Exemptia™
Adalimumab

Zydus Adalimumab Phase 3 vs Originator in Rheumatoid Arthritis

Cadila Healthcare Limited
Ahmedabad, India

Adalimumab Study Title

- "A multicentric, randomized, active controlled parallel group study to evaluate efficacy, tolerability and safety of Adalimumab (Zydus) and Adalimumab (Reference) in patients with Rheumatoid Arthritis."

  – Study Number: ADA.12.002.01.PROT

Zydus Adalimumab Clinical Study

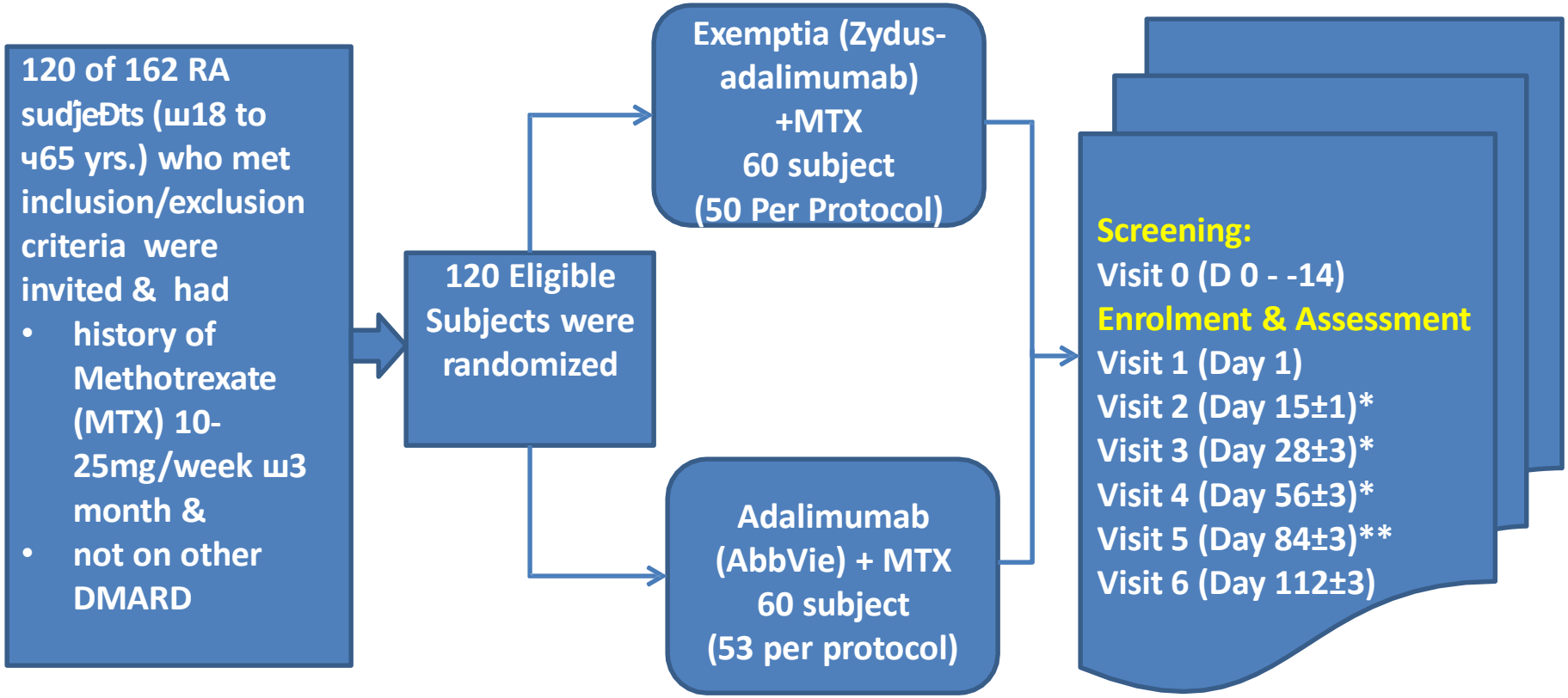
- Clinical Trial Registry:
  - WHO Clinical Trial Registry:
    - http://apps.who.int/trialsearch/Trial2.aspx?TrialID=CTRI/2013/10/004040
  - Clinical Trial Registry – India
    - **CTRI/2013/10/004040**
    - http://www.ctri.nic.in/Clinicaltrials/pmaindet2.php?trialid=7595

Zydus Adalimumab Study: Study Design

ADA.12.002.01 - Phase III – Study Design

- Study Design:
  - Multicentric, prospective, randomized, double blind, active controlled parallel arm study
- Study Phase : III
- Study Drugs:
  - Investigational Product: Adalimumab (Zydus) - 40 mg in 0.8 mL in a single-use prefilled glass syringe
  - Reference Product: Adalimumab (AbbVie) - 40 mg in 0.8 mL in a single-use prefilled glass syringe
- Study Population:
  - Moderate to severe active seropositive Rheumatoid Arthritis patients
- Treatment Duration:
  - 12 Weeks
- Number of Subjects:
  - 120
- Dosage Schedule & Dose(s):
  - Adalimumab 40 mg (Zydus/AbbVie); SC every other week

Zydus Adalimumab Study: Design & Methodology



- *Adalimumab Dose & Dose Schedule: Adalimumab 40 mg (Zydus/AbbVie); SC every other week*
- *Primary Endpoint: ACR20 on Day 84*
- *Secondary Endpoints: ACR50, ACR70 & DAS28-CRP on Day 84 & Safety analysis*
- ** Intention to treat ** Per Protocol Population*

Zydus Adalimumab Study: Evaluation Criteria

- Primary Evaluation Criteria
  - Pharmacodynamics (efficacy) of Adalimumab (Zydus) and Adalimumab (Reference) in subjects with RA on Day 84 as compared to baseline
    - Proportion of patient with an **ACR 20 response** in both the treatment groups.
- Secondary Evaluation Criteria
  - Pharmacodynamics (efficacy) of Adalimumab (Zydus) and Adalimumab (Reference) in subjects with RA on Day 84 as compared to baseline
    - Change from baseline in **Disease Activity Score 28 C-Reactive Protein** (DAS 28-CRP)
    - Proportion of patient with an **ACR 50 response** in both the treatment groups.
    - Proportion of patient with an **ACR 70 response** in both the treatment groups.
- Immunogenicity assessment:
  - Percentage of subjects who develop detectable anti-drug antibodies
    - Day 1, Day 28 and Day 84 (Week 12).

Zydus Adalimumab Study: ACR Response Evaluation

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- •Patients was considered ACR 20 responders if they have:
- –≥20% improvement in tender joint count;
- –≥20% improvement in swollen joint count;
- –≥20% improvement in at least 3 of 5 remaining ACR core measures:
- •patient assessment of pain;
- •patient global assessment of disease activity;
- •physician global assessment of disease activity;
- •self-assessed disability (disability index of the Health Assessment Questionnaire [HAQ]); and
- •acute phase reactant: ESR or C-reactive protein.
- •Similarly ACR 50 and ACR 70 were assessed, where ≥50% and ≥70% improvements in above mention criteria were considered, respectively.

Zydus Adalimumab Study: DAS 28 CRP Assessment

DAS28 is calculated using the formula:

–DAS28 - CRP = 0.56√tender 28 + 0.28√swollen 28 + 0.36 ln (CRP+1) + 0.014GH + 0.96

–Where;

•tender 28 is the number of tender joints (of the 28 assessed [n]);

•swollen 28 is the number of swollen joints (of the 28 assessed [n]);

•In (CRP) is the natural logarithm of the patients CRP level (mg/L) and

•General Health (GH) is the patient's general health or the patient's global assessment of the disease activity, measured on a 100-mm VAS (mm).

- Results/ Interpretation:-
  - DAS score > 5.1 - High disease activity
  - DAS score < 3.2 – Low disease activity
  - DAS score < 2.6 – Remission of disease

- Improvement in DAS Score of at least 0.6 is considered to be clinically significant

Zydus Adalimumab Study: Criteria of Safety

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- All adverse events (AEs) were captured and notified:
  - Non serious AEs were captured in the AE form provided with the CRF
  - Serious Adverse Events (SAE) were reported in the CIOMS form and
  - all AEs were assessed for causality, severity and seriousness.
- Clinical (General and Systemic) Examinations:
  - cardiovascular system (CVS),
  - Respiratory system (RS),
  - Gastro-intestinal System (GI) and
  - Central Nervous System (CNS).
- Safety Laboratory assessment:
  - Liver Function: AST, ALT, serum bilirubin,
  - Renal Function: serum creatinine, Blood Urea Nitrogen,
  - Hematology: CBC.
- The frequency of AE that occurs in both treatment groups

Zydus Adalimumab Study:
Rationale for Sample Size Estimation

Zydus Adalimumab Study: Rationale for Sample Size Estimation

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- Sample size for the study was estimated based on the results of ACR20 response at week 12 with 40 mg of Adalimumab using 80% power and 5% level of significance.
- Thus following estimates were considered for the calculation of sample size:
  - % ACR20 at week 12 for Reference- Rx - 55%
  - % ACR20 at week 12 for Test- Tx (Assumed) - 55%
  - Alpha (α) = 5%
  - Power = 80%
  - Delta margin (Δ) = 28.5%
  - Ratio of allocation: 1:1
- As per sample size calculation, 120 subjects was to be enrolled (60:60), of which 96 (48:48) was to be qualify for per-protocol analyses, assuming 20% dropout.

