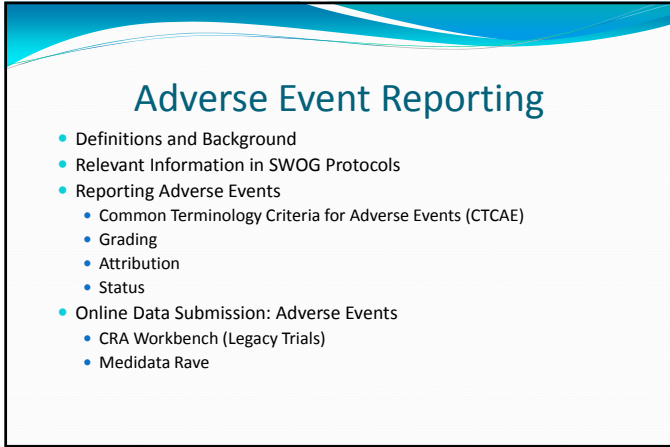


Adverse Event Reporting

SWOG Clinical Trials

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SWOG Statistics and Data
Management Center (SDMC)



Adverse Event Reporting

- Definitions and Background
- Relevant Information in SWOG Protocols
- Reporting Adverse Events
 - Common Terminology Criteria for Adverse Events (CTCAE)
 - Grading
 - Attribution
 - Status
- Online Data Submission: Adverse Events
 - CRA Workbench (Legacy Trials)
 - Medidata Rave



Definitions and Background

Adverse Event (AE):
 Any change in the patient's condition from the day protocol treatment began, regardless of cause.

Examples of Adverse Events

- Nausea and/or vomiting caused by treatment
- Sinusitis from seasonal allergies
- Breaking a leg
- Increasing cancer symptoms

Toxicity:
 Adverse symptom(s) caused or possibly caused by the drugs or treatment used in the study.

<u>Tissue</u>	<u>Toxicity</u>
Bone marrow	Myelosuppression
Mucous membranes	Nausea/Vomiting
Hair follicles	Alopecia

Serious Adverse Event (SAE):
 An unexpected or severe reaction to protocol treatment.

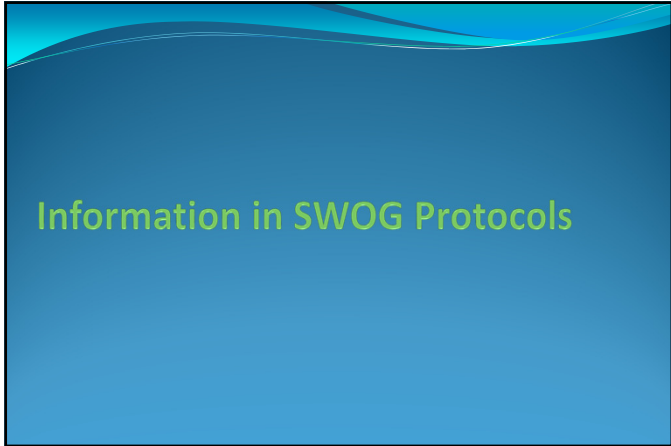
Adverse Event Reporting

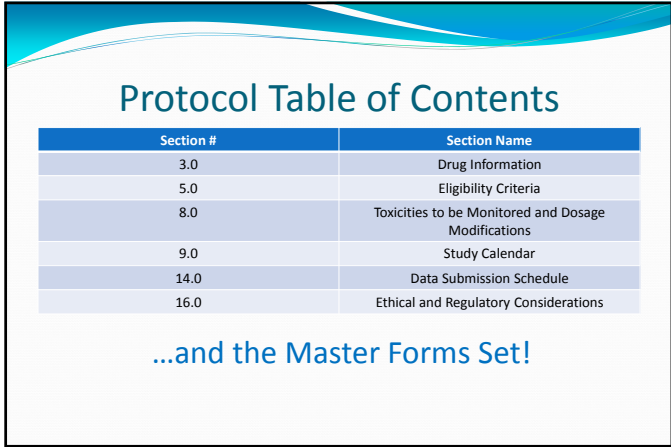
Expedited reporting: Serious Adverse Events

