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Musculo-skeletal

North Bristol NHS Trust

DOES A STRUCTURED PROTOCOL INCREASE IMPLEMENTATION OF BIOLOGIC THERAPY DOSE REDUCTION AMONG CLINICIANS AND PATIENTS?

A PILOT STUDY

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1. Introduction

- Biologic therapies (e.g. tumour necrosis factor inhibitors (TNFi)) used in the management of inflammatory arthritis are associated with potential risks (including local reactions, infections and possible malignancy).
- Increasing RCT evidence (1-3) suggests stable patients can dose-reduce without increased disease activity and a previous patient engagement event (4) explored patient perceptions of dose reduction.
- There are no clear guidelines or protocols reported in literature to facilitate implementation in clinical practice.
- For 2 years at NBT, stable patients (out of the 460 patients on subcutaneous TNFi) have been offered the opportunity to reduce their dose on an ad hoc basis with variable regimes.

2. Aims and Objectives

Aim:

- To determine if a structured protocol for standardising dose reduction of subcutaneous TNFi therapy will increase implementation amongst clinicians and patients.

Objectives:

a) Develop a structured protocol for dose reduction of biologic therapies

b) Evaluate impact of the protocol on uptake in clinical practice

c) Evaluate the contribution of a specialist pharmacist in design and implementation

d) Identify further work to further support dose reduction in biologic therapies

3. Methodology

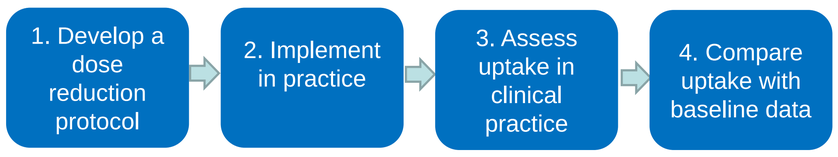
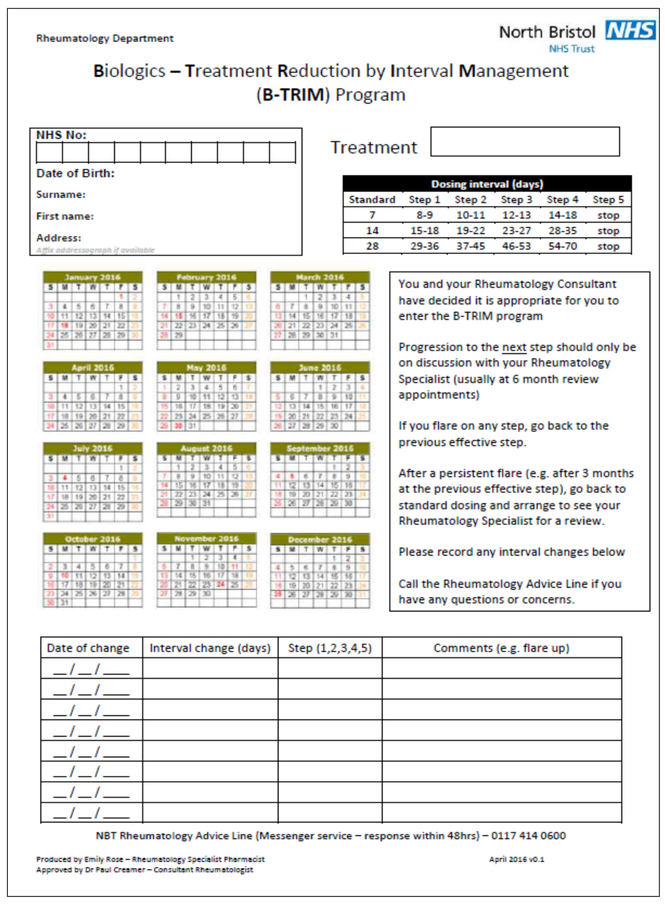


Figure 1: Methodology

- An inflammatory arthritis TNFi 5-step dose reduction program was developed by the Rheumatology Specialist Pharmacist (30% interval extension for 3 steps, followed by a 60% extension, before stopping treatment)
- The pharmacist produced a patient information leaflet and compliance record (informing of treatment escalation following a disease flare up) and checklists for prescribers.
- The program was reviewed by a Consultant Rheumatologist and patient representative group and presented to the clinical team.
- Patients with stable disease at 2 years on TNFi therapy and deemed appropriate by their clinician were offered to participate.
- Data were collected for patients started on dose reduction scheme.

Standard interval	Interval in days: Step 1	Step 2	Step 3	Step 4	Step 5
7	8-9	10-11	12-13	14-18	Stop
14	15-18	19-22	23-27	28-35	Stop
28	29-36	37-45	46-53	54-70	stop

Figure 2: NBT B-TRIM stepwise protocol for dose reduction


Rheumatology Department

North Bristol NHS Trust

Biologics – Treatment Reduction by Interval Management (B-TRIM) Program

NHS No:

Date of Birth:

Surname:

First name:

Address:

Treatment

Dosing interval (days)					
Standard	Step 1	Step 2	Step 3	Step 4	Step 5
7	8-9	10-11	12-13	14-18	stop
14	15-18	19-22	23-27	28-35	stop
28	29-36	37-45	46-53	54-70	stop

You and your Rheumatology Consultant have decided it is appropriate for you to enter the B-TRIM program

Progression to the next step should only be on discussion with your Rheumatology Specialist (usually at 6 month review appointments)

If you flare on any step, go back to the previous effective step.

