Date: October 15, 2008

Topic: CTCAE v3.0 Help Desk Tickets – WG # 7 SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps)

From: Ann Setser

I have been reviewing the new CTCAE v3.0 grading scheme, as I am currently developing new clinical trials that require the new CTCAE. I have a few questions and clarifications required. Could you please review and let me know what needs to be done in the instances listed below?

Myelodysplasia Grade 3 states '(blasts <5%)' Grade 4 states (blasts > 5%) What happens at =5%, should this be incorporated in to Grade 3 or 4? Ann's Reply:

CTEP Response: GRADE 3 SHOULD READ 'LESS THAN OR EQUAL TO 5%; GRADE 4 IS LESS THAN 5%

Suggestions for addition to CTCAE v4.0: Oncologic emergencies

* MedDRA: Pericardial effusion malignant SOC Neoplasms benign, malignant and unspecified (incl cysts and polyps)
* MedDRA: Leukostasis SOC Neoplasms benign, malignant and unspecified (incl cysts and polyps)
* hemorrhage melanoma lesion – not in MedDRA
  + Could this be LLT Hemorrhagic tumor necrosis?; LLT Tumor hemorrhage?

Date: October 15, 2008

Topic: CTCAE v3.0 Help Desk Tickets SOC: General disorders and administration site conditions

From: Ann Setser

**Death**

I am currently going over our default grading rules and was somewhat surprised to see that while there is no Grade 4 for Acne there is Grade 5 - Death.

Constitutional Symptoms - **Rigors/chills** - Grade 2 - states 'incidated', should this state 'indicated'?

CTEP Response: YES THE WORD IS A TYPO AND SHOULD BE INDICATED.

Thank you for looking into this issue for us.  I have appended the information from the CTEP link.   We are interested in getting additional guidance on CTCAE terms 'death' and 'sudden death' , beyond that what is provided below in order to better guide our clinical sites on the selection criteria around the use of these terms ( ie use in the setting of normal ADL, seen within an hour of death,  (yes/no) cardiac or respiratory risk factors etc.).

Sites recently have started to use the term 'DEATH'  in circumstances when a subject dies at home or in a hospice setting, when no autopsy is done, and the only known information is provided in an obituary column.  Sites are calling these 'unexplained death or unattended death' which codes to death in MedDRA.

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| **Lower Level Term** | **Preferred Term** | **High Level Term** | **High Level Group Term** | **SOC** | **Primary** |
| Death | Death | Death and sudden death | Fatal outcomes | Genrl | Y |

In the past these deaths would be called out as disease progression (underlying malignancy grade 5) as often the subject had been on treatment for a period of time, may have been withdrawn from treatment because of radiographic confirmed disease progression or the investigator had no other known reason to select . If the subject was losing weight, had fatigue, loss of appetite etc the site may select the AE term cachexia grade 5.

It was rare to have AEs of 'SUDDEN DEATH' reported , however, recently, sites are using the term 'sudden death' for those cases similar to those described above, primarily because the death was unattended or unwitnessed.  Sometimes the sites also select the AE terms grade 5 cardiac arrest, or cardiopulmonary arrest.  Perhaps you could also provide CTCAE guidance on when to use these terms of cardiac arrest vs sudden death.   Please note that sudden death codes under the secondary SOC of cardiac disorders under the HLT of ventricular arrhythmias and cardiac arrest in MedDRA.

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| **Lower Level Term** | **Preferred Term** | **High Level Term** | **High Level Group Term** | **SOC** | **Primary** |
| Sudden death | Sudden death | Death and sudden death | Fatal outcomes | Genrl | Y |
| Sudden death | Sudden death | Ventricular arrhythmias and cardiac arrest | Cardiac arrhythmias | Card | N |

Suggestions for addition in CTCAE v4.0:

* MedDRA LLT & PT Temperature intolerance
* MedDRA LLT & PT Extravasation