Date: October 15, 2008

Topic: CTCAE v3.0 Help Desk Tickets – WG # 9 SOC Renal and urinary disorders

From: Ann Setser

Issue: AE Term – Renal failure

Subject: Need help with definition of Renal Failure Only 2 grades are allowed:

3 or 4 for RENAL FAILURE Since renal failure is not an entity alone, but a medical decision based on multiple facts, one has to assume that the grading of an AE is based, not on clinical judgment, but on an objective fact. There is no question regarding the meaning of Renal Failure in CTC version 2. But version 3 left a door open not to assume dialysis, but to factor in renal failure criteria but not have the person on chronic dialysis. I am at a deadend in attempting to understand why the distinction was not continued from version 2 with no explanation of what version 3 means from an objective and measurable framework. Version 2 had said: Grade 3: "requires dialysis but reversible" - the assumption was acute dialysis; Grade 4: "requires dialysis and irreversible" - the assumption was chronic dialysis. Version 3 says: Grade 3: "chronic dialysis not indicated" - the assumption was acute dialysis was indicated Grade 4: "chronic dialysis or renal transplant indicated" - assumption that chronic dialysis was indicated or patient was waiting for renal transplant. Now you can tell that I am not well-schooled in this discipline. I am a nurse attempting to work with physicians and patients. I need the easy answer as to the criteria to evaluate CTCAE Version 3 for Grade 3 Renal Failure.

V3.0:

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| RRenal failure | RRenal failure | - | - | Chronic dialysis not indicated | Chronic dialysis or renal transplant indicated | Ddeath |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| RRenal failure | n | - | - | rrequiring dialysis, but reversible | requiring dialysis and irreversible |

V2.0:

CTEP Response: Since dialysis is mentioned in both descriptions of Grade 3, yes, Grade 3 means dialysis.

Dear CTEP,

NCI CTC is a great grading tool for cancer treatment related toxicities.  It is important to promote its use in all clinical studies for accurate reporting of safety profiles and the comparability among publications.  We observed inconsistencies of reporting among international investigators.  To better follow CTCAE, I would like to confirm with you several common AE reporting practices and post some questions.

1. although CTC terms are matched into MedDra.  However, renal failure, renal failure acute, renal disorder, renal impairment, blood creatinine increased, creatinine renal clearance decreased, glomerular filtration rate decreased, azotaemia, Nephropathy toxic, etc. in MedDra are all potentially reported and grade for GFR or renal failure according to CTC.  How much freedom for term selection, by CTC or MedDra?  Either way could affect reporting sensitivity and specificity in the final analyses.  In other words, a good reporting practice should enable us to identify unique undefined events and keep accurate counting for incidences

In my view, CTC is grading system, but not a dictionary.  CTC should be carefully followed when reporting cancer-treatment related toxicities.  Other events should be reported and coded by MedDra.  Training on CTC should be given to promote good reporting

Consider adding to CTCAE v4.0:

* dysuria (separate it from cystitis)
  + Dysuria = MedDRA LLT & PT

Date: October 15, 2008

Topic: CTCAE v3.0 Help Desk Tickets – SOC Investigations

From: Ann Setser

Issue: AE Term- **Calcium**

Quick question about the formula published in CTCAE v3.0 for corrected

calcium. Shouldn't the formula be: corrected calcium - total calcium +

0.8... vs. -0.8? Using subtraction, you actually get an even lower level vs.

correcting to a high (more normal) level. We are trying to set up a

programming solution in C3D and one of the programmers was questioning this.

CTEP Response: This has generated a couple of queries.

Here is an example:

The formula is:

Corrected Ca = total Ca - (0.8)(albumin-4)

Note that the supra text " 4 " in the CTCAE is a reference, not the value to

the 4th power.

An example of application of the formula. A patient's measured Ca is 10 and

albumin is 2.

Therefore, Corrected CA = 10 - (0.8) (2-4) = 10 - (0.8)(-2) = 10 - (-1.6)=

10 + 1.6 = 11.6.

What I think throws people is the double minus part of the equation, but the

equation is in fact correct.

Alternatively, we could have written the equation as:

Corrected CA = total ca + (0.8)( 4- albumin)

Which is mathematically equivalent to the formula in the CTCAE.

Issue: **Hyperuricemia**

Patient with UA of 10.1 but with no physiological consequences is graded higher (gr 4) than a patient with UA of 10 with physiological consequences (gr 3). Consider a modification for CTC v. 4 including physiological consequences or life-threatening physiological consequences in definition of grade 4.

I have been reviewing all of the updates for CTCAE in the caDSR to make

sure that all entries match for CTEP clinical trials that use both CTCAE

and the CDEs.

I noticed a typographical error for the Grade of one Blood/Bone Marrow

adverse event in the CTCAE document dated December 12, 2003.

For the Adverse Event, **Lymphopenia**

for Grade 3, the " / " is missing after " 200 ".

The range of laboratory values should read

<500 - 200/mm3

<0.5 - 0.2 x 109 /L

in order to match the other laboratory range values for the other grades for this AE.

'Hypercholestremia' confirm spelling, should it be **'Hypercholesteremia'**?

CTEP Response: YES THIS IS A TYPO AND SHOULD BE HYPERCHOLESTEREMIA.

**CD4 count**, grade 3 change 2nd value from: <0.2 x 0.05 x 109/L, to: <0.2 - 0.05 x 109/L

**Lymphopenia**, grade 1 change 2nd value from: <LLN x 0.8 – 109/L, to: <LLN - 0.8 x 109/L

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**Fibrinogen**

Grade 1 change 2nd value from: or <25% decrease from baseline, to: or <25% decrease from baseline

Grade 2 change 2nd value from: or 25 – <50% decrease from baseline, to: or >25 – 50% decrease from baseline

Grade 3 change 2nd value from: or 50 – <75% decrease from baseline, to: or >50 – 75% decrease from baseline

Grade 4 change 2nd value from: or 75% decrease from..., to or >75% decrease from...

I would like to suggest adding and defining the adverse event term of **Pancytopenia** to CTCAE v4.0

Please consider adding to CTCAE v4.0 “hyperammonemia”

There is no Grade 1 **hypophosphatemia** as the LLN of results in CRIS is 2.5mg/dL. Therefore, any of our patients that have a phosphorous lower than 2.5 are automatically being graded as at least Grade 2. I am wondering if this was an error or intentional

For reporting pediatric AEs, the CTCAE v3.0 online instructions and guidelines advise that "unless otherwise specified, **pediatric** criteria are identical to those for adults." Under Metabolic / Laboratory

category, **Creatinine** contains such pediatric-specific criteria in the remark "Adjust to age-appropriate levels for pediatric patients." I understand this adjustment to refer to the Creatinine normal range, though I'm not clear on why this particular remark is only found with

Creatinine (of the quantitative lab-based AEs) when other lab tests also consider age in determining the normal range.

"Local lab normal ranges always take precedence for reporting purposes over the CTCAE values" because Kim described an experience where they were debating the grade to repoort on a cooperative group trial and when they consulted with the cooperative group, they were told to ignore the normal ranges, because the CTCAE ranges were the final authority.

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1. if at baseline WBC=3500, ANC=2000; cycle 1 WBC=875, ANC=500 [same differential percentage due to ANC decrease], should G4 WBC, G3 ANC or both be reported?

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