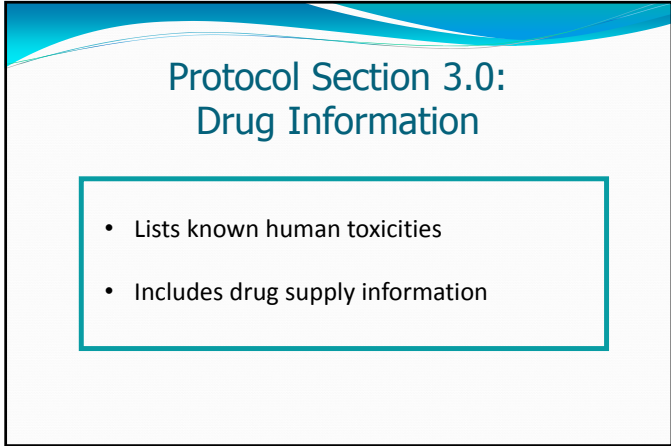
Routine reporting: All adverse events, regardless of attribution or grade (unless otherwise specified in forms or protocol)

Why do we collect routine AE's?

- **Phase I trials:**
 - Primary objective: to assess the safety of an experimental regimen and determine the maximum tolerated dose
- **Phase II single-arm trials:**
 - Secondary objective: to estimate the frequency and severity of toxicities in trial regimen
- **Phase II/III randomized trials:**
 - Secondary objective: to compare the frequency and severity of toxicities associated with each regimen







**Protocol Section 8.0:
Toxicities to be Monitored and Dose Modifications**

- Lists certain toxicities that may be seen on treatment
- Details dosage changes required during treatment in response to AEs

**Protocol Section 8.0:
Toxicities to be Monitored and Dose Modifications**

Dose Modifications – Talazoparib (BMN 673)

Dose modifications should be made based on the observed toxicity, as summarized in the tables below.

DRUG	DOSE LEVEL	DOSE
Talazoparib BMN 673	Full	1000 mcg/day
	-1 Level	750 mcg/day
	-2 Level	500 mcg/day
	-3 Level	250 mcg/day
	-4 Level	Discontinue

Table 1: Renal Impairment Dose Modifications

Toxicity	Dose Modification
Grade 3	No hold on treatment required, treatment may continue at next lower dose
Grade 4	Hold protocol treatment until resolution to \leq Grade 2, treatment may then resume at the next lower dose

**Protocol Section 8.0:
Toxicities to be Monitored and Dose Modifications**

- Lists drugs to aid in symptom management
- Lists names of physicians to call for assistance

**Protocol Section 9.0:
Study Calendar**

- Indicates how often to assess adverse events while receiving protocol treatment

**Protocol Section 16.0:
Ethical and Regulatory Considerations**

Includes instructions for reporting SAE's

Master Forms Sets/All Forms Packet

- Contains all study forms, including those used to document adverse events

Reporting Adverse Events

Common Terminology Criteria for Adverse Events (CTCAE)

About the Common Terminology Criteria for Adverse Events (CTCAE)

- Provides a list of specific adverse events (“CTCAE terms”), a description of each adverse event term, and guidelines on how to grade each event.
- Organized by System Organ Class categories.
- Can find a copy of the CTCAE at <ctep.cancer.gov>
 - Version 4.0: In use since October 2009
 - Version 5.0: Starting April 1, 2018, all patient data submitted to CTEP must use version 5.0.