Zydus Adalimumab Study: Results

Zydus Adalimumab Study: Subject Disposition

Number of subjects randomized, dropped out, completed			
	ADA-Zydus	ADA-AbbVie	Total
No. of Subjects Randomized	60	60	120
No. of Subjects Dropped Out / Withdrawn	3	1	4
• Due to Adverse event*	2	0	2
• Lost to follow-up	0	1	1
• Subject's voluntary withdraw	1	0	1
No. of Subjects Completed	57	59	116
No. of Subjects Analyzed for Safety	60	60	120
No. of Subjects Analyzed for ITT	60	59	119
No. of Subjects Analyzed for PP	50	53	103
**Subject EGR111 and Subject EGB057*			

Distribution subjects in two arms was similar in both groups

Zydus Adalimumab Study: Subject Disposition

- A total 162 subjects screened at 11 investigational sites in India. Of which, 120 subjects were enrolled in the study, 60 subjects in each group viz. Adalimumab (Zydus) and Adalimumab (Reference).
- Total 103 subjects were qualified as per protocol criteria and 119 subjects qualified ITT criteria were included for efficacy analysis, respectively.
- Over all the mean age was 45 ± 10.95 years, with the range among groups of 19 to 65 years in safety population.
- The groups were similar in age distribution, with majority of female subjects. There was no statistically significant difference in demographic & ACR/DAS scores between two arms.

Zydus Adalimumab Study: Primary Efficacy-ACR20

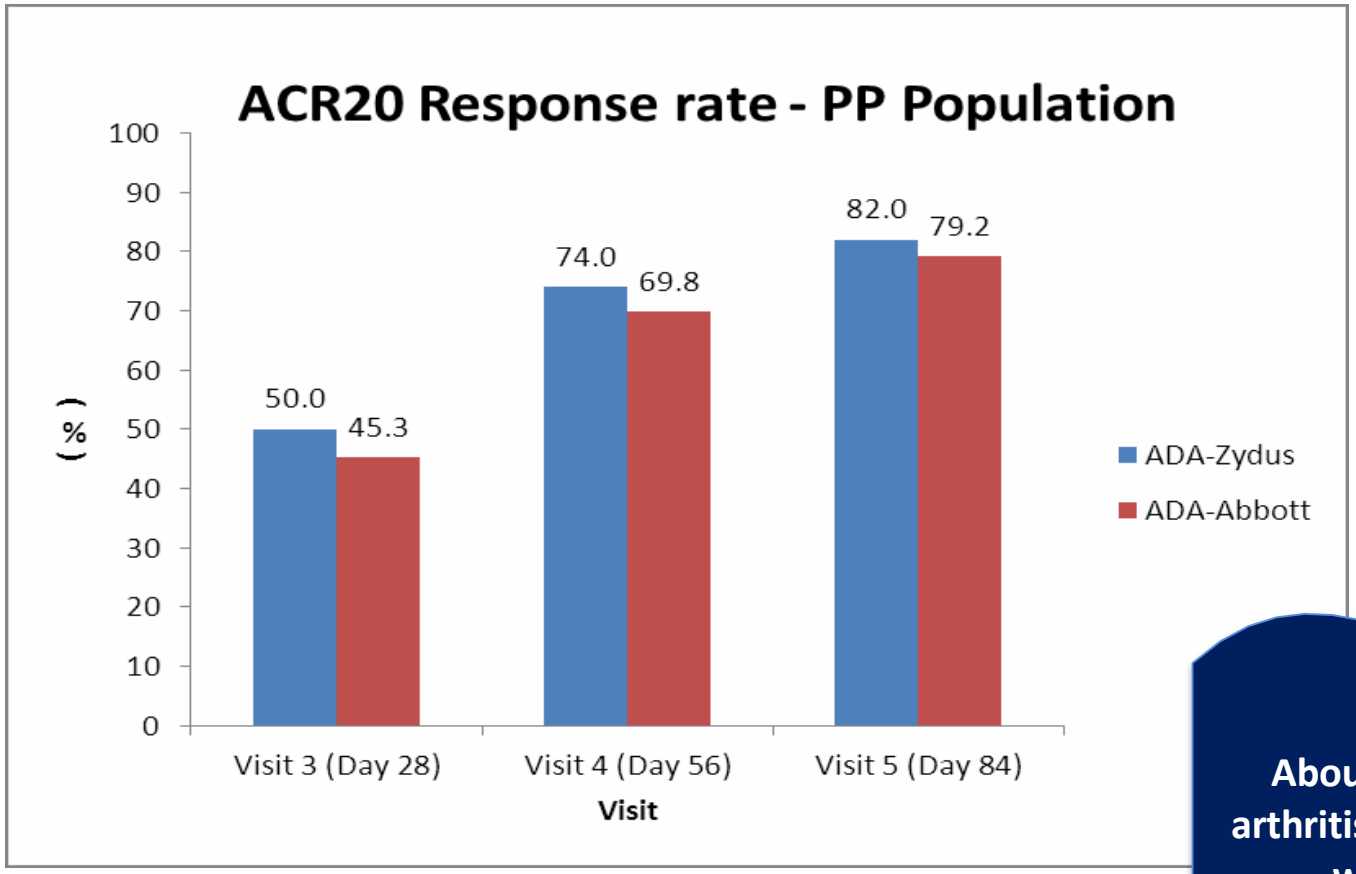
Analysis of ACR20 response on Visit 5 (Day 84) by treatment groups (PP population)			
Responder	ADA-Zydus (N = 50) n (%)	ADA-AbbVie (N = 53) n (%)	p-value*
Yes	41 (82.0%)	42 (79.2%)	0.7239
No	9 (18.0%)	11 (20.8%)	

Abbreviations: N = number of subjects in specified treatment; n = number of subjects at specified category.
ACR20 responders:>=20% improvement in tender and swollen joint count; and >= 20%improvement in at least 3 of 5 remaining ACR core measures: patient assessment of pain; patient and physician global assessment of disease activity; self-assessed disability [HAQ]; and CRP or ESR.
** p - values are calculated from Pearson's Chi-square test.*

