Table 2. Efficacy endpoints at week 24

	TIL 200 mg Q4W (N = 78)	TIL 200 mg Q12W (N = 79)	TIL 100 mg Q12W (N = 77)	TIL 20 mg Q12W (N = 78)	PBO (N = 79)
PASI 75*, %	64.2***	79.6***	55.6***	46.3*	16.7
PASI 90*, %	47.2***	50.0***	38.9**	36.6*	7.1
Swollen joint count, median change from BL	-6.0*	-6.0	-6.0*	-6.0	-5.0
Tender joint count, median change from BL	-9.0	-10.0*	-11.0*	-10.0	-8.5

*Response rates only calculated in patients with BSA $\geq 3\%$ at baseline, missing responses were imputed as nonresponses. *P < 0.05; **P < 0.001; ***P < 0.0001 vs PBO. BL, baseline; BSA, Body Surface Area; PASI, Psoriasis Area and Severity Index; PBO, placebo; Q4W, every 4 weeks; Q12W, every 12 weeks; TIL, tildrakizumab.

*P < 0.05; **P < 0.001; ***P < 0.0001 vs PBO. ACR, American College of Rheumatology response criteria; PBO, placebo; Q4W, every 4 weeks; Q12W, every 12 weeks; TIL, tildrakizumab.

Figure 1. ACR20/50/70 response rates

tender joint count at week 24. Safety assessments included monitoring of treatment-emergent adverse events (TEAEs).

Results: Of 500 patients screened, 391 patients met inclusion criteria (including =18 years old, PsA diagnosis with symptoms for 6 months, and =3 tender and =3 swollen joints). Demographics and baseline disease characteristics are shown in Table 1. There were significantly greater proportions of ACR20/50/70 and PASI 75/90 responders with TIL vs PBO at week 24, and in some cases differences in parameters were noted as early as week 8 (Figure 1 and Table 2).

The most frequent TEAEs through week 24 included nasopharyngitis (pooled TIL arms: 5.4% [17/312]; PBO: 6.3% [5/79]); and diarrhoea (TIL: 1.3% [4/312]; PBO: 0). There were no reports of candidiasis, inflammatory bowel disease, major adverse cardiac events, or malignancy. No patients discontinued treatment due to TEAEs and no deaths were reported. Serious TEAEs occurred in 2.2% (7/312) of TIL-treated patients vs 2.5% (2/79) in PBO-treated patients.

Conclusion: By week 24, TIL was significantly more efficacious than PBO in treatment of joint and skin manifestations of PsA. Furthermore, there was a clear separation between TIL and PBO as early as 8 weeks for ACR20 (TIL 200 mg Q4W and 100 mg) and 12 weeks for ACR50 (all TIL groups). Shortening the dosing interval from Q12W to Q4W for the 200-mg dose did not result in a measurable increase in skin or joint response scores. There was a low rate of TEAEs in the TIL-treated group.

Acknowledgement: Editorial support by Marie-Louise Ricketts, PhD & Claire Daniele, PhD, of AlphaBioCom, King of Prussia, PA, funded by Sun Pharma.

