REAL-WORLD EFFECTIVENESS OF GENE THERAPY ONASEMNOGENE ABEPARVOVEC (ZOLGENSMA) FOR SPINAL MUSCULAR ATROPHY: A REVIEW

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BACKGROUND & IMPORTANCE

- Spinal Muscular Atrophy (SMA) is an autosomal recessive neurodegenerative disorder, with an incidence of approximately 1 in 10 000 newborns.
- Depending on the symptoms severity and age of onset, SMA is divided into different phenotypes. SMA I phenotype is one of the most severe, and SMA I infants have a lifespan of <2 years if not treated.
- Zolgensma® is an innovative drug of gene therapy and one strategy for SMA patients. However, there remains considerable uncertainty in the long-term sustainability of Zolgensma® clinical effect.

AIM & OBJECTIVES

- Our study aims to provide a critical review of the literature regarding the clinical outcomes in SMA infants in the real-world setting after the one-time Zolgensma® dosing.

MATERIAL & METHODS

- A review of the literature was constructed, comprising 5 phases: (a) identifying the research question; (b) searching for relevant studies; (c) selecting studies; (d) analyzing data; and (e) presenting results. Data was collected and analyzed until May 2021.

RESULTS

Two real-world studies analyzing Zolgensma® effectiveness were identified:

I. Prospective Long-Term Follow-Up (LTFU) study (13 patients):

- 100% of SMA I infants in the therapeutic-dose cohort were alive and free of permanent ventilation (>5 years after Zolgensma® GRT one-time dosing);
- 20% of SMA infants achieved the additional milestone of standing with assistance (>5 years after Zolgensma® GRT one-time dosing);
- SMA infants improved their Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND) scores (≥ 4-points).

II. Retrospective cohort study of SMA I (3 patients) and SMA II infants (4 patients):

- 43% of SMA patients had meaningful increases in the CHOP-INTEND score;
- 57% had increases in the Hammersmith Functional Motor Scale-Expanded (HFMSE) score (Table 1).

CONCLUSIONS & RELEVANCE

- Despite the limited observation period and considering the available data, we conclude that Zolgensma® is effective in SMA I pediatric patients since no clinical regression or waning of effect had been reported.

Table 1: **Functional Outcomes and Motor Milestone Acquisition Observed in SMA Infants from the Retrospective Cohort Study**.

PATIENT	BASELINE CHOP-INTEND	3 MONTHS CHOP-INTEND	BASELINE HFMSE	3 MONTHS HFMSE	12 MONTHS HFMSE	NEW MOTOR MILESTONES ACHIEVED
1	-	-	23	33	39	Standing, Crawling, Walking Independently
2	-	-	11	22	23	Rolling, Standing
3	53	58	5	6	18	Sitting > 30 seconds, Standing
4	48	49	-	6	-	Sitting > 30 seconds
5	-	-	7	16	-	Rolling
6	38	50	-	-	-	Sitting > 30 seconds
7	40	58	-	-	-	Sitting > 30 seconds

[1] JERRY R. MENDELL, SAMIAH A. AL-ZAIDY, Kelly J. Lehman - Five-Year Extension Results of the Phase 1 START Trial of Onasemnogene Abeparvovec in Spinal Muscular Atrophy. JAMA Neurology. 2021).
[2] MATESANZ, Susan E. *et al.* - Clinical Experience With Gene Therapy in Older Patients With Spinal Muscular Atrophy. Pediatric Neurology. ISSN 18735150. 118:2021) 1–5. doi: 10.1016/j.pediatrneurol.2021.01.012.

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