REFERENCES

- [1] Clowse, et al. Effects of Infertility, Pregnancy Loss, and Patient Concerns on Family Size of Women With Rheumatoid Arthritis and Systemic Lupus Erythematosus. *Arthritis Care & Research*.2012; 64 (5):668–674
- [2] Vinet et al. Systemic Lupus Erythematosus in Women: Impact on Family Size. *Arthritis & Rheumatism (Arthritis Care & Research)*.2008; 59 (11):1656–1660

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.4441

AB1295

DISCREPANCIES BETWEEN THE RHEUMATOID ARTHRITIS PATIENT POPULATION IN RANDOMIZED CONTROLLED TRIALS OF BIOLOGICS AND THAT IN REAL-WORLD SETTINGS: A STUDY USING THE IORRA COHORT

Eri Sugano¹, Eiichi Tanaka¹, Eisuke Inoue¹, Mai Abe¹, Mika Kawano¹, Kumiko Saka¹, Naohiro Sugitani², Yoko Shimizu¹, Moeko Ochiai¹, Rei Yamaguchi¹, Naoki Sugimoto¹, Katsunori Ikari¹, Ayako Nakajima², Atsuo Taniguchi¹, Hisashi Yamanaka¹. ¹*Institute of Rheumatology Tokyo Women's Medical University, Tokyo, Japan*; ²*Mie University Hospital, Center for Rheumatic Diseases, Mie, Japan*

Background: Randomized controlled trials (RCTs), which are currently considered to provide the highest level of evidence, include patients with high disease activity and exclude those with comorbidities often seen in real-world settings. With the increasing recognition of the importance of real-world evidence, attention is being paid to discrepancies between RCT-based evidence and the patient population in routine clinical practice; however, few reports assessing these gaps in the context of rheumatoid arthritis (RA) are available.

Objectives: To evaluate the proportion of patients meeting the inclusion criteria in RCTs of biologics for the treatment of RA conducted in Japan using the real-world IORRA cohort.

Methods: The inclusion criteria used in Phase 2 or Phase 3 RCTs of the following biological DMARDs (bDMARDs) were extracted: infliximab (IFX), etanercept (ETN), adalimumab (ADA), golimumab (GLM), certolizumab (CZP), abatacept (ABT), tocilizumab (TCZ), and infliximab BS (IFX-BS). Patients participating in the IORRA study during the period when each RCT was conducted (Cohort A) and those who initiated treatment with each bDMARD at our institute in 2016 (Cohort B) were included in the analysis. The proportion of RA patients in Cohorts A and B who met the RCT inclusion criteria was assessed.

Results: A total of 19 RCTs were conducted in Japan (IFX, 2; ETN, 1; ADA, 2; GLM, 2; CZP, 3; ABT, 2; TCZ, 6; IFX-BS, 1). Key trial inclusion criteria were age, RA duration, tender joint count (TJC), swollen joint count (SJC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), methotrexate (MTX) use, corticosteroid use, and prior bDMARD therapy. The number of patients participating in the IORRA analysis during the period when each RCT was conducted ranged from 1,777 to 6,843 (mean: 5,470) (Cohort A). The median/average [range] proportion of RA patients meeting all RCT inclusion criteria was 0.6%/2.3% [range: 0.0%-16.2%]. The proportion by criterion was 93.9%/92.4% [59.7%-99.9%] for age, 68.9%/57.1% [9.0%-99.6%] for RA duration, 11.6%/16.0% [4.5%-33.0%] for SJC, 14.6%/17.2% [3.7%-33.9%] for TJC, 27.8%/32.1% [20.1%-49.8%] for CRP, 60.2%/58.7% [43.7%-66.8%] for ESR, 14.8%/40.6% [13.1%-73.9%] for MTX use, 99.5%/99.3% [98.5%-99.8%] for prednisolone (PSL) use, and 91.9%/92.0% [85.6%-98.0%] for prior bDMARD use. In Cohort A, the proportion of RA patients meeting the RCT inclusion criteria was low, particularly with respect to SJC, TJC, and MTX use. Among 337 patients who initiated bDMARD therapy at our institute in 2016, a total of 139 biologic-naïve patients (IFX, 3; ETN, 33; ADA, 11; GLM, 21; CZP, 17; ABT, 25; TCZ, 28; IFX-BS, 1) were included in the analysis (Cohort B). In Cohort B, the median/average [range] proportion of RA patients meeting all RCT inclusion criteria was 0%/8.2% [0.0%-54.2%]. The proportion by criterion was 100%/99.1% [94.1%-100%] for age, 20.8%/26.5% [0.0%-57.1%] for SJC, 11.8%/17.0% [0.0%-50.0%] for TJC, 33.3%/34.9% [0.0%-66.7%] for CRP, 58.3%/57.3% [0.0%-75.0%] for ESR, 23.5%/35.5% [0.0%-100%] for MTX use, and 100%/100% [100%] for PSL use. As in Cohort A, the proportion of RA patients meeting the inclusion criteria was low in Cohort B, particularly with respect to SJC, TJC, and MTX use.

