Outcome measures for ALS clinical trials

Traynor et al. studied the predictive value of outcome measures in 97 placebo-treated ALS patients enrolled in a randomized clinical trial. FVC% and ALSFRS (but not MVIC arm or grip) declined linearly over a 12-month period and were prognostic for survival.

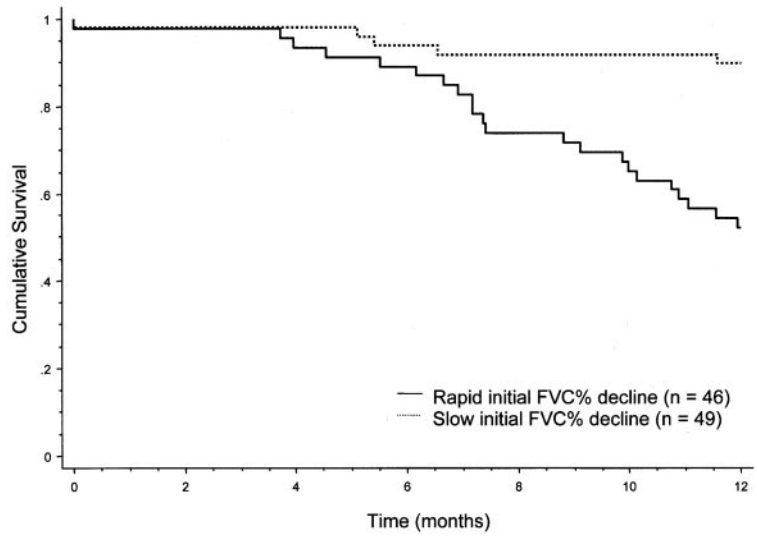
see page 1933

Finding a treatment for ALS: A practical, meaningful clinical endpoint

Commentary by Robert C. Griggs, MD

From January 1997 to January 2005, *Neurology* will have published over 150 articles on ALS. In addition, we have had 10 editorials or commentaries. Many have considered treatment. None has reported a home run[1] but four have reported supportive treatments and one a treatable ALS look-alike.[2] Many have considered clinical trial outcomes. There are now many new treatment strategies that deserve study in clinical trials. Survival was the outcome in the successful trials of riluzole in ALS. However, as Traynor et al. note, it is a costly endpoint requiring long follow-up of a large number of patients. Manual or machine motor testing quantitate the effect of motor neuron loss on strength and have an irresistible, intuitive appeal. However, they are costly and have either not performed well or not been used in most trials.

As an important by-product of the North East ALS (NEALS) Consortium failed topiramate trial,[3] Traynor et al. report that two low-cost, easily performed tests of motor function—forced vital capacity (FVC) and ALS Functional Rating Score (ALSFRS)—decline linearly and predict survival. Machine-based mechanical motor testing did neither.



Survival of placebo-treated ALS patients according to their rate of decline of FVC%.

Should these measures be adopted in new ALS trials? They clearly stack up well vs survival and expensive labor-intensive tests that cannot be used by everyone in all sites.

Complete proof of concept will require their successful use in an effective treatment but their assessment even in other negative trials should confirm their potential value.[4]

References

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see page 1933

