AB0381

CERTOLIZUMAB PEGOL IN AUTOIMMUNE DISEASES. REAL LIFE EXPERIENCE IN PREGNANCYRenato Guzman Moreno^{1,2}, Karina Guzman Roa³, Gladys Roa Montes⁴.¹IDEARG, Immunorheumatology, Bogota, Colombia; ²Foundation Universitaria Juan N Corpas, Immunology and Internal Medicine, Bogota, Colombia; ³IDEARG, ImmunoRheumatology, Bogota, Colombia; ⁴IDEARG, Immunorheumatology, Bogota, Colombia

Background: Certolizumab pegol (CZP) is a Pegylated, Fc free monoclonal antibody that is useful in different autoimmune conditions. It does not bind FcRn and is not expected to undergo transfer across the placenta and probably there is a minimal placenta transfer of CZP in humans. On the other hand, most chronic inflammatory diseases are prevalent in women and 50% of these diseases need active treatment. We describe our experience for more than 7 years in patients with inflammatory arthritis and pregnancy that received CZP.

Objectives: We describe our experience in patients with inflammatory arthropathy that received CZP during their pregnancy.

Methods: We review our cohort of patients with Rheumatoid Arthritis, Spondyloarthritis and psoriatic arthritis from 2011 to 2017 that received CZP and analyzed those cases of pregnancy and described the clinical characteristic, the medication concomitant and the course of the pregnancy.

Results: We review more than 750 patients with inflammatory arthritis that received CZP and found 15 cases that was in pregnancy. See table 1.

Table 1. The use of CZP was effective, good tolerated and the profile of safety for the mother and the product was acceptable.

Age (years)	Disease	Drug exposure (months)	Clinical course	Breastfeeding. Comments
28	RA. (Rheumatoid Arthritis).	5	Normal.	+
30	RA	7.5	Preterm. 34 weeks.- 1500 grams	+ 3 month
38	RA	2	Miscarriage. 8 weeks.	Methotrexate Use. NA.
48	RA	5	Miscarriage. 5 weeks. uterine curettage. previous tubal ligation.	Methotrexate use. NA
32	Seronegative Spondyloarthritis.	4	Normal.	-
36	RA	8	Caesarean section. 1400 grams. Gestational age 31weeks. Preterm.	+
24	Seronegative Spondyloarthritis	9	Normal	+
29	RA	9	Normal.	+
31	RA	4	Normal.	+
33	Seronegative Spondyloarthritis	9	Normal. Caesarean section. (C-section).	+
37	RA	8	Preterm. 33 weeks. Arterial Hypertension, Gestational Diabetes.	Baby Kangaroo. 1640 grams.
32	RA	9	Normal. Caesarean section. (C-section).	+
31	Psoriatic Arthritis	6.5	Normal	NA
20	RA	10	Normal	+
21	Psoriatic Arthritis	9	Normal.	+

Conclusion: CZP is a useful alternative of treatment for pregnant patients and with inflammatory arthropathies that required therapeutic agent. This topic has been recently review and show that this agent is safe for pregnant women and for those breastfeeding and support continuation of CZP during pregnancy, when considered necessary.

There has been clear evidence during the last few years that this is the treatment of choice for women in fertile age with autoimmune diseases which requires immunomodulation.

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AB0382

TROUGH VERSUS NON-TROUGH ADALIMUMAB DRUG LEVEL MEASUREMENTSFemke Hooijberg¹, Merel J. L'ami¹, Lea C. Berkhout^{2,3}, Sadaf Atiqi¹, Michael Nurmohamed¹, Annick de Vries⁴, Charlotte L. Krieckaert⁵, Theo Rispens^{2,3}, ^{1,2}Gert-Jan Wolbink³. ¹Amsterdam Rheumatology and Immunology Center, location Reade, Amsterdam, Netherlands; ²Department of Immunopathology, Sanquin Research, Amsterdam, Netherlands; ³Landsteiner Laboratory, Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands; ⁴Biologicals Lab, Sanquin Diagnostic Services, Amsterdam, Netherlands; ⁵Amsterdam Rheumatology and immunology Center, location VUmc, Amsterdam, Netherlands

Background: Over the last years there has been an increasing interest for measuring drug levels to guide decision-making. Serum samples used for these measurements are often obtained prior to the next injection, at trough level. However, Jani et al. (2015) analyzed drug levels of randomly acquired serum samples from patients with rheumatoid arthritis (RA) treated with either etanercept or adalimumab and found a significant relationship with clinical disease activity. This indicates that random drug level measurements might also be useful (1). However, more aspects should be considered before deciding to use non-trough measurements.

