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ORIGINAL ARTICLE

Ahead of print publication

Real-life efficacy and safety of biosimilar adalimumab (zrc-3197) in patients with plaque psoriasis: A tertiary care center experience

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Introduction

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- Psoriasis is a chronic, immune-mediated, inflammatory skin disorder affecting up to 3% population globally and 0.3% of Asians.
- The underlying pathophysiology involves abnormal interactions between multiple immune cell types
- Plaque type psoriasis is manifested thick, red, scaly lesions
- Biologics have revolutionized the management of Psoriasis patients
- The accessibility and affordability of biologic therapies are always a concern
- Affordable biosimilar versions of those biologics have entered the market after having passed though rigorous comparative evaluation pathway

- ZRC-3197 (ExemptiaTM; Cadila Healthcare Ltd, India); is one such adalimumab biosimilar that has been approved for use in India since 2014
- The physicochemical, functional and clinical comparability of this adalimumab biosimilar (bADA) to reference adalimumab
- This study represent the real world data on the effectiveness and tolerability of the bADA after 16 weeks of clinical use in patient with plaque psoriasis

Method

- Patients with moderate-to-severe plaque psoriasis were prospectively treated with bADA therapy for 16 weeks-80 mg subcutaneously initially, followed by 40 mg every other week from week 1 in real-life setting.
- Psoriasis Area and Severity Index (PASI) responses, Dermatology Life Quality Index (DLQI) outcomes, and Physician's Global Assessment (PGA) for psoriasis were analyzed.
- Safety and tolerability evaluations included reported adverse events.

Results

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Table 1: Baseline demographic and clinical characteristics of patients with plaque psoriasis

Characteristics	*n*=29
Age (years)	37.10±06.90
	38 (25.00-56.00)
Gender	
Male	15 (52%)
Female	14 (48%)
Race (Asian)	100%
Height (cms)	166.03±10.22
	168 (158-184)
Weight (kg)	67.85±10.42
	68 (50-88)
BMI (kg/m^2)	24-84±2.26
BMI (kg/m^2)	24.6 (19-30)
>25	14 (48%)
Duration of disease (years)	7.78±5.44
	06 (01.00-20.00)

Patient with psoriatic arthritis	11 (38%)
Prior psoriasis treatment	
Methotrexate	25 (86%)
Infliximab	2 (6%)[a]
Narrow band phototherapy	14 (48%)
Topical therapy	29 (100%)
Steroids	29 (100%)
Mean PASI score	35.03±11.83
	22-42
Mean DLQI score	12.03±3.95
	11 (7-22)
PGA score	
Moderate psoriasis	12 (41%)
Severe psoriasis	11 (38%)
Very severe psoriasis	6 (21%)

Efficacy Outcomes

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Table 2: Efficacy outcomes in patients with plaque psoriasis after treatment with biosimilar adalimumab for 16 weeks

Efficacy assessments	16 weeks post biosimilar adalimumab treatments (*n*=29)
PASI response	
Mean PASI score	05.24±07.43* [*P*<0.0001]
PASI 75	7 (24%)
PASI 90	4 (14%)
PASI 100	16 (55%)
Cumulative PASI ≥75	27 (93%)
Improvement in DLQI score	
Mean DLQI	1.72±1.62; 1 (0-7)
Mean DLQI change [absolute]	10.31±3.52 * [*P*<0.0001]
Mean DLQI change [percentage]	86±10 (%)
Patients with DLQI of 0/1	15 (52%)
PGA at 16 weeks	
PGA, clear, or minimal	27 (93%)
PGA, clear	20 (69%)