Statistically no significant difference between two groups

Exemptia is biosimilar to reference adalimumab

Zydus Adalimumab Study: Primary Efficacy-ACR20



About 80% rheumatoid arthritis patients responded within 12 weeks

Zydus Adalimumab Study
Comparison with Other Adalimumab Studies

- Reference: Study Protocol DE019

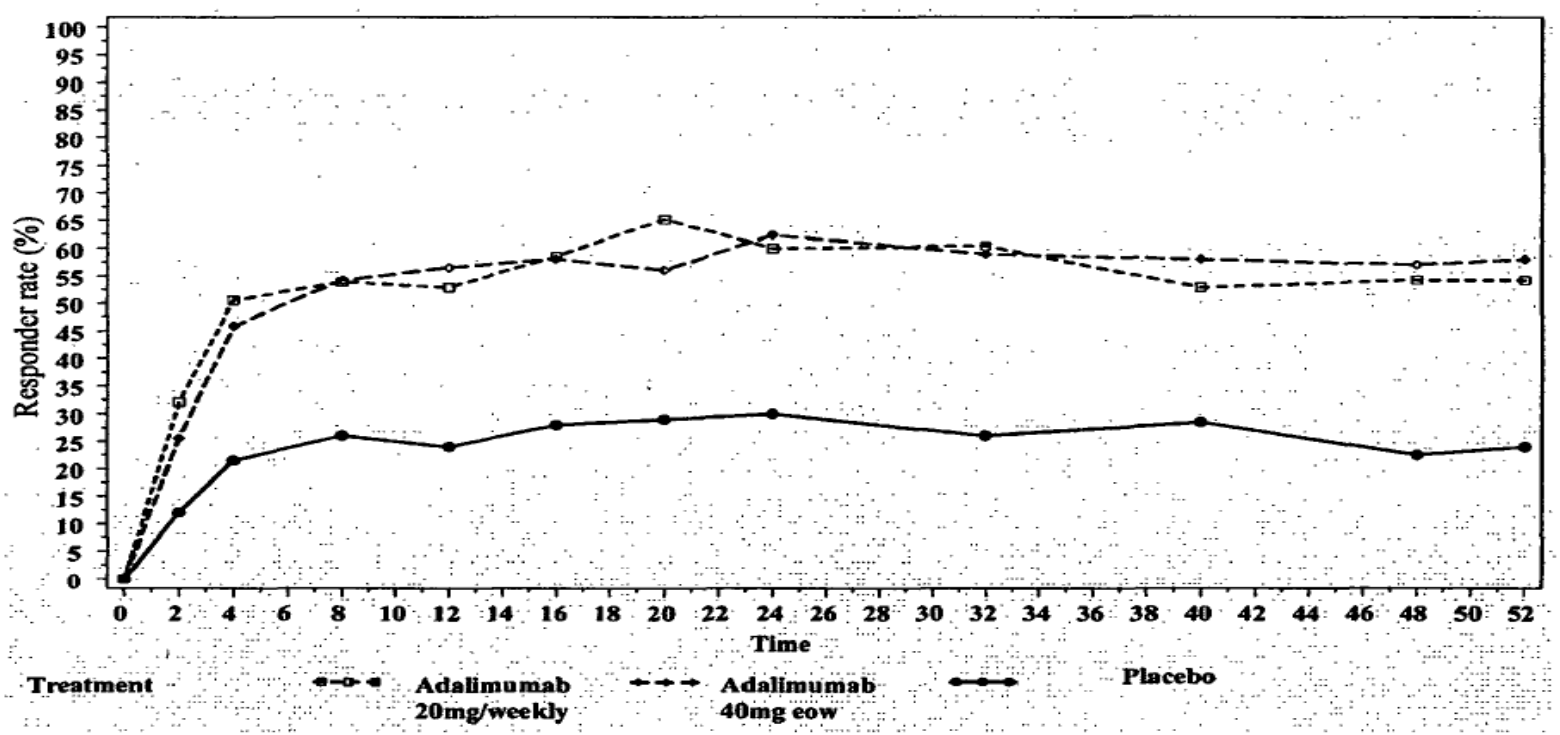


Figure 3. Responder rates according to ACR20 - full analysis set (missing as non-responders).

Zydus Adalimumab Study: Secondary Efficacy Criteria-ACR50

Exemptia Adalimumab

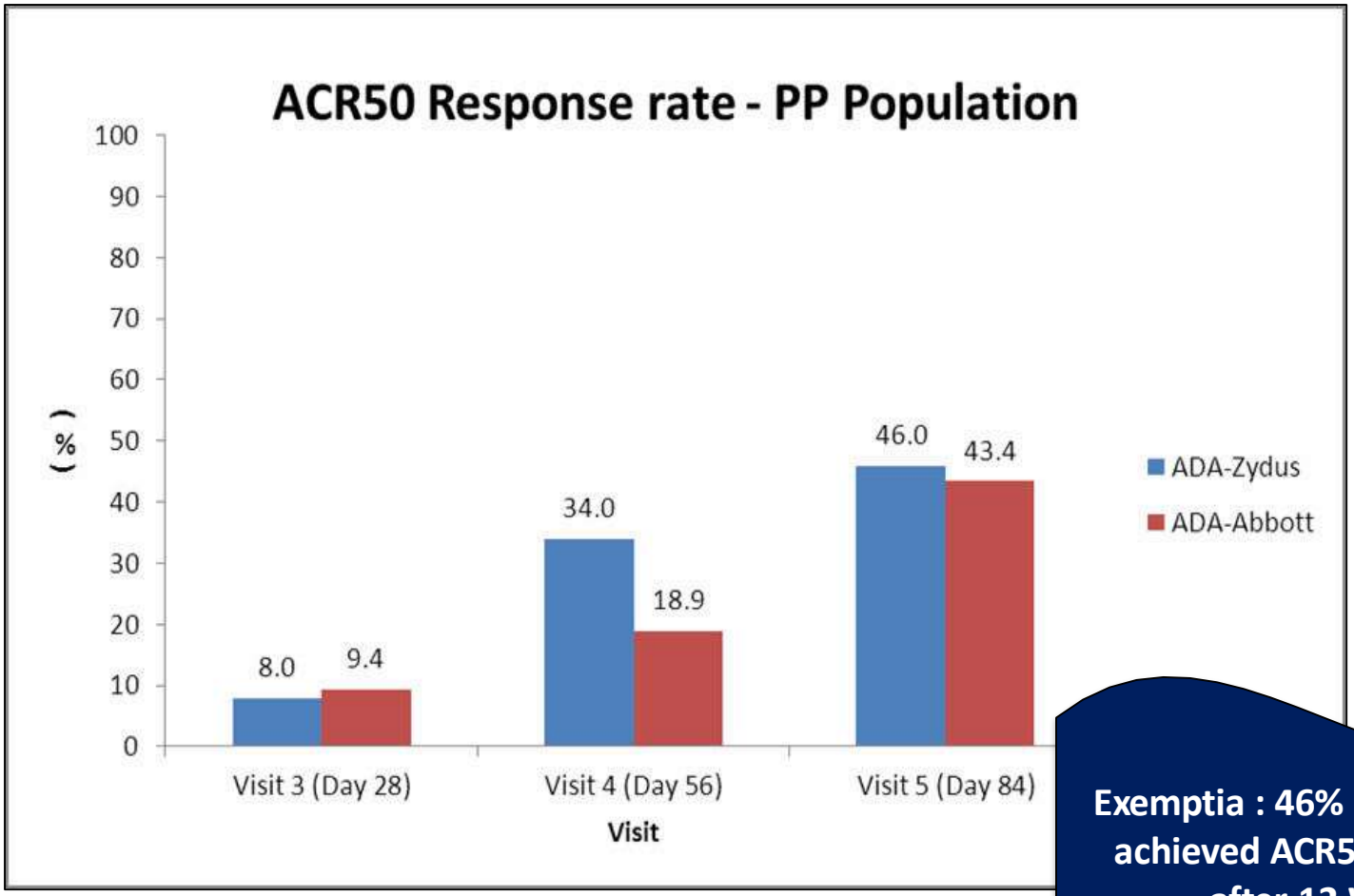
Analysis of ACR50 response on Visit 5 (Day 84) by treatment groups (PP population)			
Responder	ADA-Zydus (N = 50) n (%)	ADA-AbbVie (N = 53) n (%)	p-value*
Yes	23 (46.0%)	23 (43.4%)	0.7905
No	27 (54.0%)	30 (56.6%)	

Abbreviations: N = number of subjects in specified treatment; n = number of subjects at specified category.
ACR50 responders:>=50% improvement in tender and swollen joint count; and >= 50%improvement in at least 3 of 5 remaining AC R core measures: patient assessment of pain; patient and physician global assessment of disease activity; self-assessed disability [HAQ]; and CRP or ESR.
** p - values are calculated from Pearson's Chi-square test.*

Statistically no significant difference between two groups

Exemptia is biosimilar to reference adalimumab

Zydus Adalimumab Study: Secondary Efficacy Criteria-ACR50



Exemptia : 46% Patients had achieved ACR50 response after 12 Week

Zydus Adalimumab Study: Secondary Efficacy Criteria-ACR70

Exemptia Adalimumab

Analysis of ACR70 response on Visit 5 (Day 84) by treatment groups (PP population)			
Responder	ADA-Zydus (N = 50) n (%)	ADA-AbbVie (N = 53) n (%)	p-value*
Yes	7 (14.0%)	8 (15.1%)	0.8750
No	43 (86.0%)	45 (84.9%)	