Blood and lymphatic system disorders					
Adverse Event	Grade				
	1	2	3	4	5
Anemia	Hemoglobin (Hgb) <LLN - 10.0 g/dL; <LLN - 6.2 mmol/L; <LLN - 100 g/L	Hgb <10.0 - 8.0 g/dL; <6.2 - 4.9 mmol/L; <100 - 80 g/L	Hgb <8.0 g/dL; <4.9 mmol/L; <80 g/L; transfusion indicated	Life-threatening consequences; urgent intervention indicated	Death
Definition: A disorder characterized by a reduction in the amount of hemoglobin in 100 ml of blood. Signs and symptoms of anemia may include pallor of the skin and mucous membranes, shortness of breath, palpitations of the heart, soft systolic murmurs, lethargy, and fatigability.					
Bone marrow hypocellular	Mildly hypocellular or <=25% reduction from normal cellularity for age	Moderately hypocellular or >25 - <50% reduction from normal cellularity for age	Severely hypocellular or >50 - <=75% reduction cellularity from normal for age	Aplastic persistent for longer than 2 weeks	Death
Definition: A disorder characterized by the inability of the bone marrow to produce hematopoietic elements.					
Disseminated intravascular coagulation	-	Laboratory findings with no bleeding	Laboratory findings and bleeding	Life-threatening consequences; urgent intervention indicated	Death
Definition: A disorder characterized by systemic pathological activation of blood clotting mechanisms which results in clot formation throughout the body. There is an increase in the risk of hemorrhage as the body is depleted of platelets and coagulation factors.					
Febrile neutropenia	-	-	ANC <1000/mm3 with a single temperature of >=38.3 degrees C (101 degrees F) or a sustained temperature of >=38 degrees C (100.4 degrees F) for more than one hour.	Life-threatening consequences; urgent intervention indicated	Death
Definition: A disorder characterized by an ANC <1000/mm3 and a single temperature of >=38.3 degrees C (101 degrees F) or a sustained temperature of >=38 degrees C (100.4 degrees F) for more than one hour.					

CTCAE Terms

- The terms might not always be listed the way you expect. Below are some examples of common AE's and the appropriate CTCAE v 5.0 term:
 - Pneumonia** *Lung infection*
 - Thrombocytopenia** *Platelet Count Decreased*
 - Neutropenia** *Neutrophil count decreased*
- Each system category also includes an "Other" option (for example, "Investigations – Other"), but only use as a last resort.

CTCAE Grades

- Grade 1** Mild
- Grade 2** Moderate
- Grade 3** Severe or medically significant but not immediately life-threatening
- Grade 4** Life-threatening consequences
- Grade 5** Death related to AE

Blood and lymphatic system disorders					
Adverse Event	Grade				
	1	2	3	4	5
Anemia	Hemoglobin (Hgb) <LLN - 10.0 g/dL; <LLN - 6.2 mmol/L; <LLN - 100 g/L	Hgb <10.0 - 8.0 g/dL; <6.2 - 4.9 mmol/L; <100 - 80g/L	Hgb <8.0 g/dL; <4.9 mmol/L; <80 g/L; transfusion indicated	Life-threatening consequences; urgent intervention indicated	Death
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Definition: A disorder characterized by an ANC <1000/mm3 and a single temperature of >38.3 degrees C (101 degrees F) or a sustained temperature of >=38 degrees C (100.4 degrees F) for more than one hour.					

Attribution

The attribution code describes, **in the opinion of the investigator**, how likely it is that the adverse event is due to protocol treatment:

Relationship	Attribution	Description
Unrelated to Investigational Agent/Intervention	1- Unrelated	The AE is <i>clearly not</i> related to the intervention
	2- Unlikely	The AE is <i>doubtfully</i> related to the intervention
Related to Investigational Agent/Intervention	3- Possible	The AE <i>may be</i> related to the intervention
	4- Probable	The AE is <i>likely</i> to be related to the intervention
	5- Definite	The AE is <i>clearly</i> related to the intervention

Status

The status code describes the state of the adverse event at various points throughout the study:

- New
- Continues at the same or lower grade
- Increased grade OR improved then worsened

General Rules for AE Reporting

- Record and report adverse events as they occur
- List all adverse events, regardless of clinical significance
 - Exception: Only report AEs present at baseline if they worsen
- On each cycle or reporting period: record the most severe grade experienced
- Avoid using "Other" CTCAE terms unless no specific CTCAE term applies
- When in doubt, document it!