Disclosure of Interests: Philip J Mease Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Leo, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries, Inc., and UCB., Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Galapagos, Gilead, Janssen, Leo, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries, Inc., and UCB., Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Genentech, Janssen, Leo, Merck, Novartis, Pfizer, and UCB., Saima Chohan: None declared, Ferran J Garcia Fructuoso Grant/research support from: AbbVie, Gedeon Richter, Lilly, MedImmune, Nichi-Iko, Pfizer, Sanofi-Aventis, Takeda, and UCB., Consultant for: AbbVie, Gedeon Richter, Lilly, MedImmune, Nichi-Iko, Pfizer, Sanofi-Aventis, Takeda, and UCB., Richard C Chou Consultant for: Receives consultation fees from Sun Pharmaceutical Industries, Inc., Kristine E Nograles Shareholder of: Holds shares in Celgene Corporation and Cara Therapeutics, Employee of: Sun Pharmaceutical Industries, Inc., Alan M Mendelsohn Shareholder of: Holds individual shares in Johnson and Johnson, and as parts of retirement account/mutual funds, Employee of: Sun Pharmaceutical Industries, Inc., Michael E Luggen Grant/research support from: AbbVie, Amgen, Genentech, Eli Lilly, Nichi-Iko, Novartis, Pfizer, R-Pharm; and Sun Pharmaceutical Industries, Inc., Consultant for: AbbVie, Amgen, Genentech, Eli Lilly, Nichi-Iko, Novartis, Pfizer, R-Pharm; and Sun Pharmaceutical Industries, Inc., Speakers bureau: AbbVie, Amgen, Genentech, Eli Lilly, Nichi-Iko, Novartis, Pfizer, R-Pharm; and Sun Pharmaceutical Industries, Inc.

DOI: 10.1136/annrheumdis-2019-eular.8669

WEDNESDAY, 12 JUNE 2019

RA therapy –JAK inhibitors and beyond

OP0023

ACPA-POSITIVE RHEUMATOID ARTHRITIS PATIENTS BENEFITED MORE FROM ADVANCED TREATMENT STRATEGIES THAN ACPA-NEGATIVE RHEUMATOID ARTHRITIS PATIENTS: 25-YEAR RESULTS OF A LONGITUDINAL COHORT STUDY

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Background: Over the last 25 years, treatment of rheumatoid arthritis (RA) has changed considerably, and clinically relevant joint damage and deformations have become infrequent. It is unclear to what extent the long-term outcomes mortality, sustained drug-free remission (DFR) and physical functioning have improved, and whether ACPA+ and ACPA- patients have benefited equally from treatment-improvements.

Objectives: To investigate the influence of treatment strategies that have been improved for 25-years on mortality, DFR and functionality, and whether these effects differed for ACPA+ and ACPA- RA-patients.

Methods: In the Leiden early arthritis cohort, 1291 patients with RA (1987 criteria) were included between 1993-2016. Patients were treated in routine care; initial and subsequent treatment changed over time; divided in 5 inclusion periods. Patients included between 1993-1996 (n=168) received initial NSAIDs and started DMARDs with delay, patients included 1997-2000 (n=185) were treated early with mild DMARDs (e.g. hydroxychloroquine, penicillamine), in 2001-2005 (n=210) patients started early with methotrexate, in 2006-2010 (n=338) early methotrexate was followed by treat to target treatment adjustments; in 2011-2016 (n=390) this was similar and additional efforts were undertaken for very early referral. Patients were followed yearly including assessments of swollen joints, DAS28-ESR and health assessment questionnaires (HAQ). Mortality data were obtained from the civic registry. DFR was defined as the persistent absence of synovitis after cessation of DMARD-therapy during all available follow-up (≥ 1 year). DAS28-ESR and HAQ data were analysed with linear mixed models; mortality and time to DFR with multivariable and univariable Cox regression. Inclusion period 1993-1996 was used as reference. Analyses were stratified for ACPA-status (anti-CCP2).

Results: Baseline age, sex and antibody status did not differ between inclusion periods. With 1993-1996 as reference, the DAS28-ESR decreased in the first year and thereafter remained lower in all inclusion periods (all p<0.05).

Compared to 1993-1996, mortality was decreased in all inclusion periods (1997-2000 HR 0.67 (0.46;0.99); 2001-2005 HR 0.66 (0.45;0.97); 2006-2010 HR 0.64 (0.42;0.98); 2011-2016 HR 0.31 (0.14;0.68)). DFR achievement was faster in 2006-2010 (HR 2.68 (1.68;4.29)) and 2011-2016 (3.37 (1.97;5.74)), compared to 1993-1996. Additionally, HAQ over time was lower in 2006-2010 (-0.25 (-0.36;-0.14)) and 2011-2016 (-0.21 (-0.32;-0.10)).

