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Clinical use of ZRC3197 (Adalimumab Biosimilar) in Patients with Inflammatory Arthritis: A Real-life Experience

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Background/Purpose & Methods

- The study assessed, review of real-life data on the clinical use of biosimilar Adalimumab in patients with inflammatory arthritis.

- This was a single-centre, retrospective review of real-life data on the clinical use of biosimilar Adalimumab in patients with inflammatory arthritis.

- Medical records retrieval was performed from electronic data base of Niramaya Health Care (Dedicated Rheumatology Centre), Jaipur, Rajasthan.

- Records were evaluated for patients with inflammatory arthritis– Spondyloarthropathy (SPA) and rheumatoid arthritis (RA) who had received treatment with ZRC3197 (Adalimumab Biosimilar) and, for whom, data was available for more than 3 months of follow-up. Records with less than 3 months of follow-up data were excluded from the analysis.

Background/Purpose & Methods

- All the patients had received biosimilar Adalimumab 40 mg every 15 days for initial 3 months Post 3 months, an ‘on-demand modified dosing approach’ was followed.

- Disease activity was monitored through BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) scores in SPA patients and by DAS28 (Disease Activity Score) in RA patients.

- The 3, 6- and 12-months’ follow-up data was collected and BASDAI/DAS28 score were analyzed.

Result

- A total of 90 patients' records, meeting the evaluation criteria, were retrieved and analysed: 39 patients had SPA; 51 patients had RA.

- The median disease duration for the SPA and the RA group was 7 years and 7.5 years, respectively.

- All SPA patients were refractory to a full dose NSAIDs treatment and 15% of these patients was DMARDs naïve. All RA patients had failed prior DMARDs therapy. Most of the patients (87-94%) were biologics naïve.

Result

- All patients were prescribed biosimilar Adalimumab and BASDAI/DAS-guide dose reduction by increasing dosing interval was done for all patients.

- Methotrexate was administered concomitantly in 12 patients with SPA and 44 patients with RA, while steroids were given to 14 patients with RA. Other DMARDs given to these patients included sulfasalazine, hydroxy chloroquine and leflunomide.

- The patient pool included a total of 9 juvenile cases:7 patients with juvenile AS and 2 patients with juvenile idiopathic arthritis.

Baseline demographic and disease characteristics of the patients

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Parameters	Spondyloarthropathy (SpA) [N = 39]	Rheumatoid arthritis (Ra) [N = 51]
Age; years (mean±SD)	38.4 ± 14.5	47.5 ± 12.9
Male: Female	26:13	10:41
Disease duration; yrs (median; range)	7.5 (0.5-36)	7 (0.5-25)
Positive/Negative MT	11/28	10/41
CXR PA (Normal)	39; All	49 [2 pts had old healed TB]
Mean ESR at baseline	-	52.11 ± 33.21
DMARDs naïve patients (%; n)	15%; 6	None
NSAIDs (full dose > 6 weeks) refractory	39; All	-
No. of prior DMARDs (median; range)	1 (0-3)	2 (1-3)
DMARDs failure: Triple/Double/ Monotherapy	-	25/21/5
Patients with prior corticosteroids (n)	3	14
Biologics naïve patients (%; n)	87%; 34	94%; 48

Data presented as: mean±standard deviation; median (min-max); percentage (%) of patients; N = total number of patients; n = number of analysable patients

Clinical characteristics and diagnosis of patients

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Spondyloarthropathy (SPA)	**N = 39**
Diagnosis	
Ankylosing Spondylitis	13
Juvenile Ankylosing Spondylitis	7
Inflammatory Bowel disease	2
Psoriatic Arthritis (PsA)	8
Spondyloarthropathy, unclassifiable	9
Axial SPA	12
Peripheral SPA	7
Axial + Peripheral	15
HLA B27: Positive/Negative/NA	23/8/8
Rheumatoid Arthritis (RA)	**N = 51**
Diagnosis	
Rheumatoid Arthritis	49
Juvenile Idiopathic arthritis, polyarticular	2
RF and ACCP Positive	20
Only RF Positive	33
Only ACCP Positive	32

Data presented as: n = number of analysable patients

Result

- 91% SPA patients achieved BASDAI 50% at 3 months followed by 45% achieved BASDAI 70%
- At 3 months, 88% showed a reduction in DAS28 > 1.2 from baseline. At 12 months, 94% of the evaluable SPA patients and 58% of evaluable RA patients showed clinical remission or low disease activity
- The 3, 6- and 12-months' follow-up data revealed a significant reduction in disease activity scores (BASDAI/DAS28).
- Biosimilar Adalimumab was well-tolerated with no serious or unexpected side effects
- Despite the modified dosing, the clinical response following biosimilar Adalimumab was comparable to the published data for the standard Adalimumab treatment.

