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Virtual Trials: Access and Equity

Innovative opportunities for patients with amyotrophic lateral sclerosis (PALS)

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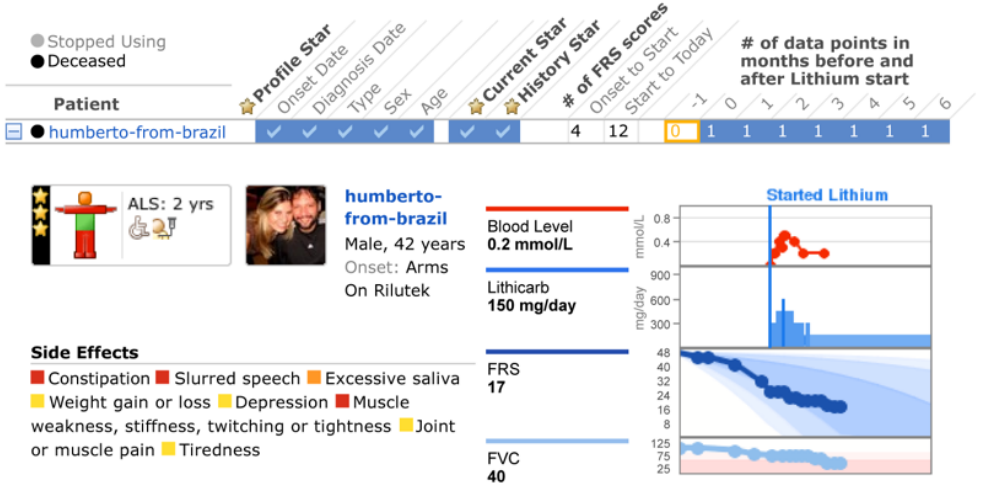
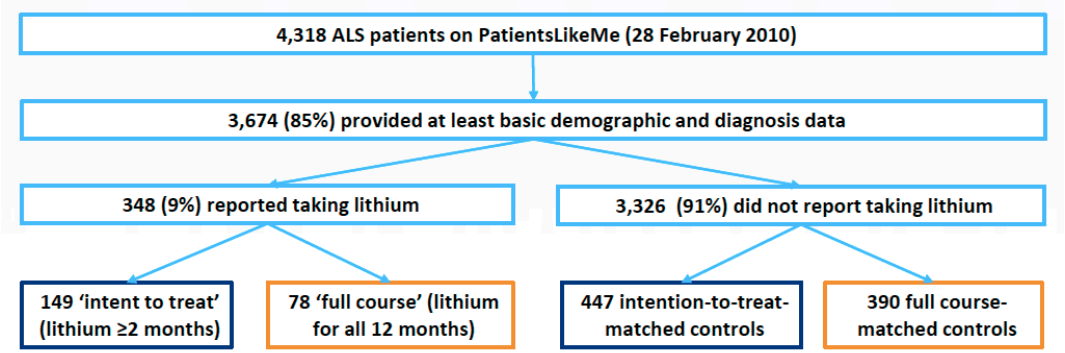
Topics

Patient initiated research in ALS	• Lithium carbonate • ALSUntangled
Hybrid virtual trial completed	• Lunasin
Virtual trials in planning stage	• ALS Reversals • Curcumin

Patient-initiated study: lithium carbonate





- Small non-randomized trial reported lithium carbonate slowed progression of ALS[1]
- PLM collected data from PALS members prescribed lithium off-label by their providers
- A matching algorithm on pre-treatment ALSFRS progression scores was developed to create historical controls
- Beneficial effect not corroborated in virtual trial - no difference found at 12 months in both groups[2]
- Results repeated in subsequent NIH studies
- Recent meta-analysis of ALS trials suggests pharmacogenetic interaction of lithium in PALS with UNC13A genotype[3]. Future study planned with external researchers.

