Patented Clinical Trial Designs

8th EFSPi Statistics Leaders Meeting

Ludwigshafen, 04-Jul-2017
Background

The SPCD

Questions and Discussion
Patented Clinical Trial Designs

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In 2003 at Massachusetts General Hospital, a new clinical trial design was invented – the Sequential Parallel Comparison Design (SPCD).

The Problem of the Placebo Response in Clinical Trials for Psychiatric Disorders: Culprits, Possible Remedies, and a Novel Study Design Approach

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Background

Sequential Parallel Comparison Design (SPCD)

- Reducing both the placebo response rate and the sample size
- Particularly interesting for indication with high placebo response rates, like psychiatric disorders

On September 3, 2014, PPD acquired an exclusive license

- Trimentum™

The SPCD was used in more than 30 trials and by several companies

- Alkermes – ALKS 5461, depression
- Janssen Pharmaceuticals – esketamine, depression → FDA approval 2016
- Avanir Pharmaceuticals – AVP 923, Alzheimer disease
Background

The SPCD

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SPCD – The Sequential Parallel Comparison Design

**Basic SPCD design.**
Sequential parallel comparison design (SPCD) involves a two-stage design. In the first stage of the trial, the majority of patients are randomized to placebo. In the second stage of the trial, placebo non-responders are re-randomized to active or placebo treatment.
Data from the patient groups in the grey box are pooled for the final analysis.

**From:** Asher Mullard: Paring down the placebo response.


http://www.nature.com/nrd/journal/v15/n12/full/nrd.2016.255.html?WT.feed_name=subjects_clinical-trials
SPCD – The Sequential Parallel Comparison Design

Stage 1

- Patients are randomized to drug/ placebo-drug/ placebo.
- Allocation ratio is $1-2a/ a/ a$, e.g., $2/ 3/ 3$, with $a=0.375$

Stage 2

- Stage 1 responders $\rightarrow$ exit double-blind treatment
- Stage 1 non-responders $\rightarrow$ receive their randomized treatment

Analysis

- Stage 1 response rates ($p_1$ and $q_1$)
- Stage 2 response rates in placebo non-responders ($p_2$ and $q_2$)
- Estimate/ test a pooled weighted difference $w(p_1-q_1)+(1-w)(p_2-q_2)$

Choice of $a$ and $w$ $\rightarrow$ maximize power
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1. Are there any other patented clinical trial designs known?

2. How can patented clinical trial designs affect
   – commercial clinical research,
   – academic clinical research,
   – the freedom of science?

3. What is the potential for further patented clinical trial designs?

4. Is there a need/ does it make sense to take action and which?

5. Is there any other aspect to patented clinical trial designs?

Five breakout groups
Discussion (20 min)
Presentation of results to the group (20 min)