SUICIDAL IDEATION AND BEHAVIOR: INCLUSION AND ASSESSMENT IN CLINICAL TRIALS

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How is “suicidal” defined? Are there minimum and maximum thresholds or cut-offs?

We recommend using the definitions of suicidal ideation and behavior found in the Columbia Classification Algorithm of Suicide Assessment:

- Suicidal Ideation (SI)
  - Passive (1)
  - Active: Nonspecific (no method, intent, or plan) (2)
  - Active: Method but no intent or plan (3)
  - Active: Method and intent but no plan (4)
  - Active: Method, intent, and plan (5)
- Suicidal Behavior (SB)
  - Preparatory actions towards imminent suicidal behaviors (1)
  - Aborted Attempt (2)
  - Interrupted Attempt (3)
  - Suicide Attempt (4)
  - Completed Suicide (5)
- Self-injurious behavior (IB)
  - No suicidal intent (6)

What degree of SI/B is appropriate for inclusion in a general MDD trial versus a study specifically targeting SI/B or prevention of suicide?

- We recommend not summarily excluding patients with *any* SI/B from psychiatric trials
- General trials: consider exclusion of those with imminent suicidal risk (i.e., C-SSRS: SI 4 to 5 or any SB) requiring acute intervention
- Recent past SB or serious SI: no set time period policy, investigator discretion on safety (case by case)

How should a trial be structured to support the inclusion of such subjects? Should safety planning and/or inpatient treatment be required?

- SI/B endpoint trials: we strongly recommend standard-of-care intervention within study design (i.e., inpatient settings if clinically warranted, active controls/treatment, etc.)
- Ethics and safety are paramount when including subjects with SI/B: **clinical care is not the same thing as research**

What is an adequate plan to manage suicidal behavior?

- Determined by clinician judgment
- Study programs should incorporate independent clinical assessment and appropriate clinical triage and treatment for patients with SB

Given that evidence for predictors of suicide is poor, on what basis would there be restrictions for inclusion?

- Again, imminent suicidal risk is main exclusion factor for general trials (non-SI/B endpoint) depending on ability to include standard-of-care measures for these patients
- If appropriate clinical assessment, triage, and referral to standard-of-care treatment are ensured, restrictions may be unnecessary

In studies targeting SI/B, what efficacy endpoints should be used? Occurrence of Ideation and Behaviors versus scores?

- Should code to C-CASA criteria
- For now, primary underlying psychiatric illness should still be measured as primary efficacy endpoint with appropriate scale
- SI/B should be measured as secondary endpoint (flexible for now on endpoint used)
- Important to assess relationship between underlying condition and SI/B in any given study
- Ballard et al (2015) noted rapid SI/B change may be easier to detect on less granular outcome measures (efficacy vs. safety as goal)
- Multidiagnostic SI/B endpoints may be considered in future

Ballard ED et al, *J Psychiatr Res* Sep 2015; 68:68-73.

In studies targeting SIB, what should the comparator treatment be (are placebo-controlled trials ethical and what evidence is there that treatment-as-usual is effective?)

- Placebo control may not be adequate/ethical without standard-of-care measures being included in study design for someone with imminent SI/B if condition may require medication: active treatment option should be incorporated
  - Consider superiority trials comparing new drug to active control, or comparing to placebo with standard of care as background therapy
  - Consider time to rescue designs with standard of care triage as outcome measure
- Evidence for standard-of-care interventions for SI/B: history of psychiatric research and care—treating underlying illnesses may improve SI/B and care must be individualized

In studies targeting SI/B, when is SI/B considered an adverse event (AE)?

- Impractical and less informative to report every SI/B event as an AE in SI/B endpoint study
- Recommend any change in baseline SI/B severity level (per C-CASA coding) to be reported as AE in these studies, and as serious AE if clinically warranted (prolonged hospitalization, change in clinical management, study discontinuation, significant clinical worsening, etc.)
- For general (non-SI/B endpoint) trials: recommend C-SSRS SI 4 or 5 and/or any SB be reported as an AE, with usual SAE criteria (hospitalization, etc.)


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