



Real-life Safety Profile of ZRC3197 (Adalimumab Biosimilar) in Indian Patients with Common Rheumatic Diseases

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Background/Purpose & Methods

- ZRC3197 (Adalimumab Biosimilar); Cadila Healthcare Ltd., India has been developed and approved for use in India since 2014, a monoclonal antibody targeting TNF- alfa.
- A biosimilar product is highly similar to the licensed originator biologic with no clinically meaningful differences in term of safety, purity and potency.
- This study is conducted to investigate real-life safety profile of biosimilar Adalimumab in patients with chronic inflammatory arthritis and other autoimmune conditions.

Background/Purpose & Methods

- All patients initiated on ZRC3197 (Adalimumab Biosimilar) in the departments of Clinical Immunology and Rheumatology and Pediatric Rheumatology, Christian Medical College, Vellore, during the period of December 2014 till August 2016, and had continued treatment for at least 3 months were included in this study.
- As a standard protocol, all patients undergo a high-resolution computed tomography (HRCT) thorax and Quantiferon TB Gold / Mantoux test as part of the screening protocol prior to TNFi administration in the institution.

Background/Purpose & Methods



- A retrospective electronic medical records (EMR) review was conducted for all the included patients after obtaining consent from the institutional review board.
- All these patients had assessments done every 3 months up to 1 year of biosimilar Adalimumab treatment.
- Safety information including serious adverse events (SAEs) and non-serious adverse events (AEs) as reported and recorded in the EMR, from the first dose of biosimilar adalimumab through 70 days (5 half-lives) after the last dose, was collected.

Result

- Real-time safety profile of biosimilar adalimumab similar to that already seen in a context of its controlled clinical trial.
- A total of 116 patients had received ZRC3197 (Adalimumab Biosimilar) during the study period. However, complete EMR data could be retrieved only for 78 patients, of which 50 (64.1%) were males. The indications for use of biosimilar included AS/spondyloarthritis, JIA, PsA, RA and refractory Takayasu Arteritis (TA) who had failed conventional immunosuppression (Figure 1).
- Majority of the patients were biologics naïve [69 (88.5%) patients].
- Treatment adherence amongst these patients, Sixty-one (78.2%) patients had completed the biosimilar adalimumab treatment, while it was ongoing for 8 (10.3%) patients at the time of analysis. Remaining nine patients (11.5%) either dropped out or were lost to follow up.

Result

- From the 78 EMRs retrieved, 4 non-serious AEs (5.1%) – nausea (1), injection site reactions (1) and abdominal pain (2); and 3 SAEs (3.8%) – psoriasis flare, pneumonia and TB reactivation (initiated elsewhere) were recorded. Tuberculosis reactivation was reported only in 1 patient’s record.
- No new safety signals reported with biosimilar treatment.

