not changed in any way.

SCEPTER III Steering Committee

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Sedation Consortium on Endpoints and Procedures for Treatment, Education, and Research (SCEPTER-III)
Clinical Trials to Evaluate Patient-Centered Outcomes of Sedation in Mechanically Ventilated Patients in the Adult ICU

MEETING AGENDA

Wednesday, March 27, 2019		
7:00 – 9:00 PM	**Reception and Dinner**	**Mayfair Court**
Thursday, March 28, 2019		
7:30 – 8:00 AM	**Continental Breakfast**	
8:00 – 8:30	Welcome and Introductions	Bob Dworkin
8:30 – 8:45	Procedural Sedation – SCEPTER 1 & 2. Goals for SCEPTER 3	Denham Ward
8:45 – 10:00	Panel Discussion: Current Clinical Guidelines - SCCM PADIS guidelines: Pain, Agitation/Sedation, Delirium, Immobility and Sleep Impairment	Douglas Coursin (moderator), John Devlin Yoanna Skrobik
10:00 – 10:30	Break	
10:30 – 11:00	Patient and family perspective	David Brown
11:00 – 11:30	Establishing core outcome measures and instruments: a case study in evaluating post-discharge status of ICU survivors	Dale Needham
11:30 – 12:00	Q&A and Panel discussion: How to incorporate the patient's and families' perspective	Pam Flood (moderator), David Brown, Dale Needham, Ingrid Egerod
12:00 – 1:00 PM	**Lunch**	**Mayfair Court**
1:00 – 1:30	SEDCOM, MENDS, MIDEX & PRODEX – Lessons learned for study design, outcomes and measures	Richard Riker
1:30 - 2:00	Evaluating efficacy in ICU sedation clinical trials: a regulatory perspective	Martha Van Clief
2:00 - 2:30	Q&A and panel discussion: current controversies, and unmet needs	Gil Fraser, Douglas Coursin (moderators), Yoanna Skrobik, Mervyn Maze, Richard Riker, Martha Van Clief
2:30 -3:00	Break	
3:00 - 3:30	Design issues for clinical trials of ICU sedation	Daniel Sessler
3:30 - 4:00	Clinical Trials for new ICU Sedation Protocols	Leanne Aitken
4:00 - 4:30	Statistical issues in clinical trial design for ICU sedation	Elizabeth Colantuoni
4:30 – 5:00	Q&A and Panel discussion: Clinical trial design	Steve Shafer(moderator), Daniel Sessler, Leanne Aitken, Franklin Dexter, Elizabeth Colantuoni, Yahya Shehabi
7:00 – 9:00	**Dinner**	**Mayfair Court**

Friday, March 29, 2019		
7:30 – 8:00 AM	**Continental Breakfast**	**Washington Ballroom**
8:00 – 8:30	Defining and measuring light vs moderate sedation / analgesia	Pratik Pandharipande
8:30 – 9:00	Case Study: Approval of Dexmed for ICU sedation	Mervyn Maze
9:00 – 10:00	Who should be studied and how? • Controls and patient inclusion / exclusion criteria? • Overall trial design.	Avery Tung (moderator)
10:00 – 10:30	**Break**	
10:30 – 12:00	Evaluating acute use of ICU sedation / analgesia. • How best to measure level of sedation? • Patient and family perspective. • Sleep state? • Efficacy of the sedation / analgesia? • Safety measures during sedation?	Yoanna Skrobik (moderator)
12:00 – 1:00	**Lunch**	**Mayfair Court**
1:00 – 2:30	Acute, Subacute and chronic outcomes after ICU sedation. • Sedation outcome domains, measures, and items? • Improving medical outcomes, short term and post discharge? • Outcomes that are more likely to have a strong correlation with sedation?	Tim Girard (moderator)
2:30 – 3:00	Group Discussion: SCEPTER 3 next steps	Denham Ward

How satisfied are you with the currently available sedative pharmacologic agents for use in the ICU?									
Not satisfied			Satisfied			Very satisfied			N/O
1	2	3	4	5	6	7	8	9	

How satisfied are you with the currently available analgesic pharmacologic agents for use in the ICU?									
Not satisfied			Satisfied			Very satisfied			N/O
1	2	3	4	5	6	7	8	9	

How satisfied are you with the currently available (natural or physiological) sleep-inducing pharmacologic agents for use in the ICU?									
Not satisfied			Satisfied			Very satisfied			N/O
1	2	3	4	5	6	7	8	9	

How important is it that a new safe, comfort enhancing medication (sedative-analgesic) be developed for use in the ICU?									
Not important			Important			Very important			N/O
1	2	3	4	5	6	7	8	9	

What do you think the likelihood is that Pharma would be willing to invest in developing a new sedative-analgesic for use in the ICU?									
Not likely			Likely			Very likely			N/O
1	2	3	4	5	6	7	8	9	

How important is the patient and/or family perspective in addressing issues with current sedative/analgesic use in the ICU?									
Not important			Important			Very important			N/O
1	2	3	4	5	6	7	8	9	

How satisfied are you that current validated sedation scales adequate for clinical trials?									
Not satisfied			Satisfied			Very satisfied			N/O
1	2	3	4	5	6	7	8	9	

How satisfied are you that current validated pain scales adequate for clinical trials?									
Not satisfied			Satisfied			Very satisfied			N/O
1	2	3	4	5	6	7	8	9	

How satisfied are you that current validated delirium scales adequate for clinical trials?									
Not satisfied			Satisfied			Very satisfied			N/O
1	2	3	4	5	6	7	8	9	

Should patient and family contribution apply to all phases of research including trial design, result review and preparation of publication?									
Not important			Important			Very important			N/O
1	2	3	4	5	6	7	8	9	

How important is it that the FDA has qualified clinical outcome assessments (COA) for sedation, analgesia and delirium in the ICU (there currently are none)?									
Not important			Important			Very important			N/O
1	2	3	4	5	6	7	8	9	

Supplemental Table 1. Information Survey Questions

		*	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%

		*	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.

		*	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%

		*	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.

		*	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%

		*	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.

		*	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.

		*	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.