

**PATIENTS WHO HAVE 50-75% REDUCTION IN SEIZURE FREQUENCY AFTER STARTING A NEW THERAPY SHOULD NOT BE CONSIDERED AS IMPROVED BECAUSE THIS IS NOT A MEANINGFUL IMPROVEMENT IN SEIZURE CONTROL: NO**

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The goal of therapy in epilepsy is seizure freedom. A seizure-free patient can lead a normal life, can drive a car, has few job restrictions, and his seizure worry is greatly reduced. Unfortunately, this goal can be achieved in up to 70% of patients with epilepsy, and all the rest have to contend with incomplete seizure control. For these patients who are not seizure free life is not much different if a new therapy decreases their seizure frequency by 50-75% or by 75-90%; in both cases there is partial improvement, a partial decrease in seizure burden. A dividing line between 50-75% reduction and 76-90% reduction would be arbitrary and not evidence-based.

Regulatory authorities both in the US and in Europe have chosen a greater than 50% reduction in seizure frequency or a 50% responder rate as primary endpoints in clinical trials of new AEDs, and they have done so for a reason. This is a reasonable compromise between choosing the maximal possible efficacy endpoint (100% seizure reduction) and the practicality of sample size, statistical power and cost. Raising the bar for treatment success from a 50% seizure reduction in half of the patients to a 75% or 90% seizure reduction in an equally high percentage of patients would be very impractical because the studies would be both time-consuming and expensive.

These clinical trials, using the >50% criterion, have led to the approval of many important, efficacious and useful new AEDs from the 1990s until today. It is difficult enough to achieve this endpoint with statistical significance versus placebo; raising the bar to >75% seizure reduction would mean that many potentially efficacious new AEDs will not be approved and will not reach the market.

Some studies of AEDs which have included health outcome instruments suggest that >50% seizure reduction is associated with improved quality of life. One study, for example, found that as seizure frequency decreases, patients report less impaired health-related quality of life, regardless of time since last seizure, gender, and comorbid status.

In conclusion, patients who achieve a 50-75% reduction in seizure frequency should be considered as improved.