Disease activity outcomes and biosimilar adalimumab treatment details

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Description	SPA N = 39	RA N=51
Disease activity score	BASDAI	DAS28
Baseline	6.19±1.05 (n=35)	6.26±1.0 (n=47)
3 months	2.24±1.15 * (n=35)	3.58±0.93 * (n=44)
6 months	2.18±1.18 * (n=25)	3.32±1.21 * (n=42)
12 months	1.98±0.91 * (n=15)	3.12±1.16 * (n=31)
Actual Duration of ZRC3197(Adalimumab Biosimilar) treatment: Median (range)	5 (2-19) months	6 (2.5-18 months)
ZRC3197(Adalimumab Biosimilar) (40 mg) - Total NUMBER of Doses		
Standard/Recommended: 40 mg (1 dose) every 15 days calculated for actual duration of treatment above:	10 (4-38); 13.5±7.79	12 (5-36); 15.4±8.89
Actual:	10 (4-27); 11.1±5.12.4 *	11 (5-30); 12.6±6.4 *
Number of patients requiring overall ≥ 3 ZRC3197(Adalimumab Biosimilar) doses less than Standard regimen	14 out of 39 patients (36%)	21 out of 51 patients (41%)
Number of Patients receiving Steroids: *baseline vs. 3 months vs. 6 months vs. 12 months*	Not available	14 vs. 8 vs. 4 vs. 3
Mean steroid dose reduction		4.14±1.8 mg (baseline) 1.23±2.89 mg (12 mon) *

Data presented as: mean±standard deviation; median (min-max); percentage (%) of patients; number of analysable patients; *Paired Student's T test. P<0.001. Statistically significant reductions as compared to baseline/standard.

Disease Activity Scores over 12 months in patients with inflammatory arthritis treated with biosimilar adalimumab

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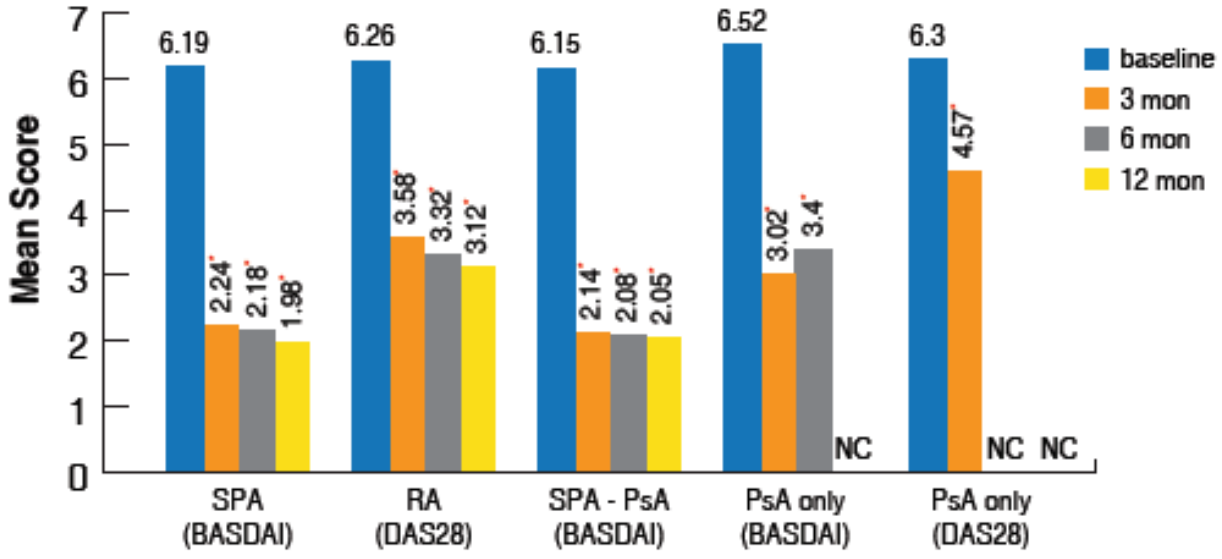

Data presented as: mean±standard deviation; median (min-max); percentage (%) of patients; number of analyzable patients.
Paired Student's T test; *P<0.001; #p<0.05 Statistically significant reduction as compared to baseline/standard; NC = not calculate

Conclusion

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- ZRC3197 (Adalimumab Biosimilar) serves as an accessible and cost-effective anti TNF-α therapy for patients with inflammatory arthritis in India.

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 spondylitispatients 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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