

Timing of the Last Dose of Biologic Therapy and Risk of Post-Surgical Infections in Patients with Psoriasis

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CONCLUSIONS

We found a non-statistically significant decrease in the risk of post-surgical infection with adherence to the recommended stopping time prior to surgery.

Analysis in large multi-national datasets may be needed to further understand the association between the timing of the last biologic dose and the risk of post-surgical infection and flare of psoriasis.

Alternative approaches should also be considered e.g. pragmatic randomized controlled trials; investigation of biologic drug level at surgery and associated risk of infection.

BACKGROUND

- 1 There is little evidence to guide clinical practice regarding the ideal time to stop biologic therapy prior to elective surgery.
- 2 Both post-surgical infections, which may be associated with significant morbidity / mortality, and loss of disease control may be important patient concerns.
- 3 British Association of Dermatologists' (BAD) guidelines for biologic therapy for psoriasis in 2017 states:

"In people undergoing elective surgery...advice stopping biologic therapy 3-5 times the half-life of the drug in question or the length of the treatment cycle (whichever is longer) between the last dose of therapy and the planned surgery."

AIM

Does stopping biologic therapies for psoriasis according to the BAD guidelines prior to surgery reduce the risk of post-surgical infection?

METHODS

British Association of Dermatologists Biologic Interventions Register (BADBIR) - prospective safety registry of patients with psoriasis on systemic therapies established in 2007 in the UK and the Republic of Ireland³.

Inclusion criteria:

Surgical procedures identified by adverse events entered under "Event of Special (ESI) - Surgery" and/or coded under MedDRA Single Organ Classification (SOC) of "Surgical and medical procedures".

Patients starting etanercept, infliximab, adalimumab, ustekinumab for plaque psoriasis with an entered last biologic dose date prior to surgical procedure eligible for inclusion.

Post-surgical infections: identified by adverse events entered under ESI for serious infection and/or coded under MedDRA SOC "Infections and infestations" occurring within 30 days after surgical procedure or flagged as post-surgical infection.

Analysis:

Descriptive summary of recorded surgeries within BADBIR; number and type of post-surgical infections

Crude and adjusted (age, sex, number of comorbidities) logistic regression to obtain odds ratio (OR) for adherence to BAD biologics guideline recommendation and risk of post-surgical infection

