LETTER TO EDITOR

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A New Hope in the Treatment of Rett Syndrome: Trofinetide

Rett Sendromu Tedavisinde Yeni Bir Umut: Trofinetid

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Dear Editor;

Rett syndrome (RTT) is a rare neurodevelopmental disorder that almost exclusively affects women. Andreas Rett first described the syndrome in the German medical literature in 1966. The disorder is characterized by a period of normal development during infancy, followed by a period of regression that leads to severe cognitive and motor skill impairments. Patients diagnosed with classic Rett Syndrome usually exhibit developmental stagnation and regression, acquired loss of speech and purposeful hand use, development of stereotypic hand movements, and may also develop microcephaly, seizures and autistic features between the ages of 6 and 18 months (1). Rett syndrome can present significant challenges for affected individuals and their families. Therefore, it is crucial to increase awareness of the disease and enhance treatment options. Researchers are actively working to gain a better understanding of the disease's causes and effects and to develop more effective treatments.

In March 2023, the United States approved Trofinetide for the treatment of Rett syndrome in adults and pediatric patients aged 2 years and older. Trofinetide, an oral, small molecule, synthetic analogue, is derived from the N-terminal tripeptide of insulin-like growth factor-1 (IGF-1). The phase 3 study showed a significant improvement in communication and social cognition with trofinetide treatment compared to placebo (2). Another study published in Nature Medicine reported significant enhancements in the Rett Syndrome Behaviour Questionnaire (RSBQ) and Clinical Global Impression-Improvement (CGI-I) scores with trofinetide treatment. Systematic review and meta-analysis further supported the efficacy of trofinetide, particularly at the 200 mg dosage, in improving RSBQ and CGI-I scores (3). Clinical trials have underscored Trofinetide's effectiveness in enhancing Rett syndrome behavioral scores, suggesting a notable advancement in syndrome treatment, potentially through its impact on neuronal morphology and synaptic functioning (4). Noteworthy, trofinetide demonstrated efficacy in treating the core symptoms of Rett syndrome in Phase 3 studies. Common side effects observed during treatment included mostly mild to moderate diarrhea, along with vomiting, fever, seizure, anxiety, and fatigue. Trofinetide is not recommended for patients with moderate or severe renal impairment. The FDA's approval of trofinetide marks the first authorized treatment for Rett syndrome, a condition that has lacked effective treatment options for over five decades (5).

The approval of Trofinetide by the FDA represents a significant advance in the management of rare and difficult-to-treat diseases such as Rett syndrome. This approval is a promising step for both patients and their families because it could potentially have a major impact on managing symptoms. However, it should be noted that Trofinetide does not treat the disease and aims to manage symptoms. In this context, it is important to consider the potential role of future research in the development of innovative approaches, such as a true cure for diseases such as Rett syndrome or perhaps even genetic correction therapies. In particular, the approval of Trofinetide could further motivate the scientific and clinical community to better understand the complex mechanisms underlying such disorders and develop more effective treatments. In this process, it is also important to consider measures such as raising awareness in the community and improving opportunities for early diagnosis, which could significantly improve the quality of life of patients and their families.

The FDA's approval of Trofinetide can be considered a promising step towards the treatment of rare and difficult-to-treat diseases such as Rett Syndrome. Trofinetide is designed to manage symptoms, not to treat Rett Syndrome. However, this drug could be of great value if it can provide a noticeable increase in patients' quality of life. It is of paramount importance to conduct further research in order to enhance the improvement offered by Trofinetide and to identify a genuine cure for Rett Syndrome.

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