinal muscular atrophy: current knowledge and existing gaps". *Developmental Medicine and Child Neurology* 61.1 (2019): 19-24.

5. Aartsma-Rus Annemieke and David R Corey. "The 10th Oligonucleotide Therapy Approved: Golodirsen for Duchenne Muscular Dystrophy". *Nucleic Acid Therapeutics* 30.2 (2020): 67-70.

6. Lim Kenji Rowel Q., *et al*. "Eteplirsen in the treatment of Duchenne muscular dystrophy". *Drug Design, Development and Therapy* 11 (2017): 533-545.

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