



Switching from Other Biologics to ZRC3197
(Adalimumab Biosimilar) in Patients with
Spondyloarthropathy: A Prospective Evaluation from
Real-Life Clinical Practice

Sanjiv Kapoor

Sanjivni Rheumatology Centre and ISIC Superspeciality Hospital, New Delhi

Published in: JAPI, 2017/May/65(5)

Background/Purpose & Methods

- Tumour necrosis factor inhibitors (TNFi) like Infliximab, Etanercept and Adalimumab have been successfully studied in controlled clinical trials and are currently recommended in the treatment of patients with Spondyloarthritis (SPA).
- Significant proportion of patients in clinical studies have, however, failed to achieve a desired clinical response, or, are discontinued from the therapy due to secondary inefficacy or side effects.
- Switching of Indian patients with SPA with inadequate response to other TNFi to ZRC 3197(Adalimumab Biosimilar) treatment available in India, was monitored and reported.

Background/Purpose & Methods

- Patients with SPA who were treated previously with biologics (INF, ETA), and who met criteria below were considered for switching to biosimilar ADA therapy:
 - adults with at least 18 years of age with SPA according to ASAS axial SpA criteria or ASAS peripheral SpA criteria (2011); BASDAI ≥ 4 and failure of ≥ 2 nonsteroidal anti-inflammatory drugs (NSAIDs); and prior treatment with ETA discontinued ≥ 3 weeks and IFX was discontinued ≥ 2 months before the first biosimilar ADA injection.
- Strategy of switching to biosimilar Adalimumab therapy was as per the ASAS consensus recommendations:
 - active disease > 4 weeks; BASDAI on previous TNFi > 4 (0-10). Inadequate response to INF was indicated by a $< 50\%$ decline in previous BASDAI.

Background/Purpose & Methods

- Biosimilar Adalimumab therapy was initiated at 40 mg subcutaneously (s.c.) every other week; tapering and discontinuation of treatment over 1 year was guided by the disease activity, and was primarily done by increasing the dosing interval rather than decreasing the dose.
- The aim of the biosimilar ADA treatment was to maintain the BASDAI below 50% of the baseline scores.
- Data is presented for two groups of patients: (1) Typical cases group comprising of routine patients with SPA; and (2) atypical cases wherein use of biosimilar Adalimumab and its effectiveness has been discussed with unusual comorbid conditions.

Result-Typical Cases

- Data of 15 patients with SPA, who were switched to biosimilar Adalimumab from other TNF- α inhibitors.
- Out of 13 patients (86%) who previously received INF; 1 patient (7%) who initially received INF followed by ETA; and 1 patient (7%) on ETA; who were switched to biosimilar ADA therapy.
- Reasons for switching to biosimilar ADA in this patient group included: secondary inefficiency in 10 patients (66.6%); uveitis flare-up with IFX in 3 patients (20%); and no improvement in psoriasis in 2 patients (13.3%). Patient follow-up was done every 15 days for initial 3 months and every month thereafter.

Result-Typical Cases

- All the patients showed insufficient responses for all parameters (BASDAI, VAS (pain) and ESR scores) while on treatment with previous other biologics, prior to switching. There was a substantial drop in all these scores when the patients were switched to biosimilar ADA, suggestive of efficacy of the treatment.
- Post 1 year of treatment with biosimilar ADA; all the patients were continuing on the biosimilar Adalimumab therapy. There was no inefficacy or serious adverse events noted in these patients.

