|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | \* | Not Important (1,2,3) | Important but not critical (4,5,6) | Critical (7,8,9) |
| The indications for the initiation of sedation (separate from the indication for enrollment in the study) are fully specified in the study protocol. | Round 1 | 30 | - | 24% | **76%** |
| An illness score (APACHE II, SOFA, SAPS II, etc.) is recorded for all patients at the time of enrollment. | Round 1 | 30 | - | 7% | **93%** |
| The risk of substance withdrawal (e.g., opioids, alcohol, etc.) is assessed with a validated tool prior to enrollment. | Round 1 | 30 | - | **72%** | 28% |
| Round 2 | 27 | 8% | **73%** | 19% |
| Round 3 | 25 | - | **91%** | 9% |
| Baseline pain is measured before study initiation using a validated scale. | Round 1 | 30 | 3% | 38% | 59% |
| Round 2 | 27 | 4% | 26% | **70%** |
| Baseline pain is treated to a pre-specified level using a validated scale prior to enrollment | Round 1 | 30 | 24% | 48% | 28% |
| Round 2 | 27 | 15% | 67% | 19% |
| Round 3 | 25 | 4% | **72%** | 24% |

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|  |  | \* | Immedi-ately | 1 hr | 6 | 12 | 24 | 48 |
| Enrollment is to occur no later than    [make selection]   after initiation of "usual" practice sedation (non-protocol) | Round 1 | 30 | 4% | 23% | 15% | 8% | 38% | 12% |
| Round 2 | 26 | - | - | 9% | 13% | **74%** | 4% |
| Round 3 | 25 | - | - | 9% | - | **87%** | 4% |

**Supplemental Table 2A. Enrollment and Study Initiation**. Questions were removed from a subsequent round if consensus was reached for the recommendation being “critical” (see text). APACHE II - Acute Physiology and Chronic Health Evaluation II. SOFA – Sequential Organ Failure Assessment. SAPS II – Simplified Acute Physiology Score II. \* Total number of respondents for each round. The percentages are based on the number who indicated a response 1-9, excluding “No Opinion” option.

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | |  | | \* | Not Important (1,2,3) | | Important but not critical (4,5,6) | | Critical (7,8,9) |
| A “non-inferiority" trial design compared to “usual practice” is an acceptable RCT design for a study of a new ICU sedative or protocol. | Round 1 | | 30 | | 13% | 43% | | 43% | | |
| Round 2 | | 27 | | - | 52% | | 48% | | |
| Round 3 | | 25 | | 4% | **72%** | | 24% | | |
| A pragmatic RCT design (e.g., “usual practice” as the comparison group) is acceptable for a study of a new ICU sedative or protocol. | Round 1 | | 29 | | 14% | 54% | | 32% | | |
| Round 2 | | 27 | | - | **81%** | | 19% | | |
| Round 3 | | 25 | | - | **92%** | | 8% | | |
| Complete blinding (patients, family, clinicians and study personal) for the study conduct and analysis is: | Round 1 | | 30 | | 7% | 52% | | 41% | | |
| Round 2 | | 27 | | 4% | 58% | | 38% | | |
| Round 3 | | 25 | | - | **76%** | | 24% | | |
| For new ICU sedation agents (or combinations) adequate Pk/Pd data must be available for the specific ICU patient population to be studied | Round 1 | | 30 | | 7% | 36% | | 57% | | |
| Round 2 | | 27 | | - | 24% | | **76%** | | |
| Former ICU patients and families should be explicitly consulted in the design phase of an ICU sedation clinical trial | Round 1 | | 30 | | 14% | 31% | | 55% | | |
| Round 2 | | 27 | | 11% | 30% | | 59% | | |
| Round 3 | | 25 | | 4% | 24% | | **72%** | | |
| All outcome assessments for sedation, pain and/or delirium should be conducted by fully trained research personnel | Round 1 | | 30 | | 13% | 27% | | 60% | | |
| Round 2 | | 27 | | 4% | 22% | | **74%** | | |
| Documentation of adequate training for all personnel (study or clinical) who measure study outcomes must be made | Round 1 | | 30 | | 3% | 23% | | **73%** | | |