Result

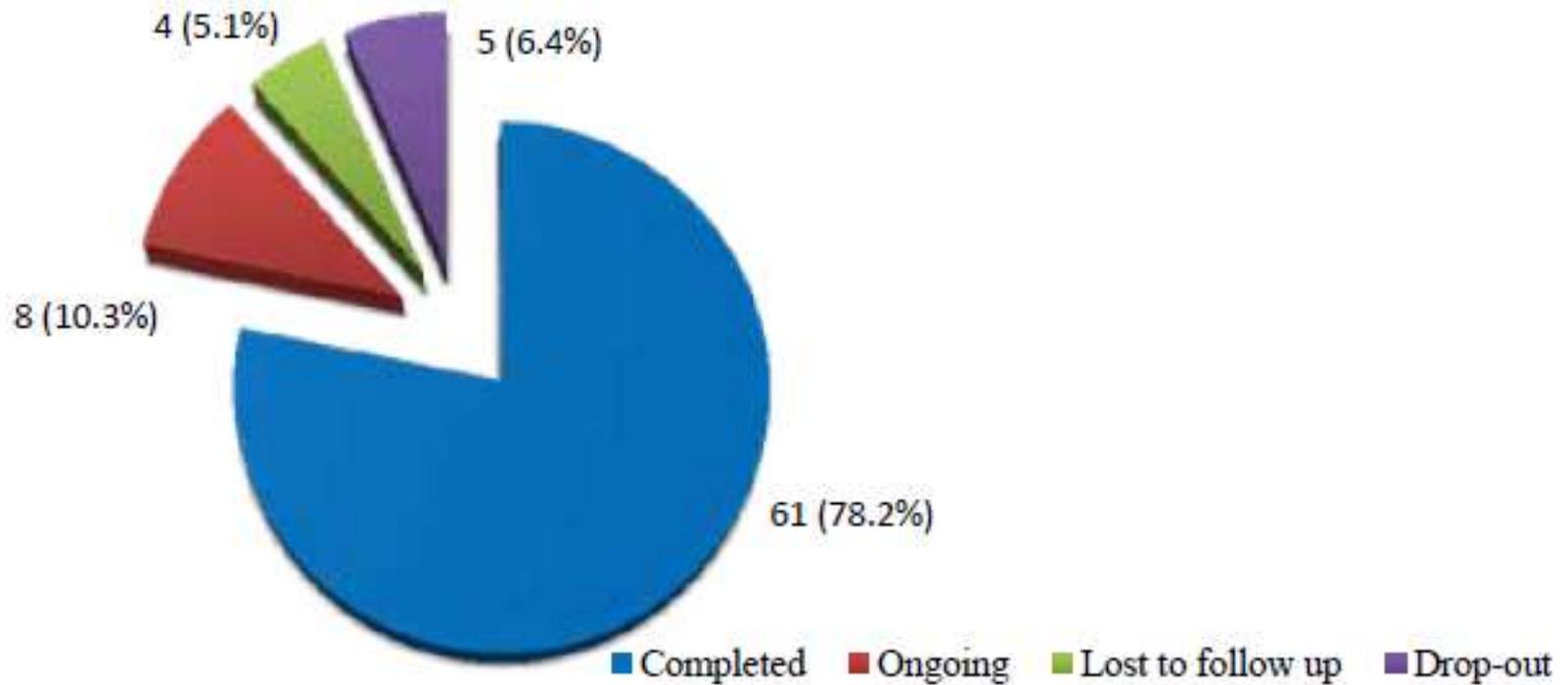


Fig. 2: Adherence to biosimilar adalimumab treatment

Result

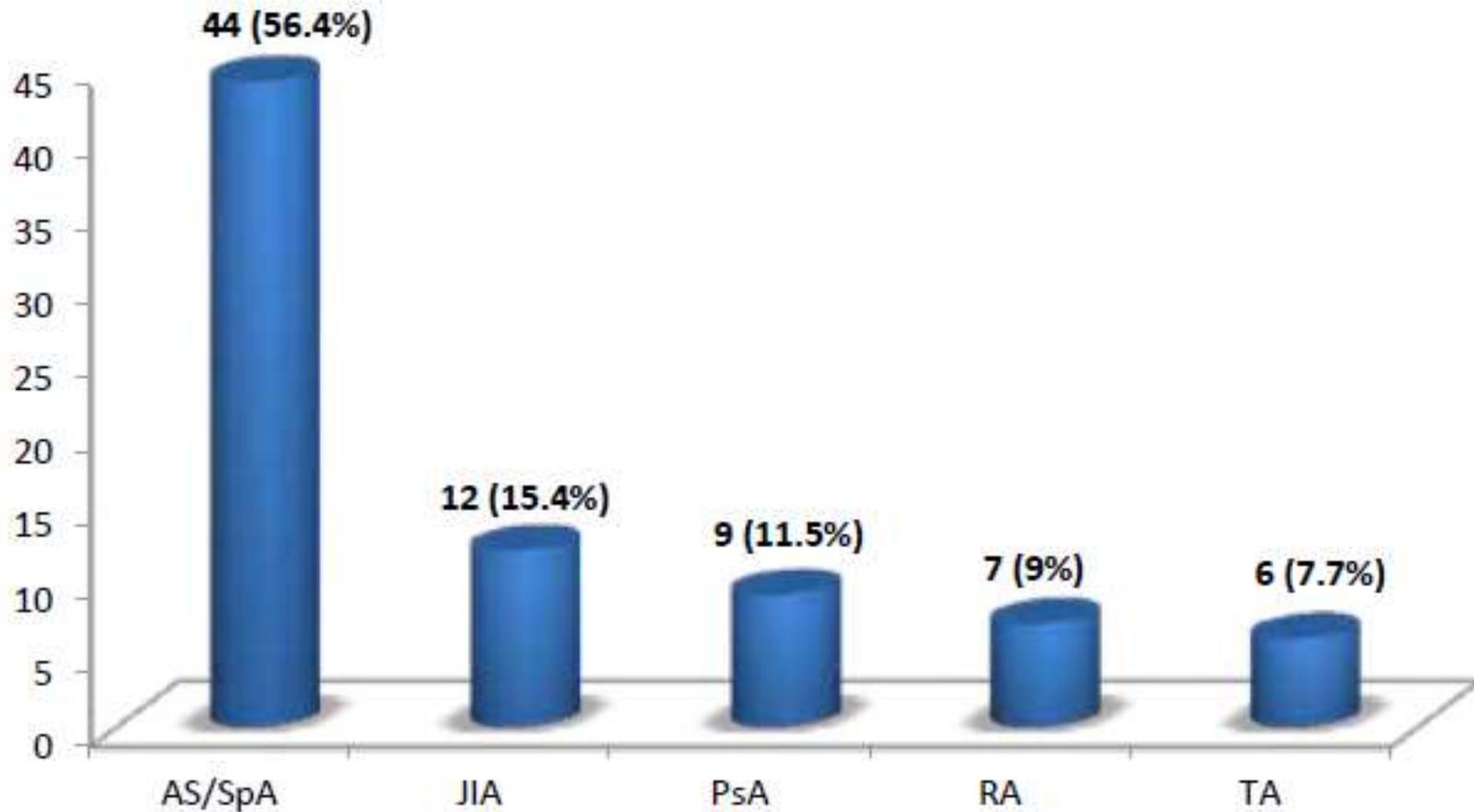


Fig. 1: Indications for initiating ZRC3197 (Adalimumab Biosimilar)

Conclusion



- This analysis provides vital information on the real-time safety of biosimilar adalimumab in patients from routine clinical practice.

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.

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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:

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Thank you