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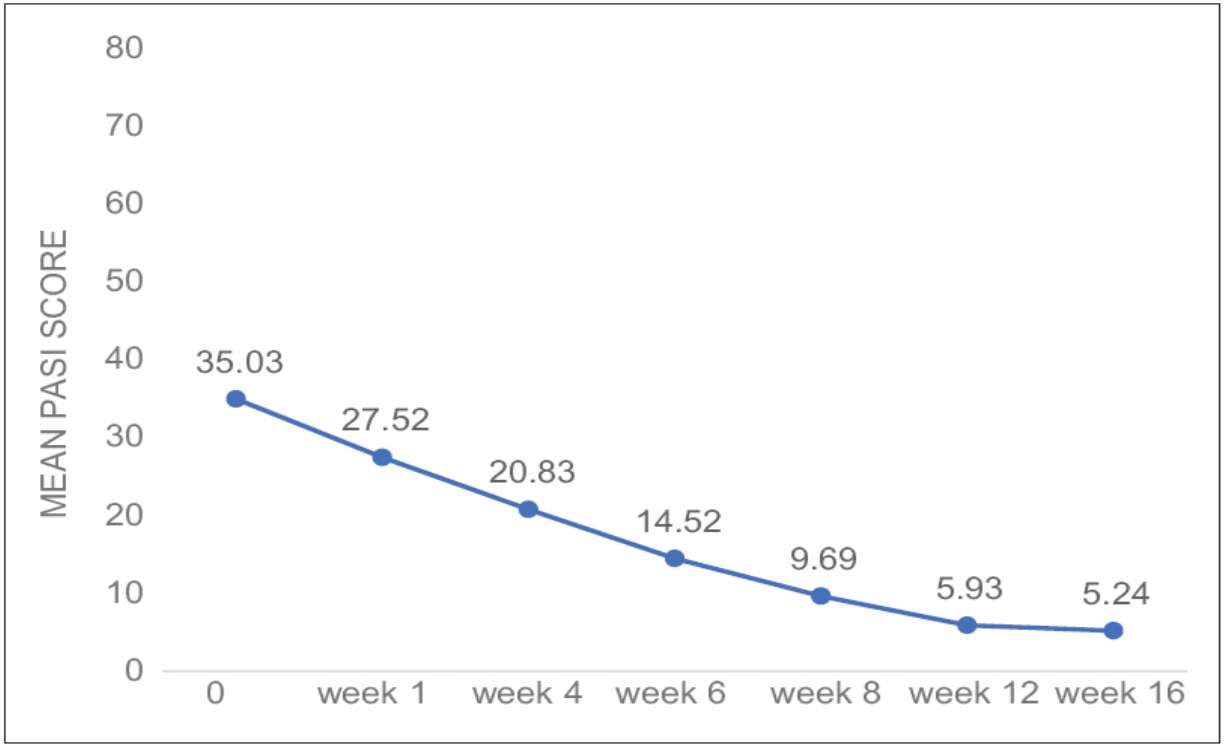
Figure 1: Change in mean PASI score over 16 weeks of biosimilar adalimumab therapy



Conclusion

- This report serves as a first-hand, real-life evidence of the efficacy and tolerability of the biosimilar adalimumab (Exemptia™) therapy in patients with plaque psoriasis.
- Ongoing real-life safety monitoring is crucial in the clinical use of biosimilars. Reports like these shall further strengthen and guide the treatment choices for clinicians in day-to-day clinical practice.

Key take out from the study

- A biosimilar adalimumab (EXEMPTIA) which is comparable to the originator in clinical efficacy as well as safety, is developed and approved for use in Psoriasis in India
- Current study evaluating the real life clinical use of this bADA Psoriasis patients in India. This study is also reflective of the real time prescription patterns and clinical practice of managing such patients.
- Psoriasis disease outcome measures i.e. PASI, PGA and DLQI score showed a gradual and significant decrease ($p<0.0001$ for all) in patients after 16 week bADA therapy
- 93% patients achieved ≥75% reduction in their baseline PASI scores
- PASI75, PASI90, and PASI100 responses were achieve in 24%, 14%, and 55% patients, respectively
- Real life data demonstrated clinical effectiveness and tolerability of biosimilar adalimumab in patient with Psoriasis, who had received treatment for up to 16 weeks.

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-alpha 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 EXEMPTIA™. 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 ≥ 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 EXEMPTIA™ 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 ≥ 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 EXEMPTIA™ 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 EXEMPTIA™ and begin antiviral therapy• Demyelinating disease: Exacerbation or new onset, may occur• Heart failure: Worsening or new onset, may occur• Lupus-like syndrome: Stop EXEMPTIA™ 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 EXEMPTIA™ 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 EXEMPTIA™. •Cytochrome P450 Substrates- The formation of CYP450 enzymes may be suppressed by increased levels of cytokines (e.g., TNFα, IL-6) during chronic inflammation. Upon initiation or discontinuation of EXEMPTIA™ 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. **UNDESIRED 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.

Please refer to the full Prescribing Information before starting EXEMPTIA™.

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

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