ProTECT III

Second Annual Investigators' Meeting
April 2011

Monitoring

ProTECT III

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Frequency

- First visit occurs after the second subject is discharged or reaches 30 days at each Hub.
- Subsequent monitoring will occur after every 10 pts are enrolled or 6 months (whichever is more frequent).

What to expect during a monitor visit

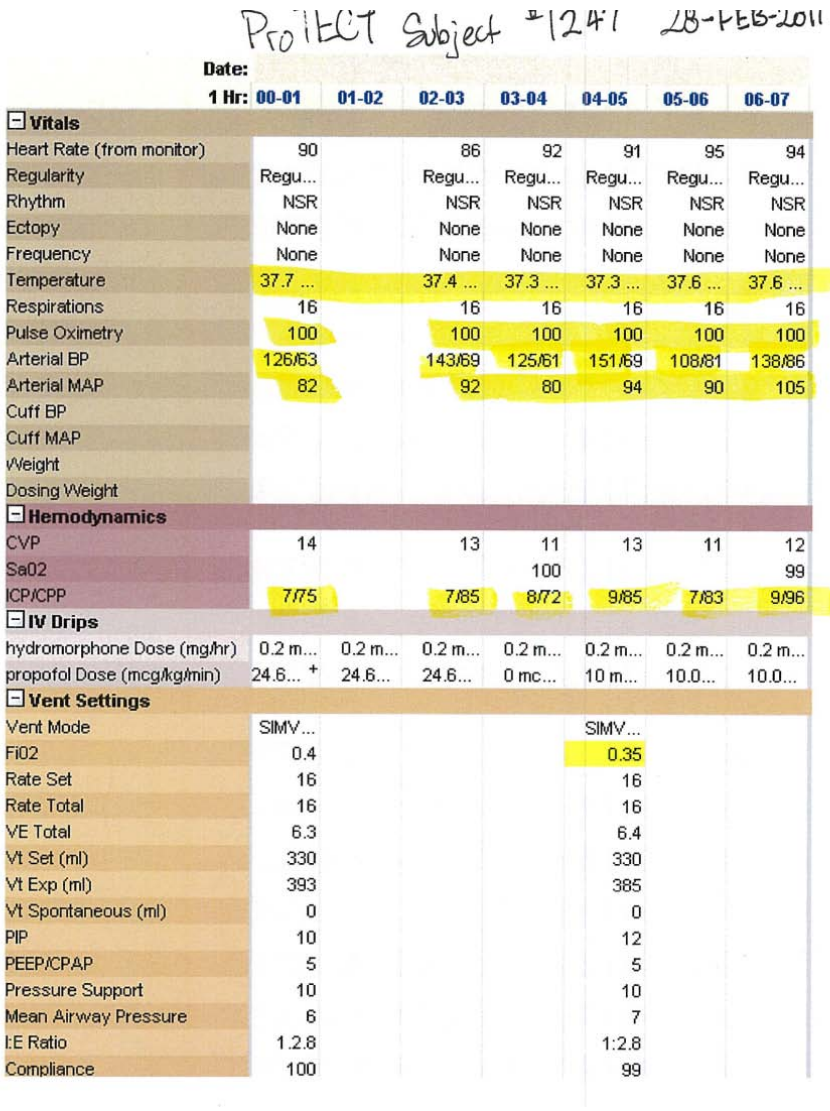
- Verification of CRF data against source documents
- Review and discussion of screening and enrollment
- Review of informed consent documents
- Regulatory review
- Visit to pharmacy for study kit supply, storage and drug accountability review
- Data clarification requests
- Meeting with the Hub Principal Investigator and/or Primary Study Coordinator to review findings, give and receive feedback

Source documents

- Source documents include

1. Electronic medical records
2. Paper medical records
3. Study worksheets (if used)
4. Video/audio recordings (with approval of protocol version 7)

