Results: Demographics were similar between combination and monotherapy pools (mean age 52 years; 81–83% female), and 38.7% and 8.5% of patients had received prior bDMARDs. Cumulative drug exposure was 7,985.5 and 798.7 patient-years (PY), with maximum duration 7.3 and 3.5 years. Exposure-adjusted rates of TEAEs, serious AEs, and TEAEs leading to discontinuations were similar (Table). Infections were the most common AEs. Rates of serious infection were 3.7 and 1.0/100 PY for combination and monotherapy, respectively, and were not associated with decreased absolute neutrophil counts (ANCs). Incidences of ALT >3× upper limit of normal and ANC <1.0 giga/L were 10.3% and 12.7% for combination, respectively, and 5.5% and 14.9% for monotherapy. Rates of confirmed GI perforation for combination and monotherapy were 0.1 and 0/100 PY. Analyzing data by 6-month intervals showed no increase in rate over time for serious infections, malignancy, major adverse cardiac events, or ANC <1.0 giga/L.

	Sarilumab+csDMARD (N=2887)	Sarilumab monotherapy (N=471)
Safety overview: n/Y_{FE} (IR/100 PY)^a		
TEAEs	2489/1726 (144.2)	386/254 (151.8)
Serious TEAEs	685/7270 (9.4)	52/770 (6.7)
TEAEs leading to death	31/8187 (0.4)	5/812 (0.6)
TEAEs leading to discontinuation	705/8061 (8.7)	53/805 (6.6)
AEs: number of events (IR/100 PY)^b		
Infections	4451 (54.4)	446 (54.9)
Serious infections	301 (3.7)	8 (1.0)
Opportunistic infections	76 (0.9)	6 (0.7)
Herpes zoster ^c	53 (0.6)	4 (0.5)
Tuberculosis ^c	4 (0.0)	1 (0.1)
Leukopenia ^d	1482 (18.1)	244 (30.0)
Thrombocytopenia ^d	147 (1.8)	8 (1.0)
Hepatic disorders	726 (8.9)	58 (7.1)
Confirmed GI perforations ^e	9 (0.1)	0
Elevation in lipids ^f	498 (6.1)	18 (2.2)
Major adverse cardiovascular events ^g	45 (0.5)	2 (0.2)
Hypersensitivity	444 (5.4)	48 (5.9)
Anaphylaxis	0	0
Injection site reactions	1934 (23.6)	279 (34.3)
Malignancy	56 (0.7)	5 (0.6)
Malignancy excluding NMSC	38 (0.5)	4 (0.5)
Lupus-like syndrome	5 (0.1)	0
Demyelinating disorders	0	1 (0.1)

n, number of patients; Y_{FE}, cumulative years at risk of first event; IR, incidence rate; GI, gastrointestinal; NMSC, non-melanoma skin cancer; PY, patient-years. ^aExposure period is cumulative time at risk of first event. ^bAEs were investigator reported; exposure period is cumulative total TEAE period; ^cherpes zoster was reported as an opportunistic infection per protocol requirement; all cases of tuberculosis were reported as opportunistic infections; ^dindividual events were reported and laboratory abnormalities were not necessarily persistent; ^e3 upper, 6 lower; ^fMACE includes cardiovascular death, myocardial infarction, stroke, hospitalization for either unstable angina and/or transient ischemic attack.

Conclusion: The long-term safety profile of sarilumab, either as monotherapy (observed for >3.5 years) or with csDMARD (observed for >7 years), remains stable and consistent with the anticipated profile of an IL-6R blocker.

Acknowledgement: Study funding and editorial support (Helen Johns, Adelphi) were provided by Sanofi and Regeneron Pharmaceuticals, Inc. These data were previously presented at the 2018 American College of Rheumatology annual meeting.