After a persistent flare (e.g. after 3 months at the previous effective step), go back to standard dosing and arrange to see your Rheumatology Specialist for a review.

Please record any interval changes below

Call the Rheumatology Advice Line if you have any questions or concerns.

Date of change	Interval change (days)	Step (1,2,3,4,5)	Comments (e.g. flare up)
__/__/____			
__/__/____			
__/__/____			
__/__/____			
__/__/____			
__/__/____			
__/__/____			
__/__/____			

NBT Rheumatology Advice Line (Messenger service – response within 48hrs) – 0117 414 0600

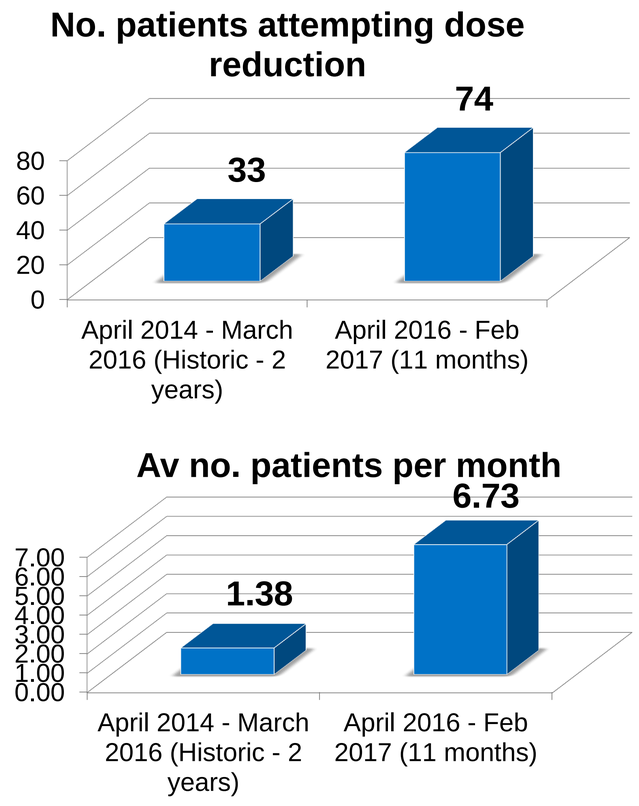
Produced by Emily Rose – Rheumatology Specialist Pharmacist

Approved by Dr Paul Creamer – Consultant Rheumatologist

April 2016 v0.1

Figure 3: NBT B-TRIM Patient handheld compliance record

4. Results



Of the 74 additional patients commenced on an extended interval regime between Apr 2016 – Feb 2017, 76% followed the BTRIM program for dose reduction whereas 24% had their interval extended via an alternative schedule.

5. Discussion

- As previously discussed in literature (1-3) patients have been known to successfully reduce dose of biologic therapy by extending dose intervals, however little guidance exists on implementing dose reduction in clinical practice.
- The pilot study showed adopting a structured dose reduction program, developed by the Rheumatology Specialist Pharmacist, increased implementation in clinical practice.
- It is unclear whether this was attributable to increased patient and / or clinician confidence in initiating dose reduction or raised clinician awareness of dose reduction.
- The pilot data collection only includes patients who agreed to participate in dose reduction, therefore reasons for patients opting out of dose reduction were not assessed (and may have influenced data).
- The pilot demonstrated the benefit of having a Rheumatology Specialist Pharmacist to facilitate implementation of the program, with support of a Consultant Rheumatologist.
- The pilot has also been associated with significant financial savings, evaluated as ~£145,755 for our commissioners over the 11 month implementation period.
- The pilot is an example of work to be adopted as part of efficiency work in sustainability and transformation plans.

Acknowledgments:
Rheumatology Patient Representative Group, North Bristol NHS Trust
Rheumatology Clinical Team, North Bristol NHS Trust

6. Conclusions and Future Work

- Our aim was to bridge the gap between dose reduction studies reported in literature and practical implementation of dose reduction in the clinical setting, without increasing resource utilisation or inconveniencing patients with more frequent follow up appointments. We also aimed to allow competent patients to self-manage their dosing interval under the guidance of their Rheumatology clinician. The pilot study achieved this.
- Further work has been identified following the pilot, including:
  - Research patient perspectives of biologic therapy dose reduction (research project currently recruiting patients).
  - Investigate relevance of drug level and anti-drug antibody assays and ultrasound in identifying patients' suitability to enter dose reduction programs or progress to subsequent dose intervals.
  - Roll out to other non TNFi therapies and intravenous biologic therapies.

7. References

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