Conclusion: It is important to note that evidence from RCTs of bDMARDs is based on a limited RA population in real-world settings.

Disclosure of Interests: Eri Sugano: None declared, Eiichi Tanaka Speakers bureau: Abbvie, Asahi Kasei pharma co., Bristol Myers Squibb,

Chugai Pharmaceutical, Daiichi Sankyo Co., Eisai Pharmaceutical, Janssen Pharmaceutical K.K., Nippon Kayaku, Pfizer, Takeda Pharmaceutical, Taisho Toyama Pharmaceutical Co., and UCB Pharma., Eisuke Inoue: None declared, Mai Abe: None declared, Mika Kawano: None declared, Kumiko Saka: None declared, Naohiro Sugitani: None declared, Yoko Shimizu: None declared, Moeko Ochiai: None declared, Rei Yamaguchi: None declared, Naoki Sugimoto: None declared, Katsunori Ikari: None declared, Ayako Nakajima Grant/research support from: Asahi Kasei pharma co., Chugai Pharmaceutical, Daiichi Sankyo Co., Pfizer, Kissei Pharmaceutical Co., and Mitsubishi Tanabe Pharma Corporation., Atsuo Taniguchi: None declared, Hisashi Yamanaka Grant/research support from: AbbVie, Eisai, Bristol-Meyers, Novartis, Behringer, Astellas, Kaken, Nippon-Shinyaku, Pfizer, UCB, Ayumi, Ono, Daiichi-Sankyo, Taisyo-Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Torii, YLbio, Speakers bureau: Bristol-Meyers, Astellas, Pfizer, Daiichi-Sankyo, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, YLbio

DOI: 10.1136/annrheumdis-2019-eular.6570

AB1296

PREGNANCY IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS: MATERNAL AND FETAL COMPLICATIONS

Tatiana Kirsanova¹, Olga Tsatsulina², Maria Vinogradova¹, Tatiana Fedorova¹, Nina Rozina², Elizaveta Rumyantseva². ¹*Federal State Budget Institution "Research Center for Obstetrics, Gynecology and Perinatology", Moscow, Russian Federation*; ²*Moscow State University, Fundamental Medicine, Moskva, Russian Federation*

Background: Systemic lupus erythematosus is a chronic autoimmune disease often affecting women in fertile age. The physiological changes in T-helpers (Th1/Th2) activity balance during pregnancy can cause SLE flare. Women with SLE are at high risk for maternal and fetal complications. The high SLE activity is associated with higher risk of PE and lower birth weight, compared with population controls. Nevertheless, no detailed analysis of the relationship between clinical features/laboratory parameters and unfavorable pregnancy outcome in patients with SLE has been carried out in the recent studies.

Objectives: This study aimed to analyze influence of SLE activity, laboratory parameters and medications on risk of maternal and fetal complications.

Methods: A retrospective single-center cohort study 11/2014-12/2018: 43 pregnancies in 42 patients with proved SLE and > 20 weeks of gestation, mean age was 31,5 years. Renal function at conception and after delivery, pregnancy outcomes, clinical and laboratory parameters were collected. PE was diagnosed by the 2008 WHO criteria. The sFIT/PIGF ratio was used as the main differential marker to exclude lupus nephritis exacerbation in cases of increased proteinuria.