1. Fornai F, Longone P, Cafaro L, Kastsiuchenka O, Ferrucci M, Manca ML, et al. Lithium delays progression of amyotrophic lateral sclerosis. Proc. Natl. Acad. Sci. U.S.A. 2008;105:2052–7.
2. Wicks P, Vaughan TE, Massagli MP, Heywood J. Accelerated clinical discovery using self-reported patient data collected online and a patient-matching algorithm. Nat Biotchnol. 2011;29(5):411-4.
3. Van Eijk, Ruben P.A. et al. "Meta-Analysis of Pharmacogenetic Interactions in Amyotrophic Lateral Sclerosis Clinical Trials." *Neurology* 89.18 (2017): 1915–1922. *PMC*. Web. 19 Oct. 2018.

Scientific review of alternative off-label treatments in ALS

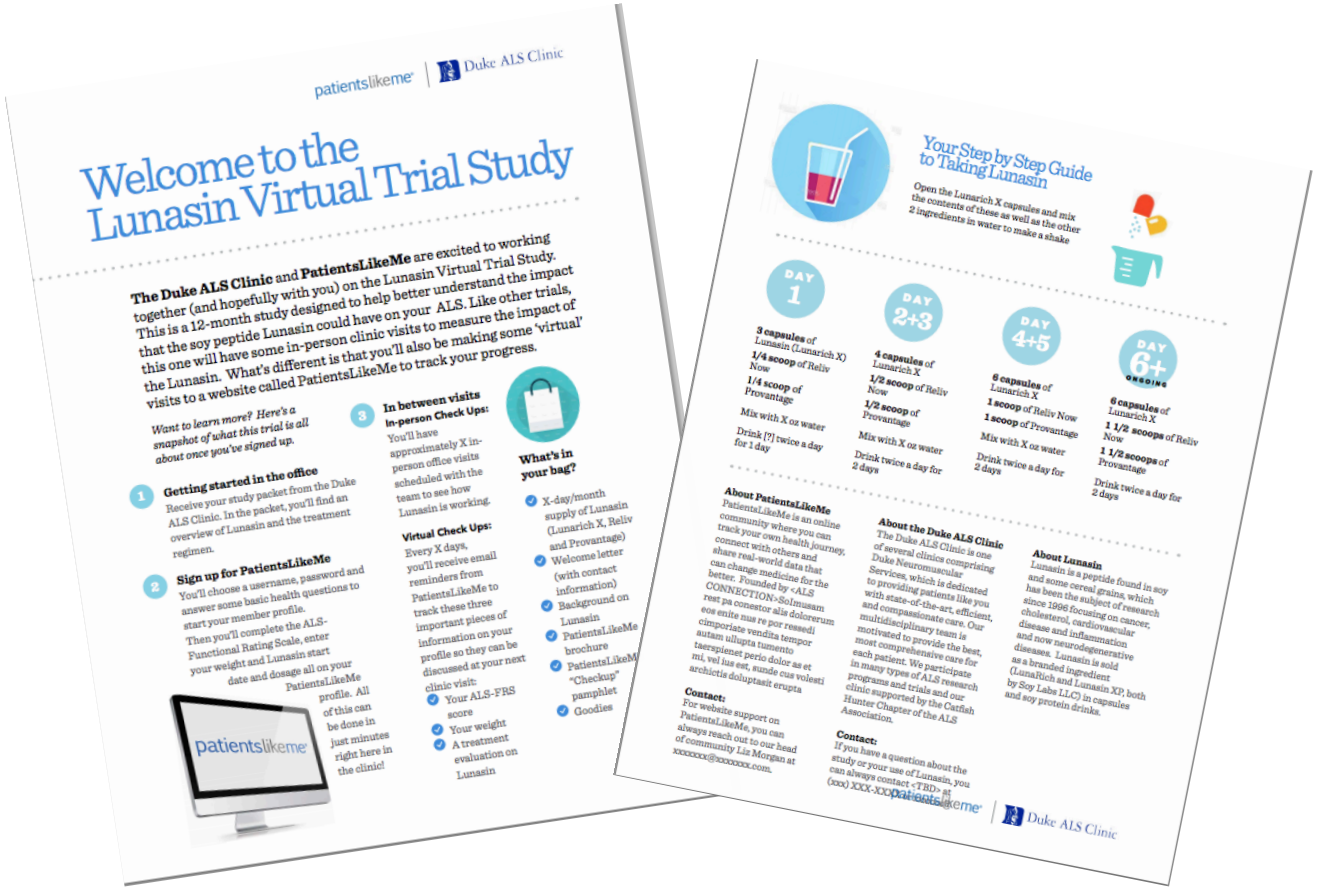
Product	Mechanism	Pre-clinical	Cases	Trials	Risks
Sodium Chlorite					
A. NP001	A	D	U	C	B
B. WF10	A	D	D	U	C
C. ORAL	F	U	D	U	F
Deanna Protocol	B	C	D	U	B
Fecal Transplant	D	U	D	U	B
Propofol	C	U	D	U	D
Rife Machine	F	U	D	U	B
Vitamin D	C	C	F	D	B
Ursodiol	C	U	D	D	C
Lunasin	C	U	C	U	B
Curcumin	C	C	B	C	B (PO) D (IV)