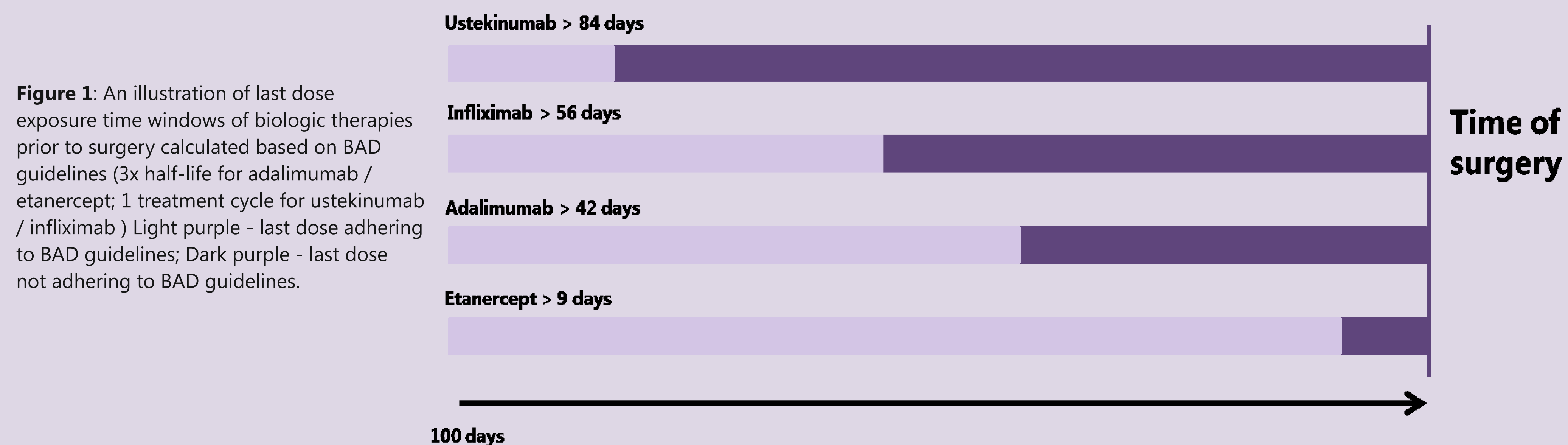


Figure 1: An illustration of last dose exposure time windows of biologic therapies prior to surgery calculated based on BAD guidelines (3x half-life for adalimumab / etanercept; 1 treatment cycle for ustekinumab / infliximab). Light purple - last dose adhering to BAD guidelines; Dark purple - last dose not adhering to BAD guidelines.

RESULTS

N=709 recorded surgeries
Post-surgical infections = 33 (4.7%)

Biologic	Number of surgeries	Median time between last dose of biologic and surgery (days; IQR)	Proportion stopping in accordance with guideline
Etanercept	41	24 (37)	28 (68.3%)
Infliximab	90	48 (104)	37 (40.7%)
Adalimumab	92	17 (30)	22 (23.9%)
Ustekinumab	486	56 (60)	127 (26.1%)

Table 1: Descriptive summary of surgical procedures and the last dose of the biologic therapy before surgery

DISCUSSION

- 1 This is the first study to utilise a large psoriasis treatment registry to investigate the optimal time to stop biologic therapy before elective therapy in patients with psoriasis.
- 2 Recent cohort study of patients (4288 post-elective knee/hip arthroplasty) with immune-mediated inflammatory diseases (including psoriasis) showed no increased risk of hospitalisation for infection for infliximab stopping <4 weeks compared with stopping 8-12 weeks¹.
- 3 Small single centre study of 77 procedures in psoriasis patients found no significant difference with risk of post-surgical complications in those who stopped biologic therapies vs those who continued².

Category	N (%)
Bone and joint therapeutic procedures	174 (24.8)
Skin and subcutaneous tissue therapeutic procedures	104 (14.8)
Head and neck therapeutic procedures	81 (11.5)
Gastrointestinal therapeutic procedures	59 (8.4)
Therapeutic procedures and supportive care	50 (7.1)

Table 2: The five most common surgical procedures coded by MedDRA high-level group term

	Non-adherence to BAD guidelines (n=495)	Adherence to BAD guidelines (n=214)
Number of post-surgical infections	28 (5.7%)	5 (2.4%)
Crude OR	/	0.40 (95% CI 0.15,1.06)
Adjusted OR	/	0.40 (95% CI 0.15,1.06)

Table 3: Number of post-surgical infections in both exposure groups and the OR for adherence to BAD guidelines and risk of post-surgical infections. OR - odds ratios; CI - confidence intervals

Strengths and weaknesses of the study

- ✓ Real-world data
- ✓ Fully industry independent data analysis
- ✗ Incomplete information re: whether surgery was elective
- ✗ Small sample size
- ✗ Lack of dose date data for etanercept and adalimumab
- ✗ Loss of disease control not consistently recorded
- ✗ Date of re-initiation of biologic only available for ESIs

Category	N (%)
Postoperative wound infection	8 (24.2)
Post procedural infection	4 (12.1)
Urinary tract infection	3 (9.1)
Nasopharyngitis	3 (9.1)
Lower respiratory tract infection	3 (9.1)
Sinusitis	2 (6.1)
Ear infection	2 (6.1)
Abscess	1 (3.0)
Skin infection	1 (3.0)
Cellulitis	1 (3.0)
Infected tenosynovitis	1 (3.0)
Tooth infection	1 (3.0)
Influenza	1 (3.0)
Gastroenteritis	1 (3.0)
Infected cyst	1 (3.0)

Table 4: List of post-surgical infections in participants on biologic therapies in BADBIR coded by MedDRA preferred term

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