INITIATIVE ON METHODS, MEASUREMENT, AND PAIN ASSESSMENT IN CLINICAL TRIALS

IMMPACT-VI (REVISED TO IMMPACT-VII)

“RANDOMIZED CLINICAL TRIALS FOR CHRONIC PAIN TREATMENTS: PLACEBO-CONTROLLED DESIGNS AND THEIR ALTERNATIVES”

June 8-10, 2006
Ritz Carlton Pentagon City
Arlington, Virginia

Thursday, June 8

7:00 PM                    RECEPTION AND DINNER
                            at the Ritz Carlton

Friday, June 9

7:00–8:00 AM            CONTINENTAL BREAKFAST

8:00–8:30 AM            Welcome, introductions, update, objectives
                        Dennis Turk, PhD

8:30–9:00 AM            Epilepsy clinical trials: state-of-the science, with focus
                        on add-on designs
                        Jacqueline French, MD

9:00–9:30 AM            Depression clinical trials: state-of-the science, with
                        focus on placebo group response
                        Michael Thase, MD

9:30–10:00 AM           Analyzing and interpreting onset of effect, durability of
effect, and time to exit in clinical trials
                        Susan Ellenberg, PhD

10:00–10:30 AM          COFFEE BREAK

10:30–11:00 AM           1. The Phase III chronic pain clinical trial
                        2. Establishing an IMMPACT “Resource for Evaluating
                           Procedures and Outcomes of Randomized Trials”
                           (REPORT)
                        Bob Dworkin, PhD

11:00 AM –12:30 PM       Study populations
                        moderator: Dennis Turk, PhD

                        1. General considerations, for example
- identifying best clinical condition(s) for a particular treatment, for example, relatively homogeneous conditions (e.g., diabetic neuropathy) vs. heterogeneous groups of patients (e.g., neuropathic pain)
- difficulties of studying neglected clinical conditions

2. Specific inclusion and exclusion criteria, for example
   - minimum baseline pain (e.g., ≥ 4/10, ≥ 5/10, ≥ 3/10)
   - can patients be trained to rate pain with greater reliability and validity?
   - minimum pain duration (e.g., ≥ 3 mos, ≥ 6 mos)
   - excluding patients refractory to multiple prior treatments

3. How can IMMPACT interrogate existing data and generate new data?

12:30–1:30 PM
LUNCH

1:30–3:00 PM
Types of controlled superiority trials
moderator: John Farrar, MD, PhD

1. Investigational treatment
   - single vs. multiple fixed dosages
   - identifying non-effective and maximum dosages
2. Placebo
   - no other treatments allowed
   - rescue allowed (e.g., acetaminophen)
   - add-on designs (e.g., pre-specified vs. any stable regimen)
3. Active comparator
4. Both of the above comparison groups
5. Studying combination therapy
6. Situations in which a non-inferiority trial would be informative
7. Randomization
   - equal allocation vs. fewer patients randomized to placebo
8. How can IMMPACT interrogate existing data and generate new data?

3:00–3:30 PM
COFFEE BREAK

3:30–5:00 PM
Trial components and duration
moderator: Bob Dworkin, PhD

1. Run-in periods
   - identifying placebo responders
   - identifying treatment responders
   - identifying poor treatment tolerability
- identifying poor adherence
2. Titration phase
3. Taper phase
4. Overall trial duration
5. Placebo group
   - anatomy of placebo group response: placebo effect, regression to the mean, natural history
   - estimating placebo group response
   - attenuating placebo group response
   - inert vs. active placebo
6. Methods to improve subject retention
7. How can IMMPACT interrogate existing data and generate new data?

6:45 PM  Meet in hotel lobby for transport to dinner
7:00–9:30 PM  RECEPTION AND DINNER

Saturday, June 10

7:00–8:00 AM  CONTINENTAL BREAKFAST
8:00–9:30 AM  Situations that require alternative designs for Phase III clinical trials
moderator: Dennis Turk, PhD
1. Treatments
   - opioid analgesics
   - disease modifying agents
   - prevention of chronic pain
   - others?
2. Conditions
   - osteoarthritis
   - rheumatoid arthritis
   - low back pain
   - fibromyalgia
   - visceral pain
   - others?

9:30–10:00 AM  COFFEE BREAK
10:00–12:00 PM  Alternative designs for Phase III clinical trials
moderator: Nat Katz, MD
1. Randomized withdrawal
2. Enriched enrollment
3. Flexible dosing
4. Crossover designs
5. Superiority
6. Adaptive allocation and Bayesian approaches
7. Others?
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<td>12:00–1:00 PM</td>
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| 1:00–2:30 PM | **How will IMMPACT interrogate existing data?**<br>How can IMMPACT generate new data?**  
moderator: Bob Dworkin | 1. Action plan for coming year |
| 2:30–3:00 PM | COFFEE BREAK                      |                                                                         |
| 3:00–4:30 PM | **How will IMMPACT interrogate existing data?**<br>How can IMMPACT generate new data?**  
moderator: Bob Dworkin | 1. Action plan for coming year  
2. Identify members of implementation team |
| 4:30 PM      | ADJOURN                           |                                                                         |