ISCTM RAAD

Assessment of Methods and Endpoints for Rapid-Acting Antidepressants-RAADs Working Group

17FEB2023

In this working group we reviewed the progress made since the inception of the group in 2019 including the ongoing challenges in defining what rapid-action means across a range of compounds that have different mechanisms of action. This challenge has implications for the recommendations of specific endpoints to measure change across time in clinical trials and these were discussed alongside the paper that was submitted to Frontiers in Psychiatry for their special issue on rapid-acting antidepressants. While recommendations for scales – both new and legacy – were provided in the paper and discussed during the working group, there remain concerns around the appropriateness of these and whether changes seen during treatment with RAADs are adequately captured by these instruments. The group also discussed concerns about trial participants and whether screening could be improved.

There were two questions put to the working group that generated significant discussion including:

- What scales have working group members used in RAAD trials? Any digital endpoints?
- What can be done to improve screening to mitigate risk? Better scales, better histories or something else?

The first question was answered succinctly by a range of working group members who are directly involved in clinical trials with RAADs: they have not used any digital endpoints and the scales used as endpoints have been either unmodified versions of standard depression instruments (e.g., MADRS, HAMD, IDS) or modified versions of these scales that do not include items that are not typically subject to rapid change such as sleep and appetite changes.

The second question generated very thoughtful commentary by a range of professionals at the site, sponsor, CRO and academic level. There was wide agreement that screening should be improved to mitigate risk and that a consistent framework should be developed along the lines of what the known risk factors are in the use of these types of compounds.

While this was described to working group members as potentially the final iteration of the group, there was clear interest in continuing to work towards improving the safety and efficacy of trials in this space.