Objectives: To assess the effect of non-trough measurements, compared to trough measurements, on serum drug level.

Methods: Patients with RA starting adalimumab treatment were included in this prospective observational cohort study, named the Reade Rheumatology Registry. Serum samples were obtained during every visit and these were analyzed for drug levels using a regular enzyme-linked immunosorbent assay (Sanquin, Amsterdam). The date of a patients' last injection with adalimumab was documented. Samples were included in the analyses if the interval between the last injection and serum sampling did not exceed 28 days, as in general patients do not have such long dosing-intervals. The analysis was performed using Spearman correlation.

Results: In total, 121 RA patients were included in this study. The median follow-up period of these patients was 156 (interquartile range (IQR) 78-247) weeks. Drug level measurements were performed in all serum samples that were obtained. In total, 310 measurements were included in the analyses, as from this subset the date of the previous injection with adalimumab was documented. The median drug level during adalimumab treatment was 6.6 (IQR 4.2-9.8) µg/ml, and the median number of days between the previous injection of adalimumab and serum sampling was 8 (5-13). The latter was divided into quartiles and plotted against drug level (Figure 1). The first quartile (median 2 (IQR 1-3) days) had a median drug level of 8.0 (4.7-11.0) µg/ml, the second quartile (7 (6-8) days) of 6.9 (5.4-10.0) µg/ml, the third quartile (11 (10-12) days) of 6.1 (3.4-9.5) µg/ml, and the fourth quartile (14 (13-14) days) of 5.7 (3.1-8.5) µg/ml. A weak association was found between the number of days between the previous injection of adalimumab and serum sampling and adalimumab drug level (Spearman's ρ : -0.182, $p=0.001$).

Figure 1

Conclusion: The growing interest to apply therapeutic drug monitoring (TDM) within the field of rheumatology forces us to discuss which measurements, trough or non-trough, are most informative. We found a correlation between the number of days between the previous injection of adalimumab and serum sampling, and adalimumab drug level. This might suggest that the timing of serum sampling affects the measured drug level, which could have consequences for treatment decisions based on these drug levels.

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AB0383

LATENT TUBERCULOSIS INFECTION SHOULD BE MONITORED IN BOTH TUMOR NECROSIS FACTOR INHIBITORS AND NON-TUMOR NECROSIS FACTOR INHIBITORS IN BIOLOGIC-NAÏVE PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The risk of latent tuberculosis infection (LTBI) increased during the treatment of biologic agents for patients with rheumatoid arthritis. Taiwan rheumatology association recommend performing at least annual interferon-gamma release assays (IGARs) testing during biologic treatment course because of the moderate prevalence of tuberculosis in Taiwan.[1] Although increased tuberculosis reactivation rate in patients with TNF inhibitor is reported, the risk of LTBI in patients with RA treated by non-TNF inhibitors is limited.

Objectives: The aim is to use serial interferon-gamma release assays (IGARs) as a diagnostic tool for LTBI in biologic-naïve patients with rheumatoid arthritis treated with TNF and non-TNF inhibitors in Taiwan.

Methods: We retrospectively collected 313 biologic-naïve patients with rheumatoid arthritis receiving biologic agents between 2013 to 2017 in Chang Gung Memorial hospital in Taiwan. All RA patients underwent semi-annual IGRA test during biologic agent treatment. Cox proportional hazard model was used for analysis to compared RA patients with TNF and non-TNF inhibitors.