Result-Typical Cases

Total No. of Patients = 15

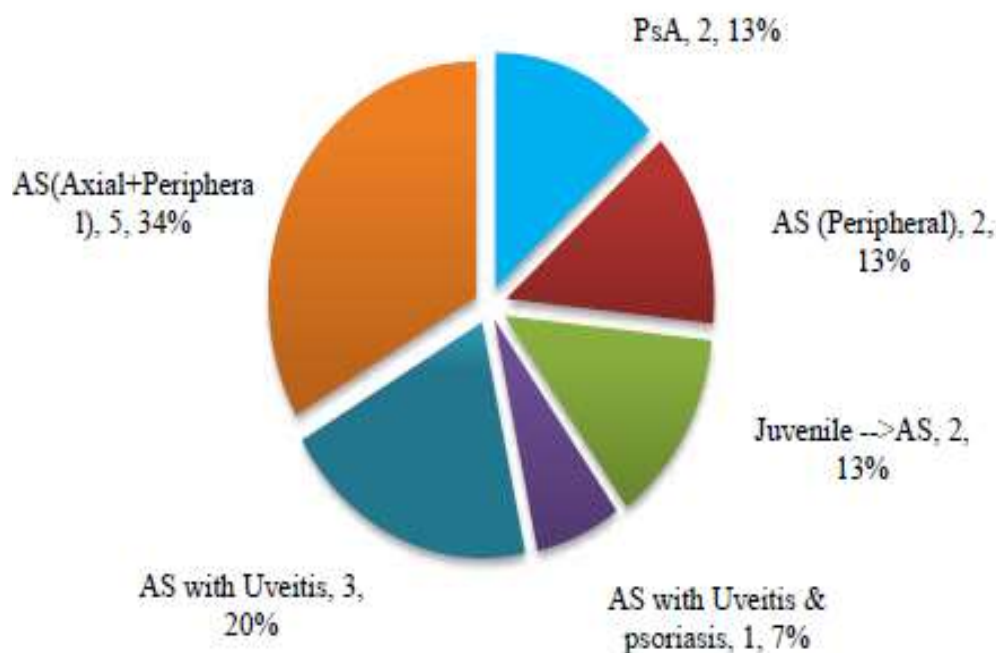


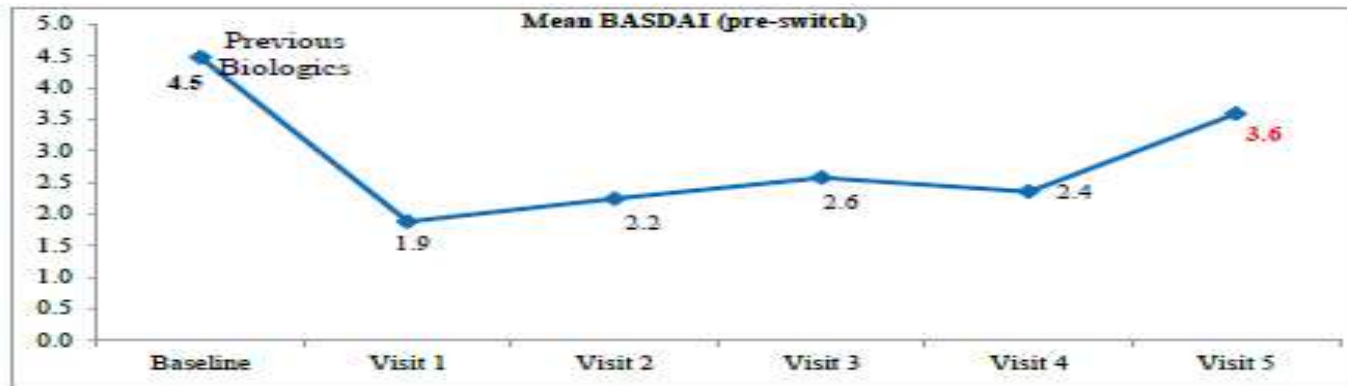
Fig. 1: Indication-wise distribution of patients who were switched to biosimilar Adalimumab

Table 1: Baseline demographic and clinical characteristics of patients

| Parameters | N = 15 |
|-----------------------------------|---------------|
| Age (in years) | 40.5±9.26 |
| Male/Female | 13/2 |
| Average Disease duration | 11 years |
| HLA – B27 Positive | 80% (12/15) |
| Extra Articular Manifestation | |
| <i>Enthesitis</i> | 7/15 (47%) |
| <i>Uveitis</i> | 4/15 (26%) |
| <i>Psoriasis</i> | 3/15 (20%) |
| Mean BASDAI | 4.2 |
| Mean ESR (mm/hr) | 54 |
| Mean CRP (mg/l) | 50.4 |
| Mean Hb (g/dl) | 12.6 |
| Concomitant Therapy | |
| <i>DMARDs</i> | 13/15 (86.6%) |
| <i>Steroids (Intra-articular)</i> | 4/15 (26.6%) |
| <i>NSAIDs</i> | 6/15 (40%) |
| <i>Infliximab mean duration</i> | 4.9 years |