Disclosure of Interests: Roy Fleischmann Grant/research support from: AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Celtrion, Genentech, GSK, Janssen, Lilly, Novartis, Pfizer Inc, Sanofi-Aventis, UCB, Consultant for: AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Celtrion, Genentech, GSK, Janssen, Lilly, Novartis, Pfizer Inc, Sanofi-Aventis, UCB, Yong Lin Shareholder of: Sanofi Genzyme, Employee of: Sanofi Genzyme, Gregory St John Shareholder of: Regeneron Pharmaceuticals Inc, Employee of: Regeneron Pharmaceuticals Inc, Désirée van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, Union Chimique Belge, Chunfu Qiu Shareholder of: Sanofi Genzyme, Employee of: Sanofi Genzyme, Juan Jose Gomez-Reino Grant/research support from: Biogen, Gilead, Eli Lilly, Merck Sharp & Dohme, Pfizer, Roche, Consultant for: Biogen, Gilead, Eli Lilly, Merck Sharp & Dohme, Pfizer, Roche, Jose Antonio Maldonado-Cocco Consultant for: Pfizer, Merck Sharp Dohme, Sanofi – Aventis, Novartis, Bristol Myers Squibb, Roche, Boehringer Ingelheim, Schering – Plough, Abbott, UCB, Eli Lilly, Gilead, Speakers bureau: Pfizer, Merck Sharp Dohme, Sanofi – Aventis, Novartis, Bristol Myers Squibb, Roche, Boehringer Ingelheim, Schering – Plough, Abbott, UCB, Eli Lilly, Marina Stanislav Consultant for: R-Pharm, Bruno Serio: None declared, Gerd Rüdiger Burmester Consultant for: Roche, Sanofi-Genzyme, Speakers bureau: Roche, Sanofi-Genzyme

DOI: 10.1136/annrheumdis-2019-eular.245

SAT0126

A PHASE 2 STUDY OF E6011, AN ANTI-FRACTALKINE MONOCLONAL ANTIBODY, IN PATIENTS WITH RHEUMATOID ARTHRITIS INADEQUATELY RESPONDING TO BIOLOGICS

Yoshiya Tanaka¹, Tsutomu Takeuchi², Hisashi Yamanaka³, Toshihiro Nanki⁴, Hisanori Umehara⁵, Nobuyuki Yasuda⁶, Fumitoshi Tago⁷, Yasumi Kitahara⁷, Makoto Kawakubo⁷, Hayato Hisaki⁷, Seiichi Hojo⁷, Tetsu Kawano⁶, Toshio Imai⁶.
¹University of Occupational and Environmental Health, Japan, Kitakyushu, Japan;
²Keio University, Tokyo, Japan; ³Tokyo Women's Medical University, Institute of Rheumatology, Tokyo, Japan; ⁴School of Medicine, Faculty of Medicine, Toho University, Tokyo, Japan; ⁵Nagahama City Hospital, Division of Rheumatology and Immunology, Shiga, Japan; ⁶KAN Research Institute, Inc., Kobe, Japan; ⁷Eisai Co., Ltd., Tokyo, Japan

Background: Fractalkine (CX3CL1, designated as FKN hereafter) is the sole member of the CX3C-chemokine which leads to dual actions, chemotaxis and cell adhesion for leukocytes expressing the cognate receptor, CX3CR1, during their migration. We have conducted clinical trials of E6011, a novel humanized anti-FKN monoclonal antibody, for patients with rheumatoid arthritis (RA) in Japan¹. This is the first report of a Phase 2, multicenter, randomized, double-blind, placebo-controlled, parallel-group comparison study of E6011 in RA patients inadequately responding to biologics (NCT02960490).

Objectives: To evaluate efficacy and safety of E6011 compared with placebo.

Methods: During the 24-week double-blind period, patients with moderately to severely active RA of inadequate response to biologics were randomly assigned to E6011 400 mg or placebo groups at a 1:1 ratio. Patients who continued the study beyond Week 12 were further allocated to E6011 200 mg or 400 mg at a 1:1 ratio within the initially assigned group. Patients received either E6011 400 mg or placebo at Weeks 0, 1, 2, and every 2 weeks subsequently until Week 10 and then E6011 200 mg or 400 mg every 2 weeks between Weeks 12 and 22 in a double-blind manner. This abstract reports the results from the first 12-week placebo controlled period.

Results: A total of 64 subjects (33 in the placebo group and 31 in the E6011 400 mg group) received study drug. Of the 64 subjects, 55 completed and 9 discontinued study treatment prematurely during the 12-week placebo controlled double-blind period. The ACR20 response rate at Week 12 (non-responder imputation), the primary endpoint, was 27.3% (9/33 subjects) in the placebo group and 22.6% (7/31 subjects) in the E6011 group. ACR50 and ACR70 response rate at Week 12 were 3.0%, 0% in the placebo group and 9.7%, 3.2% in the E6011 group, respectively. Numerically greater improvement from baseline was found for some parameters of the ACR components in the E6011 group, however, no statistically significant differences were found in any of the ACR components between the placebo and E6011 groups. From the exploratory PK exposure analysis, there was a tendency that the effect of E6011 became clearer in the subjects who achieved higher serum trough E6011 concentration. Adverse events that occurred in at least 2 subjects in the E6011 group were stomatitis, injection site erythema, nasopharyngitis, and blood creatine phosphokinase increased. As a results, E6011 was well tolerated with no notable safety concerns at doses of 400 mg when administered subcutaneously for 12 weeks.