- In 2009 a consortium of patients, clinicians, and researchers began scientific reviews of alternative off-label treatments in ALS
- Patients and caregivers submit names of alternative therapies and then vote for the ones they most want to learn about
- The global team has completed over 40 reviews grading each therapy on the mechanistic plausibility, the strength of relevant preclinical data; case reports; identified/potential risks and costs
- Engages many stakeholders and empowers patients and providers with data to support more informed decisions about options in ALS care

1. The ALSUntangled Group (2015) ALSUntangled: Introducing The Table of Evidence, Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, 16:1-2, 142-145, DOI: 10.3109/21678421.2014.987476

ALSUntangled No. 26: Lunasin

Amino acid peptide from soy, rye, barley & wheat



- Review prompted after reports of dramatic improvements in PAL taking lunasin
- Found insufficient evidence to support use; recommended pilot study[1]
- PLM and Duke ALS Clinic collaborated on hybrid virtual trial design with goals to:
  - Demonstrate feasibility, strengths, limitations of design to rapidly test reports of ALS reversals
  - Validate correlation of PRO ALSFRS scores captured online with CRO ALSFRS scores done in clinic
- Findings:
  - No evidence that Lunasin slowed ALS (n=50)
  - Patients accurately measured ALSFRS scores and recorded monthly online
  - Fastest enrollment of any ALS trial in history
  - Diverse population represented
  - Retention rate above average

1. The ALSUntangled Group (2014) ALSUntangled No. 26: Lunasin, Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, 15:7-8, 622-626, DOI: 10.3109/21678421.2014.959297
2. Bedlack R, Spector A, Morgan E, Wicks P, Vaughan T, Blum R, Dios A, Sadri-Vakili G (2017) Final results from an open-label, single-center, hybrid-virtual 12-month trial of Lunasin for patients with ALS. 28th International Symposium on ALS/MND 2017, Boston, MA, USA, December 8-10, 2017 (Poster)

Virtual trials in planning stage

- PLM and Duke ALS Clinic currently in planning stages for two virtual trials
- Trial design building on the experience developed in the lunasin trial
- Both studies will include a range of phenotypic data entered online by patients as well as multi-omics data from in-home biospecimen collections

ALS Reversals[1]

- Build on compiled database of 36 cases of ALS reversals that studied differences in demographics, disease characteristics, treatments, and comorbidities between patients with ALS reversals and those with typically progressive ALS

ALSUntangled No. 44 Curcumin[2]

- Published trials in varying formulations show clinical benefits in different diseases
- Oral curcumin found to be inexpensive and safe
- Curcumin found to have at least four potential mechanisms relevant to ALS

1. Daniel Harrison, Paul Mehta, Michael A. van Es, Elijah Stommel, Vivian E. Drory, Beatrice Nefussy, Leonard H. van den Berg, Jesse Crayle, Richard Bedlack & the Pooled Resource Open-Access ALS Clinical Trials Consortium (2018) “ALS reversals”: demographics, disease characteristics, treatments, and co-morbidities,Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, DOI: 10.1080/21678421.2018.1457059
2. Richard Bedlack & ALSUntangled Group (2018): ALSUntangled 44: curcumin, Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, DOI: 10.1080/21678421.2018.1440738