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SHORT REPORT

Switching infliximab in psoriatic patients during COVID-19 pandemics: A real-life retrospective study comparing intra-versus interclass switching strategies

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Abstract

During this pandemic, dermatological infusion centers were partially unavailable, suspended or even reconverted to guest COVID-19 patients, consequently infliximab (IFX) infusions became challenging for their both logistic arrangement and also for patients' COVID-19 phobia. This 48 weeks follow-up retrospective observational study included 37 PsO patients that underwent IFX SB2 during pandemic in two primary dermatological referral centers. In 23 (62.1%) we had to switch from IFX to other biologics, not motivated by adverse reactions, contraindication or even loss of response but only to pandemic related conditions. Nine patients underwent interclass switching and 15 underwent intraclass switching; interestingly 2 patients that underwent adalimumab SB-5 switched back to IFX. Interclass switching was privileged in elder patients and smokers. All patients at week 48 achieved PASI 100. Intra- and interclass switchings are both safe and effective strategies in psoriatic patients with COVID-19 phobia and/or difficulties to undergo infliximab infusions.

KEYWORDS

biologics, COVID-19 pandemic, infliximab, interclass switching, intraclass switching, psoriasis, switching, teledermatology

1 | INTRODUCTION

Although COVID-19 pandemic continues to challenge healthcare systems worldwide, medical decisions should be directed by the evidence-based medicine principles[1,2]; at the same time, contradicting data on psoriasis (PsO) and biologics are present in literature and social media[3–5] ending up to influence patients' compliance.[6]

Infliximab (IFX), a humanized IgG1 monoclonal antibody targeting tumor necrosis factor (TNF)-α, was the first biologic drug authorized for PsO. Among biologics, only infliximab and its biosimilars, such as SB-2, has a pro-kilo parenteral administration that forces patients every 8 weeks to undergo a ≃60 min infusion and a total of 3 h hospitalization for each infusion.[7] This laborious protocol, that maintains patients hospitalized longer than other biologics, virtually, also exposes them to a higher possibility of SARS-CoV-2 infection.

During this pandemic, dermatological infusion centers were partially unavailable, suspended or even reconverted to guest COVID-19 patients, consequently IFX infusions became challenging for their both logistic arrangement and also for patients with COVID-19 phobia.

Andrea Conti and Giovanni Damiani contributed equally to this study.

Thus, several IFX responders asked to switch to another anti-psoriatic biologic drug and, at the moment, no indications are present to orient intraclass or interclass switchings.[8–10]

2 | MATERIALS AND METHODS

2.1 | Study design

This a retrospective observational study that included PsO patients that underwent IFX SB2 during pandemic in two primary referral dermatological centers in Northern Italy (University Hospital of Modena, Italy and IRCCS Istituto Ortopedico Galeazzi in Mian, Italy) between February 2020 and March 2021.

Adult patients with a diagnosis of plaque PsO, with or without psoriatic arthritis (PsA), responders, treated in-label (intravenously every 8 weeks) with IFX originator or its biosimilar in monotherapy were enrolled and followed during COVID-19 pandemic.

Demographics (age, gender), clinical data (body mass index [BMI], comorbidities, smoking, PsO duration) and pharmacological history (previous anti-psoriatic biologic drugs and their drug-survival) were carefully collected using institutional databases. Patients underwent dermatological assessment every visits.

2.2 | Dermatological assessment

During the entire study, patients were clinically assessed by two board certified dermatologists (A. C., G. D) that performed Psoriasis Area Severity Index (PASI),[11] Psoriasis Epidemiology Screening Tool (PEST),[12] ClASsification criteria for Psoriatic Arthritis (CASPAR).[13] Patients were evaluated at T0 (Baseline), T1 (4 weeks), T2 (16 weeks), T3 (32 weeks), T4 (40 weeks), and T5 (48 weeks) during in-person and teledermatological visits. Patients treated with IFX SB-2 were evaluated in person during the infusions at T0, T1, T2, T3, T4 and T5, while patients switched to subcutaneous biologics were evaluated in person only at T0, T2, and T4 and in teledermatology at T1, T3, and T5. Interclass switching was privileged in case of needle-phobia due to the lower number of injections per year (50 injections/year vs. 32 injections/year or 17 injections/year, respectively for Adalimumab and its biosimilars, secukinumab, and ixekizumab).