Conclusion: E6011 400 mg was well tolerated but did not show clear efficacy at Week 12 compared with placebo in RA patients with inadequately responding to biologics. Further investigation to seek an optimal clinical dose and evaluation period of E6011 are warranted.

REFERENCE

[1] Tanaka Y, et al., *Mod Rheumatol* (2018) 28, 58-65

Acknowledgement: The authors wish to thank the study investigators.

Disclosure of Interests: Yoshiya Tanaka Grant/research support from: AbbVie, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Mitsubishi-Tanabe, MSD, Ono, Taisho-Toyama, Takeda, Speakers bureau: AbbVie, Asahi-kasei, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eli Lilly, Eisai, Glaxo-Smithkline, Janssen, Mitsubishi-Tanabe, Novartis, Pfizer Japan Inc, Sanofi, Takeda, UCB, YL Biologics, Tsutomu Takeuchi Grant/research support from: Astellas Pharma Inc, Chugai Pharmaceutical Co., Ltd., Daiichi Sankyo Co., Ltd., Takeda Pharmaceutical Co., Ltd., AbbVie GK, Asahikasei Pharma Corp., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Eisai Co., Ltd., AYUMI Pharmaceutical Corporation, Nipponkayaku Co. Ltd., Novartis Pharma K.K., Grant/research support from: AbbVie, Asahi Kasei, Astellas, AstraZeneca, AYUMI, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Eli Lilly Japan, Janssen,

Mitsubishi Tanabe, Nippon Kayaku, Novartis, Pfizer Japan Inc, Taiho, Taisho Toyama, Takeda, Teijin, Grant/research support from: Astellas Pharma Inc., Bristol Myers Squibb, Chugai Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Santen Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Teijin Pharma Ltd., AbbVie GK, Asahi Kasei Pharma Corp., Taisho Toyama Pharmaceutical Co., Ltd., Symbio Pharmaceuticals Ltd., Janssen Pharmaceutical K.K., Celltrion Inc., Nipponkayaku Co. Ltd., and UCB Japan, Consultant for: Astra Zeneca K. K., Eli Lilly Japan K.K., Novartis Pharma K.K., Mitsubishi Tanabe Pharma Co., Abbvie GK, Nipponkayaku Co.Ltd, Janssen Pharmaceutical K.K., Astellas Pharma Inc., Taiho Pharmaceutical Co. Ltd., Chugai Pharmaceutical Co. Ltd., Taisho Toyama Pharmaceutical Co. Ltd., GlaxoSmithKline K. K., UCB Japan Co. Ltd., Consultant for: AbbVie, Asahi Kasei, Astellas, AstraZeneca, AYUMI, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Eli Lilly Japan, Janssen, Mitsubishi Tanabe, Nippon Kayaku, Novartis, Pfizer Japan Inc, Taiho, Taisho Toyama, Takeda, Teijin, Consultant for: Astra Zeneca K.K., Eli Lilly Japan K.K., Novartis Pharma K.K., Mitsubishi Tanabe Pharma Co., Asahi Kasei Medical K.K., AbbVie GK, Daiichi Sankyo Co., Ltd., Bristol Myers Squibb, and Nipponkayaku Co. Ltd., Speakers bureau: Astellas Pharma Inc., Bristol Myers Squibb, Chugai Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Santen Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Teijin Pharma Ltd., AbbVie GK, Asahi Kasei Pharma Corp., Taiho Toyama Pharmaceutical Co., Ltd., Symbio Pharmaceuticals Ltd., Janssen Pharmaceutical K.K., Celltrion Inc., Nipponkayaku Co. Ltd., and UCB Japan, Speakers bureau: AbbVie, Asahi Kasei, Astellas, AstraZeneca, AYUMI, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Eli Lilly Japan, Janssen, Mitsubishi Tanabe, Nippon Kayaku, Novartis, Pfizer Japan Inc, Taiho, Taisho Toyama, Takeda, Teijin, Speakers bureau: AbbVie GK., Bristol-Myers K.K., Chugai Pharmaceutical Co. Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Astellas Pharma Inc, Daiichi Sankyo Co. Ltd., Eisai Co. Ltd., Sanofi K.K., Teijin Pharma Ltd., Takeda Pharmaceutical Co. Ltd., Novartis Pharma K.K., 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, Toshihiro Nanki Grant/research support from: Chugai, Eisai, Takeda, Teijin, Eli Lilly, Bristol-Myers, AbbVie, Ono, Novartis, Asahikasei, Mitsubishi-Tanabe, Astellas, Ayumi, Pfizer, Daiichi Sankyo, Shionogi, Sanofi, Nippon Kayaku, Yutoku, Actelion, UCB, Bayer, Nihon Pharmaceutical., Consultant for: UCB, Eisai, Chugai, Ono, Gilead., Speakers bureau: Mitsubishi-Tanabe, Chugai, Eisai, Takeda, Astellas, Janssen, Eli Lilly, Ayumi, Pfizer, Asahikasei, Sanofi, Daiichi Sankyo, Otsuka, AbbVie, Ono, Teijin, Nippon Kayaku, UCB., Hisanori Umehara: None declared, Nobuyuki Yasuda Shareholder of: Eisai Co., Ltd., Employee of: KAN Research Institute, Inc. (subsidiary of Eisai Co., Ltd.), Fumitoshi Tago Employee of: Eisai Co., Ltd., Yasumi Kitahara Shareholder of: Eisai Co., Ltd., Employee of: Eisai Co., Ltd., Makoto Kawakubo Shareholder of: Eisai Co., Ltd., Employee of: Eisai Co., Ltd., Hayato Hisaki Shareholder of: Eisai Co., Ltd., Employee of: Eisai Co., Ltd., Seichiro Hojo Employee of: Eisai Co., Ltd., Tetsu Kawano Employee of: KAN Research Institute, Inc. (subsidiary of Eisai Co., Ltd.)