Figure 1

Results: The age of patients and disease duration are 55.9 13.1 year-old and 5.2 2.0 years (Table 1). The LTBI rate in patients with rheumatoid arthritis after biologic treatment is 6.7%. Out of the 21 patients with LTBI, 12(6%) patients were treated with TNF inhibitors, 9(8%) patients were treated with non-TNF inhibitors (Figure 1). 42.9%(9/21) received chemoprophylactic therapy by isoniazid but no patient suffered from active TB till the end of study period. Patients with TNF inhibitors was associated with a hazard ratio (HR) of 4.43 (95% CI, 0.80-24.39) after adjusted age, sex, diabetes history, prednisolone use and disease duration. This

Cox regression analysis of RA patients found that the risk of LTBI was not different in TNF or non-TNF inhibitors.

Conclusion: Our study revealed biologic-naïve patients with rheumatoid arthritis have the same risk of LTBI. All RA patients who need either TNF or non-TNF inhibitors should be monitored LTBI in moderate prevalence TB area.

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Table 1. Baseline characteristics in patients with RA treated with TNF or non-TNF inhibitors

	Total (n=313)	TNF inhibitors (n=200)	Non-TNF inhibitors (n=113)	p- value
Gender, female	259 (82.7%)	169(84.5%)	90(79.6%)	0.109
Age (Mean± standard deviation)	55.9	55.0	57.6	0.102
Disease duration (Mean± standard deviation)	13.1 5.2	12.3 5.5	14.4 4.7	0.001*
Diabetes mellitus	2 (0.6%)	1.8 (0.9%)	2.2 (1.9%)	0.019*
Liver cirrhosis	2(0.6%)	2(1.0%)	0(0.0%)	0.280
Prednisolone mean dose (mg/day)	223 (71.2%) 8.0	145(72.5%) 8.2	78 (69.0%) 7.6	0.479 0.623
	7.7	9.1	3.8	

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AB0384

PROMISPAIN INTERFERENCE 6B AND FATIGUE 7A SHORT FORMS AND PROFILE-29 IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TNF INHIBITORS

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Background: PROMIS (Patient Reported Outcomes Measurement Information System) has been used in rheumatoid arthritis (RA) patients (Pts) to assess disease activity across multiple domains (i.e. physical function, fatigue, pain interference). AWARE (Comparative and Pragmatic Study of Golimumab IV Versus Infliximab in Rheumatoid Arthritis) is an ongoing Phase 4 study designed to provide a real-world assessment of intravenous Tumor Necrosis Factor inhibitor (TNFi) medications in RA pts. The study utilizes PROMIS and Clinical Disease Activity Index (CDAI) to assess effectiveness.

Objectives: This analysis examined select PROMIS measures to assess (1) relationship between baseline (BL) CDAI and PROMIS-scores, (2) responsiveness of PROMIS after initiation of TNFi and (3) relationship between PROMIS T-scores of the 4 item Profile29v2 Fatigue and Pain Interference domains and respective PROMIS Short Forms (SF).

Methods: AWARE is a prospective, noninterventional, 3-year study at 100 US sites. RA pts were enrolled when initiating TNFi treatment. Treatment decisions are at the discretion of the treating rheumatologist. We report on data from Pts' BL PROMIS Pain Interference 6b (PI), Fatigue7a (F), Profile29v2 and CDAI. PROMIS T-scores were compared across CDAI disease category (high, moderate etc) using ANOVA. We dichotomized pts based on whether their BL T-score was within 0.5SD of the population mean (i.e. 'normal') or not to evaluate for effect modification in the subsequent change in PROMIS T-scores. Data shown are mean ± std dev.

Results: Pts (N=1220) were 59.5± 13.2 yrs, disease duration 8.2 ± 9.9 yrs, 83.4% female, body weight 85.1± 24.2 kg, BMI 31.4 ± 8.51, BL CDAI 32.4 ± 15.6. A significant relationship between PROMIS T-scores (PI, F) and BL CDAI disease activity category was confirmed. There was minimal change in T-score of pts with BL PI and F T-scores <=55 and PF>=45 over 5 infusions (approx. 5-7 months). Depending on domain,