**Supplemental Table 2B. Study Design**. Questions were removed from a subsequent round if consensus was reached for the recommendation being “critical” (see text). RCT – Randomized Controlled Trial. ICU – Intensive Care Unit Pk/Pd – pharmacokinetic / pharmacodynamic. . \* Total number of respondents for each round. The percentages are based on the number who indicated a response 1-9, excluding “No Opinion” option.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | \* | Not Important (1,2,3) | Important but not critical (4,5,6) | Critical (7,8,9) |
| In a sedation clinical trial, the Richmond Agitation and Sedation Scale (RASS) is included as an efficacy outcome measurement of the sedation level | Round 1 | 28 | - | 58% | 42% |
| Round 2 | 27 | - | 58% | 42% |
| Round 3 | 25 | - | 63% | 38% |
| In a sedation clinical trial, the Sedation Agitation Scale (SAS) is included as an efficacy outcome measurement of the sedation level | Round 1 | 28 | 13% | 39% | 48% |
| Round 2 | 27 | 4% | **73%** | 23% |
| Round 3 | 25 | 8% | **79%** | 13% |
| In a sedation clinical trial, the Ramsey Sedation Scale (RSS) is included as an efficacy outcome measurement of the sedation level | Round 1 | 28 | 57% | 30% | 13% |
| Round 2 | 27 | 77% | 19% | 4% |
| Round 3 | **25** | **92%** | 8% | - |
| The use of pre-specified rescue medications (e.g., which medications and indications for use) is included as an outcome | Round 1 | 28 | - | 19% | **81%** |
| A composite efficacy outcome (e.g., components of sedation, pain and [lack of] delirium) is not used as a primary outcome | Round 1 | 28 | 29% | 38% | 33% |
| Round 2 | 27 | 28% | 56% | 16% |
| Round 3 | 25 | 16% | 64% | 20% |
| A validated tool for patient and/or family satisfaction with sedation is included as an efficacy outcome. | Round 1 | 28 | 4% | 50% | 46% |
| Round 2 | 27 | - | 56% | 44% |
| Round 3 | 25 | - | 68% | 32% |

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| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | \* | Hour | 2 hrs | 4 | 8 | 12 | Day |
| As an efficacy outcome the sedation level should be measured every | Round 1 | 28 | 8% | 16% | 60% | 12% | 4% | 0% |
| Round 2 | 26 | 4% | - | **96%** | - | - | - |

**Supplemental Table 2C. Efficacy Outcome Measurements**. Questions were removed from a subsequent round if consensus was reached for the recommendation being “critical” (see text). \* Total number of respondents for each round. The percentages are based on the number who indicated a response 1-9, excluding “No Opinion” option.

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| --- | --- | --- | --- | --- | --- |
|  |  | \* | Not Important (1,2,3) | Important but not critical (4,5,6) | Critical (7,8,9) |
| In patients who can self-report pain a numeric rating scale (NRS) is used | Round 1 | 28 | - | 19% | **81%** |
| In patients who cannot self-report pain the Critical Care Pain Observation Tool (CCPOT) is used. | Round 1 | 28 | 4% | 23% | **73%** |
| In patients who cannot self-report pain the Behavioral Pain Scale (BPS) is used. | Round 2 | 27 | 8% | 46% | 46% |
| Round 3 | 25 | - | 29% | **71%** |
| Pain is measured and recorded only by study personnel fully trained in the use of the scale: | Round 1 | 27 | 19% | 31% | 50% |
| Round 2 | 27 | 15% | 11% | **74%** |
| Ability of the patient to communicate with family and staff is included as an outcome. | Round 1 | 28 | 4% | 56% | 41% |
| Round 2 | 27 | 4% | 62% | 35% |
| Round 3 | 25 | 4% | **80%** | 16% |
| Assessment of amnesia (without specification as to whether amnesia is good or bad from a patient’s perspective) is included as an outcome measurement: | Round 1 | 28 | 35% | 42% | 23% |
| Round 2 | 27 | 15% | **81%** | 4% |
| Round 3 | 25 | - | **96%** | 4% |
| Assessment of sleep (subjective or objective sleep assessment scores) is included as an outcome measurement: | Round 1 | 28 | 15% | 52% | 33% |
| Round 2 | 27 | 11% | **70%** | 19% |
| Round 3 | 25 | 4% | **84%** | 12% |