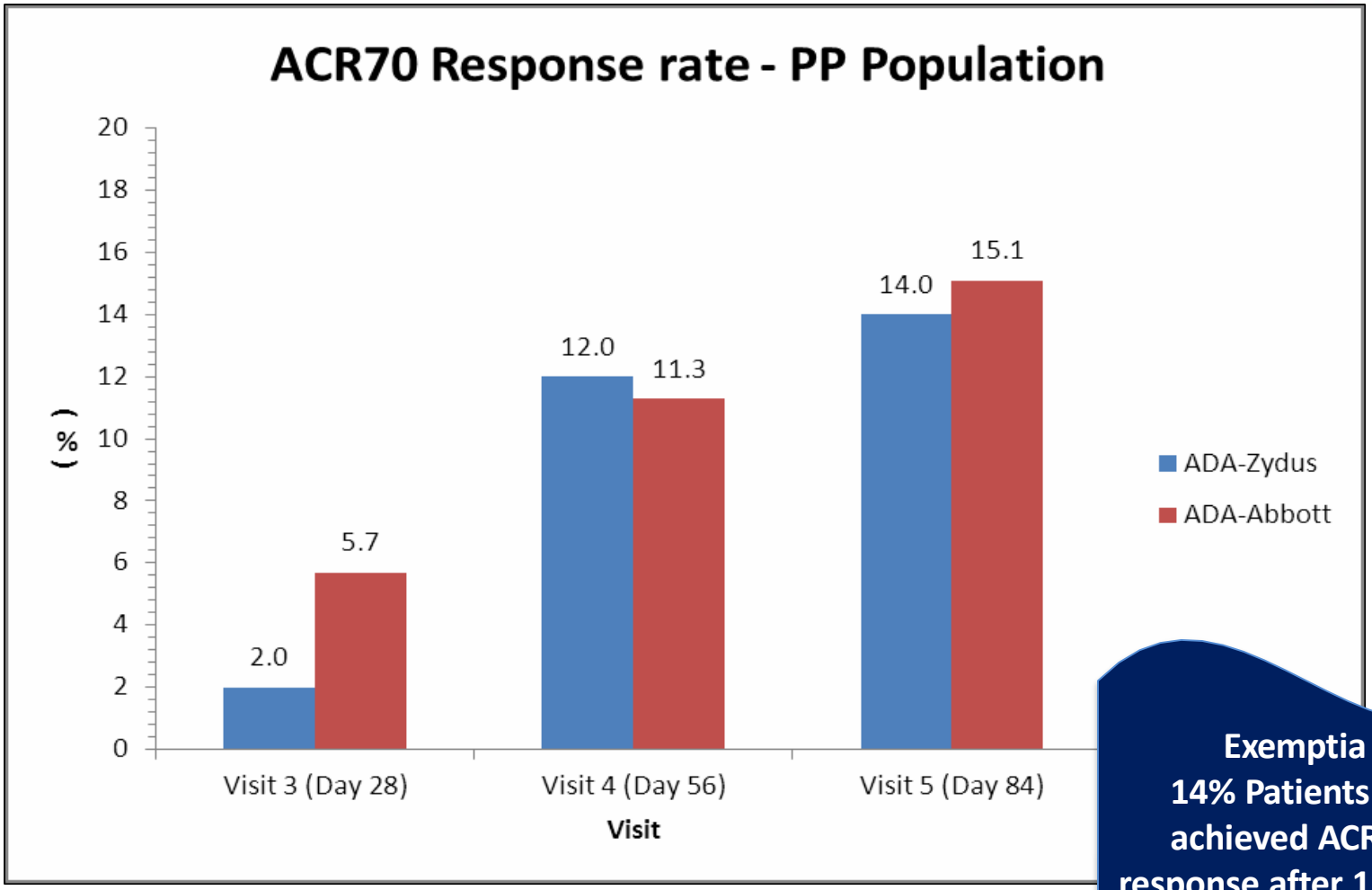
Abbreviations: N = number of subjects in specified treatment; n = number of subjects at specified category. ACR70 responders:>=70% improvement in tender and swollen joint count; and >= 70%improvement in at leas t 3 of 5 remaining ACR core measures: patient assessment of pain; patient and physician global assessment of disease activity; self-assessed disability [HAQ] ; and CRP or ESR.

** p - values are calculated from Pearson's Chi-square test.*

Statistically no significant difference between two groups

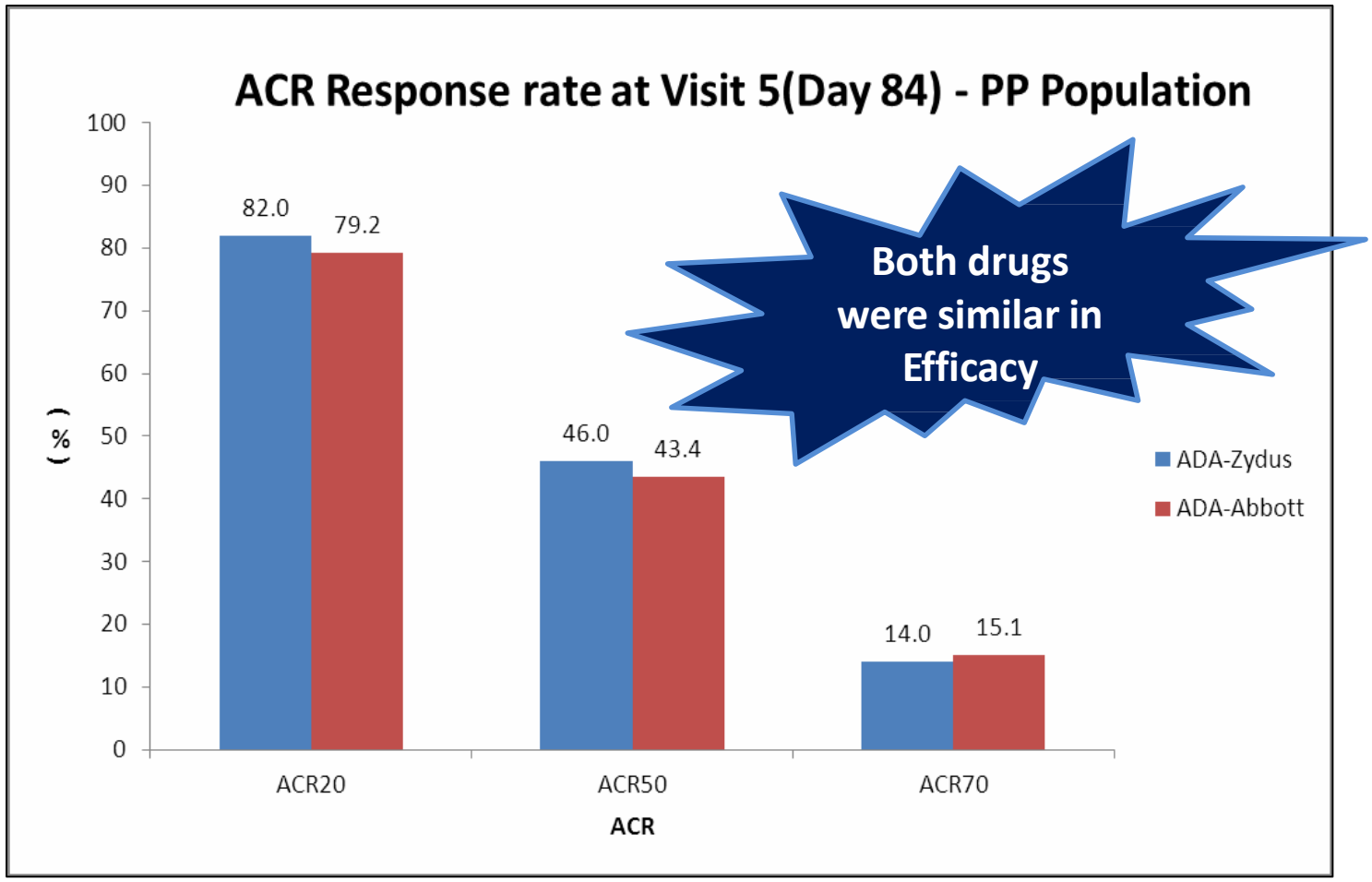
Exemptia is biosimilar to reference adalimumab

Zydus Adalimumab Study: Secondary Efficacy Criteria-ACR70



Exemptia : 14% Patients had achieved ACR70 response after 12 Week

Zydus Adalimumab Study: Efficacy Criteria-ACR 20, 50 & 70



Zydus Adalimumab Study: Summary of ACR Core Component

Exemptia Adalimumab

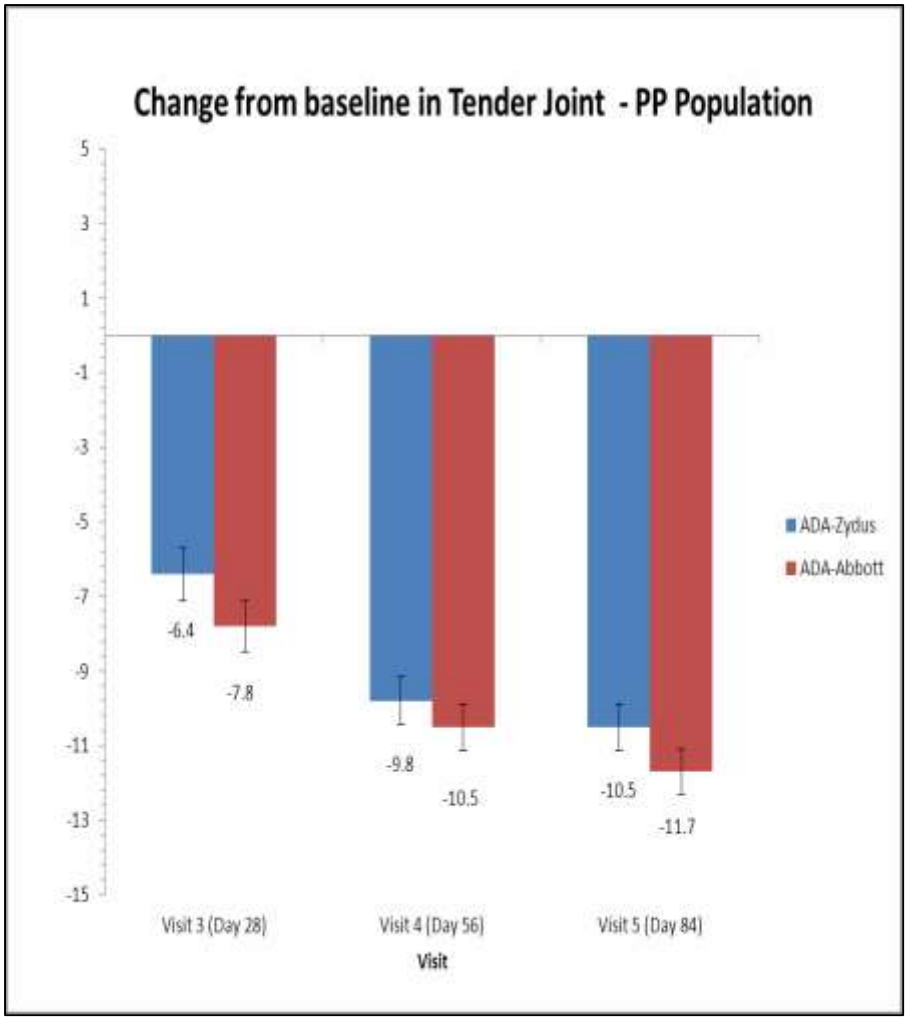
Baseline and change from baseline to Visit 3 (Day 28) and Visit 5 (Day 84)		
ACR Core component	**ADA-Zydus (N=50)**	**ADA-AbbVie (N=53)**
Tender joint count score (0-28)		
Visit 1 (Day 1)	16.6 ± 6.09	17.4 ± 6.32
Change from baseline at Visit 3 (Day 28)	-6.4 ± 5.67*	-7.8 ± 6.21*
Visit 5 (Day 84)	-10.5 ± 5.95*	-11.7 ± 7.19*
Swollen joint count score (0-28)		
Visit 1 (Day 1)	11.7 ± 5.57	12.4 ± 5.24
Change from baseline at Visit 3 (Day 28)	-5.5 ± 5.00*	-6.5 ± 5.81*
Visit 5 (Day 84)	-8.2 ± 5.77*	-9.2 ± 6.02*

