# OCTRI Research Forum
## Adverse Event Coding

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# Why is Adverse Event Coding Important?

- Coding standardizes AE data for analysis
  - Saves time (less data cleaning – faster analysis)
  - Helps prevent misinterpretation of data
  - Helps identify drug/device related problems
- To comply with regulatory requirements for reports of AEs
  - FDA and international regulatory authority requirements
- Particularly important for studies with:
  - Safety endpoints
  - Multiple sites
    - With multiple investigators, coordinators, data managers, and IRBs
  - International trials
  - FDA and other regulated trials where study results could impact large population of patients

# Common Medical Dictionaries

- MedDRA
  - AE classification for most pharmaceutical, biologic, vaccines and drug/device combination products trials
  - Developed by International Council on Harmonization (ICH)
  - OHSU has a license (more on this later)

- CTCAE
  - coding and grading AEs in oncology trials
  - Developed by NIH
  - Free

# Common Medical Dictionaries

- WHODrug
  - Drug reference dictionary
  - Coding concomitant medications makes it easier to identify drug related problems
  - Standardizes drug names and includes information on active ingredients, anatomical and therapeutic classifications from nearly 150 countries
  - Prescription, over the counter, herbal remedies, biotech and blood products, diagnostic substances and contrast media

# More Medical Device Dictionaries

- Some dictionaries are very specific to your area of research such as:
  - Toxicity grading scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventative Vaccine Clinical Trials (FDA)

  - FDA Medical Device Report (MDR)
    - Linked to the International Medical Device Regulators Forum (IMDRF) terminologies and the NCI Thesaurus (NCIt)

  - Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events

# Best Practices

- Select the right dictionary or dictionaries for your trial
  - What is required by regulatory authorities?
  - What is used by other experts in your field of research?
- Select when you are writing your protocol
  - Consider the next protocol
    - Will you combine the data in a repository
    - Will this study be the basis of future trials (Phase I, II, III)
- Stick with the same dictionary version for the duration of the trial (and future trials)
- Train, train, train your staff
  - Standardization only works if you train the people collecting and coding the data
- Document, document, document
  - Decisions about coding, processes, queries, communications with other sites/sponsors, and training

# Who can code AEs/SAEs?

- ▶ Should have training in the clinical area being studied
- ▶ MD/RN/LIP or appropriately trained coordinators
  - ▶ Naming
  - ▶ Grading
  - ▶ Attribution must be done by an investigator
- ▶ Should be trained on the coding dictionary
- ▶ Should be trained on the protocol and reporting requirements to be able to flag issues for:
  - ▶ IRB, DSMB/C, protocol required reporting

# Documenting Adverse Events and Con meds Real World Examples using CTCAE

# CTCAE

▶ What is the definition of an Adverse Event?

- <u>NEW</u> or <u>WORSENING</u> symptom or lab value from baseline

▶ Which version of CTCAE are you using? Version 4?  Version 5? Version 6?

# CTCAE – Version 5

▶ If you would like to follow along in CTCAE

▶ https://view.officeapps.live.com/op/view.aspx?src=https%3A%2F%2Fctep.cancer.gov%2Fprotocoldevelopment%2Felectronic_applications%2Fdocs%2FCTCAE_v5.0.xlsx&wdOrigin=BROWSELINK

# Baseline

- ▶ Importance of detailed baseline history
  - ▶ Non gradable
    - ▶ ie.  Diabetes
    - ▶ Surgical history
    - ▶ H/o Chron's disease
    - ▶ H/o DVT

  - ▶ Gradable
    - ▶ **MUST** use CTCAE terminology

# Baseline:

- ▶ Patient has the following baseline history:

| Term | Start Date | End Date |
|------|-----------|----------|
|      |           |          |
|      |           |          |

- ▶ Patient has the following baseline symptoms:

| CTCAE v5Term | Start Date | End Date | Grade |
|--------------|-----------|----------|-------|
|              |           |          |       |
|              |           |          |       |

- ▶ Patient is on the following baseline meds:

| Medication | Dose | Indication | Route | Frequency | Start Date | End Date |
|-----------|------|-----------|-------|-----------|-----------|----------|
|           |      |           |       |           |           |          |
|           |      |           |       |           |           |          |

## On Study Intervention

▶ AE's while on Study

| CTCAE v5Term | Start Date | End Date | Grade |
|---|---|---|---|
| | | | |
| | | | |
| | | | |

▶ Medications started while on study:

| Medication | Dose | Indication | Route | Frequency | Start Date | End Date |
|---|---|---|---|---|---|---|
| | | | | | | |
| | | | | | | |

## Mr. Beckham

▶ Mr. Beckham is here on 12/24/18 for his C2 visit on the GALAXY trial. Mr. Beckham states that he has been having muscle aches similar to what he had a few years ago, however, the pain is now currently lasting longer and more difficult to treat. He is taking ibuprofen 800 mg TID and Dilaudid 2-4 mg every 3 hours to control the pain. He mentioned that he is also having chills and does not have much of an appetite. These symptoms started on 12/18/18. He also has noticed that his hair seems thinner than normal; he first noticed this about two weeks ago.

