British Association of Dermatologists Biologic Interventions Register (BADBIR)

New Starter Presentation
Aim of BADBIR

Determine whether there is an importantly increased risk of serious adverse events following the introduction of biologic therapy compared to that expected from a conventionally treated cohort with comparable disease severity

Subsidiary aim will be to collect information on their long-term effectiveness

Recommendation from the BAD and NICE

“All patients treated with biologic agents should be registered with BADBIR”
Study Design – Follow-up

Information gathered at FUP

Dermatology Team questionnaire

Patient questionnaire

Linkage with national databases

6 Monthly Follow-ups

Annual Follow-ups

STUDY END DATE

Current study end date: 31st July 2028

3 YEARS

LIFE LONG

Year 0

Year 3

Current study end date: 31st July 2028
Patient Eligibility

Two-Cohort Study

**Biologic Cohort**
- Patient has commenced treatment within the **last 6 months** on one of the biologic drugs registered with BADBIR

  - BADBIR Registered Drugs:
    - Humira (Adalimumab)
    - Stelara (Ustekinumab)
    - Taltz (Ixekizumab)
    - Cosentyx (Secukinumab)
    - Benepali (Etanercept Biosimilar)

  - Patient needs recent PASI and DLQI score

**Conventional Cohort**
- Patient has commenced treatment within the **last 6 months** and is **naïve to Biologic Therapy**

  - Patient recently stopped one conventional and started another. Cannot be the same as one just stopped (**less than a 3 month gap**)

  - Patient needs recent PASI **equal or greater than 10** and recent DLQI greater than 10

  - Patient has been receiving an ongoing conventional treatment and is now introduced to a new second concurrently

  - Patient needs recent PASI and DLQI. At some point in the patient’s history it needs to be recorded that they have had **moderate to severe generalised psoriasis**

BADBIR New Starter Presentation
• BADBIR eligibility criteria was changed to allow recruitment of patients under 16 years old.

• These patients are being exposed to immunosuppressive therapy on a comparatively immature immune system so it is important that the long term safety is evaluated. In addition, there is potentially a high lifetime exposure to these therapies which may place them at a higher risk than adults.

• We understand that it is possible that you are not necessarily managing these patients in your clinics but please could you liaise with colleagues to explore the feasibility of registering these eligible patients.
Consenting patients

- You have a 6 month window from the date the patient started their biologic/conventional therapy to consent the patient.

- The patient information sheet and consent form should be provided to the patient and they should be given time to read and ask any questions.

- We have ethical approval to allow patients to sign the consent form as soon as they are happy to do so (some clinical trials require patient to have 24 hours to think about their participation.)

- When the patient has signed consent please ensure that a copy, along with a patient information sheet, is given to the patient as well as added to the hospital notes, sent to us.

- The original consent form should be stored in section 7 of the BADBIR site file behind the completed patient enrolment log.
Consenting Patients

Consent Forms

The current BADBIR consent form should be Version 4. Any patients consented on version 3 will need to be re-consented.

Republic of Ireland have a different consent form!

Patients need to sign Irish version.

Please ensure consent form is on hospital headed paper.

Important

• Boxes should be initialled not ticked.

• The date of consent should be the same for the patient and person taking the consent.
Consenting under 16s

• Parent/guardian should be provided with adult BADBIR patient information sheet and child with age appropriate patient information sheet (guidance is provided on sheet but version used will be at the discretion of person taking consent.)

• Participants under 16 will sign Assent form and parent or guardian will sign Parent of Guardian Consent form – both forms will be required to register a patient under the age of 16.
Uploading Consent Forms

Consent forms can be upload in the following three ways:
• Faxed to the BADBIR office on **0161 306 1912**
• Emailed to the BADBIR office using the address BADBIR@manchester.ac.uk
• Uploaded directly to the database as shown below
Information collected at baseline..