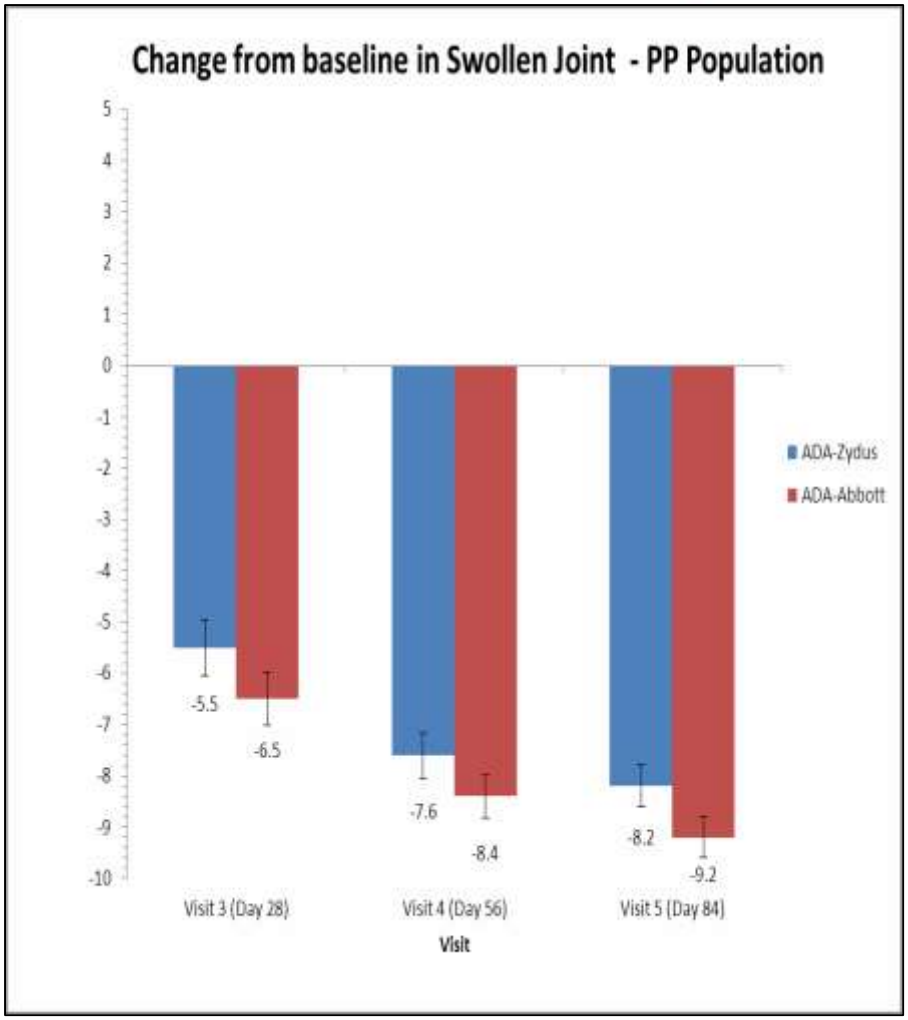
Values presented in Mean ±SD.

** Significant compare to baseline.*

 # Significant compare to ADA-Abbvie.

Zydus Adalimumab Study: Summary of ACR Core Component





Zydus Adalimumab Study: Summary of ACR Core Component

Exemptia Adalimumab

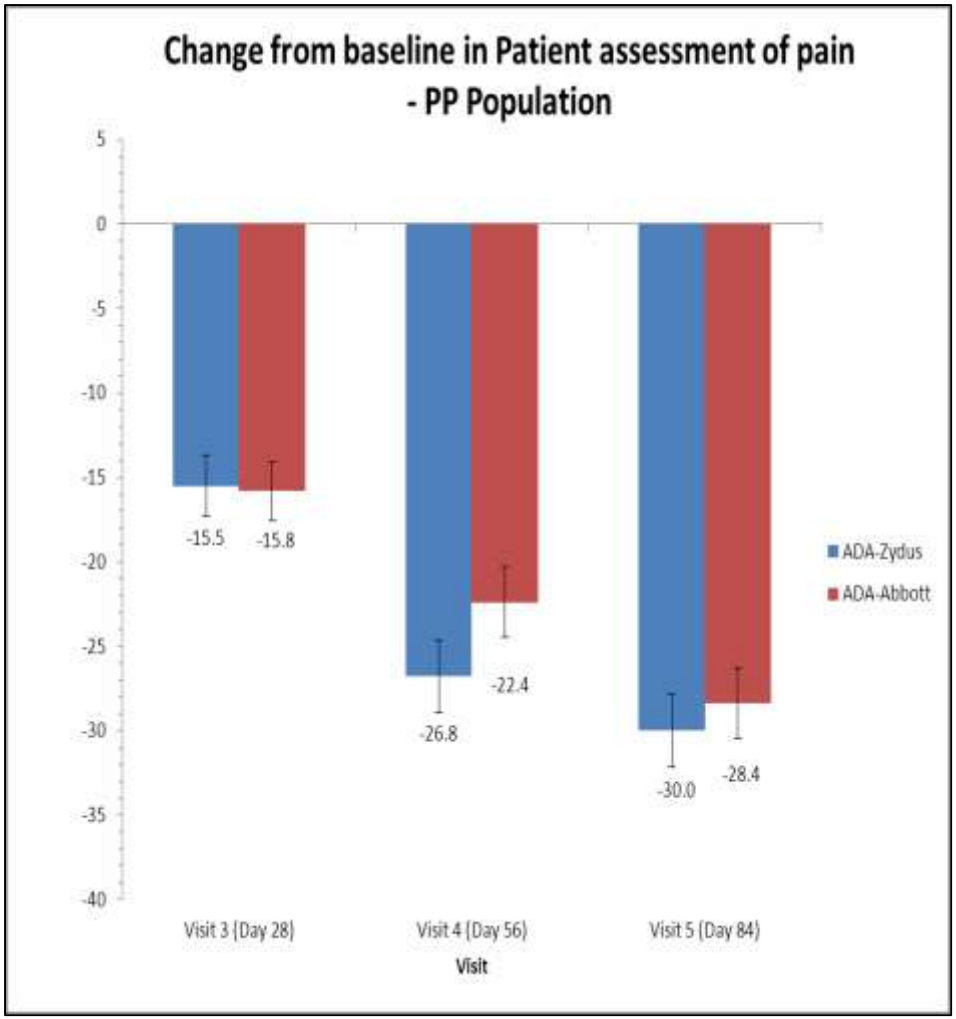
Baseline and change from baseline to Visit 3 (Day 28) and Visit 5 (Day 84)		
ACR Core component	**ADA-Zydus (N=50)**	**ADA-AbbVie (N=53)**
Patient Assessment of pain (0-100)		
Visit 1 (Day 1)	66.5 ± 12.38	66.4 ± 11.11
Change from baseline at Visit 3 (Day 28)	-15.5 ± 11.18*	-15.8 ± 14.87*
Visit 5 (Day 84)	-30.0 ± 17.66*	-28.4 ± 16.75*
Patient global assessment of disease activity (0-100)		
Visit 1 (Day 1)	66.2 ± 11.91	64.8 ± 10.57
Change from baseline at Visit 3 (Day 28)	-14.8 ± 11.47*	-16.5 ± 14.56*
Visit 5 (Day 84)	-30.5 ± 16.75*	-28.3 ± 18.11*