DOI: 10.1136/annrheumdis-2019-eular.1894

SAT0127 LONG-TERM OUTCOME OF CHILDREN BORN TO MOTHERS WITH CHRONIC ARTHRITIS AND EXPOSED TO TNF-INHIBITORS DURING PREGNANCY: A CASE-CONTROL STUDY

Maria Chiara Gerardi¹, Laura Andreoli¹, Chiara Bazzani¹, Matteo Filippini², Micaela Fredi¹, Roberto Gorla², Maria Grazia Lazzaroni¹, Cecilia Nalli², Marco Taglietti², Andrea Lojaco³, Sonia Zatti³, Mario Motta⁴, Angela Tincani¹.
¹Rheumatology and Clinical Immunology, Spedali Civili and University of Brescia, Brescia, Italy, Brescia, Italy; ²Rheumatology and Clinical Immunology, Spedali Civili, Brescia, Italy, Brescia, Italy; ³Obstetrics and Gynaecology, Spedali Civili and University of Brescia, Brescia, Italy, Brescia, Italy; ⁴Neonatology and NICU, Spedali Civili, Brescia, Italy, Brescia, Italy

Background: Treatment with tumor necrosis factors inhibitors (TNFi) during pregnancy may be required in order to control maternal disease which itself can be a threat for maternal-fetal well-being and pregnancy outcome. Information about the follow-up of in utero exposed offspring is limited

Objectives: The aim of this study was to compare the health and developmental conditions of children born to mothers with chronic arthritis who

were exposed *in utero* to TNFi with those of unexposed children born to patients with the same age at conception and disease.

Methods: An *ad-hoc* created questionnaire was used to collect data on birth and growth parameters, breastfeeding, weaning, developmental milestones, vaccinations and illnesses.

Results: 122 live births in 97 women with chronic arthritis (65 RA and 32 SpA) were observed: 59 pregnancies were exposed to TNFi at the time of conception and 63 pregnancies were TNFi-naïve. In 57/59 (97%) pregnancies, TNFi was discontinued at positive pregnancy index. In 2/59 (3%) pregnancies TNFi was maintained throughout pregnancy due to active disease at conception. TNFi was restarted in 16/57 pregnancies (28%) (10 ETA, 5 CTZ, 1 ADA) during the 2nd-3rd trimester due to moderate-severe flare (median exposure 22 weeks; discontinuation of TNFi between 32-39 gestational weeks). In second group, TNFi (1 ETA, 1 CTZ) was introduced in 2/63 (3%) pregnancies during the 2nd trimester due to a severe flare. 16 in 16/63 (25%) pregnancies were managed with an increase of prednisone (max 10mg/day). To investigate the long-term follow-up of children exposed in utero to TNFi, 61 children exposed to TNFi at conception or during 2nd-3rd trimester (median age 29 months) and 61 unexposed children (median age 49 months) were compared. No significant differences in growth parameters and developmental milestones were observed. No excess nor particular pattern of congenital defects/malformations were observed. In both groups, vaccinations were performed according to the national schedule (no live vaccines in the first year of life) without relevant complications (Figure 1).

