Background

Novel responder definitions for fibromyalgia (FM) clinical trials have been proposed by the Outcome Measures in Rheumatology (OMERACT) subcommittee as alternative methods by which to interpret key symptom and functional domains relevant to FM patients. Using sleep quality, physical function, and pain as key outcome areas, we evaluated responder data from 12 previous registration trials of 4 medications – meloxicam, pregabalin, cyclobenzaprine, and TNX 102 SL (Rho Inc., Chapel Hill, NC) – in FM patients. OMERACT proposes new definitions for key outcome areas in patients with FM. These definitions are proposed in order to better inform clinicians and patients about the clinical importance of treatment benefit. The current paper evaluates the proposed responder criteria in comparative analyses using OMERACT responder definitions.

Methods

OMERACT initially defined 24 different response definitions in an attempt to find constructs that assessed multiple domains important to fibromyalgia patients, and when used to evaluate clinical trial results were efficient in separating treatment responses from placebo responses. Using clinical data from 12 registration trials, randomized, placebo-controlled trials, and 4 different medications for the treatment of FM, each definition was evaluated. Two definitions performed best in these pooled analyses: the FM10 short version and the FM10 long version.

Both definitions required a ≥30% reduction in pain and ≥10% improvement in physical function. The definitions differed in that one (FM20 short version) required ≥30% improvement in sleep quality, and the other (FM10 long version) required ≥30% improvement in 2 of the following symptoms: sleep, fatigue, depression, anxiety, or cognition. A total of 10 additional alternative responder definitions were also evaluated using those domains. The results of the analyses are presented in the Table 1 and Figure 1 below. The two responder definitions evaluated for this analysis were:

<table>
<thead>
<tr>
<th>Definition</th>
<th>Results</th>
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<tr>
<td>FM Long Version</td>
<td>30% reduction in pain</td>
</tr>
<tr>
<td>FM Short Version</td>
<td>30% reduction in pain</td>
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Table 1: Comparison of a Pain Responder Analysis to Alternative Composite Responder Definitions

Results

Table 1 below presents the response rates obtained when each of the proposed definitions was evaluated with the data from BESTFIT. Figure 1 graphically compares the standard pain responder analysis used in BESTFIT (≥30% improvement in pain from baseline) with the proposed composite responder definitions proposed by OMERACT.

To the far right, Figure 2 presents the effects of TNX 102 SL on a number of sleep and function measures and Figure 3 presents additional responder analyses on key secondary measures from BESTFIT.


The current paper evaluates the proposed responder criteria in comparative analyses using OMERACT responder definitions. These results were then compared to the primary outcomes used in BESTFIT.

Conclusion

In the BESTFIT trial, bedtime TNX 102 SL improved multiple domains of FM, including sleep, physical and physical function. Applying composite responder definitions developed by OMERACT to the results of the study revealed consistent with the conclusions of BESTFIT, namely that the improvements in FM symptoms seen with TNX 102 SL treatment are not limited only to an analgesic response, since these composite outcomes require improvement in other somatic and functional symptoms. The proposed OMERACT response criteria provide an additional method for which to assess clinical benefit in fibromyalgia clinical trials.

References:

Disclaimer of Interest: None declared.

TNX-102 SL is an investigational New Drug and has not been approved for any indication.