Source documents from Stanford



ProTECT Subject #1241 28-FEB-2011

Date:							
1 Hr:	00-01	01-02	02-03	03-04	04-05	05-06	06-07
Vitals							
Heart Rate (from monitor)	90		86	92	91	95	94
Regularity	Regu...		Regu...	Regu...	Regu...	Regu...	Regu...
Rhythm	NSR		NSR	NSR	NSR	NSR	NSR
Ectopy	None		None	None	None	None	None
Frequency	None		None	None	None	None	None
Temperature	37.7 ...		37.4 ...	37.3 ...	37.3 ...	37.6 ...	37.6 ...
Respirations	16		16	16	16	16	16
Pulse Oximetry	100		100	100	100	100	100
Arterial BP	126/63		143/69	125/61	151/69	108/81	138/86
Arterial MAP	82		92	80	94	90	105
Cuff BP							
Cuff MAP							
Weight							
Dosing Weight							
Hemodynamics							
CVP	14		13	11	13	11	12
Sa02				100			99
ICP/CPP	7/75		7/85	8/72	9/85	7/83	9/96
IV Drips							
hydromorphone Dose (mg/hr)	0.2 m...	0.2 m...	0.2 m...	0.2 m...	0.2 m...	0.2 m...	0.2 m...
propofol Dose (mcg/kg/min)	24.6... +	24.6...	24.6...	0 mc...	10 m...	10.0...	10.0...
Vent Settings							
Vent Mode	SIMV...				SIMV...		
Fi02	0.4				0.35		
Rate Set	16				16		
Rate Total	16				16		
VE Total	6.3				6.4		
Vt Set (ml)	330				330		
Vt Exp (ml)	393				385		
Vt Spontaneous (ml)	0				0		
PIP	10				12		
PEEP/CPAP	5				5		
Pressure Support	10				10		
Mean Airway Pressure	6				7		
I:E Ratio	1.2.8				1:2.8		
Compliance	100				99		

Date:							
1 Hr:	00-01	01-02	02-03	03-04	04-05	05-06	06-07
Blood Gas							
ph (A), ISTAT				7.37			7.38
pCO2 (A), ISTAT				47.0			47.1
pO2 (A), ISTAT				202			165
HCO3 (A), ISTAT				27.3			27.9
Base Excess ISTAT				2.0			3.0
SaO2 ISTAT				100			99

Date:	02/28 0700 - 03/01 0659																
1 Hr:	07-08	08-09	09-10	10-11	11-12	12-13	13-14	14-15	15-16	16-17	17-18	18-19	19-20	20-21	21-22	22-23	23-00
Vitals																	
Heart Rate (from monitor)	100	100	103	112+	115	113	113	116	117	120	117	110+	113	115	115	119+	118+
Regularity	Regu...	Regu...	Regu...	Regu...	Regu...	Regu...	Regu...	Regu...	Regu...	Regu...	Regu...	Regu...	Regu...	Regu...	Regu...	Regu...+	Regu...
Rhythm	NSR	NSR	ST	ST	ST	ST	ST	ST	ST	ST	ST	ST	ST	ST	ST	ST+	ST
Ectopy	None	None	None	None	None	None	None	None	None	None	None	None	None	None	None	None+	None
Frequency	None	None	None	None	None	None	None	None	None	None	None	None	None	None	None	None+	None
Temperature	37.5 ...	37.6 ...	37.7 ...	37.9 ...	38 (1...	38 (1...	38.1 ...		38.4 ...			38.1 ...	38.1 ...	38.5 ...+	38.5 ...	38.2 ...+	38.2 ...
Respirations	21	20	11	11	10	11	11	18	11	11+	10	8+	9	12	12	15+	19+
Pulse Oximetry	100	100	100+	100	100	99+	99	100	100	99+	98	100+	100	100+	100	100+	100+
Arterial BP	134/80	137/85	124/89	~~93/82~~+	~~67/59~~			154/69	156/72	111/55+	106/53	140/68+	131/65	154/73	117/59	130/63+	155/81+
Arterial MAP	100	106	103	86+	61			91	95	73+	70	88+	84	95	76	82+	103+
Cuff BP				115/63	129/70	125/65	130/70	127/70	135/84								
Cuff MAP				75	81	79	85	83	97								
Weight							76.3 ...										
Hemodynamics																	
CVP	12	10	11	10+	10	9	8	6	6	3+	4	6+	6	7	7	13+	18+
Sa02				98						99							
ICP/CPP	7/93	8/98	9/94	10/97	9/52	13/66	17/68	11/80	12/83	16/57+	16/54	13/75+	13/71	14/81	7/69	5/77+	9/94+
IV Drips																	
fentanyl Dose (mcg/hr)														25 m...	25 m...	25 m...	50 m...+
hydromorphone Dose (mg/hr)	0.2 m...+	0.2 m...	0.2 m...	0.2 m...	0.2 m...	0.2 m...	0.2 m...	0.2 m...	0.2 m...	0.2 m...	0.2 m...	0.2 m...	0.2 m...	0 mg/...			
propofol Dose (mcg/kg/min)	0 mc...+	10 m...	10 m...	0 mc...+	0 mc...+		15 m...	15 m...+	0 mc...+		15 m...	0 mc...+		25 m...	25 m...	50 m...+	50 m...
Vent Settings																	
Vent Mode			PSV			PSV				PSV				SIMV...			
Fi02			0.35			0.35				0.35				0.35			
Rate Set			0			0				0				16			

