

Revised Airlie House consensus guidelines for design and implementation of ALS clinical trials

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Study objective and summary result

This study aimed to revise the 1999 Airlie House consensus guidelines for designing and implementing preclinical therapeutic studies and clinical trials involving patients with amyotrophic lateral sclerosis (ALS), and it developed a 2018 revised version of the guidelines.

What is known and what this paper adds

Consensus guidelines for clinical trials involving patients with ALS were published in 1999, but the accumulation of clinical trial experience and new information about ALS since 1999 necessitates the revision of the consensus guidelines. This study provides the needed revisions.

Participants and setting

A 3-day meeting with 140 leading members of the ALS community, including researchers, clinicians, biostatisticians, patient representatives, research-funding agency representatives, industry representatives, and regulatory agency representatives, was held at the Airlie House Conference Center in Warrenton, VA, in March 2016.

Design, size, and duration

The meeting aimed to address 9 key considerations relevant to ALS clinical trials: (1) preclinical studies; (2) the biological and phenotypic heterogeneity of ALS; (3) outcome measures; (4) disease-modifying and symptomatic interventions; (5) recruitment and retention; (6) biomarkers; (7) clinical trial phases; (8) moving beyond traditional trial designs; and (9) statistical considerations. This study used a modified Delphi consensus process to develop draft consensus guidelines that were reviewed and modified after a public consultation period.

Main results and the role of chance

This study developed a list of 112 guidelines, including 15 high-priority guidelines calling for practices such as collecting DNA whenever possible, training study examiners to ensure uniform assessments, and publishing both positive and negative results.

Table Sample guidelines

Domain	Key guidelines
Preclinical studies	Provide a firm biological rationale for advancing a therapeutic candidate to clinical trials
	Conduct independent preclinical validation studies of therapeutic candidates
Disease-modifying and symptomatic interventions	If a symptomatic intervention is effective, consider permitting its use for trial participants
	Symptomatic therapies and medical devices should be tested in controlled trials
Biomarkers	Biomarkers should be reliably quantifiable

Bias, confounding, and other reasons for caution

The quality of available evidence limited the option of a truly evidence-based approach.

Generalizability to other populations

These guidelines were written to reflect an understanding of the particular features of ALS. This may limit their generalizability as guidelines for clinical research into other conditions.

Study funding/potential competing interests

This study was funded by the NIH, various pharmaceutical companies, and various foundations. Some authors report serving on journal editorial boards, receiving funding from various foundations and governments, and receiving grants, consulting fees, lecture honoraria, and committee appointments from various healthcare companies. Dr. Gronseth reports serving as Associate Editor for *Neurology*® and receiving compensation from the American Academy of Neurology. Go to Neurology.org/N for full disclosures.

A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The authors of the full-length article and the journal editors edited and approved the final version.

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