Age of the patients, SLE activity, hemoglobin and platelet levels, glomerular filtration rate, serum creatinine, AST, ALT, fibrinogen, D-dimer, aPTT, antinuclear factor and antiphospholipid antibodies concentrations, the using/non-use of glucocorticoids, hydroxychloroquine, low molecular weight heparins and aspirin were analyzed as potential risk factors of unfavorable pregnancy outcomes: PE, premature delivery, low birth weight, low Apgar score at 1 and 5 minutes after birth.

Results: In 12 cases (27.9%) there was no activity of SLE, in 16 cases (37.2%) there was low activity, in five (11.6%) – moderate, in three (7%) – high, in seven cases (16.3%) SLE activity was not assessed. SLE activity showed significant negative correlation with week at which labor occurred ($p = 0.003$, $R = -0.477$) and birth weight ($p = 0.005$, $R = -0.461$) and we found a significant fivefold increase in preeclampsia in patients with high activity of SLE ($p = 0.011$, $OR = 4.95$, 95% CI 1.449 to 16.931). Hemoglobin levels in third trimester correlated positively with birth weight ($p = 0.04$, $R = 0.322$). The dosage of glucocorticoids showed a significant correlation with week of delivery ($p = 0.011$, $R = -0.382$). Interestingly, the increase of aPTT in the third trimester had an almost significant effect on the risk of developing PE ($p = 0.059$, $OR = 1.237$, 95% CI 0.958-1.596). Unfortunately, lupus anticoagulant (LA) at that moment was not measured. Other studied parameters were not associated with risk of PE.

Conclusion: High SLE activity significantly increases the risk of gestational complications and unfavorable pregnancy outcomes. We suggest that regular monitoring of antiphospholipid antibodies, especially LA, is needed. In this study, laboratory parameters did not significantly affect the risk of PE.

REFERENCES

- [1] Zhang J.J. et al. A systematic review and meta-analysis of outcomes of pregnancy in CKD and CKD outcomes in pregnancy//Clin. J. Am. Soc. Nephrol. 2015. V. 10. Nº 11. P. 1964–1978.
- [2] Skorpén C.G. et al. Influence of disease activity and medications on offspring birth weight, pre-eclampsia and preterm birth in systemic lupus erythematosus: A populationbased study//Ann. Rheum. Dis. 2018. V. 77. Nº 2. P. 264–269.
- [3] Wu J. et al. Therapeutics and Clinical Risk Management Dovepress Management and outcomes of pregnancy with or without lupus nephritis: a systematic review and meta-analysis//Ther. Clin. Risk Manag. 2018. P. 14–885.
- [4] Lightstone L., Hladunewich M.A. Lupus Nephritis and Pregnancy: Concerns and Management//Semin. Nephrol. 2017. V. 37. Nº 4. P. 347–353.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.7648

AB1297

CARDIOVASCULAR EVENT AND RISK FACTORS IN PRIMARY SJÖGREN'S SYNDROME FROM LATIN-AMERICAN COHORT

Valeria Valim¹, Gabriela Hernandez-Molina², Virginia Fernandes Moça Trevisani³, Maria Lúcia Lemos Lopes⁴, Aysa Cesar Pinheiro⁵, Anastasia Secco⁶, Sabrina Zanardi Machado¹, Samira Tatiyama Miyamoto¹, Patricia Sasaki⁶, Antonio Catalán-Pellet⁶. Study Group on Sjögren's Syndrome of PANLAR.

¹Universidade Federal do Espírito Santo, Vitória, Brazil; ²Universidade Federal de Pernambuco, Mexico City, Mexico; ³Universidade Federal de São Paulo and Universidade de Santo Amaro, São Paulo, Brazil; ⁴Hospital Irmandade da Santa Casa de Misericórdia de Porto Alegre and Universidade Federal de Porto Alegre, Porto Alegre, Brazil; ⁵Universidade Federal de Pernambuco, Pernambuco, Brazil; ⁶Hospital B. Rivadavia, Caba, Argentina

Background: Inflammation has been associated with higher cardiovascular risk in rheumatic autoimmune diseases. Primary Sjögren's syndrome (pSS) is associated with increased cardiovascular morbidity¹. However, few and controversy data on the prevalence of cardiovascular events in patients with pSS have been reported^{2,3} with no data regarding on Latin-American pSS patients.

