

## WEB MATERIAL

### Eliminating Ambiguous Treatment Effects Using Estimands

Brennan C. Kahan\*, Suzie Cro, Fan Li, and Michael O. Harhay

\* (b.kahan@ucl.ac.uk)

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## WEB APPENDIX 1

### Trial of Baricitinib for Atopic Dermatitis

The primary estimand aimed to address the effect of baricitinib vs. placebo in the hypothetical setting where participants did not discontinue treatment and could not receive rescue therapy. Full details are provided in Web Table 1.

**Web Table 1.** Example of reporting estimands for the trial of baricitinib for atopic dermatitis

| <b>Estimand Aspect</b>          | <b>Definition</b>   |
|---------------------------------|---|
| Population                      | Adults with atopic dermatitis (meeting the trial eligibility criteria)  |
| Treatment conditions            | Baricitinib 4-mg or 2-mg vs. placebo daily plus topical corticosteroids, without discontinuation and without rescue therapy                   |
| Endpoint                        | WPAI-AD change from baseline score at 16 weeks  |
| Summary measure                 | Difference in means   |
| Handling of intercurrent events |   |
| Incorrect treatment received    | Treatment policy strategy   |
| Treatment discontinuation       | Hypothetical strategy, pertaining to the setting where participants are kept on treatment regardless of side effects or other adverse effects |
| Use of rescue therapy           | Hypothetical strategy, pertaining to the setting where rescue therapy is not provided even if medically indicated                             |

## WEB APPENDIX 2

### Trial of Anakinra for Palmoplantar Pustulosis

The primary estimand aimed to address the effect of anakinra vs. placebo regardless of treatment discontinuation or receipt of additional therapies. Full details are provided in Web Table 2. A supplementary estimand addressed the effect of anakinra vs. placebo in the subset of participants who would receive at least 50% of daily injections under both treatment conditions, regardless of receipt of additional therapies. Full details are provided in Web Table 3 (see next page).

**Web Table 2.** Example of reporting estimands for the trial of anakinra for palmoplantar pustulosis (primary estimand)

| Estimand Aspect                 | Definition   |
|---------------------------------|--|
| Population                      | Patients with confirmed diagnosis of PPP meeting the trial eligibility criteria  |
| Treatment conditions            | 8 weeks of treatment with anakinra vs. placebo, regardless of treatment discontinuation or receipt of additional therapies |
| Endpoint                        | Change from baseline in PPPASI at week 8   |
| Summary measure                 | Mean difference  |
| Handling of intercurrent events |  |
| Study treatment discontinuation | Treatment policy   |
| Use of rescue medication        | Treatment policy   |
| Use of prohibited medication    | Treatment policy   |
| Use of other topical medication | Treatment policy   |

PPP, palmoplantar pustulosis; PPPASI, palmoplantar pustulosis area and severity score.

**Web Table 3.** Example of reporting estimands for the trial of anakinra for palmoplantar pustulosis (supplementary estimand)

| <b>Estimand Aspect</b>   | <b>Definition</b>  |
|--|--|
| Population   | Patients with confirmed diagnosis of PPP meeting the trial eligibility criteria who would comply with treatment and receive at least 50% of daily injections |
| Treatment conditions   | 8 weeks of treatment with anakinra vs. placebo, regardless of treatment discontinuation or receipt of additional therapies                                   |
| Endpoint   | Change from baseline in PPPASI at week 8   |
| Summary measure  | Mean difference  |
| Handing of intercurrent events                                       |  |
| Study treatment discontinuation (received <50% of daily injections)  | Principal stratum of participants who would receive at least 50% of daily injections under either treatment condition  |
| Study treatment discontinuation (received ≥ 50% of daily injections) | Treatment policy   |
| Use of rescue medication   | Treatment policy   |
| Use of prohibited medication   | Treatment policy   |
| Use of other topical medication                                      | Treatment policy   |

PPP, palmoplantar pustulosis; PPPASI, palmoplantar pustulosis area and severity score.