

Adverse Event CRA Orientation Presentation Case Studies

CASE # 1

CALGB Patient ID # 45719 (M.,C.) Hospital Id # 2489742, at St Francis Medical Center is a 70-year old woman with breast cancer randomized to Arm B (Capecitabine) of CALGB 49907. Her first cycle of treatment began June 05, 2007 and ended on June 26, 2007. She developed grade 2 diarrhea on day 11 of cycle 1 and stopped taking the drug on Day 14. She reported moderate fatigue and could no longer climb a flight of stairs – possible related to the study drug (per/MD). On day 16 of cycle 1, she presented to the ER with diarrhea, abdominal pain, and dehydration – all grade 3 probably related to the study drug (per/MD). She was admitted to the hospital and treated with IV fluids and anti-diarrheal medication. All labs were within normal limits and no other complaints.

1. Complete the C-719 CALGB: 49907 Adverse Event (AE) Form.

CASE # 2

CALGB Patient Id # 31438 (L., M.) was diagnosed with CD20+ B-cell Non-Hodgkin's Lymphoma and underwent treatment on CALGB 50201 with no later treatment. Approximately 2 years after protocol treatment on the study, he presented to his physician with shortness of breath, body aches, fatigue, and fever. His CBC's showed a WBC of 51.7×10^3 and he was diagnosed with Acute Monocytic Leukemia (AML), which was later confirmed by bone marrow.

1. Should these events be reported via AdEERS? No Yes
2. If not, how should the events be reported? _____

3. If the events should be reported via AdEERS, provide the appropriate MedDRA code(s).

CASE # 3

CALGB Patient Id # 13015 (H., R.) is a 65-year-old man diagnosed with hormone refractory prostate cancer who was registered to CALGB 90004. His blood draw from week 2 of cycle 3 showed an ANC of $450/\mu\text{l}$ and a platelet count of $35,000/\mu\text{l}$.

1. Should these events be reported via AdEERS? No Yes
2. If not, how should the events be reported? _____

3. If the events should be reported via AdEERS, provide the appropriate MedDRA code(s).

CASE # 4

CALGB Patient Id # 29359 (D., J.) was a woman diagnosed with metastatic colon cancer and registered to CALGB 80203. She was randomized to Arm D (Oxaliplatin/5-FU/Leucovorin with Cetuximab (C225). During the first cycle of therapy the patient developed a Grade 2 acneiform skin rash and her ANC was $950/\text{mm}^3$.

1. Are these adverse events expected or unexpected? Expected Unexpected
2. Should these events be reported via AdEERS? No Yes
3. If not, how should the events be reported? _____

Adverse Event CRA Orientation Presentation

CALGB 49907

18.1 Phase 2 and 3 Trials Utilizing an Agent under a CTEP IND or non-CTEP IND: AdEERS Expedited Reporting Requirements for Adverse Events That Occur Within 30 Days¹ of the Last Dose of the Investigational Agent (CALGB 49907 Arm B)

	Grade 1	Grade 2	Grade 2	Grade 3		Grade 3		Grades 4 & 5 ²	Grades 4 & 5 ²
	Unexpected and Expected	Unexpected	Expected	Unexpected with Hospitalization	without Hospitalization	Expected with Hospitalization	without Hospitalization	Unexpected	Expected
Unrelated Unlikely	Not Required	Not Required	Not Required	10 Calendar Days	Not Required	10 Calendar Days	Not Required	10 Calendar Days	10 Calendar Days
Possible Probable Definite	Not Required	10 Calendar Days	Not Required	10 Calendar Days	10 Calendar Days	10 Calendar Days	Not Required	24-Hrs; 5 Calendar Days	10 Calendar Days
¹ Adverse events with attribution of possible, probable, or definite that occur <u>greater</u> than 30 days after the last dose of treatment with an agent under a CTEP IND or non-CTEP IND require reporting as follows: AdEERS 24-hour notification followed by complete report within 5 calendar days for: <ul style="list-style-type: none"> • Grade 4 and Grade 5 unexpected events AdEERS 10 calendar day report: <ul style="list-style-type: none"> • Grade 3 unexpected events with hospitalization or prolongation of hospitalization • Grade 5 expected events 									
² Although an AdEERS 24-hour notification is not required for death clearly related to progressive disease, a full report is required as outlined in the table.									

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Note: All deaths on study require both routine and expedited reporting regardless of causality. Attribution to treatment or other cause should be provided.

