Research Strategy and Publication Plan for British Association of Dermatologists Biologic Interventions Register (BADBIR)

General Principles

1) Key outcomes from BADBIR will be published in high-quality, peer-reviewed journals.
2) BADBIR will publish key outcomes in abstract form (at clinical and research meetings such as the BAD annual meeting and the European Society for Dermatological Research, [ESDR]) and subsequently in full papers preferably in the highest quality journals such as The Lancet and British Medical Journal. This principle should be adhered to when deciding about interim publications, publications from selected centres or publications limited to selected outcomes. Duplicate publication of data will be avoided. Investigators proposing to utilise BADBIR data should liaise with the Research and Steering Committees at an early stage. Publications should: be constructed with methodological rigour; adopt a similar style of reporting data; report relevant negative findings; refer back to previous BADBIR publications and; update results as necessary.
3) Timing of key publications should be governed by:-
    a) Preliminary power calculations in relation to the events being considered
    b) Preliminary analysis of event rate in the control arm of BADBIR
    c) Interim analyses as set out in the protocol.
4) The timing of publications should also take into account the importance of signals highlighted through interim analyses and input from the data monitoring committee. Reporting mechanisms are in place. On the one hand, we would want to avoid publishing early signals that may later be refuted, but we would also want to avoid undue delay in reporting important safety signals of potential health concern. Pharmacovigilance may also identify rare but highly important and thus reportable signals.
5) Publications reporting BADBIR data should be sent to the BADBIR Research and Steering Committees for review prior to publication. A 60-day delay may be required for review by the relevant pharmaceutical companies depending on the nature of the research and the data being reported.

Interim Analyses

The protocol indicates that interim analyses will be undertaken when 5,000 patient years of exposure have been accumulated in any of the exposed groups. Decisions about further interim analyses will be informed by this initial review and documented within the protocol. In addition, a review of current data sets in BADBIR (December 2012) has been undertaken to inform the chronology of principal publications that will emanate from the register.

List of Key BADBIR Papers

A primary function of BADBIR is to report rates of key, pre-specified adverse events in psoriasis patients receiving biologic therapy compared to controls (conventional therapy). Our power calculations indicate that BADBIR should have achieved sufficient power for the vast majority of key AEs by 2018 (see below). However, in addition, we will report pre-specified AEs of special interest according to a time line determined by: a) calculations of when sufficient power is achieved to report rates of clinically meaningful AEs; and b) pre-specified interim analyses. For the sake of clarity, key primary papers to be published from BADBIR are listed in chronological order. In addition, it should be noted that further studies utilising BADBIR data are currently underway but are not reported here.

- Baseline characteristics of patients with psoriasis enrolled in the British Association of Dermatologists Biologic Interventions Register (BADBIR)
- Comparison of efficacy, disease control and discontinuation of individual biologic and conventional systemic therapies in patients in BADBIR, based on projected accrual to provide comparable data with BSRBR.
- Rates of key adverse events in control and biologic arms including but not limited to death, serious infections, site specific infections
- Rates of non-melanoma skin cancer in patients receiving biologic therapy compared to controls (conventional systemic therapy)
- Comparison of baseline demographics and relevant outcomes including efficacy and adverse events from “real-life” clinical practice to data reported in clinical trials
- Incidence rates of diabetes and metabolic syndrome in patients receiving biologic therapy compared to controls (conventional systemic therapy). Could include change in weight, waist circumference, BMI. Would follow from interim analysis earlier in 2013
- Analysis of longitudinal outcome data (including cluster analysis of PASI, PGA) and comparison of outcomes to refine different modes of response/non-response in patients receiving biologic therapy compared to controls (conventional systemic therapy).

- Comparison of outcomes when switching from one biologic agent to another. Utilising data from BSRBR, BADBIR should have accrued sufficient patients (6,000 patient years) in 2015.
- Rates of hepatotoxicity in patients receiving biologic therapy compared to controls (conventional systemic therapy).
- Rates of cardiac disorders in patients receiving biological therapy compared to controls (conventional systemic therapy).
- Rates of serious and soft tissue infections (pre-specified AEs of special interest) in patients receiving biologic therapy compared to controls (conventional systemic therapy). By 2016 BADBIR is predicted to have accrued 20,000 patient years on biologic therapy.
- Rates of Tuberculosis (TB) and other opportunistic infections in patients receiving biologic therapy compared to controls (conventional systemic therapy). We should accrue sufficient data by 2018 (28,000 patient years)
- Rates of multiple sclerosis and central nervous system disorders in patients receiving biologic therapy compared to controls (conventional systemic therapy).
- Pregnancy outcomes in patients receiving biologic therapy compared to controls (conventional systemic therapy). Based on a BSRBR case control study, and current event data, we should achieve relevant power in 2018.
- Rates of key pre-specified adverse events in patients receiving biologic therapy compared to controls (conventional systemic therapy) including but not limited to death, serious infections, site specific infections, TB and other opportunistic infections, cardiovascular disease, multiple sclerosis hepatotoxicity. This is the primary function of BADBIR.