LEADING THE
FIGHT TO
END DUCHENNE

Patient experience survey results: ataluren (PTC 124)

Introduction

In July 2016, Parent Project Muscular Dystrophy (PPMD) launched a community engagement project to learn about the experiences of patients and caregivers who participated in clinical trials of ataluren. This report describes the community responses received from mid-July 2016 through August 2017. PPMD's goal was to better understand, directly from caregivers and patients, their direct experiences with the experimental therapy.

PTC has communicated publicly through press releases and presentations about the data collected from clinical trials, but this data was (as is typical for a clinical trial) of a limited scope and may not tell a complete story about individual and family experiences. Our engagement is aimed at gaining more insight directly from those involved in the clinical studies.

Our method

The information detailed below was collected using an online, mixed methods survey to facilitate our engagement efforts.

This report includes counts of responses and summaries.

For open-ended questions, we developed a codebook of recurring concepts and coded each story individually. We then identified major and supporting themes from the entire set of stories and chose representative quotations.

The information we collected was caregiver reported, as the majority of the long-term experience occurred in a pediatric population.

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Summary of engagement responses

Sixty-one (61) people responded. Thirty-nine (39) had children who participated in a clinical trial of ataluren. Though the engagement was open to caregivers or to teens/adults with Duchenne, only one of the respondents was an individual with Duchenne, most respondents were caregivers. The age at starting trial participation ranged from 3 to 18 years, and current age of participating children was from 4 to 26.

A total of twenty-one (21) children currently walk independently, five (5) walk with assistance, four (4) walk around their home independently, two (2) walks with assistance for long distances (scooter or wheelchair), four (4) indicated their sons were ambulatory but did not indicate to what degree, and twenty-five (25) are non-ambulatory.

Respondents by trial

- 004: Phase 2a for 5 years and older, 28 days of treatment with 28 days of follow up (total 56 days); biopsies required (**12)**
- 004e: Phase 2a open label extension of 004 (**7)**
- 007: Phase 2b double blind, placebo controlled dose ranging efficacy and safety study for patients 5 year and older; study was for 48 weeks. (**23)**
- 016: Extension trial (open label) for patients in the USA previously treated with ataluren **(16)**
- 019: Extension trial (open label) for patients in Europe, Israel, Australia and Canada that were previously treated with ataluren **(3)**
- 020: Phase 3, double blind, placebo controlled safety and efficacy trial for 48 weeks. (**11)**
- 020 E: Extension trial (open label) for those that participated in 020. (**11)**
- 030: Younger Patient (under 5 years old) sub study **(3)**

Those who participated in both the study and the extension study indicated so where applicable.

In addition, eleven **(11)** parents reported that their child did not participate in a clinical trial because ataluren was commercially available (Translarna) in their country through conditional approval. We included those eleven (11) responses in the summary below.

Impact of drug

Fifty one (51) parents and the one (1) patient surveyed reported seeing benefit, which they then described in an open-ended question.
Nine (9) responded they saw no direct impact of drug benefit.

When describing the benefits, parents reported:

- an increase in energy level (32);
- stopped progression (4)
- slowed progression (27)
- improvement in stability/reduced falls (17);
- regained physical abilities that had previously been lost (5);
- cognitive improvement (7);
- general increase in strength (9);
- walking maintained (8);
- generalized physical improvement (12).

When asked about timing of when the improvements began, **the majority (33 of the 61) described the benefit starting within the first 6 months of beginning the drug.**

We also asked parents a question about emotional and psychological impact:

- Seventeen (17) said that their child had no emotional/psychological change associated with trial participation.

- In an open-ended question, of those who responded to this question, the parents described that their child:

    - Had improved mood/confidence when on the drug (13)
    - Was more hopeful for the future (7)
    - Had a cognitive improvement (5)
    - Was more independent (6)
    - Improved behavior (2)

Side effects and burden

Forty-five (45) parents reported no side effects.

Fourteen (14) reported a side effect; twelve (12) of them described GI side effects (stomach aches, loose stools, nausea, vomiting), one (1) described headache, and one (1) described mild weight gain. Two (2) did not answer the question.