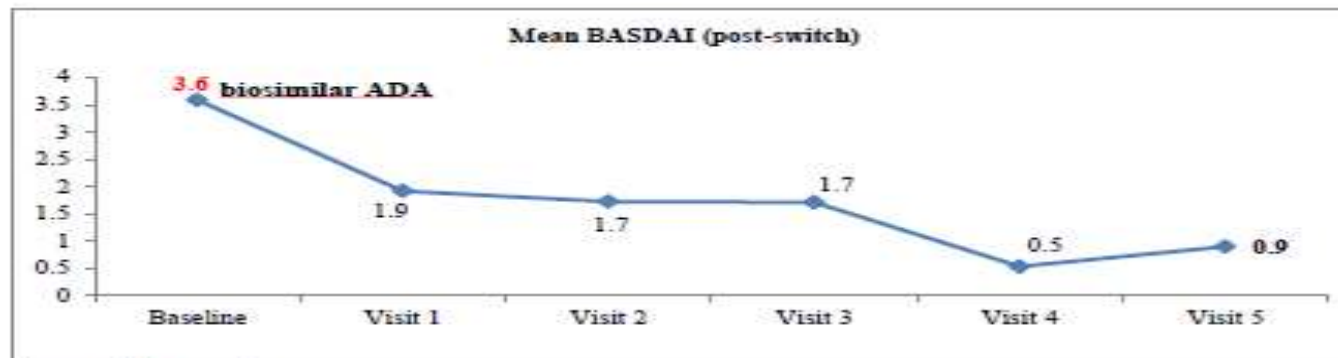
Data presented as: mean; mean±standard deviation; number of patients(n)/total number of patients (N); n/N (percentage of patients); unless specified otherwise.

Result-Typical Cases



IR: Insufficient response defined as < 50% improvement in BASDAI post infusion of previous biologics

Fig. 2a: Mean BASDAI score [Pre-Switch]

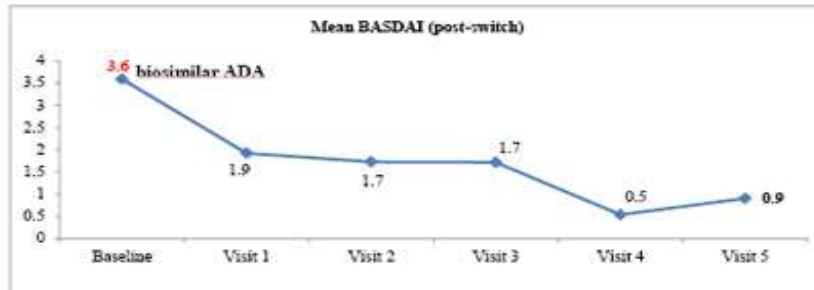


ADA: Adalimumab.

BASDAI score reduced significantly in patients who had insufficient response to previous biologics and were switched to biosimilar Adalimumab.

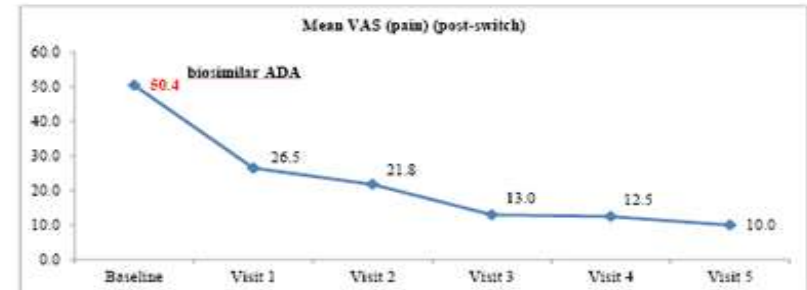
Fig. 2b: Mean BASDAI score with biosimilar Adalimumab [Post-Switch]

Result-Typical Cases



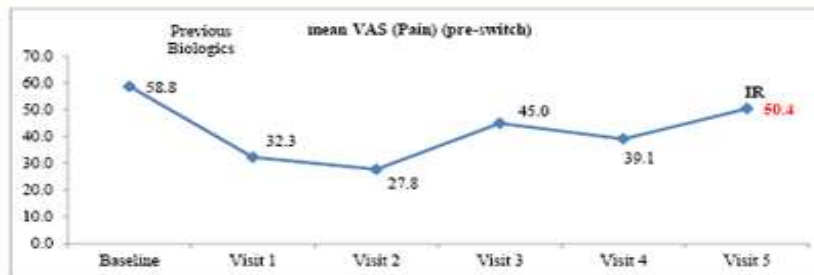
ADA: Adalimumab.
BASDAI score reduced significantly in patients who had insufficient response to previous biologics and were switched to biosimilar Adalimumab.

Fig. 2b: Mean BASDAI score with biosimilar Adalimumab [Post-Switch]



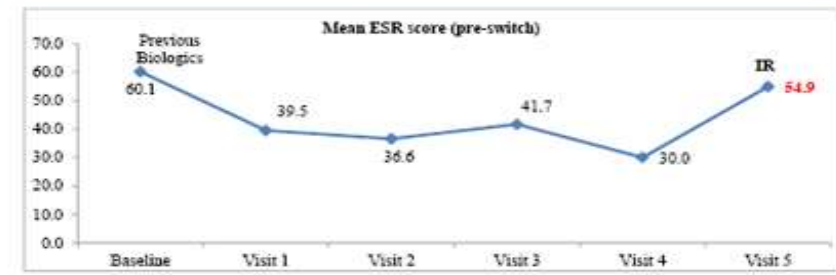
ADA: Adalimumab
VAS score showed pain reduced significantly in patients who had insufficient response to previous biologics and were switched to biosimilar Adalimumab.