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| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | \* | Hour | 2 hrs | 4 | 8 | 12 | Day |
| As an outcome, pain should be assessed every | Round 1 | 28 | 12% | 16% | 48% | 12% | 8% | 4% |
| Round 2 | 27 | 4% | 4% | **88%** | 4% | - | - |

**Supplemental Table 2D. Other Outcome Measurements**. Questions were removed from a subsequent round if consensus was reached for the recommendation being “critical” (see text). \* Total number of respondents for each round. The percentages are based on the number who indicated a response 1-9, excluding “No Opinion” option.

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| --- | --- | --- | --- | --- | --- |
|  |  | \* | Not Important (1,2,3) | Important but not critical (4,5,6) | Critical (7,8,9) |
| The ICU mortality is required as a safety outcome. | Round 1 | 28 | 4% | 15% | **81%** |
| Days on a ventilator is a required safety outcome measure. | Round 1 | 28 | 7% | 11% | **82%** |
| Lack of delirium is an important safety outcome and assessment of delirium should use the CAM-ICU scale. | Round 1 | 28 | 7% | 11% | **81%** |
| Lack of delirium is an important safety outcome and assessment of delirium should use the Intensive Care Delirium Screening Checklist (ICDSC) scale. | Round 2 | 27 | 8% | 36% | 56% |
| Round 3 | 25 | 4% | 24% | **72%** |
| Delirium measurement should distinguish between hypoactive and hyperactive types | Round 1 | 28 | 15% | 46% | 38% |
| Round 2 | 26 | 8% | 56% | 36% |
| Round 3 | 25 | 4% | 60% | 36% |
| Delirium is measured and recorded only by study personnel fully trained in the use of the scale: | Round 1 | 28 | 11% | 30% | 59% |
| Round 2 | 27 | 7% | 11% | **81%** |

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | \* | Hour | 2 hrs | 4 | 8 | 12 | Day |
| The measurement of delirium should be made every | Round 1 | 28 | - | 4% | 28% | 24% | 36% | 8% |
| Round 2 | 27 | - | - | 31% | 15% | 54% | - |
| Round 3 | 24 | - | - | 9% | 14% | **73%** | 5% |

**Supplemental Table 2E. Safety Outcome Measurements**. Questions were removed from a subsequent round if consensus was reached for the recommendation being “critical” (see text). CAM-ICU – Confusion Assessment Method for the Intensive Care Unit. \* Total number of respondents for each round. The percentages are based on the number who indicated a response 1-9, excluding “No Opinion” option.

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| --- | --- | --- | --- | --- | --- |
|  |  | \* | Not Important (1,2,3) | Important but not critical (4,5,6) | Critical (7,8,9) |
| The Core Outcome Measurement Set (Am J Crit Care Med 196 (9): 1122-1130, 2017) should be used to assess long term outcomes. | Round 1 | 28 | 4% | 32% | 64% |
| Round 2 | 26 | 8% | 15% | **77%** |
| “Institution (i.e., not at home) free days” after discharge should be a long-term outcome. | Round 1 | 28 | 4% | 63% | 33% |
| Round 2 | 27 | 4% | 73% | 23% |
| Round 3 | 25 | - | **76%** | 24% |

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | \* | 30 days | 60 days | 6 months | 1 year |
| Long term (post ICU discharge) mortality should be measured at what interval(s) (choose one or more): | Round 1 | 30 | 32% | 18% | 26% | 24% |
| Round 2 | 22 | 45% | 14% | 28% | 14% |
| Round 3 | 25 | 57% | 4% | 29% | 11% |

**Supplemental Table 2F. Long Term Outcome Measurements**. Questions were removed from a subsequent round if consensus was reached for the recommendation being “critical” (see text). \* Total number of respondents for each round. The percentages are based on the number who indicated a response 1-9, excluding “No Opinion” option.