- Type of psoriasis
- Disease Severity - PASI/PGA/psoriatic arthritis
- Current Therapy for any indication
- Treatment for Psoriasis
- All previous systemic treatments for psoriasis
- Co-morbidities
- Fitzpatrick skin type
- History of prior neoplastic or pre-cancerous lesions
- Past UV Therapy
- Lab results (preferably prior to commencement of current systemic therapy)
- Blood pressure
- Height, weight and waist
- Patient Questionnaires: Patient baseline questionnaire, CAGE, DLQI, EQ-5D, HAQ (HAQ only required if patient has diagnosis of inflammatory arthritis)

Above is the clinical information which will be obtained from the patients medical notes by your local research team, please try to document as much of the information as possible. Those highlighted in purple are required for patient eligibility so these are most important. Both the clinical and patient questionnaires can be found on our website www.badbir.org
Information collected at follow-up...

- Changes to biologic/conventional therapy
- UV therapy
- Changes to current therapy for any indication
- Lab results
- Adverse Events
- PASI and PGA
- Weight and waist
- Patient Questionnaires

Above is the information collected at follow-up. As this is a safety register the most important information to be collected is the adverse events. We also need an accurate account of the psoriasis treatment the patient is on.

It is worth noting that BADBIR follow-up payment will not be received if a PASI isn’t documented at follow-up as this is the only indicator we have to establish efficacy of the treatments.

Please ensure as much of the information as possible is documented in the patients medical notes so it can be uploaded onto the BADBIR database.
Accessing Database

To access our database you must first **register for a database account:**

1. Send your signed and dated CV

2. Register for an account on our database at:  

3. If you are completing the data entry training you will be given training access on the database straight away

4. To get access to the LIVE database you will need to be approved access by your principal Investigator (they will receive instructions on how to do this)
Your database home page will look like this. From here you will be able to access everything you need to add the required data to your patient’s records.

- You can view all your current patients as well as add new ones.
- We also let you know when follow-ups are currently due and which ones will be due soon.
- You can also see where your data has been queried by BADBIR and can easily access and answer these queries.
Database: View all Patients

Select patient by clicking on their BADBIR ID. This will take you to patient summary page.

Search bar can find patient by name or BADBIR/hospital/NHS number.

This table shows dates when patients are next due for a follow-up. Dates are colour coded so you can see the status of the follow-up.

Click show key to view icon description.
Once you have clicked on a patient’s Study ID you will be taken to the patient summary page.

Click **Select** to enter a new baseline/follow-up or to view previously entered data. You will not be able to enter a new follow-up until the due date is within 2 months.

The FUP column indicates if the query relates to a baseline or a specific follow-up.

If there are any queries for a patient they will be located here.

Any feedback or solved queries can be seen by clicking **SHOW**.
Printable summary sheet – an overview of all the data entered for this patient except adverse events

Drugs & AE Summary – can be used to provide a summary of the patient to take to clinic

Patient Charts – Graph to show patients PASI/DLQI in relation to treatments they have received.

File and Adverse Event – Adverse events are usually recorded in an open follow-up. If you wish to complete an adverse event form before a patient’s follow-up you can use file it here. The event will then be held for you in the next follow-up.

Switch to Biologic (Conventional only) – If a conventional patient starts biologic information you can click here to inform us and we shall make the appropriate changes

Flag for BSTOP – You can use this to flag patients you have consented to B-STOP. Once you have flagged a patient a grey logo will show. When we have confirmation from BSTOP this logo will change to blue.

Send Feedback – press this button to leave any important information about a patient. i.e why information is missing or of information you have forgotten to include in follow-up.
21 Day Edit Window

• When a baseline or follow-up is opened you will have 21 days to enter data before the edit window is closed.
• After the edit window is closed any serious adverse events will be reported by our pharmacovigilance team.
• If you notice any missing or incorrect data after the edit window is closed then you will need to contact the BADBIR team preferably using the feedback function on the individuals patient summary page.
Entering Patient Data

• When completing a patient’s baseline/follow-up you can navigate through the record using the tab on the **left** or using the ‘Advance to...’ button located at the bottom of the page. Below is an example of how to complete one of the follow-up pages.

• When entering the data please use the ‘Tutorials’ in order to learn how to complete each section of the patient record.
Patient Data: Adding Doses

- **Ustekinumab** doses need to be recorded

If patient is continuing therapy click **no** and update

If a patient switches from the originator drug to a biosimilar a new entry must be made for the biosimilar (and vice versa) e.g.