Patient community's comments to the FDA

Parents were invited to provide a message to the FDA about the drug.

- Of the parents who experienced a benefit, forty-two (42) provided a message to the FDA. All but one of these messages unequivocally advocated for drug approval based on the parents' perception of benefit, usually together with a comment about low risk/side effects. One other caregiver, who thought the benefit was modest, was also in favor of approval as long as it did not delay development of more effective drugs.
- Four (4) of the parents who did not think their child benefited wrote a response. Of those, three were positive regarding approval because the drug seems safe. One did not feel the drug should be approved.

Parent quotes on benefit

"The effects were dramatic. The falls for both of them stopped. They don't fall. Their energy is dramatically increased. The first 2 years their strength increased. Now there is a very slow progression."

"All movements including walking and running improved. Improved cognitive abilities and school performance."

"He now breaks into a run whenever he wants and can jump with both feet off the ground!! While we haven't seen huge academic gains, he is brighter and more talkative at school. He is much more confident in his physical abilities at the playground and in sports classes."

"The first effect was an improvement in behavior. His self-control improved hugely making it much easier for the entire family in both social and school environments. Physically, he has been much more stable and capable physically.

His North Star score increased 4 points after 6 months and his 6MWT went from 374m to 598m. Falls reduced to almost none, stamina has increased and he no longer falls asleep after days out or school."

'We saw XXX in the trial stay at the same strength, at times surpassing previous strength tests, his 6 min walk tests, we could see they stabilized at every visit, where he should have been losing strength. He was not losing strength he was maintaining what he had for strength.'

Quotes from those who reported no benefit

"I don't see any reason for the drug to be approved. Perhaps there is benefit for those that start drug very young."

'May be worth using it as no side effects and may be making a small impact that is hard to measure."

"We dont know if it works or not, every boy is different."

Parent quotes on messages to FDA:

"Translarna has seemed to stabilize my son. I don't see why with all the trials that have been done why the drug can't be approved

"When the trial stopped, we immediately saw xxxx lose his strength, that time hurt xxxx greatly, with losing strength, he would say why am I falling all the time now, why am I losing the strength I had".

"If the drug is safe and may be helpful, we should be able to use it. My friends in study whose sons noticeably improved initially may have continued to do well had trial not be stopped/started/stopped."

"This drug could be really impactful for a child who starts it at a young age, before fibrosis sets in. My son was too old when he started, then there were the

starts and stops with the drug that didn't help him. I believe if he got the right dose of the drug starting at age 4, that we'd be seeing a different progression."

"This drug works! It is proven to help maintain strength and mobility for longer which equates to immense savings in health care costs. ANY improvement or delay of progression is meaningful to patients and saves health care dollars."

"This drug doesn't just delay the progression of DMD but also has a positive effect on ability and behavior. This drug has allowed us to function a family and allowed [our son] to make friends at school, where before he was ostracized because of his [behavior]."

"The risk/benefit analysis must be in favor of benefit. I am certain our son has thrived until the age of 21 because of the drug, even though we cannot personally quantify it. There are no safety concerns. We have nothing to lose and everything to gain."

"Listen to the families from around the world, as well as the USA, whose boys are taking the drug. Also listen to the regulators such as NICE who have extremely robust procedures for considering new medicines in rare conditions, resulting in the 5 year Managed Access Agreement."

Implications

The FDA must make important and often challenging decisions that determine access to potential treatments. Many of these decisions rely on qualitative assessments that are based on quantitative data, balancing patient need and opportunity, speed and certainty, and benefits and risks

In cases of rare, progressive diseases that are 100% fatal, like Duchenne, it is a serious challenge for those who haven't "lived it" to understand meaningful benefit to patients and families. Mixed method engagement surveys are an appropriate method for soliciting parent reported feedback about their perspective of therapy benefit and harm in a clinical trial. All stakeholders can greatly benefit from collection of information that provides a richer understanding of the complex complete experience of those with experience on drug.

We encourage the FDA to consider the demonstrated preferences and experiences of patients and their caregivers when making determinations about new drug applications in Duchenne.