Genital Bleeding in MTN 020

Annual Meeting
February 22, 2012
Background

- Genital Bleeding is common
  - Includes menses
  - Includes intermenstrual bleeding (IMB)

- Determining whether genital bleeding constitutes an “adverse event” will vary by protocol
The VOICE Experience

- “Only unexpected bleeding is an AE”

- Expected bleeding includes
  - Menses
  - Bleeding from missed oral contraceptive pill (ocp)
  - Spotting within one year of starting depo
  - Spotting within 3 months of ocp initiation

- Unexpected bleeding includes
  - Heavy or prolonged menses
  - Unexplained bleeding in between menses
VOICE AEs

- 11,500 Adverse Events
- Genital Bleeding Assessment Form
- 484 for bleeding events to date (4.2%)
  - Menorrhapsia (137)
  - Metrorrhaphia (276)
  - Menometrorrhaphia (57)
  - Post coital bleeding (14)
Your Feedback
The MTN 020 Response

- Simplify

  And

- Don’t disregard bleeding presumed to be due to another cause
Genital Bleeding in MTN 020

☐ Is this bleeding event consistent with the participant’s baseline bleeding pattern?
  ■ Yes = NO AE
  ■ No  = AE
Implications

- Obtaining an accurate baseline bleeding history will be imperative
- The level of detail will be at the site’s discretion
- Goal: A reasonable person reading the baseline history can determine whether a current bleeding event is consistent with baseline or not
Scenario #1

- 22 year old woman at screening describes regular moderate flow menstrual periods occurring every 24-32 days and lasting 3-6 days
  - She is started on depo-provera during the screening period
  - One month after enrollment she reports a 14 day bleeding episode occurring 30 days after her last menses
  - Has an AE occurred?
Scenario #2

- 22 year old woman describes regular moderate flow menstrual periods occurring every 24-32 days and lasting 3-6 days at screening

- She is started on depo-provera during the screening period

- One month after enrollment she reports 3 days of spotting 2 weeks after her last menstrual period

- Has an AE occurred?
Scenario #4

- 22 year old woman describes unpredictable spotting on depo-provera at the screening visit. The spotting lasts 2-7 days, is light in flow, and can occur anywhere from 2 weeks to 3 months apart.

  - 2 month after enrollment she reports 3 days of spotting 2 months after her last spotting episode
  - Has an AE occurred?
One BIG caveat

- Multiple bleeding episodes deemed to be AEs may ultimately be captured as one open ended AE once a new pattern is identified.
Ongoing Metrorrhagia

- 22 year old with monthly menses lasting 4-6 days at enrollment is enrolled into MTN 020
- In the screening period she has an implant placed for contraception
- At Month 1 she reports a 3 day period of light vaginal bleeding 2 weeks after her last menstrual period.
  - An AE for metrorrhagia is filed
Ongoing Metrorrhagia

- At month 2, the participant reports another episode of light bleeding this time lasting 5 days and occurring 2 weeks after the last episode
  - Pelvic exam is unremarkable

- Is this a new AE or a continuation of the previously filed AE?

- Clinician discretion
  - File a new AE and consider an open ended AE with her next event  OR
  - Update the last AE to be ongoing
Recurring Bleeding AEs in VOICE

- 11,500 Adverse Events
- 484 for bleeding events
  - Menorrhagia (137 events in 120 pts)
  - Metrorrhagia (276 events in 215 pts)
  - Menometrorrhagia (57 in 49 pts)
  - Post coital bleeding (14 in 14 pts)
- 56 participants with 2 or more identical bleeding AEs
  - 19 of these with >2 AEs
Amenorrhea

- Unexplained amenorrhea should be recorded as a pre-existing condition.
- Amenorrhea secondary to contraceptive use need not be recorded as pre-existing.
- Amenorrhea in follow-up is an AE if it is different from baseline and NOT explained by contraception or pregnancy (as per the tox table).
Evaluating Abnormal Bleeding

- A new AE for genital bleeding should prompt a pelvic exam
- Whether bleeding in the context of an open AE should be evaluated is per clinician discretion
Please Tell Us….

☐ Is this clear? Logical?

☐ What challenges to this reporting method do you foresee?

☐ Will you miss the genital bleeding assessment form?

☐ How detailed should training at your site be regarding genital bleeding assessment, documentation and reporting?
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