Patients undergoing infusions had to stay at the hospital for 60 min on average while patients undergoing adalimumab and its biosimilars had to stay 30 min.

2.3 | Statistics

Data were reported as mean ± SD, median [interquartile range] or percentages (%). The software MedCalc Statistical Software version v19.0.5 (MedCalc Software bvba, Ostend, Belgium) was used for all the statistical.

3 | RESULTS

3.1 | Clinical characteristics

We enrolled 25 PsO patients and 12 PsO&PsA patients with a male prevalence (81.1%) and a median age of 58.0 [45.5–68.0]. Despite the low Charlson comorbidity index the patients were globally overweight (BMI = 28.0 [22.5–31.0]), while only 13 (35.1) were smokers.

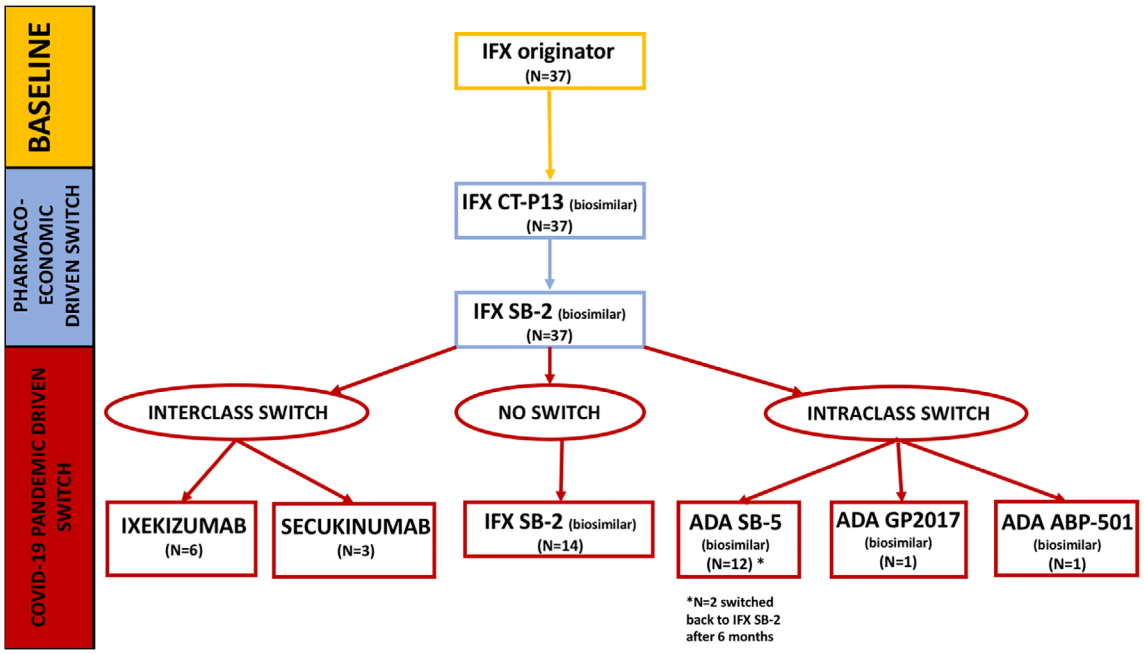

FIGURE 1 Switchings over the patients' journey in the enrolled cohort

Demographics and clinical data are summarized in Table S1. The entire cohort started with IFX originator (116.0 [91.5–142.8] duration), underwent two pre-pandemic pharmaco-economic driven switched to IFX CT-P13 (18.0 [16.0–21.0] duration) and then to IFX SB-2 (15.0 [14.0–18.0] duration) (Figure 1).