Fig. 3b: Mean VAS (Pain) score with biosimilar Adalimumab [Post-Switch]



IR: Patients with Inadequate response to previous biologics had increased Pain reported in follow-up visits

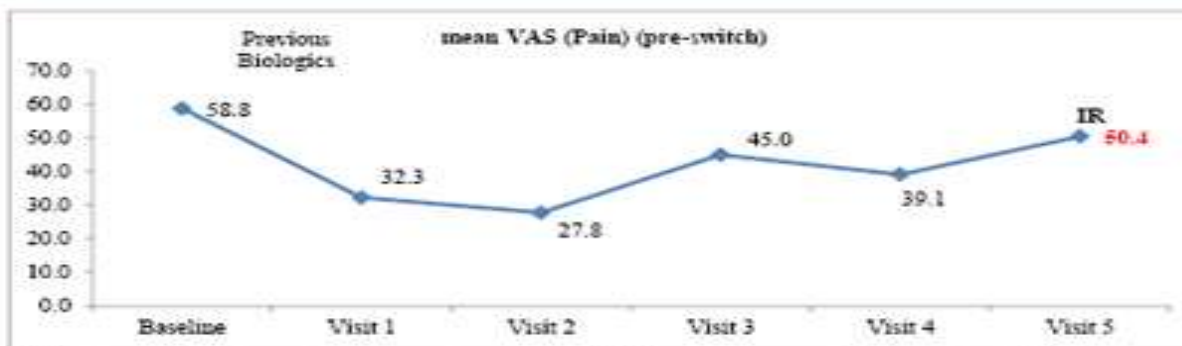
Fig. 3a: Mean VAS (Pain) score [Pre-Switch]



IR: Patients with Inadequate response to previous biologics had increased Inflammatory markers (ESR) reported in follow-up visits

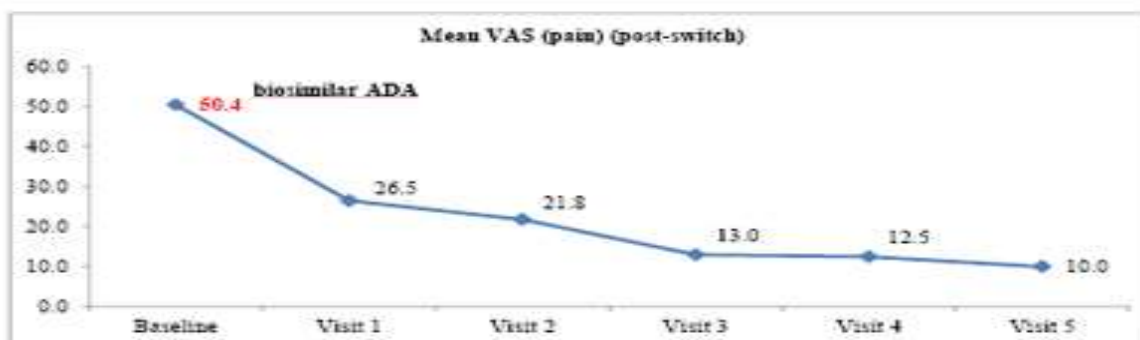
Fig. 4a: Mean ESR score [Pre-Switch]

Result-Typical Cases



IR: Patients with Inadequate response to previous biologics had increased Pain reported in follow-up visits

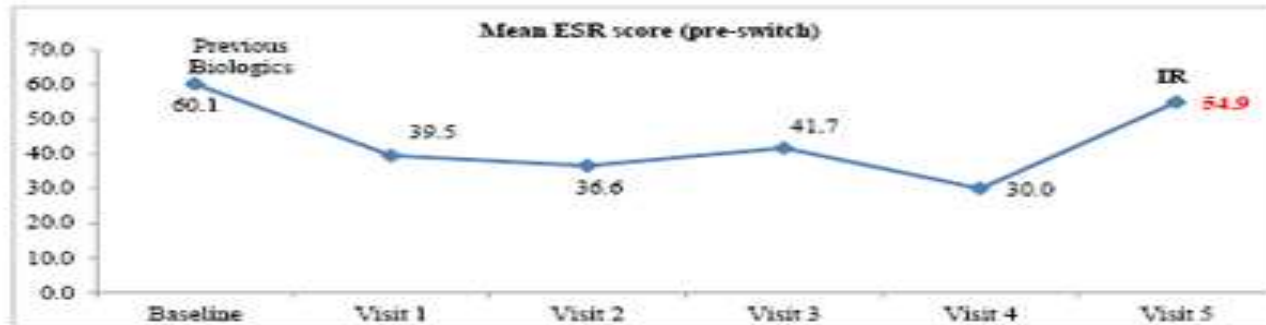
Fig. 3a: Mean VAS (Pain) score [Pre-Switch]



ADA: Adalimumab
VAS score showed pain reduced significantly in patients who had insufficient response to previous biologics and were switched to biosimilar Adalimumab.

