'It's Like Yelp for ALS Research': Rating System for Patient Centricity in ALS Clinical Trials is Disrupting Research in the Best Way Possible

'I AM ALS' Furthers CTTI's 'Transforming Trials 2030' Vision

SUMMARY

After abysmal experiences with burdensome clinical research protocols that put patients with ALS (amyotrophic lateral sclerosis, also known as Lou Gehrig's disease) through the wringer, patient advocacy group I AM ALS decided to take patients' power back. The group, which includes a representative on CTTI's Steering Committee, developed the Patient-Centered Trial Design Rating System (PaCTD), a publicly shared five-star rating tool that objectively ranks ALS trials across nine elements of patient-centeredness. By holding trialists accountable for developing accessible and patient-centered protocols, PaCTD brings CTTI's Transforming Trials 2030 vision to life.

GOAL(S)

Imagine receiving an ALS diagnosis. You're probably exhausted even before you hear the news, having been in and out of doctors and specialists due to the fact that there is no definitive test for the condition. Now, you are told your prognosis: that the neuromuscular disorder will make talking, swallowing, moving, and, eventually, breathing progressively difficult. There's no cure, but novel treatments in the pipeline have potential to meaningfully slow progression — if you can take part in the research.

What would you give to participate? Would you drive for six hours to the site with no hotel reimbursement? Would you go weekly for blood draws? Would you go back on an ad hoc basis to complete surveys? Would you still do all of that even if I told you that you won't have the option to continue treatment once the trial concludes?

Hope is a powerful force, which is why some ALS patients have historically accepted these terms — but they shouldn't have to. Faced with a grim disease prognosis and only a handful of promising, but burdensome active ALS trials, I AM ALS wanted to motivate clinical trialists to build protocols more aligned to the needs of patients. The group believed that if patients were embedded deeply into the research process, outcomes for the ALS community and researchers alike would improve.

CHALLENGES

Just four years ago, progress in ALS research was frustrating on many fronts. Riluzole, a mildly effective treatment for ALS, had received marketing authorization in 1995. However, from that time until 2018, over 60 molecules had been investigated as possible treatments for ALS, and the overwhelming majority of those failed, either because they couldn't demonstrate clinical efficacy or due to a lack of participation. Despite patient engagement in research being increasingly recognized as important across all therapeutic areas, many of the researchers in ALS did not have a direct line to the ALS community. This dynamic was problematic for everyone: researchers were faced with failing and expensive clinical trials, and patients were left without therapies that could meaningfully disrupt the progression of their disease.

SOLUTION(S)

I AM ALS needed to develop a resource that could amplify the voice and needs of ALS patients despite this lack of dialogue between researchers and the ALS community. To that end, they developed the Patient-Centered Trial Design Rating System (PaCTD), a publicly shared five-star rating tool that objectively ranks ALS trials across nine elements of patient-centeredness (many of which align with CTTI's Transforming Trials 2030 vision). I AM ALS believed this tool would inform people living with ALS of their clinical trial options, while driving participation to those protocols that had invested in patient-centric tactics, such as open label extension, considered eligibility criteria, or use of novel methods to minimize travel when possible. I AM ALS’s broad patient reach made it influential, so PaCTD's developers hoped a high rating would serve as a carrot for drug developers to craft considered, patient-friendly protocols.

TAKING ACTION

I AM ALS used nine elements to assess clinical trial design. These elements fell into three primary categories and were given percentage weighting for the overall rating as listed below:

- **Optimizing access to investigational therapies (60%).** This category addresses whether a trial includes the following elements:
  - *Open-label extension*, allowing trial participants to continue to access the treatment after the participation commitment in the trial has ended
  - *Minimized placebo usage*, giving more participants the chance at life-changing therapies
  - *An Expanded Access Program*, allowing patients who did not meet the inclusion or exclusion trial criteria access to the therapy of study
- **Advancing scientific progress (30%).** This category addresses whether a trial includes the following elements:
  - *Consideration of disease heterogeneity* (i.e. through the use of crossover design), given ALS is marked by different clinical, biochemical and genetic features
  - *Use of scientifically justified eligibility criteria* to stop the tendency of trialists to cut and paste these criteria from past trials, potentially limiting participation without cause
  - *Investigation of one or multiple biomarkers* to help future researchers better understand ALS
  - *Independent unblinded review panel* for interim efficacy check-ins if warranted
- **Being patient friendly (10%).** This category addresses whether a trial includes the following elements:
  - *Use of minimal run-in observation period*, reducing the time span from which a patient is accepted to the trial and starts treatment
  - *Reduce travel burden* by use of novel methods where possible, such as wearable technology or telemedicine, and financial reimbursement

The team makes it clear that PaCTD ratings do *not* measure or evaluate the treatment's safety or efficacy. A high rating on its scale does not indicate promising science and a low rating on this scale does not mean the treatment is ineffective — it purely measures the design of the trial from the patient and caregiver perspective across the criteria outlined.

IMPACT

Today, the ranking system offers much-needed information for people with ALS who are interested in clinical trial participation, but aren't sure which trial to pursue. The rating tool gives a snapshot of every active ALS trial, where they stand on nine dimensions of high interest to patients, and their overall PaCTD ranking. But, perhaps even more importantly, I AM ALS's theory was correct: the tool is prompting ALS trialists to reach out to I AM ALS to optimize their score, resulting in meaningful change across ALS research.

"Two years ago, expanded access was a unicorn," said one I AM ALS leader who helped design PaCTD. "Now, not only is expanded access more common, but every single ALS trial today – even phase 2 trials – have an open label extension. Sponsors now see that incorporating these aspects is helping their trials succeed, and that in turn helps the whole ALS community by giving potential new treatments the best chance to get to market."

Since the tool launched, I AM ALS has also successfully lobbied the FDA to update their guidance document for ALS Clinical Trials and organized an "ALS Caucus" of representatives and senators in Washington to push forward legislation supporting people living with ALS.

ADVICE

I AM ALS has momentum, and the group is not stopping anytime soon. 2022 has seen an influx of new potential ALS treatments in the pipeline, and the group is hard at work collaborating across its ALS research network to ensure those protocols have the best chance of success. For other patient groups hoping for similar progress in their disease area, the group suggests building connections and alliances across organizations that share a common mission.

"We can't go it alone," says one I AM ALS leader. "The only way we will make progress is by sharing out what we know, and taking back the learnings of other groups. Find organizations like CTTI that align with your mission, partner to amplify your impact, and be relentless in the pursuit of continuous improvement. I see a future where tactics like decentralized trials, novel endpoints and modeling and simulation can bring us research outcomes much faster than we've historically seen. We've got to join forces and fight for those, not just across ALS, but for all indications."

ORGANIZATION

I AM ALS

CONTACT

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ORGANIZATION TYPE

Patient

IMPLEMENTATION DATE

2019

TOPIC

Clinical Trials Transformation

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