3.2 | Interclass versus intraclass switching

During pandemic 23 (62.1%) patients had to switch to other biologics for COVID-phobia ($N = 9$ [39.1%]) or for impossibility to undergo regular IFX infusions ($N = 14$ [60.9%]) (Figure 1). Remarkably, none of them exhibited a lack of response to IFX SB-2. Medical history and clinical data are described in detail in Table 1.

Interclass switching involved 9 patients ($N = 6$ with ixekizumab and $N = 3$ with secukinumab), while the intraclass switching involved 14 patients and was directed only to adalimumab biosimilars ($N = 12$ to ADA SB-5, $N = 1$ to ADA GP2017 and $N = 1$ to ADA ABP-501).

Interestingly, interclass switching was preferred in elder patients ($p < 0.001$) and smokers ($p < 0.001$), while disease duration, gender, BMI, and psoriatic arthritis did not differ among intra and interclass switched patients. After a 48 weeks follow-up, patients maintained the response to the prescribed anti-psoriatic drug, except for two patients (16.7%) switched to ADA SB-5 that after 6 months had to switch back to IFX originator.

After 48 weeks follow-up, IFX SB-2 patients spent more time in the hospital than patients that switched to subcutaneous injections (18 vs. 1.5 h, $p < 0.001$).

4 | DISCUSSION

IFX remains an effective biologic drug for both PsO and PsA patients, but its infusions were difficult to deliver during COVID-19 pandemic due to both patient-related (i.e., COVID-19 phobia or Cabin fever syndrome) and hospital-related (i.e., infusions room unavailability) causes.[14] Furthermore, during pandemic chronic patients undergoing immunosuppressive drugs globally decreased their compliance[6] due to media disinformation and fake news,[15] discordant position on therapies, COVID-19, and related outcomes.[3,4,16,17] In line with National Psoriasis Foundation recommendations,[18] The Italian Society of Dermatology (SIDeMaST) suggested not to discontinue biologics in absence of COVID-19,[19] while in case of COVID-19, symptomatic or asymptomatic, positions remain still discordant. In fact, anti-TNF alpha (i.e., IFX) seems to increase SARS-CoV-2 infection rate,[4] protect and care cytokine storm,[20] prevent COVID-19-related PsA flares,[21] and ICU admissions.[4]

During lockdown we experienced the need to switch patients from IFX to other biologics not motivated by adverse reactions, contraindication or even loss of response, indeed. Demographics and socio-economic characteristics are reported to influence biologics response,[22,23] but, unlike biomarkers,[24,25] unable to predict single-patient response to a certain biologic from the baseline.

Scattering data are present in literature to orient clinicians interclass or intraclass switching, so we performed this retrospective study.

Intraclass switching from IFX to ADA biosimilars is motivated by the same targeted cytokine, the administration (intravenous vs. subcutaneous), the cytokine storm protection in case of severe

TABLE 1 Clinical evaluation of intra- and inter-class switching

		Interclass switch ($N = 9$)		Intraclass switch ($N = 14$)		
Clinical characteristics	**No switch ($N = 14$)**	**Ixekizumab ($N = 6$)**	**Secukinumab ($N = 3$)**	**ADA SB-5 ($N = 12$)**	**ADA GP2017 ($N = 1$)**	**ADA ABP-501 ($N = 1$)**
Age, median [IQR], yoa	47.5 [43–59]	65.0 [59.8–69.5]	61.0 [59.5–63.5]	56.5 [45.0–70.5]	36.0	66.0
Male, *N* (%)	11 (78.6)	5 (83.3)	3 (100.0)	9 (75.0)	1 (100.0)	1 (100.0)
BMI, median [IQR], kg/m^2	27.8 [23.8–28.9]	28.9 [27.5–29.8]	29.2 [28.6–30.1]	28.8 [24.7–30.4]	25.5	26.4
Disease duration, median [IQR], years	25.5 [21.5–29.0]	32.5 [31.0–38.5]	25.0 [24.0–28.0]	27,5 [22.5–32.3]	17.0	40.0
Psoriatic arthritis, *N* (%)	3 (21.4)	2 (33.3)	1 (33.3)	4 (33.3)	1 (100.0)	0 (0)
Smokers, *N* (%)	4 (28.6)	4 (66.7)	2 (66.7)	2 (16.7)	0 (0)	1 (100.0)
Therapeutic parameters						
PASI (T0), median [IQR]	0 [0–1]	0	0	0 [0–0.3]	0	0
PASI (T1), median [IQR]	0 [0–1]	0	0	0	0	0
PASI (T2), median [IQR]	0 [0–1]	0	0	0	0	0
PASI (T3), median [IQR]	0 [0–1]	0	0	0[a]	0	0
PASI (T4), median [IQR]	0 [0–1]	0	0	0	0	0
PASI (T5), median [IQR]	0 [0–1]	0	0	0	0	0