1 Hr:	07-08	08-09	09-10	10-11	11-12	12-13	13-14	14-15	15-16	16-17	17-18	18-19	19-20	20-21	21-22	22-23	23-00
Neuro																	
LOC	Seda...	Seda...	Seda...	Seda...	Seda...	Seda...	Seda...	Seda...	Seda...	Seda...	Seda...	Seda...	Seda...	Seda...	Seda...	Agita...+	Seda...
Orientation	Unab...	Unab...	Unab...	Unab...	Unab...	Unab...	Unab...	Unab...	Unab...	Unab...	Unab...	Unab...	Unab...	Unab...	Unab...	Unab...	Unab...
Hand Grips Right	Mod;...	Mod;...	Mod;...	Mod;...	Mod;...	Mod;...	Mod;...	Mod;...	Mod;...	Mod;...	Mod;...	Mod;...	Mod;...	Mod;...	Mod;...	Mod;...	Mod;...
Hand Grips Left	Mod;...	Mod;...	Gros...	Gros...	Wea...	Gros...	Gros...	Gros...	Gros...	Gros...	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Neuro Expanded																	
Gag Reflex	Impai...	Impai...	Impai...	Impai...	Impai...	Impai...	Impai...	Impai...	Impai...	Impai...	Impai...	Impai...	Impai...	Impai...	Impai...	Impai...	Impai...
Pupil Reaction Right	Slug...	Slug...	Slug...	Slug...	Slug...	Slug...	Slug...	Slug...	Slug...	Brisk	Slug...	Slug...	Slug...	Slug...	Slug...	Slug...	Slug...
Pupil Reaction Left	Slug...	Slug...	Slug...	Slug...	Slug...	Slug...	Slug...	Slug...	Slug...	Slug...	Slug...	Slug...	Slug...	Slug...	Slug...	Slug...	Slug...
Pupil Size R/L	2 mm...	2 mm...	3 mm...	2 mm...	3 mm...	3 mm...	3 mm...	3 mm...	2 mm...	3 mm...	3 mm...	3 mm...	3 mm...	3 mm...	3 mm...	3 mm...	3 mm...
RUE Response	Spon...	Spon...	Spon...	Spon...	Spon...	Spon...	Spon...	Spon...	Local...	Spon...	Spon...	Spon...	Spon...	Spon...	Spon...	Spon...	Spon...
LUE Response	Spon...	Spon...	Spon...	Spon...	Spon...	Spon...	Spon...	Spon...	Spon...	Spon...	Spon...	Spon...	Spon...	Spon...	Spon...	Spon...	Spon...
RLE Response	With...	With...	With...	With...	With...	With...	With...	With...	With...	With...	With...	With...	With...	With...	With...	With...	With...
LLE Response	With...	With...	With...	No m...	With...	No m...	No m...	No m...	With...	With...	With...	With...	With...	With...	With...	With...	With...
Eye Opening	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Best Verbal Response	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Best Motor Response	5	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
Glasgow Coma Scale Score	7	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6

Baseline

- Pre-hospitalization documentation (EMS/flight trip sheets)
- ED documentation
- Documentation of attempts to locate LAR
- Informed Consent Form

Treatment Phase

- Study drug infusion documentation
- Documentation of PI/CO-I assessment of adverse events
- Documentation of PI/CO-I assessment of lab results
- Point-Of-Care glucose values

Adverse Events

- AEs are recorded for the first 7 days after enrollment
- After 7 days, only new SAEs and PAAEs are recorded and followed through end of study.
- Non-serious AEs must be submitted within 5 days from time of discovery by the study team.
- SAEs and PAAEs must be submitted within 24 hours from time of discovery by the study team.

Adverse Events

- Any untoward events or complications that were not previously identified;
- Or that occur with greater frequency or severity than previously reported;
- Occur during or after the protocol intervention;
- Are reported whether or not they are considered (possibly/probably/definitely) related to the protocol intervention.