Grade						
MedDRA	Adverse Event	0	1	2	3	4
10012174	Dehydration	none	dry mucous membranes and/or diminished skin turgor	requiring IV fluid replacement (brief)	requiring IV fluid replacement (sustained)	physiologic consequences requiring intensive care; hemodynamic collapse
Also consider Diarrhea, Vomiting, Stomatitis/pharyngitis (oral/pharyngeal mucositis), Hypotension.						
10012745	Diarrhea Patients without colostomy:	none	increase of < 4 stools/day over pre-treatment	increase of 4-6 stools/day, or nocturnal stools	increase of 7 stools/day or incontinence; or need for parenteral support for dehydration	physiologic consequences requiring intensive care; or hemodynamic collapse
90004048	Patients with a colostomy:	none	mild increase in loose, watery colostomy output compared with pretreatment	moderate increase in loose, watery colostomy output compared with pretreatment, but not interfering with normal activity	severe increase in loose, watery colostomy output compared with pretreatment, interfering with normal activity	physiologic consequences, requiring intensive care; or hemodynamic collapse
90004052	Diarrhea associated with graft versus host disease (GVHD) for BMT studies, if specified in the protocol.	none	>500 - 1000ml of diarrhea/day	>1000 - 1500ml of diarrhea/day	>1500ml of diarrhea/day	severe abdominal pain with or without ileus
90004056	<i>For Pediatric BMT studies, if specified in the protocol.</i>		<i>>5 - ≤10 ml/kg of diarrhea/day</i>	<i>>10 - ≤15 ml/kg of diarrhea/day</i>	<i>>15 ml/kg of diarrhea/day</i>	-
Also consider Hemorrhage/bleeding with grade 3 or 4 thrombocytopenia, Hemorrhage/bleeding without grade 3 or 4 thrombocytopenia, Pain, Dehydration, Hypotension.						
10013836	Duodenal ulcer (requires radiographic or endoscopic documentation)	none	-	requiring medical management or non-surgical treatment	uncontrolled by outpatient medical management; requiring hospitalization	perforation or bleeding, requiring emergency surgery
10013946	Dyspepsia/heartburn	none	mild	moderate	severe	-
10030220	Dysphagia, esophagitis, odynophagia (painful swallowing)	none	mild dysphagia, but can eat regular diet	dysphagia, requiring predominantly pureed, soft, or liquid diet	dysphagia, requiring IV hydration	complete obstruction (cannot swallow saliva) requiring enteral or parenteral nutritional support, or perforation
Note: If the adverse event is radiation-related, grade <u>either</u> under Dysphagia- esophageal related to radiation <u>or</u> Dysphagia- pharyngeal related to radiation.						
10048899	Dysphagia- <u>esophageal</u> related to radiation	none	mild dysphagia, but can eat regular diet	dysphagia, requiring predominantly liquid, pureed or soft diet	dysphagia requiring feeding tube, IV hydration or hyperalimentation	complete obstruction (cannot swallow saliva); ulceration with bleeding not induced by minor trauma or abrasion or perforation
Also consider Pain due to radiation, Mucositis due to radiation. Note: Fistula is graded separately as Fistula- esophageal.						
10013950	Dysphagia - <u>pharyngeal</u> related to radiation	none	mild dysphagia, but can eat regular diet	dysphagia, requiring predominantly pureed, soft, or liquid diet	dysphagia, requiring feeding tube, IV hydration or hyperalimentation	complete obstruction (cannot swallow saliva); ulceration with bleeding not induced by minor trauma or abrasion or perforation

Grade						
MedDRA	Adverse Event	0	1	2	3	4
10000573	Vision- night blindness (nyctalopia)	normal	abnormal electro-retinography but asymptomatic	symptomatic and interfering with function, but not interfering with activities of daily living	symptomatic and interfering with activities of daily living	-
10034960	Vision- photophobia	normal	-	symptomatic and interfering with function, but not interfering with activities of daily living	symptomatic and interfering with activities of daily living	-
90004080	Ocular/Visual-Other (Specify, _____)	normal	mild	moderate	severe	unilateral or bilateral loss of vision (blindness)
PAIN						
10000085	Abdominal pain or cramping	none	mild pain not interfering with function	moderate pain: pain or analgesics interfering with function, but not interfering with activities of daily living	severe pain: pain or analgesics severely interfering with activities of daily living	disabling
10003239	Arthralgia (joint pain)	none	mild pain not interfering with function	moderate pain: pain or analgesics interfering with function, but not interfering with activities of daily living	severe pain: pain or analgesics severely interfering with activities of daily living	disabling
Arthritis (joint pain with clinical signs of inflammation) is graded in the MUSCULOSKELETAL category.						
10006002	Bone pain	none	mild pain not interfering with function	moderate pain: pain or analgesics interfering with function, but not interfering with activities of daily living	severe pain: pain or analgesics severely interfering with activities of daily living	disabling
10008479	Chest pain (non-cardiac and non-pleuritic)	none	mild pain not interfering with function	moderate pain: pain or analgesics interfering with function, but not interfering with activities of daily living	severe pain: pain or analgesics severely interfering with activities of daily living	disabling
10013935	Dysmenorrhea	none	mild pain not interfering with function	moderate pain: pain or analgesics interfering with function, but not interfering with activities of daily living	severe pain: pain or analgesics severely interfering with activities of daily living	disabling
10013944	Dyspareunia	none	mild pain not interfering with function	moderate pain interfering with sexual activity	severe pain preventing sexual activity	-
Dysuria is graded in the RENAL/GENITOURINARY category.						