1) **Inflectra/Remsima** (infliximab biosimilars)

2) **Benepali** (etanercept biosimilar)

To add doses or add a stop date click **edit**

If dose dates are not available please ask patient if they have stuck to a standard dosing schedule and inform us of the answer in feedback so we can add estimated doses accordingly.
Patient Data: Adding Doses

- For Stelara and Remicade individual doses will need to be recorded on the database.

- This is done at patient follow-up. Click the edit button to the left of the biologic treatment, circled in image a.

- Enter the dose date and dose as shown in image b. Then click ‘Save drug dose or batch details’. This will then be added to our system as seen in c.
Patient Data Collection (I)

When possible please complete the BADBIR follow-up face-to-face with the patient.

Tips on what to ask the patient:

- If they have suffered any new illnesses in the last 6 months/year.
- Have they suffered any relapses/exacerbations of any ongoing illnesses.
- Have they had to visit the doctors or have any hospital visits?
- Ask the patient to be ask specific as possible with dates, when any events have occurred and how long.
- Have there been any changes in their current medication, and if so why?
- If they have missed or delayed any of their biologic doses and if so, why?

Use Drugs & AE summary sheet from patients summary page.
As it is not always possible to see all BADBIR patients in clinic we ask that as much information as possible to be obtained from the patients hospital notes and entered onto the BADBIR database.

To help with the quality of the BADBIR data please:

• Put a process in place for BADBIR patient questionnaires to be completed

• Ensure clinic letters are to contain as much information as possible (PASI’s, Adverse events etc...)
What is An Adverse Event

• Any untoward medical occurrence which affects the patient’s health whilst he/she is on the Register
  • e.g. Any new illness, diagnosis, symptoms, accidents, drug reactions, side effects, clinically significant lab results, hospitalisations, surgery including elective, exacerbations of any illness

• **Does not require a relationship with treatment**

• Applies equally to Conventional Cohort and Biologic Cohort even if the patient is not currently on any systemic treatment

• Without accurate and complete adverse event data, safety analysis for the register could be incomplete
Database – Adverse Events

Once you enter all the adverse event data and click save, you will be navigated to this page where you can add the applicable ESI categories. Once you have selected the ESI category you can select ‘Add form’ in the ESI column to complete the ESI form.

You can view the full list of all adverse events entered for the patient at every follow-up here. This should prevent entering the same adverse event more than once.

At follow-up previously entered adverse events should be reviewed and any additional/missing information updated.
An event is serious if it results in...

- Death
- Overnight hospitalisation / prolonging an existing hospitalisation
- Significant loss of function or disability
- Congenital malformation
- Life threatening (immediately)
- IV antibiotics / antifungals or antivirals
- Medically important event (events of special interest)
Event of Special Interest

For certain **serious adverse events** we collect extra information on Events of Special interest (ESI) forms.

- Aplastic anaemia, pancytopenia, serious neutropenia
- Cerebrovascular Accident (CVA)
- Hepatitis B Reactivation
- Lymphoproliferative Disease
- Malignancy (not including skin)
- Melanoma Or Skin Cancer including Bowens Disease
- Myocardial Infarction/Acute Coronary Disease
- Pregnancy
- Pulmonary Embolism
- Serious Congestive Heart Failure
- Serious Demyelination/ Optic Neuritis
- Serious Hepatic Dysfunction/ Failure
- Serious Hypersensitivity Reaction
- Serious Infection (excl. TB)
- Serious Lupus/ Lupus like illness
- **Serious Psoriasis Flare** - this is only required if the patient was hospitalised overnight
- Serious Skin Reaction (e.g. Stevens Johnson syndrome, erythema multiforme toxic epidermal necrosis)
- Surgery (Overnight Hospitalisation)
- Tuberculosis (Not Latent)

Tip!
Your follow-up data entry training exercise includes a Serious Psoriasis Flare.
If you have entered any adverse events which we require an ESI form for they will be listed on your centre home page:

- **Querying System** 48 NEW out of 51 UNSOLVED queries
- **Pharmacovigilance Queries** 2 NEW out of 3 UNSOLVED queries
- **Serious Adverse Event Queries** 2 NEW out of 3 UNSOLVED queries
- **Patient Queries and Feedback** 46 NEW out of 48 UNSOLVED queries

**Missing ESI Forms (9 ESI Forms Pending)**
List of all missing ESI for your centre. You can choose ESI Forms in this page.