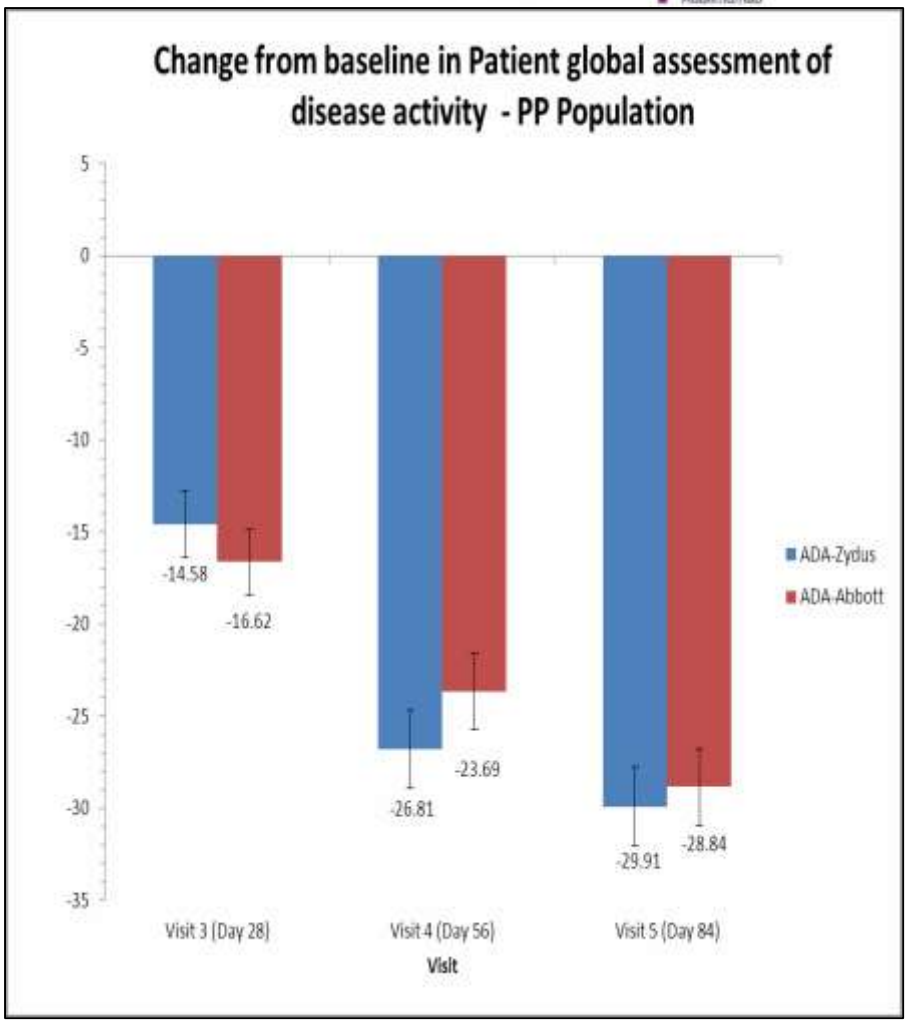
Values presented in Mean ±SD.

** Significant compare to baseline.*

 # Significant compare to ADA-Abbvie.

Zydus Adalimumab Study: Summary of ACR Core Component





Zydus Adalimumab Study: Summary of ACR Core Component

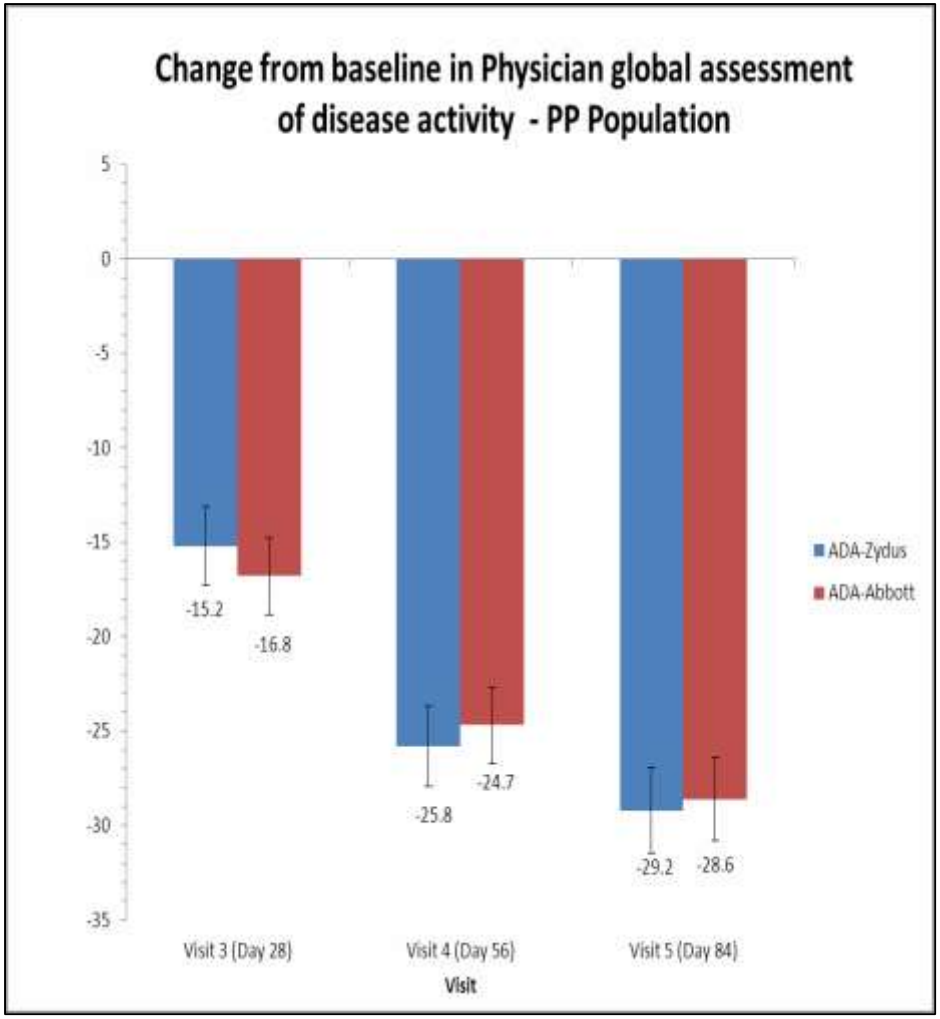
Baseline and change from baseline to Visit 3 (Day 28) and Visit 5 (Day 84)		
ACR Core component	**ADA-Zydus* (N=50)**	**ADA-AbbVie* (N=53)**
Physician global assessment of disease activity (0-100)		
Visit 1 (Day 1)	63.4 ± 12.02	63.9 ± 10.39
Change from baseline at Visit 3 (Day 28)	-15.2 ± 13.86*	-16.8 ± 16.05*
Visit 5 (Day 84)	-29.2 ± 18.35*	-28.6 ± 18.02*
Disability Index of the HAQ (0-3)		
Visit 1 (Day 1)	1.7 ± 0.62	1.6 ± 0.61
Change from baseline at Visit 3 (Day 28)	-0.5 ± 0.48*	-0.5 ± 0.48*
Visit 5 (Day 84)	-0.8 ± 0.63*	-0.7 ± 0.60*