Objectives: To assess the cardiovascular event and to evaluate its association with traditional and disease associated risk factors in pSS.

Methods: We included 455 patients with pSS according to AECG 2002 or ACR-EULAR 2016 classification criteria, attending tertiary referral centers from Brazil (n=183), Mexico (n=236) and Argentina (n=36). We retrospectively registered demographics, disease duration, cardiovascular event (CE) (coronary heart disease, cerebrovascular accident, peripheral arterial disease), smoking, and use of prednisone (PDN), immunosuppressors and antimalarials. We evaluated traditional risk factors and scored the ESSDAI, ESSPRI and SSDDI at last follow-up.

Results: Most patients were female, miscigenous ethnicity, with median disease duration of 9.5 years. RF was positive in 48.5%, ANA in 85.6%, anti-Ro-SSA in 78.9% and anti-La-SSA in 43.1%. ESSDAI mean was 3.2 ±4.4, SSDDI 2.54±1.78 and ESSPRI 5.03±2.38. Fifty five percent used glucocorticoid in the past and 20% are currently using it, 33.4% are using immunosuppressors, 44% antimalarials and 10.3% biological therapy. It was found 26 (5.7%, CI95% 3.73-8.37) CE. The prevalence of hypertension was 35.6%, diabetes 11.2%, dyslipidemia 27.7% and smoking 17.5%. In univariate regression analysis, aging, hypertension, diabetes, dyslipidemia and smoking were associated with CE. Beyond traditional risk factors, prednisone > 20mg/day, ESSDAI constitutional domain and ESSPRI fatigue were associated with CE. In multivariate analysis, aging OR= 1.037 (1.001-1.075, p= 0.043), hypertension OR=2.509 (1.028-6.128, p=0.043) and diabetes OR= 2.736 (1.059-7.070, 0.038) were independent risk for CE.

Conclusion: Traditional risk factors are independent risk for CE in pSS. Disease-associated factors, such as glucocorticoid, fatigue and disease activity seem to be associated and should be explored in larger samples.

REFERENCES

- [1] Beltai A, et al. Cardiovascular morbidity and mortality in primary Sjögren syndrome: a systematic review and meta-analysis. Arthritis Care Res. 2018 (Epub ahead of print);
- [2] Valim V, et al. Atherosclerosis in Sjögren's syndrome: evidence, possible mechanisms and knowledge gaps. Gerds Clin Exp Rheumatol.34(1):133-42, 2016.
- [3] Berardicurti O, et al. Cardiovascular Disease in Primary Sjögren's Syndrome. Rev Recent Clin Trial 13(3):164-169, 2018.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.3846

AB1298

SAFETY AND EFFICACY OF PRIMARY YELLOW FEVER VACCINATION IN AUTOIMMUNE DISEASE: A PROSPECTIVE CONTROLLED STUDY

Valeria Valim¹, Arthur Dalmaso Pinto¹, Priscila Costa Martins Rocha¹, Samira Tatiyama Miyamoto¹, Érica Vieira Serrano¹, Ruben Horst Duque¹, Maria Bernadete Renoldi DE Oliveira Gavi¹, Lidia Balarini¹, Valquiria Garcia Dinis¹, Ketty Lysie Libardi Lira Machado¹, Thais Zanon Casagrande¹, Ana Paula E Gianórdoli¹, Sônia Alves Gouvêa¹, Larissa Carvalho Caser¹, Sheila Maria Barbosa DE Lima², Emilly Hime Miranda², Gisela Freitas Trindade², Ana Carolina Campi Azevedo³, Andréa Teixeira Carvalho³, Vanessa Peruhype Magalhães³, Ana Lidia Silva DE Souza¹, Ana Paula Neves Burian Lima¹, Lauro Ferreira Da Silva Pinto Neto⁴, Carolina Zorzaneli Costa⁴, Luiza Correia Rodrigues¹, Maria Fátima Bissoli¹, Raquel Altoé Giovel⁴, Luciana D. Moura¹, João Gabriel Fragoso Dias¹, Flavia Zon Pretti⁵, Karine G. Oliveira¹, Maryella S. Giacomini⁵, Luiz Felipe F Genelhu⁵, Daniela L. Merlo⁵, Laiza H. Dias⁵, Brunela P. Borjaile⁵, Leticia R. Brandão⁵, Daniela B. Pereira⁵, Ingrid O. Koehler⁵, Bruna CM Moura¹, Fernanda Mn Batista¹, Elisandra TI Polito¹, Thalles B. Clemente¹, Enan S. Magalhães¹, Marcela M. Thebit¹, Olindo Assis Martins Filho³. ¹UFES, Vitória, Brazil; ²Fiocruz, Rio de Janeiro, Brazil; ³Fiocruz, Belo Horizonte, Brazil; ⁴EMESCAM, Vitória, Brazil; ⁵SORES, Vitória, Brazil

