EPH127

Understanding the Burden of Aromatic L-Amino Acid Decarboxylase Deficiency (AADC deficiency): Results from a Clinician Expert Survey

Paul Castellano[1], Steven Hill[1], Jonathan Gibson[2], Andrew Mumford[2], Phillip Pearl[3]

1 – PTC Therapeutics, New Jersey, USA; 2 – Initiate Consultancy, London, United Kingdom; 3 – Boston Childrens Hospital, Boston, USA

1. Background and objectives

Background

Aromatic L-amino acid decarboxylase (AADC) deficiency is a life-limiting and debilitating rare genetic neurological disorder that causes widespread central nervous system dysfunction, developmental delay, and often premature death. Pathologic variants in the dopa decarboxylase (*DDC*) gene result in deficiency of the AADC enzyme, leading to a severe combined deficiency of monoamine neurotransmitters, as well as impairments in motor development, cognitive and language development, and autonomic function[1,2]. Eladocagene exuparvovec is a recombinant adeno-associated virus serotype 2 containing the human DDC gene, approved in Europe on July of 2022 for treatment of patients aged 18 months and older with a clinical, molecular, and genetically confirmed diagnosis of AADC deficiency with a severe phenotype. In a single dose, eladocagene exuparvovec delivers a functioning *DDC* gene directly into the putamen, a major area of dopamine activity in the healthy brain, thereby restoring dopamine production and improving patient motor function. In addition, eladocagene exuparvovec administration results in measurable improvements in cognitive function and language skills, an increase in body weight, and reductions in floppiness, oculogyric crisis (OGC) episodes, and dystonia. AADC deficiency has a predicted birth rate of between 1/64 000-1/90 000 in the United States. Due to the rarity of the disease, there is a paucity of data surrounding the disease burden.

Objectives

The objectives of this clinician expert survey were:

- To gain insight into the importance of motor development in AADC deficiency progression
- To validate assumptions made in health economic models

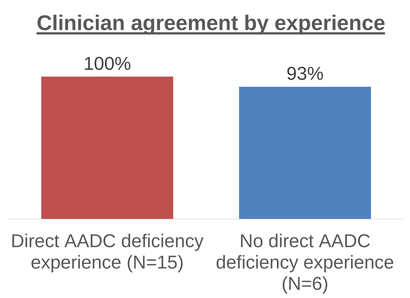
2. Methods

Twenty-four clinicians from various geographical regions (US, EU, Asia, Middle East, South America) were asked to complete an online survey (2020). All active participants were asked to participate in real-time voting, accompanied by a group discussion of the clinical assumptions. Twenty-one clinicians completed the survey, providing feedback regarding disease proxies and motor milestones in relation with age, life expectancy, cognitive symptoms and resource utilization. Fifteen (71%) clinicians had direct experience in treating AADC deficiency.

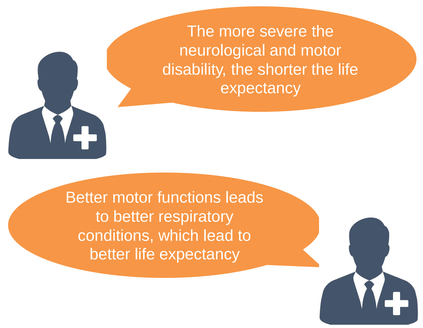
3. Results

Mortality

Would you anticipate differences in life expectancy depending on the motor milestones that patients are achieving?

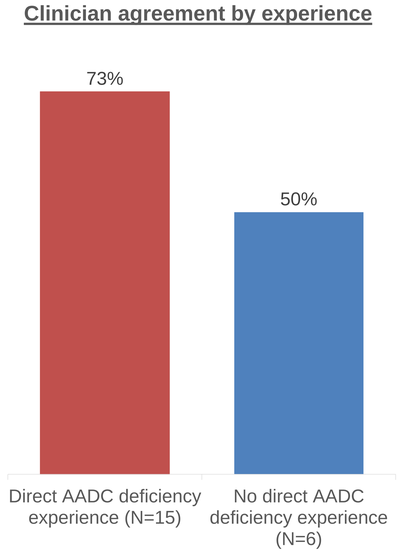


Clinician insights



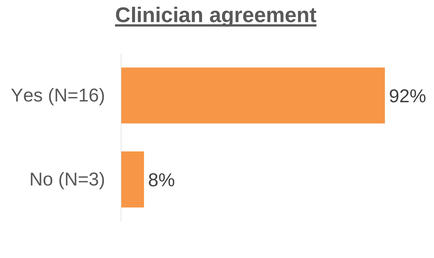
Proxy

While some of the other diseases may be more similar to AADC deficiency in terms of severity and/or disease characteristics, there is a lack of available data that can be used with regards to survival. In this situation, could cerebral palsy (CP) be a suitable proxy?



Cognition

Would you agree that there is a correlation between motor function and other symptoms such as cognitive functioning, oculogyric crisis (OGC), dystonia, and other behavioral aspects?

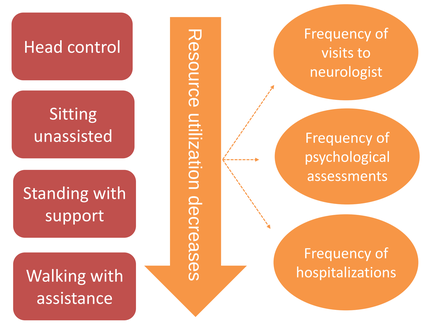


Clinician insights - continued

Resource use

Would you agree that medical resource utilization is significantly different per motor milestone state?

- All 21 clinicians (100%) agreed that resource utilization significantly decreases at each achieved motor milestone state
- All clinicians agreed with the example statement “a bed ridden patient requires greater resource utilization than a patient who can walk with assistance”
- All clinicians agreed that resource utilization for patients with AADC deficiency includes, but is not limited to neurologist visits, psychological assessments, and screening tests



4. CONCLUSIONS

- **Overall, clinicians agreed with the following assumptions:**
  - **Development of motor milestones is expected to have an impact on life expectancy**
  - **Improvements in motor function is expected to have an impact on cognitive functioning and other symptoms of AADC deficiency**
  - **Resource use is expected to differ significantly per motor milestone state achieved in AADC deficiency**
  - **CP is a suitable proxy for survival in AADC deficiency**
- **These data provide an understanding of AADC deficiency and the influence of motor development on the progression and differential management of the disease. Eladocagene exuparvovec addresses motor function issues and is expected to improve patient outcomes. Finally, these findings can help in the development of health economic models for eladocagene exuparvovec**

References

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- JG and AM are employees of Initiate Consultancy who received funding from PTC Therapeutics for this work
- PC and SH are employees of PTC Therapeutics
- PP is a Pediatric Neurologist who received funding from PTC Therapeutics, along with all clinician experts, to participate as an expert in the original study. No funding was received to co-author this poster
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