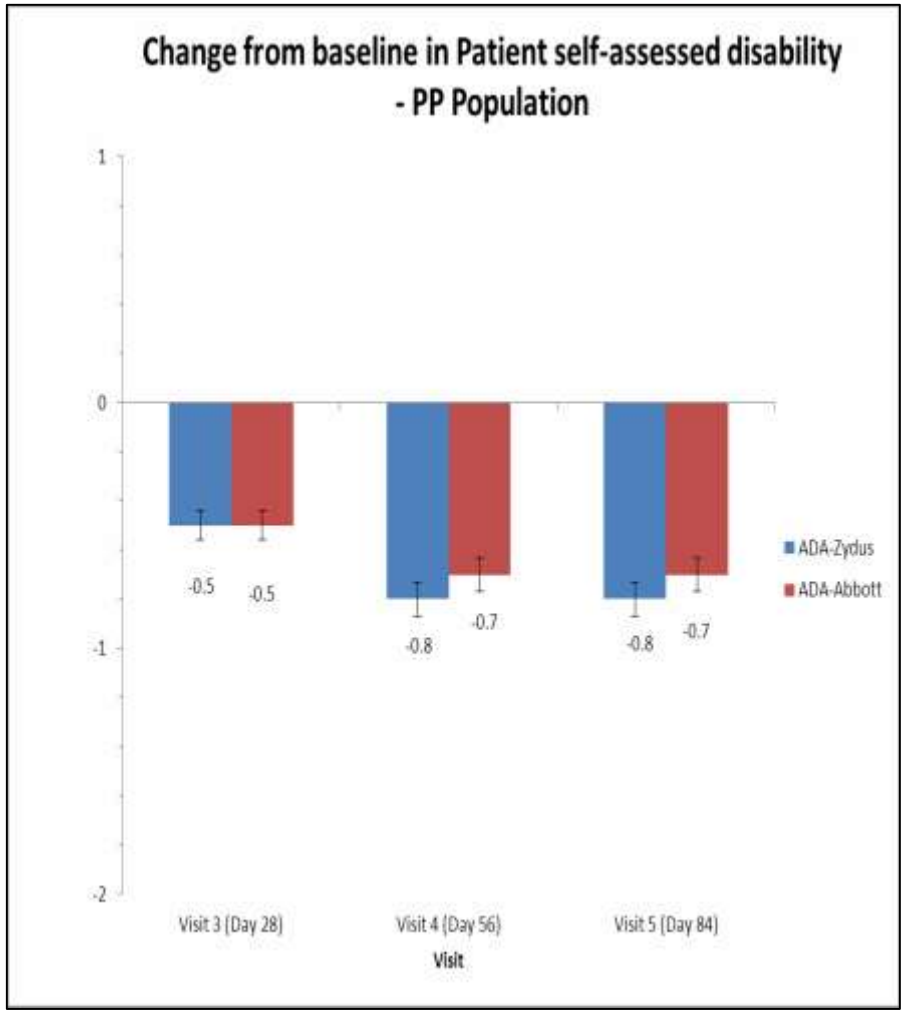
Values presented in Mean ±SD.

** Significant compare to baseline.*

 # Significant compare to ADA-Abbvie.

Zydus Adalimumab Study: Summary of ACR Core Component





Zydus Adalimumab Study: Summary of ACR Core Component

Summary of ACR Core Component: Baseline value and change from baseline to Visit 3 (Day 28) and Visit 5 (Day 84)		
ACR Core component	**ADA-Zydus* (N=50)**	**ADA-AbbVie* (N=53)**
CRP (mg/L)		
Visit 1 (Day 1)	11.0 ± 12.72	10.5 ± 12.90
Change from baseline at Visit 3 (Day 28)	-2.5 ± 19.36	-6.8 ± 12.77*
Visit 5 (Day 84)	-5.5 ± 12.66*	0.7 ± 26.98
ESR (mm/hr)		
Visit 1 (Day 1)	53.9 ± 21.45	53.2 ± 20.33
Change from baseline at Visit 3 (Day 28)	-5.4 ± 16.82*	-2.5 ± 15.62
Visit 5 (Day 84)	-8.6 ± 19.76*	-5.4 ± 17.35*

Values presented in Mean ± SD.

** Significant compare to baseline.*

 # Significant compare to ADA-Abbvie.

No significant difference between treatment groups

Zydus Adalimumab Study: Secondary Efficacy Criteria-DAS-28 CRP

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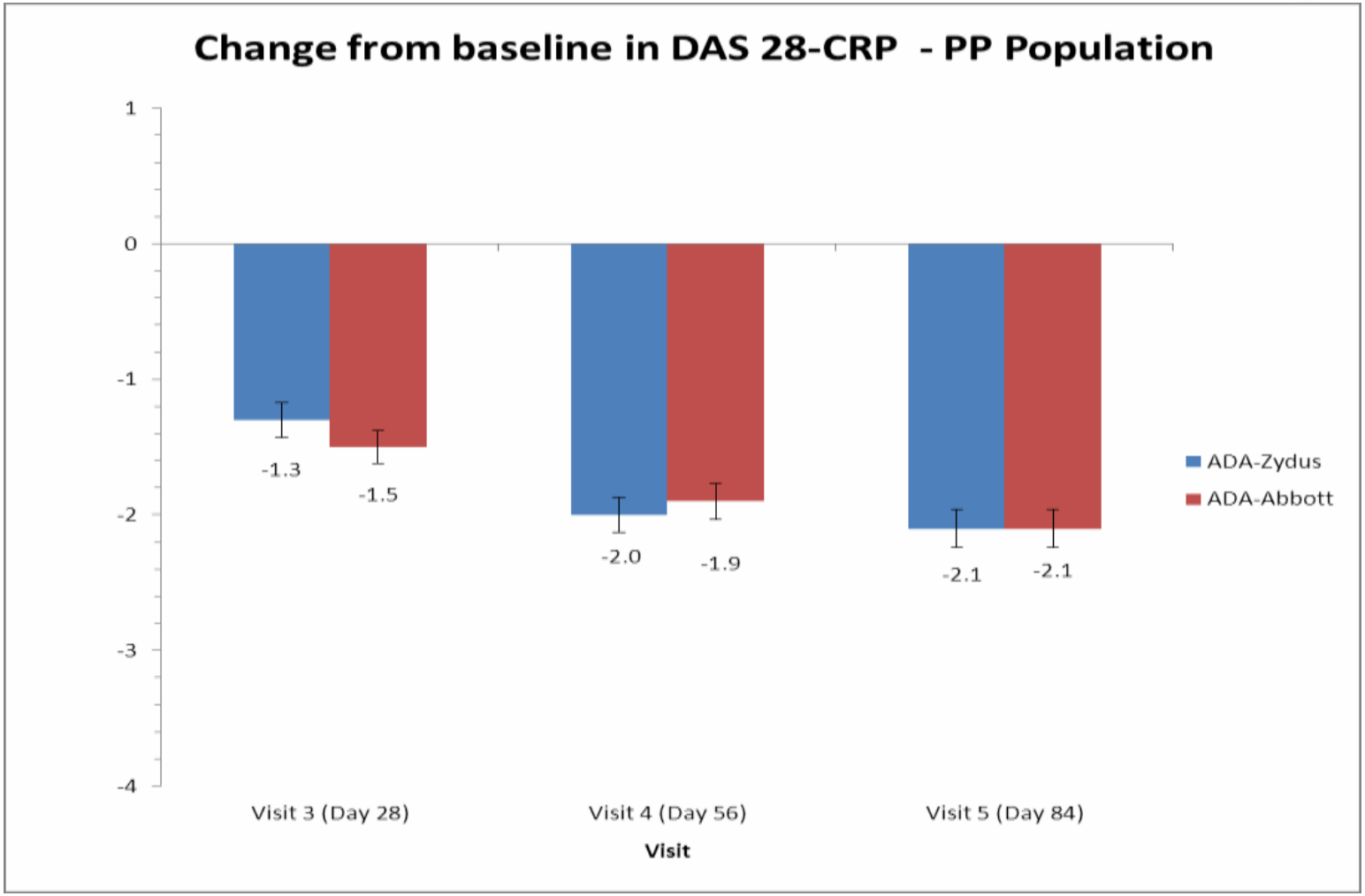
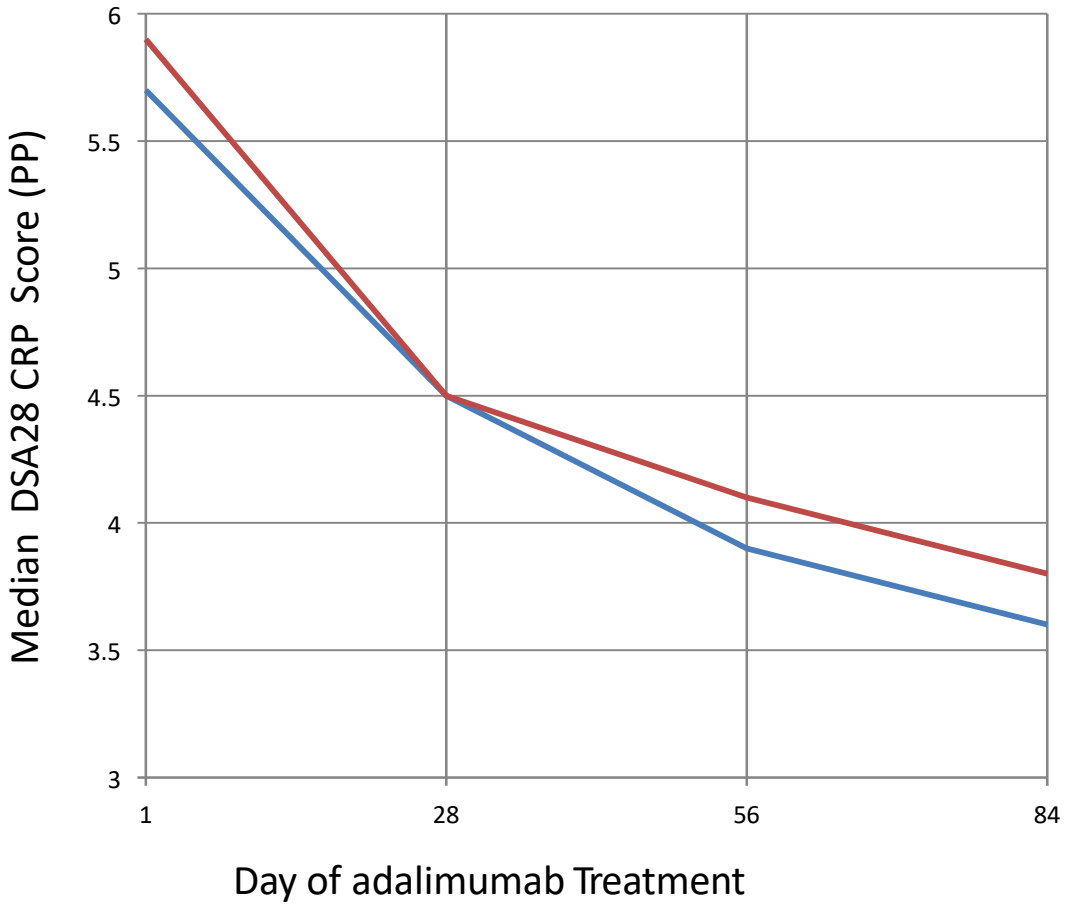
Summary of DAS 28-CRP score by visit and treatment groups (PP population)			
Visit		ADA-Zydus (N=50)	ADA-AbbVie (N=53)
Visit 1 (Day 1)	Mean ± SD	5.8 ± 0.88	5.8 ± 0.83
	Median	5.7	5.9
Visit 3 (Day 28)	Mean ± SD	4.5 ± 1.06	4.3 ± 0.93
	Median	4.5	4.5
Visit 4 (Day 56)	Mean ± SD	3.8 ± 0.97	4.0 ± 0.98
	Median	3.9	4.1
Visit 5 (Day 84)	Mean ± SD	3.7 ± 1.12	3.7 ± 0.94
	Median	3.6	3.8
Abbreviations: N = number of subjects in specified treatment;			