- **Recruitment Report by month**
  Patient recruitment numbers shown in a monthwise breakup for both centres.

- **Site File Documents**
  View the documents for site file that BADBIR has for your centre.

This page lists any outstanding forms you have.
Website – Events of Special Interest

- You can then download ESI forms from the website so that it can be completed on paper and then added to the database when the information has been collected.
Once you have gone through and filled out a patient’s baseline/follow-up you should **always** check what queries BADBIR will raise.

**Preview Queries** – Allows you to view queries that will be raised against a follow-up (see next slide)

**Close 21 Day Window** – used when there is no further information available to enter. If there are any queries on the data these will be generated quicker

**Feedback/Comments** – can be used to enter additional information or to notify us of any missing data to avoid data queries
Database – Preview Queries

Once completed, this page will show you the queries BADBIR will raise. These queries will be raised if there is missing or incorrectly entered data. To stop us querying missing data please leave feedback using the Feedback / Comments button.

In this example no queries would be raised as it has been stated in the feedback that patient weight and waist were not collected.

= Potential data queries

= Example feedback entry
Cohort Switches

• We will have to perform a cohort switch if a conventional patient begins one of the BADBIR registration biologic drugs. To do this you will need to inform BADBIR by pressing the button ‘Switch to Biologic’ found on the Patient Summary Page.

What we need from you:
✓ Complete the latest follow-up, dated before the switch, as normal.
✓ Click ‘Switch to Biologic’ and enter biologic drug name, start date, dose and frequency.
✓ After the switch the patient’s Study ID will begin with a 3 and they will start from a new baseline. Please carry on follow-ups as normal.

<table>
<thead>
<tr>
<th>Patient Study ID number correlates with cohort:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Biologic (190112733)</td>
</tr>
<tr>
<td>2 Conventional (290112761)</td>
</tr>
<tr>
<td>3 Switched from conventional to biologic cohort (390113285)</td>
</tr>
</tbody>
</table>
Patient Transfer

• If a BADBIR patient is moving to a different area please inform BADBIR

• If a patient has been referred to your centre who is already on BADBIR we may contact you to ask if you would carry on their BADBIR follow-ups.
Site file and Audit

- Please find out where the BADBIR site file is kept within your hospital.
- We now have an electronic site file which can be located on the homepage.
- We conduct centre audits each year - part of the audit we will check that your CV is in section 7 of the site file and that all staff working on BADBIR are present on the delegation log.
- We will also check every patient consented to BADBIR has their original consent form filed in section 6 of the site file.
- During the audit will request a certain number of patients notes who have consented to BADBIR, for these patients we will do 100% source document verification to ensure the data entered onto the database is accurate and complete.
Section 7: Delegation Log

- Patients must only be consented by members of staff who are on the delegation log.

- The Principal Investigator must approve access for every member of staff to confirm the named person is capable of the study responsibilities.

- When a staff member leaves the trust or no longer wishes to take part in BADBIR responsibilities please provide an end date and inform BADBIR so access to the database can be removed.

Every member of staff named on the delegation log should have a CV filed in section 7 of the site file.
Collection of data
Financial assistance available

Extra Work Involved
Identify and consent patient
Complete baseline questionnaire and enter onto web-based database
Complete follow-up forms and enter onto web-based database

BADBIR Financial Assistance – 6 monthly intervals
£120 per baseline questionnaire
£30 per follow-up questionnaire up to Follow up 6
£15 per follow-up questionnaire Follow up 7 onwards

Recruiting 2 patients per month
24 patients in year 1
Baseline @ £120 = £2880
12 F-up @ £30 ea = £360
Total in year 1 = £3240

Recruiting 8 patients per month
96 patients in year 1
Baseline @ £120 = £11520
48 F-up @ £30 ea = £1440
Total in year 1 = £12,960
Conclusion

• BADBIR will help to answer important questions about the long-term safety of biologic drugs in patients treated for psoriasis

• Provide more accurate and better quality information to be available to patients

• Added value through links with other studies such as the biomarker study BSTOP and adherence study iMAP

Acknowledgements

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