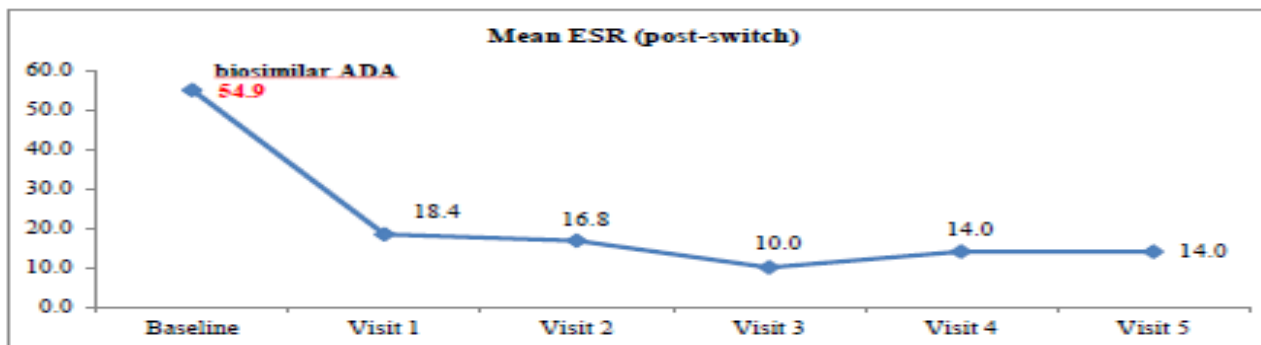
Fig. 3b: Mean VAS (Pain) score with biosimilar Adalimumab [Post-Switch]

Result-Typical Cases



IR: Patients with Inadequate response to previous biologics had increased Inflammatory markers (ESR) reported in follow-up visits

Fig. 4a: Mean ESR score [Pre-Switch]



Inflammatory marker (ESR) showed significant reduction in patients who had insufficient response to previous biologics and were switched to biosimilar Adalimumab.

Fig. 4b: Mean ESR score with biosimilar Adalimumab [Post-Switch]

Result-Atypical Cases

- Atypical experience with biosimilar ADA therapy in 5 patients with AS.
- Cases # 1 and 2: AS with Achilles Tendonitis:

Two patients were diagnosed of AS with enthesitis. Both the patients had persisting Achilles Tendonitis. Patients had received IFX, and were switched to biosimilar ADA 40mg s.c. After persistence of Heel enthesitis. The patients received 3 doses of biosimilar ADA and responded completely for Achilles Tendonitis.
- Case # 3: AS with hip involvement:

A 38 years old male patient was diagnosed of AS and was receiving IFX for 5 years. Patient had undergone a left hip replacement. After 2 months, patient developed severe right hip pain, and increased disease activity on IFX. Patient was switched to biosimilar ADA therapy, and his hip pain was relieved post 3 doses of the treatment.

Result-Atypical Cases

- Case # 4: AS with Uveitis Flare:

A 31 years old male patient was diagnosed of AS (peripheral) with Uveitis flare in spite being treated with IFX. The duration of the disease was 15 years and HLA B27 tested negative. The patient had received IFX. After inadequate response to Uveitis, the patient was switched to biosimilar ADA. Figure 5 shown the improvement in clinical parameters post switching to biosimilar ADA.

- Case # 5: AS with chest enthesitis resistant to IFX:

A male patient was diagnosed on AS involving axial and peripheral symptoms, with chest enthesitis. The patient was also hypertensive. The patient developed a flare in chest enthesitis leading to difficulty in breathing, while on IFX treatment for 5 months. Treatment was switched to biosimilar ADA and there was an immediate improvement in the overall condition of the patient. The changes in the clinical parameters are shown in Figure 6. Biosimilar ADA therapy was tapered to slow withdrawal.