Conclusion: TNFi may be required in patients that experienced flare during pregnancy and they are effective in controlling maternal disease and ensures a good pregnancy outcome without complications for the health and growth of exposed children.

Table 1. Long-term follow up of children

	Pregnancies exposed to TNFi (n=61)		P value	Pregnancies unexposed to TNFi (n=61)	P value
	TNFi until positive pregnancy index (n=41)	TNFi during the 2 nd -3 rd trimester (n=20)			
Age at interview, mths.	32(10-86)	29(7-153)		49(7-169)	
Children growth					
Weight					
-at 0 mths, g	7250(7000-7600)	7550(6959-8178)	0.95	8000(7250-8245)	0.61
-at 12 mths, g	9350(8950-9850)	9975(9360-10838)	0.09	9600(8948-10673)	0.61
-at 24 mths, g	13050(11760-13625)	11250(10776-12825)	0.16	12680(11275-13510)	0.98
Length					
-at 0 mths, cm	67(65-68)	66(65-68)	0.95	68(65-70)	0.06
-at 12 mths, cm	75(74-77)	77(74-79)	0.29	76(73-78)	0.18
-at 24 mths, cm				90(85-92)	0.15
Head circumference					
-at 0 mths, cm	43(42-44)	44(42-44)	0.61	43(42-44)	0.45
-at 12 mths, cm	46(45-47)	47(45-49)	0.31	46(45-47)	0.96
Age at seated position, mths.	6(6-7)	6(6-7)	0.41	6(6-7)	0.38
Age at walking, mths	12(11-13)	13(11-15)	0.17	13(11-14)	0.32
Age at speaking, mths	20(15-24)	19(12-24)	0.77	24(14-24)	0.52
Reactions to vaccinations (performed according to the vaccination schedule for childhood)	1 rash post measles vaccines	1 post MPR (measles, mumps, and rubella) fever, rash and conjunctivitis		1 allergic reaction to PCV (Pneumococcal Conjugate Vaccine)	
Pathological conditions during the first year of life	1 hand foot and mouth disease 1 cardiac murmur 1 cryptorchidism surgery 1 anal fissure	1 total ductocelitis 1 atopic dermatitis 1 meningitis 1 pyelonephritis		1 hydrocephalus and testicular hydrocele 1 atopic dermatitis 1 inguinal hernia 1 lactose intolerance	
Pathological conditions after the first year of life	1 autism spectrum disorder	1 amblyopia		1 language disorder 1 recurrent otitis	

All data are expressed as median (IQR)

Acknowledgement: None

Disclosure of Interests: Maria Chiara Gerardi: None declared, Laura Andreoli: None declared, Chiara Bazzani: None declared, Matteo Filippini: None declared, Micaela Fredi: None declared, Roberto Gorla: None declared, Maria Grazia Lazzaroni: None declared, Cecilia Nalli: None declared, Marco Taglietti: None declared, Andrea Lojaco: None declared, Sonia Zatti: None declared, Mario Motta: None declared, Angela Tincani: None declared, Tincani Consultant for: UCB, Pfizer, Abbvie, BMS, Sanofi, Roche, GSK, AlphaSigma, Lilly, Janssen, Cellgene, Novartis

DOI: 10.1136/annrheumdis-2019-eular.3076

SAT0128 A PHASE 4 TRIAL ASSESSING THE IMPACT OF RESIDUAL INFLAMMATION AND CLINICAL CHARACTERISTICS ON THE OUTCOME OF DOSE TAPERING OF ADALIMUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO ARE IN STABLE CLINICAL REMISSION

Paul Emery¹, Gerd Rüdiger Burmester², Esperanza Naredo³, Ivan Lagunes-Galindo⁴, Franziska Koenigsbauer⁵, Philip G. Conaghan¹.
¹University of Leeds and NIHR Leeds Biomedical Research Centre, Leeds, United Kingdom; ²Charité-Universitätsmedizin, Berlin, Germany; ³Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain; ⁴AbbVie, Inc., North Chicago, United States of America; ⁵AbbVie Deutschland GmbH and Co. KG, Ludwigshafen, Germany

Background: For rheumatoid arthritis (RA) pts in stable clinical remission (SCR) on bDMARDs, EULAR and ACR recommend to consider tapering