Clinically significant improvement in DAS28 CRP score from baseline in both groups

Zydus Adalimumab Study: Secondary Efficacy Criteria-DAS-28 CRP



Zydus Adalimumab Study: Secondary Efficacy Criteria-DAS-28 CRP



Exemptia improves DAS28 score within 28 days

Zydus Adalimumab Study: Immunogenicity Assessment

- Immunogenicity Assessment
  - Anti-drug antibody was observed on visit 5 in
    - two patients treated with **Adalimumab (Zydus)** with titer value of 25 and 800, and
    - one patient treated with **Adalimumab (AbbVie)** with titer values of 200.
    - Low level antidrug antibody was observed in two baseline samples (before the drug treatment) on Visit 1 with titer values of 25 and 50, but on Visit 5 they were found negative.
- These results indicate that the drug products Adalimumab (Zydus) and Adalimumab (AbbVie) are similar with respect to immunogenic response in patients.

Zydus Adalimumab Study: Safety Assessment

Exemptia Adalimumab

- Adverse Events (AEs):
  - 28 AEs reported in 17 subjects and
    - 13 AEs reported in 7 subjects in test group,
    - 15 AEs in 10 subjects in reference group.
    - AE reported were-
      - Abdominal Discomfort, Abdominal Pain, Accelerated Hypertension, Arthralgia, Body Tinea, Chest Pain, Diarrhoea, Dizziness, Dyspepsia, Dyspnoea, Fungal Infection, Gastritis, Headache Injection Site Reaction, Joint Swelling, Oligomenorrhoea, Pollakiuria, Polymenorrhoea, Pulmonary Tuberculosis, Pyrexia, Pyrexia, Rash, Urinary Tract Infection, Vomiting
  - 3 SAEs reported during the study
- The distribution of AEs was comparable between the treatment groups.

Zydus Adalimumab Study: Summary of Adverse Event by Severity

Association to study drug	ADA-Zydus (N=14) n (%)	ADA-AbbVie (N=17) n (%)	Total (N=31) n (%)
Not Related	5 (35.7%)	11 (64.7%)	16 (51.6%)
Possible	2 (14.3%)	2 (11.8%)	4 (12.9%)
Probable	7 (50.0%)	2 (11.8%)	9 (29.0%)
Definite	0 (0.0%)	2 (11.8%)	2 (6.5%)

Abbreviations: N = number of adverse event in the treatment group;

n = number of adverse event in the specified category.

Medical Dictionary used: MedDRA Version 17.0

Most of AEs were not related to study drugs

Zydus Adalimumab Study: Summary of Serious Adverse Event

Treatment	Reason for narrative	Preferred term (Verbatim term)	Causality	Outcome
Adalimumab (AbbVie)	SAE[1] (Hospitalization)	Dizziness (Giddiness with gastritis)	Unlikely	**Resolved**
Adalimumab (Zydus)	SAE[2] (Hospitalization)	Pyrexia (Cough and fever)	Probable	**Resolved**
	SAE[3] (Hospitalization)	Cough (Cough and coryza)	Possible	**Resolved**

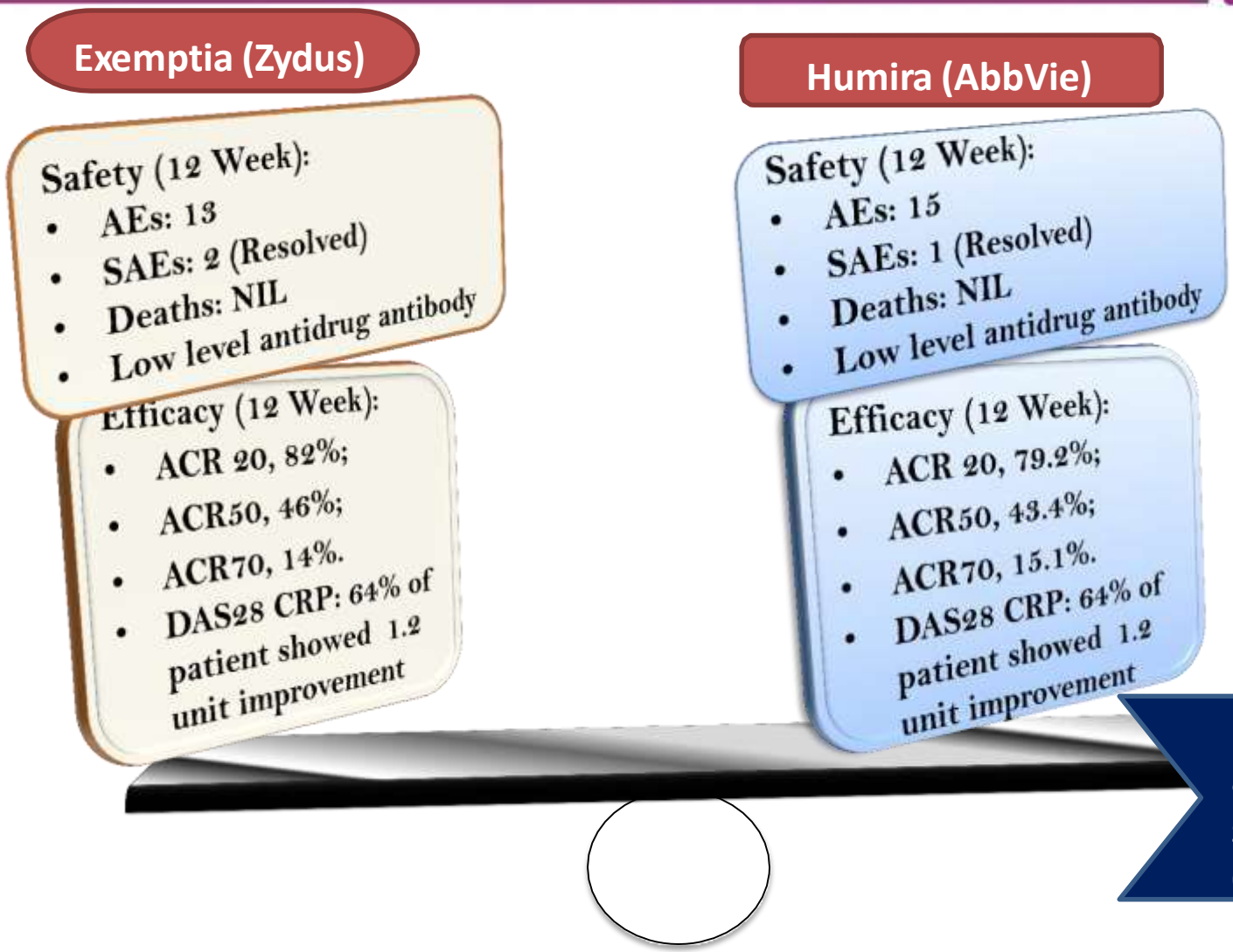
[1] Subject enrollment no. EGB063;

[2] Subject enrollment no. EGB057; Further subject was diagnosed with Pulmonary tuberculosis;

[3] Subject enrollment no. EGB063

- All SAEs resolved completely
- **Overall, both drugs were similar in Safety**

Zydus Adalimumab Study: Conclusion



Exemptia is as effective and safe as Originator

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™.

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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