Result-Atypical Cases

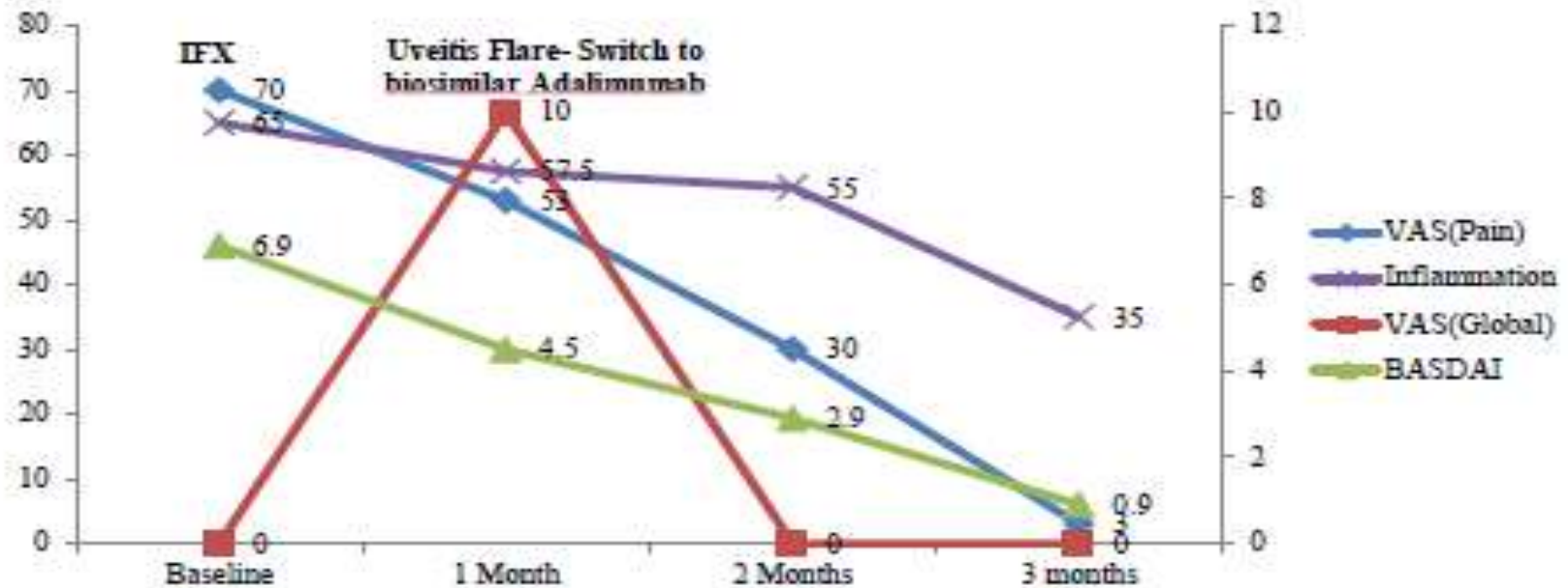


Fig. 5: Atypical case # 4: AS with uveitis flare

Result-Atypical Cases

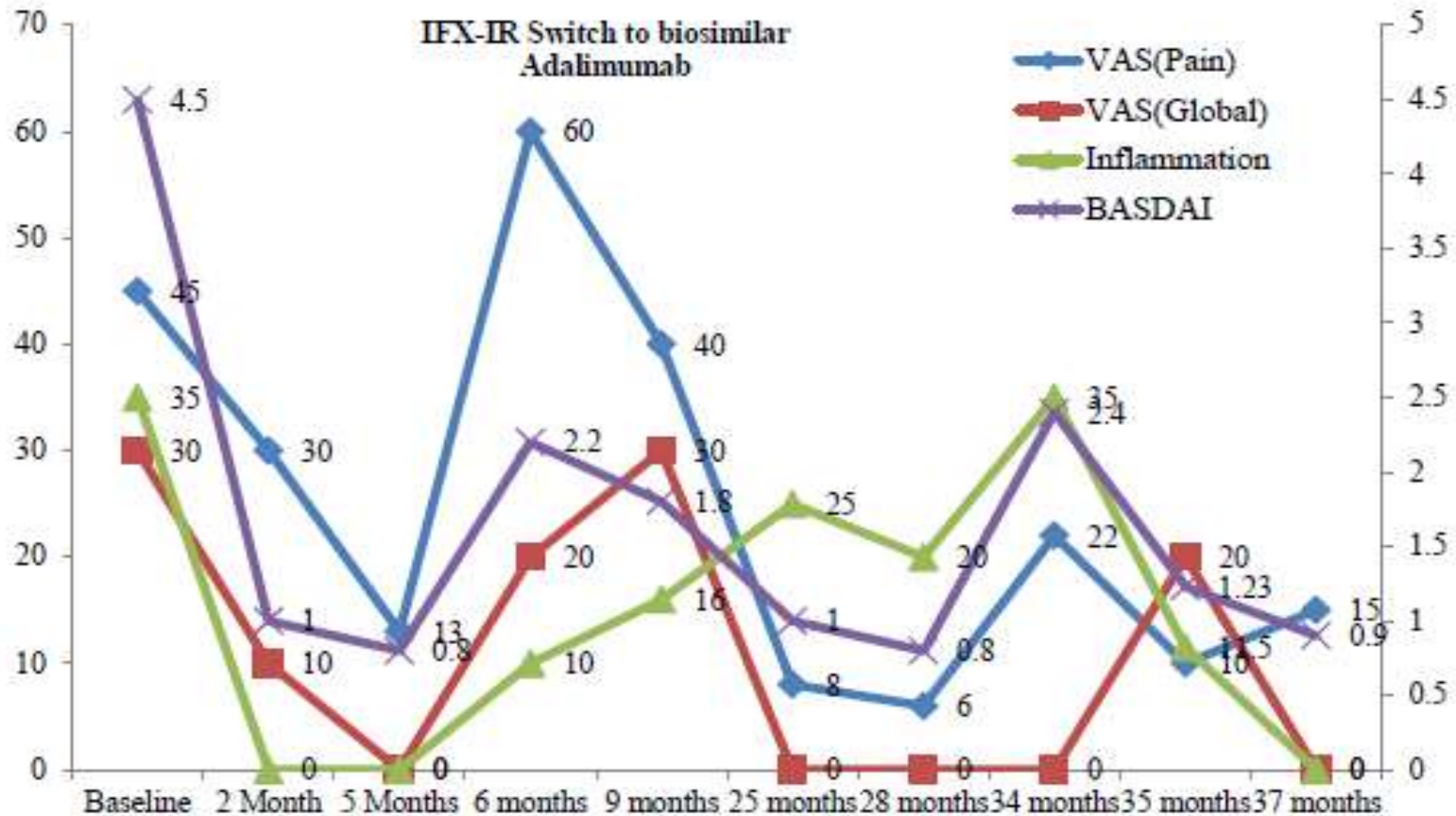


Fig. 6: Atypical Case # 5: AS with inadequate response to IFX

Conclusion

- Biosimilar ADA served as an effective option with an acceptable tolerability, for switching Indian patients with SPA not responding to other TNFi.