▶ He also reports ongoing heartburn and diarrhea since starting on study.  He is having about 4-5 bowel movements/day.

# Original baseline for Mr. Beckham

▶ Myalgias, gr 1, start 2010

▶ Baseline bowel movements 1-2/day

▶ Gr 1 Diarrhea Increase of <4 stools per day <u>over baseline</u>; mild increase in ostomy output compared to baseline

▶ Gr 2 Increase of 4 - 6 stools per day <u>over baseline</u>; moderate increase in ostomy output compared to baseline

▶ Gr 3 Increase of >=7 stools per day <u>over baseline</u>; <u>incontinence</u>; hospitalization indicated; severe increase in ostomy output compared to baseline; limiting self care ADL

# Adverse events/meds

**<u>Baseline:</u>**

Myalgias, gr 1, start 2010 <u>stop 12/23/18</u>

**<u>AE's:</u>**

▶ Myalgias gr. 2; start date 12/24/18

▶ Chills, gr 1; start date 12/18/18

▶ Anorexia, gr 1, start date 12/18/18

▶ Alopecia gr. 1; start date 12/10/18

▶ Dyspepsia, gr 1, start 12/1/18

# 35 year old breast cancer patient

Comes in for C2D1 receiving IV SOC plus an oral study drug.   She has developed a red, raised rash on her chest and face that she says is itchy and keeping her awake at night.  The lesions are pus-filled and she is starting to develop a fever (temp 99).    Her doctor wants to start her on an oral antibiotic for 10 days which she will start today.   She has noticed that since starting chemo she is having increased hot flashes which are waking her up 4-5 nights/week.  Her husband has had a "cold" this week and yesterday she noticed the onset of a sore throat, cough with yellow sputum and she feels like she has something running down the back of her throat.

# Adverse events

▶ Skin infection gr 2 (oral antibiotic)

▶ Acneiform rash, gr 2 (must list the type of rash)

▶ NO fever (too low to record per CTCAE)

▶ Sore throat, gr 1

▶ Productive cough, gr 1

▶ Postnasal drip, gr 1

▶ Hot flashes gr 2

## Upper respiratory infection (sore throat, cough, postnasal drip)

▶ Gr 2  Upper respiratory infection - Moderate symptoms; oral intervention indicated (e.g.,antibiotic, antifungal, antiviral)

▶ Gr 3  IV antibiotic, antifungal, or antiviral intervention indicated; radiologic, endoscopic, or operative intervention indicated

▶ THERE IS <u>NO</u> GRADE 1 UPPER RESPIRATORY INFECTION

## Let's practice!      C1D1    6/25/15

▶ **Patient reports the following medications at baseline:**
  ▶ Asprin 325 mg PO BID for CVA prophylaxis beginning August 1995 Changed to 325 mg PO Daily 7/8/15
  ▶ Losartan 100 mg po daily start 2014

▶ **Patient reports the following complaints at baseline:**
  ▶ Belching, Grade 1 beginning May 2015
  ▶ Numbness, gr 1,  on top of right hand feels intermittently cold,
    ▶ Began ~ 4 months ago
  ▶ High blood pressure, ??????
  ▶ Weight loss, gr 1, start June 2015
  ▶ Tremor, gr 1, not active at baseline

# On study medications

- **Patient reports the following medications since beginning treatment:**
- Pulmonary Rehab x 4 weeks during September
- Decadron 2mg tabs, 6mg TID daily starting 11/28/15. Taper starting 12/3/15: 6mg TID x 7 days, 6mg BID x 7 days, 3mg BID x 7 days, 3 mg daily x 7 days. Restarted 1/19/15 2mg PO BID.  Reduced to 1mg PO BID starting 2/9/16.

# On study Adverse Events

- Urinary tract infection, gr 1, start 7/15/15
- Hyperglycemia, gr 1, start 8/1/15
- Hypercalcemia, gr 2, start 8/1/15
- Joint pains, gr 1, start 9/12/15
- Infusion reaction, gr 2, start 9/1/15 stop 9/2/15
- Heartburn, gr 1, start 8/5/15
- Rash, gr 1, start 8/24/15

# Resources:

- MEDdra https://www.meddra.org/about-meddra/vision
  - Training courses, videos, case studies, support documentation and tools
- CTCAE https://ctep.cancer.gov/protocoldevelopment/electronic_applications/ctc.htm
  - Guidances, versions 4,5, &6
- WHODrug Global https://who-umc.org/whodrug/whodrug-global/
- Medical Device Report (MDR) https://www.fda.gov/medical-devices/mandatory-reporting-requirements-manufacturers-importers-and-device-user-facilities/mdr-adverse-event-codes#:~:text=The%20FDA%20Medical%20Device%20Report,medical%20device%20reports%20(MDRs).

# How to get access to MedDRA and WHODrug at OHSU

- Contact Julie Mitchell for MedDRA and WHODrug
  - OHSU investigator initiated projects only
  - Can't be used for Industry Sponsored or Foundation funded trials