Background: Alive vaccines should be used with caution in autoimmune diseases (AID).¹

Objectives: To evaluate prospectively adverse events and efficacy of the Yellow Fever vaccine in patients with AID.

Methods: Prospective study, including 190 individuals, 47 with Rheumatoid Arthritis (RA), 36 primary Sjögren's Syndrome (SS), 48 Ankylosing Spondylitis (AS), 8 Systemic Sclerosis (SSc), 24 Systemic Lupus Erythematosus (SLE), and 29 Healthy Controls (HC). All individuals received 17DD (Biomanguinhos-Fiocruz) YF vaccine, for the first time during the 2017 Brazilian Campaign, aged ≥ 18 years, had no or low disease activity, low immunosuppression. Exclusion Criteria: previous vaccination for yellow fever or PRNT > 1:50 at baseline, primary or secondary immunodeficiency, under treatment with cyclophosphamide, chlorambucil, mycophenolate mofetil, calcineurin inhibitors, azathioprine > 2mg/kg/day, prednisone ≥ 20mg/day, methotrexate > 20mg/week or any immunobiological drug. Viremia (CRP) and plaque reduction neutralization test (PRNT; GeoMean title) were measured before (D0) and D3, D4, D5, D6, D7, D14, D28 after vaccine. Adverse events (AE) were registered through patient report diary and medical interview at D7, D14 and D28.

Results: Mean age was 52 years old for AID and 56 for HC. No serious adverse event was reported. However, mild local AE was more reported in AID as compared to HC (34.2% vs 3.4%, p=0.000). The frequency of AE was higher in AID compared to HC (34.1 vs. 3.4%). The Risk (Odds Ratio; 95%CI) for AE was 14.53 (1.9-109.7, p=0.000) and AID subgroups: RA=14.5 (1.8-116.2, p=0.0016), AS= 9.3 (1.1-76.2, p=0.0248), SS 25.1 (3.1-204.5, p<0.0001), SLE 9.3 (1.0-84.1, p=0.0377), SSc 56.0 (4.1-769.0, p=0.0014). The PRNT levels expressed in reverse of serum dilution was lower in AID 181 (144-228, p=0.04) as well in AS 112 (73-170, p<0.001), and in SLE 143 (61-332, p=0.01) as compared to HC 440 (291-665). The seropositivity rates were lower in AID after 28 days (78% vs. 96%, p=0.04) as well as in AS (73%, p=0.02) and SLE (73%, p=0.03) as compared to HC (Figure 1). Viremia peak was slightly late and low in AID (D6=5.8 x 10³) compared to HC (D5= 8.3 x 10³). Seropositivity was statistically lower at D14 in AID as compared HC (21% vs. 75%, p=0.04) and remained lower at D28 in AS and SLE subgroups.

Conclusion: Efficacy was lower in AID, especially in SLE and AS, in spite of viremia peak at D5-D6 similar to HC. Taking together, results suggest that YF vaccine is safe in AID with low disease activity and under low immunosuppression, but probably a booster dose should be necessary.

REFERENCES

- [1] Lopez A, Mariette X, Bachelez H, et al. Vaccination recommendations for the adult immunosuppressed patient: A systematic review and comprehensive field synopsis. Journal of Autoimmunity 2017;80:10-27

Acknowledgement: SORES and FAPES

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.6424