Exemptia™ Adalimumab
EMPOWERING YOU

Prolonged effectiveness of a 12 Week Regimen of Biosimilar Adalimumab in Indian (Asian) Patients Suffering from Symptomatic Acute-Chronic Ankylosing Spondylitis (AS)

Arvind Chopra1 , Nagnath Khadke2 , Manjit Saluja3 , Toktam Kainifard4 and Anuradha Venugopalan5

1. *Center for Rheumatic Diseases, Pune, India*
2. *Rheumatolgy, Consultant, Pune, India*
3. *Rheumatology, Research Co-ordinator, Pune, India*
4. *Rheumatology, Consultant research and Dietitian, Tehran, Iran (Islamic Republic of)*
5. *Rheumatology, R & D, Lab, Center for Rheumatic Diseases, Pune, India*

Presented in: 2018 ACR/ARHP Annual Meeting

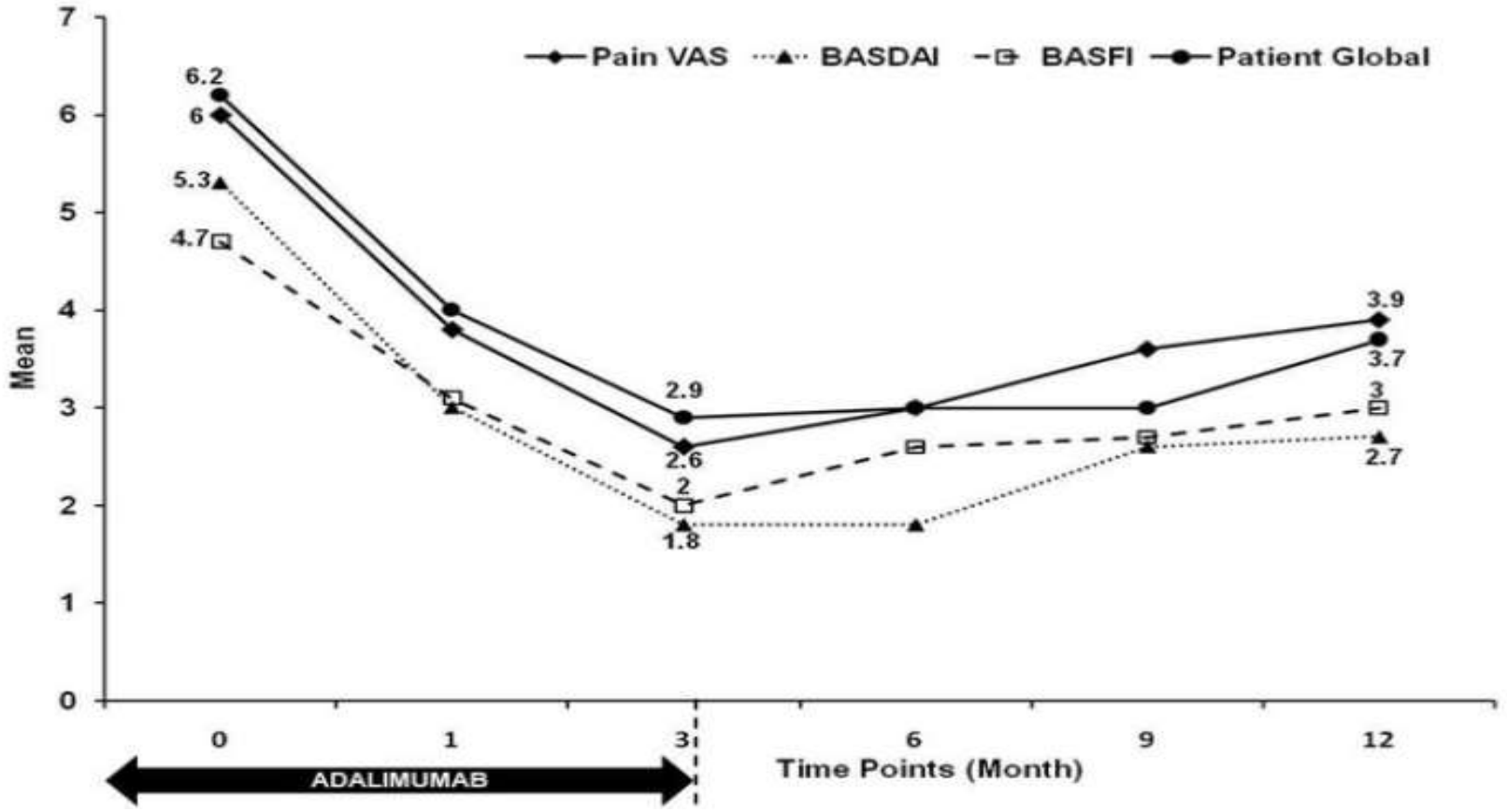
Background/Purpose & Methods

- To evaluate the effectiveness of a shorter therapeutic regimen of a Biosimilar Adalimumab in AS.

- 50 patients (42 males, mean age 31.2 years, mean duration 98.8 months) were enrolled into an observational design study in a community practice setting: mean of AS-DAS 4.6, ESR 88 mm, CRP 64 mg/dl (nephelometry, cut off 5 mg/dl). 40 mg Biosimilar Adalimumab (Bsmr-ADL) (Exemptia™) was administered sub cutaneous every fortnight for 12 weeks as per protocol and standard (ACR) clinical and laboratory monitoring performed. cytokines assay Standard intention-treat analysis was performed (Student T and matched sign rank); significant $p < 0.05$.

Result

Figure shows the mean Efficacy Measures in severe AS treated with Biosimilar Adalimumab



Result

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Table shows the proportion of patients with severe AS showing response at study end points

Index	12-14 weeks	22-26 weeks	46-52 weeks
ASAS 20 (%)	80	72	52
ASAS 40(%)	68	60	38
ASDAS (mean)	2.4	2.9	3.5
ASAS partial remission (%)	34	22	12

Result

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- Improvement was rapid (week 4- mean ESR 29.1 mm), significant and sustained (Figure).
- The Tables shows the proportion of patients showing index improvement and ASDAS change. 10 patients failed ASAS 20 at week 12 and despite additional Bsmr-ADL (2 injections, 2 week apart) did not show ASAS based improvement at later time points (data not shown).
- 12 patients withdrew (1 drug fear,4 logistics, 5 poor response, 2 unknown). None had active TB/severe AE. Cytokine assay (IL-6, TNF α and IL-17) at baseline and a-priori endpoints will be presented. We continue to monitor patients and have completed 18 months post ADA. We lacked active control and did not study structure modification.

Conclusion

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- This investigator initiated study demonstrated prolonged benefit of a 12 week regimen with Biosimilar ADA in several patients of severe AS. This is a promising way forward in our setting. But validation studies are required.

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:

Cadila Healthcare Limited
Zydus Corporate Park
Nr. Vaishno Devi Circle,
SG Highway,
Ahmedabad – 382 481
Gujarat, India.
PHONE: +91-79-71800000

Thank you