Online Data Submission: Adverse Events

- CRA Workbench (legacy trials only)
- iMedidata Rave

Online AE Submission: CRA Workbench

SWOG Patient No: 236696 SWOG Study No: S1117 Reg Step: 1 Patient Initials (L,F,M): T,MM

[Patient Info](#) | [Forms](#) | [Expectations](#) | [Queries](#)

[Baseline](#) | [On Treatment](#) | [Adverse Events](#) | [Follow-up](#)

Refresh This page to see updates.

On Treatment Forms	Date Submitted
Click to complete or amend	Click to view confirmation
S1117 Adverse Event Form	
S1117 Treatment Form	
Translation Log	
Cycle Number = 1 Cycle Number = 0	

saved without submitting 7/6/2012

Online AE Submission: CRA Workbench

Reporting Period Start Date:
(Day 1 of this period)

Reporting Period End Date:
(Day 1 of next period. If final period, date of first contact after resolution of acute adverse events.)

Date of Most Recent Adverse Event Assessment:

Were adverse events assessed during this time period?
 No (explain in Comments)
 Yes, but no reportable adverse events occurred
 Yes, and reportable events occurred (complete Step 2)

Comments

Online AE Submission: CRA Workbench

Lookup by [CTC Category](#) Lookup by Keyword: rash

Part 2b: Complete adverse event information

Adverse Event	Grade	Attribution	Status	Comments
--	--	--	--	<input type="text"/>

Online AE Submission: CRA Workbench

Keyword: rash

- [IM00](#) - Allergic reaction/hypersensitivity (including drug fever)
- [SK11](#) - Rash/desquamation
- [SK22](#) - Rash: acne/acneiform
- [SKR72](#) - Rash: dermatitis associated with radiation - Chemoradiation
- [SKR71](#) - Rash: dermatitis associated with radiation - Radiation
- [SK20](#) - Rash: erythema multiforme (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis)
- [SK13](#) - Rash: hand-foot skin reaction

Can't see the page?
Disable your Pop-Up
Blocker!

Online AE Submission: CRA Workbench

Lookup by [CTC Category](#) Lookup by Keyword: rash

Part 2a: Lookup adverse event term

Part 2b: Complete adverse event information

Adverse Event	Grade	Attribution	Status	Comments
Rash/desquamation	2	3: Possible	--	<input type="text"/>

Display Grade Definitions

1. New
2. Continues at same or lower grade
3. Inc grade OR imprv then worsened

Online AE Submission: CRA Workbench

Adverse Event	Grade	Attribution	Status	Comments
Rash/desquamation	2	3 : Possible	1 : New	

Online AE Submission: CRA Workbench

[S1007 Adverse Event Summary Form](#)

[Reporting Period = 6 mo - 1 yr: Reporting Period 08/22/2011 - 03/05/2012](#)

[Reporting Period = 0-6 months: Reporting Period 03/24/2011 - 08/22/2011](#)

Online AE Submission: CRA Workbench

Part 1: Complete general information about the adverse events assessed since the last form

Reporting Period: 0-6 months

Reporting Period Start Date: 03/24/2011
(Day 1 of this period)

Reporting Period End Date: 08/22/2011
(Day 1 of next period. If final period, date of first contact after resolution of acute adverse events.)

Date of Most Recent Adverse Event Assessment: 08/22/2011

Were adverse events assessed during this time period?
Yes, but no reportable adverse events occurred

Comments

[Edit Part 1](#)

Online Data Submission: Adverse Events

- CRA Workbench (legacy trials only)
- iMedidata Rave

Online AE Submission: Medidata Rave

Subject: 202289
Page: Adverse Events Assessment - Cycle 01

Reporting period start date: 02 Mar 2016

Reporting period end date: 18 Mar 2016

View adverse events associated during this time period? Yes No

If yes, did the patient experience any reportable adverse events during this reporting period? Yes No

Date of most recent adverse event assessment: 18 Mar 2016

Comments:

If you're not done completing this form, but want to save your work for later, check the box below and click the Save button. Note that all checks will still fire.