Abridged Prescribing Information

COMPOSITION: Exemptia™ (Adalimumab) 40 mg /0.8 mL single use pre filled syringe and 20mg /0.4 mL single use pre filled syringe **DESCRIPTION:** EXEMPTIATM (Adalimumab) is a recombinant human IgG1 monoclonal antibody specific for human tumor necrosis factor (TNF- α). EXEMPTIATM is supplied as a sterile, preservative-free solution of Adalimumab for subcutaneous administration. The solution of EXEMPTIATM is clear and colorless. **MECHANISM OF ACTION:** Adalimumab binds specifically to TNF- α and blocks its interaction with the p55 and p75 cell surface TNF- α receptors. Adalimumab also lyses surface TNF expressing cells in vitro in the presence of complement. Elevated levels of TNF- α is found in the synovial fluid of rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis patients and play an important role in both the pathologic inflammation and the joint destruction that are hallmarks of these diseases. **INDICATIONS & DOSAGE:** Rheumatoid Arthritis, Psoriatic Arthritis, and Ankylosing Spondylitis: The recommended dose of EXEMPTIATM for adult patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), or ankylosing spondylitis (AS) is 40 mg subcutaneously administered every other week. Methotrexate (MTX), other non-biologic DMARDs, glucocorticoids, nonsteroidal anti-inflammatory drugs (NSAIDs), and/or analgesics may be continued during treatment with EXEMPTIATM. Juvenile Idiopathic Arthritis: Exemptia™ dosing in JIA is based on weight; for 10 kg (22 lbs) to <15 kg (33 lbs): 10 mg s.c. every other week. For 15 kg (33 lbs) to < 30 kg (66 lbs): 20 mg s.c. every other week and for \geq 30 kg (66 lbs): 40 mg s.c. every other week. Plaque Psoriasis or Non-Infectious Uveitis: Initial dose of 80 mg, followed by 40 mg every other week starting from week one after initial dose. Hidradenitis Suppurativa: 160 mg (Day 1) (four 40 mg injections in one day or two 40 mg injections per day for two consecutive days), followed by 80 mg two weeks later (Day 15). Two weeks later (Day 29) begin a maintenance dose of 40 mg every week. Adult Crohn's Disease and Ulcerative Colitis: Initial dose (Day 1): 160 mg s.c. (four 40 mg injections in one day or two 40 mg injections per day for two consecutive days). Second dose two weeks later (Day 15): 80 mg. Two weeks later (Day 29): Begin a maintenance dose of 40 mg s.c. every other week. For patients with Ulcerative Colitis only: Only continue EXEMPTIATM in patients who have shown evidence of clinical remission by eight weeks (Day 57) of therapy. Pediatric Crohn's Disease: For weight 17 kg (37 lbs) to < 40 kg (88 lbs): Initial dose (Day 1): 80 mg s.c. (two 40 mg injections in one day). Second dose two weeks later (Day 15): 40 mg s.c.. Two weeks later (Day 29): Begin a maintenance dose of 20 mg s.c. every other week. For \geq 40 kg (88 lbs): Initial dose (Day 1): 160 mg s.c. (four 40 mg injections in one day or two 40 mg injections per day for two consecutive days). Second dose two weeks later (Day 15): 80 mg s.c. (two 40 mg injections in one day). Two weeks later (Day 29): Begin a maintenance dose of 40 mg s.c. every other week. **CONTRAINDICATIONS:** Hypersensitivity to the active substance or to any of the excipients, Moderate to severe heart failure, Active tuberculosis or other severe infections such as sepsis and opportunistic infections. **SPECIAL WARNINGS AND PRECAUTIONS:** Serious and fungal infections: Do not start EXEMPTIATM during an active infection. If an infection develops, monitor carefully, and stop EXEMPTIATM if infection becomes serious • Anaphylaxis or serious allergic reactions may occur • Hepatitis B virus reactivation: Monitor HBV carriers during and several months after therapy. If reactivation occurs, stop EXEMPTIATM and begin antiviral therapy • Demyelinating disease: Exacerbation or new onset, may occur • Heart failure: Worsening or new onset, may occur • Lupus-like syndrome: Stop EXEMPTIATM if syndrome develops **USE IN PREGNANCY AND LACTATION:** Pregnancy Category B: Adequate and well controlled studies with EXEMPTIATM have not been conducted in pregnant women. Adalimumab is an IgG1 monoclonal antibody and IgG1 is actively transferred across the placenta during the third trimester of pregnancy. Lactation: No data is available on the absorption of adalimumab from breast milk in newborn or preterm infants. Caution should be exercised when EXEMPTIATM is administered to a nursing woman. **DRUG INTERACTION** Biological Products- Concomitant administration of EXEMPTIATM with other biologic DMARDs (e.g., Anakinra and Abatacept) or other TNF blockers is not recommended • Live Vaccines- Avoid the use of live vaccines with EXEMPTIATM. • Cytochrome P450 Substrates- The formation of CYP450 enzymes may be suppressed by increased levels of cytokines (e.g., TNF α , IL-6) during chronic inflammation. Upon initiation or discontinuation of EXEMPTIATM in patients being treated with CYP450 substrates with a narrow therapeutic index, monitoring of the effect (e.g., Warfarin) or drug concentration (e.g., Cyclosporine or Theophylline) is recommended and the individual dose of the drug product may be adjusted as needed. **UNDESIRE EFFECTS:** The most serious adverse reactions include the following • Serious Infections- Tuberculosis and Opportunistic Infections • Malignancies. The Clinical experience has reported Upper Respiratory Tract Infection (URTI), Increased creatine phosphokinase, Headache, Rash, Sinusitis, Nausea, Urinary Tract Infection (UTI), Abdominal pain, Flulike syndrome, Hyperlipidemia, Back pain, Hypercholesterolemia, Hematuria, Hypertension, Increased alkaline phosphatase as common side effects. **STORAGE CONDITION:** Store between + 2°C and + 8 °C, in the carton to protect from light. Do not freeze Exemptia™. Do not use Exemptia™ if frozen, even if it has been thawed. Keep out of reach of children. **PRESENTATION:** a) Injection: 40 mg/0.8 mL in a single-use prefilled syringe b) Injection: 20 mg/0.4 mL in a single-use prefilled syringe.

Zydu Biovation – Copyright ©

Please refer to the full Prescribing Information before starting EXEMPTIATM.

Please consult full Prescribing Information before prescribing.

Zydus Cadila does not recommend the use of any product in any different manner than as described in the prescribing information.

Further information is available on request from:

Cadila Healthcare Limited

Zydus Corporate Park

Nr. Vaishno Devi Circle,

SG Highway,

Ahmedabad – 382 481

Gujarat, India.

PHONE: +91-79-71800000

Thank you