Note: T0: Baseline, T1: 8 weeks, T2: 16 weeks, T3: 32 weeks, T4: 40 weeks, T5: 48 weeks.
Abbreviations: BMI, body mass index; IQR, interquartile range.
[a]$N = 2$ patients switched back to the IFX originator due to ADA SB-5 loss of function.

COVID-19,[20] the decreased drug immunogenicity[26] and the higher efficacy to COVID-19 vaccines.[27] At the same time, intraclass switching also expose to a potential lack of response, as testified by two patients that had to switch back to IFX after 6 months of ADA SB-5.

Conversely, interclass switching from IFX to IL-17 blockers is motivated by the administration (intravenous vs. subcutaneous), the faster response, longer drug survival,[28] the lower number of administrations, the decreased drug immunogenicity,[26] the effect in ACE2 receptor utilized by SARS-CoV-2[8] and the evidence regarding COVID-19 vaccination in PsO patients.[5]

Furthermore, IL-17 blockers produce lower levels of anti-drug antibodies[29] than TNF alpha blockers (i.e., ADA and IFX)[26] limiting the potential need to introduce also methotrexate, a second immunosuppressive agent capable to increase SARS-CoV-2 infection rate. Although, also interclass switching may be hazardous since the cytokine block move from TNF-alpha to IL-17 with a potential loss of response, IL-17 blockers demonstrated excellent profiles of safety and efficacy in both trials and real-life.[30]

In conclusion, a therapeutic change of perspectives in needed from targeting a single pro-inflammatory cytokine to understanding the biological signature of the patient (precision medicine); in fact, precision medicine by combining omics, lab, and clinical data may address clinicians to a drug maximizing his response and decreasing the potential side effect occurrence.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

CREDIT STATEMENT

Andrea Conti and **Giovanni Damiani**: Conceptualization. **Andrea Conti**, **Giovanni Damiani**, **Paolo Daniele Maria Pigatto** and **Giovanni Pellacani**: Methodology. **Giovanni Damiani:** Software. **Andrea Conti** and **Giovanni Pellacani:** Validation. **Giovanni Damiani:** Formal analysis. **Andrea Conti**, **Giovanni Damiani**, **Giulia Odorici** and **Roberta Ruggeri:** Investigation. **Paolo Daniele Maria Pigatto** and **Giovanni Pellacani:** Resources. **Andrea Conti**, **Giovanni Damiani** and **Giulia Odorici:** Data curation. **Andrea Conti** and **Giovanni Damiani:** Writing - original draft. **Andrea Conti**, **Giovanni Damiani**, **Roberta Ruggeri**, **Giulia Odorici**, **Francesca Farnetani**, **Paolo Daniele Maria Pigatto** and **Giovanni Pellacani:** Writing - review & editing. **Giovanni Damiani** and **Giulia Odorici:** Visualization. **Paolo Daniele Maria Pigatto** and **Giovanni Pellacani:** Supervision. **Andrea Conti**, **Giovanni Damiani**, **Giulia Odorici** and **Roberta Ruggeri:** Project administration.

DATA AVAILABILITY STATEMENT

Data are available upon reasonable request to the Corresponding author.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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