Save this form, but don't submit to SROCC yet.

Printable Version View PDF from Key

DPF Version 012 Page Generated: 18 Mar 2016 10:54:39 Pacific Daylight Time

Save Cancel

Online AE Submission: Medidata Rave

Subject: 202289
Page: Adverse Events Assessment - Cycle 01

Reporting period start date: 02 Mar 2016

Reporting period end date: 18 Mar 2016

View adverse events associated during this time period? Yes No

If yes, did the patient experience any reportable adverse events during this reporting period? Yes No

Date of most recent adverse event assessment: 18 Mar 2016

Comments:

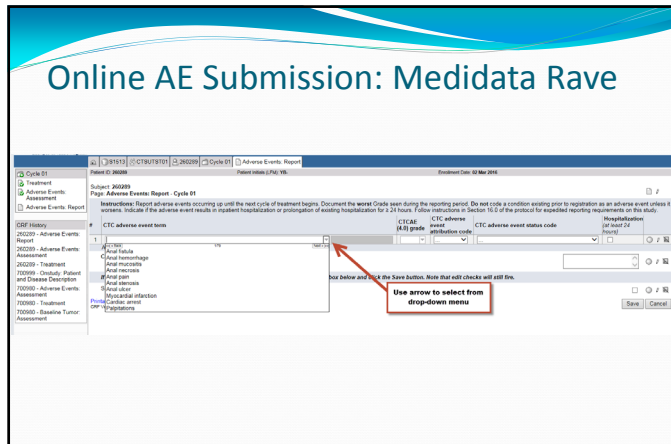
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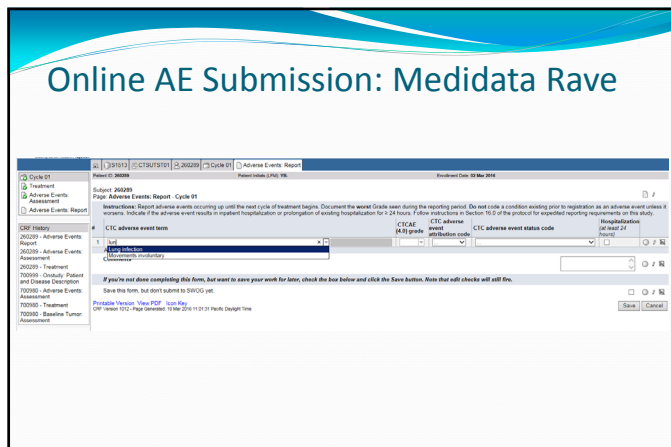
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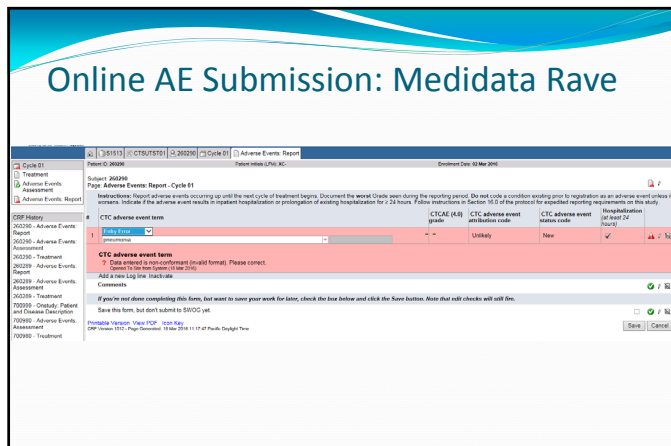
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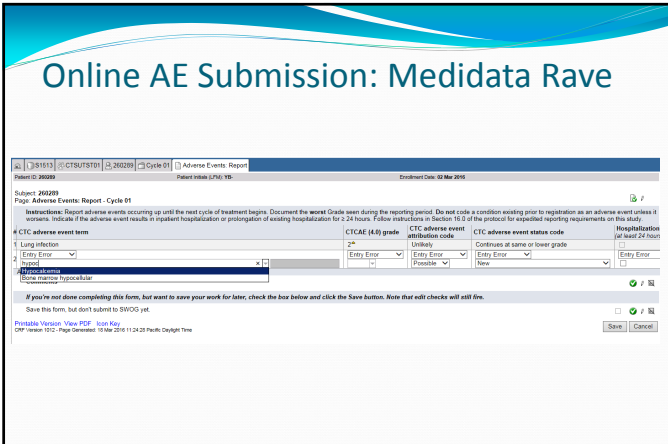
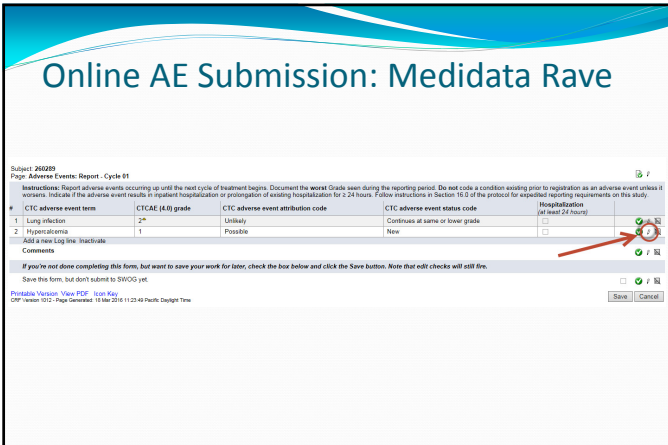
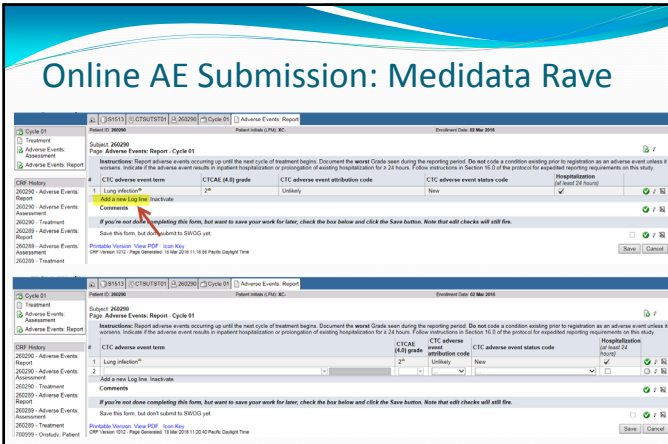
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Save Cancel









Online AE Submission: iMedidata Rave Recent Developments

Form Instructions ?

- * red asterisk before a field denotes a required response
- * Start date of DRG: 02/01/2016

Adverse event term (CTCAE v4.0)	Adverse event grade description (CTCAE v4.0)	Attribution to study intervention	Hospitalization	Life threatening	Death	Disability	Congenital anomaly/birth defect	Required intervention	Other	SAE report recommended (derived)	Date first learned (derived)	Time zone (derived)	Adverse event term (CTCAE v4.0)

Add a new Log line [Inactivate](#)

Comments [Save](#) [Cancel](#)

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Save this form, but don't submit to SWOG yet [Save](#) [Cancel](#)

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DRP version 015 - Page Generated: 10 Mar 2016 12:20:38 Pacific Daylight Time

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BreastQuestion@crab.org LungQuestion@crab.org
 CancerControlQuestion@crab.org LymphomaQuestion@crab.org
 GIQuestion@crab.org MelanomaQuestion@crab.org
 GUQuestion@crab.org MyelomaQuestion@crab.org
 GYNquestion@crab.org S1400Question@crab.org
 LeukemiaQuestion@crab.org

And refer to the ORP Manual available at
www.SWOG.org