Adverse Events

- Abnormal laboratory findings that are considered by the PI/Co-I to be clinically significant, or any lab result that requires a procedure or medication are included as adverse events.
- Example: potassium = 3.0 on day 5. Potassium chloride bolus administered IV.
- Enter AE CRF.
- Provide severity, date of onset, outcome, date of resolution (if available), relationship to study drug, and actions taken. Please note what the lab value was in the general comment section.

Adverse Events

- Example: PLTs = 80,000/mm3 on day 6. Subject received PLTs transfusion.
- Enter AE CRF.
- Provide severity, date of onset, outcome, date of resolution (if available), relationship to study drug, and actions taken. Please note what the lab value was in the general comment section.

Adverse Events

- Transgressions do NOT have to be entered as adverse events in WebDCU™.
- Example: hemoglobin = 7.8 g/dl on day 3
- Enter "Yes" on Daily Checklist for hemoglobin transgression.
- Complete hemoglobin transgression CRF.

Potentially Associated Adverse Events

Based on known potential risks of progesterone administration, the following could be associated with study drug infusion:

- Deep vein thrombosis and pulmonary embolism
- Myocardial infarction or ischemic stroke
- Allergic reactions (to Intralipid)
- Marked (unexplained) liver function abnormalities
- Serious infections such as pneumonia, sepsis, meningitis (Must meet CDC definition).
- DVT, pulmonary embolism, MI or stroke would require that the study drug infusion be stopped.

Serious Adverse Events

Any adverse events that results in the following:

- Death due to any cause;
- A life-threatening adverse experience (i.e., the subject was at immediate risk of death from the event as it occurred);
- In-patient hospitalization or prolongation of existing hospitalization. (Hospitalizations scheduled before enrollment for an elective procedure or treatment of a pre-existing condition that has not worsened during participation in the study is not considered a serious adverse event);

Serious Adverse Events

Cont'd

- A persistent or significant disability/incapacity (i.e., a substantial disruption of one's ability to conduct normal life functions);
- A congenital anomaly/birth defect;
- An important medical event that may not result in death, be life-threatening, or require hospitalization, but may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

Serious Adverse Events

Required elements on the SAE CRF:

- Title, date and time of onset;
- Seriousness and severity;
- Action taken as a result of the SAE, the outcome and date of resolution (if applicable or known), and a narrative of the event.
- Assessment of PI/CO-I of the relatedness to the investigational drug.

Serious Adverse Events

- Example: cerebral herniation on day 5.
- Enter AE CRF.
- Provide severity, date of onset, outcome, date of resolution (if available), relationship to study drug, and actions taken.
- Descriptive narrative should include: mechanism of injury, date/time of randomization, start/stop time and date of study drug infusion, summary of patient's status leading up to the AE (including GCS, ICP readings, neuro exam, etc.); summary of pertinent test results (CT/MRI scans, cerebral perfusion, etc), interventions and outcome of actions taken.

Serious Adverse Events

- The ProTECT™ III Project Manager (PM) will review the PAAE/SAE for completeness of information in WebDCU™.
- If a request for additional information or clarification is requested, you are expected to provide that informationwithin 24 hrs of the request.

Any SAE categorized as "probably/definitely related" to the study drug will prompt cessation of the infusion and a medical safety review.

When in doubt, CALL THE HOTLINE!

Following up PAAEs and SAEs

- Monitors review source documents (nursing notes, lab report, CT reports, chest x-rays, Medication Administration Record) for verification of dates, diagnostic procedures, medications given, and other action taken in relation to the SAE/PAAE.
- If a SAE/PAAE is marked ongoing, we will request a follow-up to resolve the SAE/PAAE.

Monthly Follow-up Phase

Monthly follow-up documentation:

- Use of a telephone log is recommended as a best practice
- Include details of the interview and participants (i.e. date, time, conversation) in a progress note
- Monthly follow up visit window +/- 14 days

QA Monitoring

- QA visits will be conducted yearly by the PM
- 10%of subjects at each Hub/spoke will be monitored in their entirety (including all transgressions)
- Visit is meant to be educational/informative not punitive

Payment

- Payment can occur when all Data Clarification Requests have been responded to by the site and closed by site monitors/SDMC/QA monitor, *and* images have been sent to Emory.

Regulatory Review

- WebDCU™ is the primary source of regulatory recordkeeping for the NETT.
- All regulatory documents must remain current throughout the course of the trial.

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