Stratification for ACPA revealed that ACPA+ patients in the first two inclusion periods remained to have a higher DAS28-ESR over time (1993-1996 β 0.76 (0.42;1.10); 1997-2000 β 0.40 (0.07;0.74)); thereafter there was no difference in DAS28-ESR between ACPA+ and ACPA- patients. The decrease in mortality was similar for ACPA+ and ACPA- patients. The increased rate of DFR was more prominent in ACPA+ patients than ACPA- patients in the two most recent inclusion periods (2006-2010 HR ACPA+: 3.85 (1.25;11.9); ACPA- 2.27 (1.34;3.83); 2011-2016 HR ACPA+: 6.48 (1.89;22.2); ACPA- 3.04 (1.66;5.55)). Within ACPA+ RA, the HAQ over time had improved in 2001-2005 (-0.19 (-0.34;-0.04)), 2006-2010 (-0.35 (-0.49;-0.22)) and 2011-2016 (-0.26 (-0.40;-0.13)), compared to 1993-1996. This effect was absent ACPA- RA.

Figure 1. Disease outcomes over time stratified for inclusion period

Conclusion: Improvements in treatment strategies during the last 25 years have resulted in lower disease activity, less mortality, more DFR and better physical functioning of RA-patients. ACPA+ patients, traditionally the most severe subset, benefited most from these improvements and have become more similar to ACPA- patients.

Disclosure of Interests: Xanthe Matthijssen: None declared, Ellis Niemantsverdriet: None declared, Thomas Huizinga Consultant for: Merck, UCB, Bristol Myers Squibb, Biotest AG, Pfizer, GSK, Novartis, Roche, Sanofi-Aventis, Abbott, Crescendo Bioscience Inc., Nycomed, Boehringer, Takeda, Zydus, Epirus, Eli Lilly, Annette van der Helm - van Mil Grant/research support from: The research leading to these results has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (Starting grant, agreement No 714312) and from the Dutch Arthritis Foundation.

The funding source had no role in the design and conduct of the study.

DOI: 10.1136/annrheumdis-2019-eular.3229

OP0024

PATIENT DISCUSSIONS OF GLUCOCORTICOID-RELATED SIDE EFFECTS WITHIN AN ONLINE HEALTH COMMUNITY FORUM

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Background: Social media websites are an important, largely untapped source of data about patients' experience of living with disease and its treatment. This includes information on drugs such as the occurrence, nature and impact of side effects. However, there are few published studies reporting drug safety profiles using such data.

Health Unlocked (HU), Europe's largest social media network for health that supports patients and health care providers, hosts over 200 communities including the UK's National Rheumatoid Arthritis Society (NRAS). Using the example of glucocorticoid (GC) therapy, this study aims to explore the potential of HU posts in providing information about the occurrence and nature of drug side effects.

Objectives:

1. Evaluate the accuracy of a computerised system for automated suspected adverse drug reaction (sADR) detection from posts from HU compared to human annotation.
2. Explore themes of discussion about GC-related ADRs within posts from HU.

Methods: HU provided a dataset of de-identified posts from the NRAS community from December 2015 to December 2016. Posts mentioning GCs were processed by automated Natural Language Processing software, which identified the drug and health issues, mapped them to the Medical Dictionary for Regulatory Activities (MedDRA®) dictionary and categorised as a sADR or not. A sample (n=50) of sADR posts were randomly selected and manually reviewed to determine whether they were true ADRs. Additionally, a sample (n=50) of the posts that included GC and were labelled as having a health issue but not thought to have an ADR, were also assessed for true ADRs.

Posts identified as containing GC ADRs from manual analysis were reviewed to identify themes.

Results: Of the 35,904 posts from 1,998 users, 2,409 posts mentioned GCs, of which 324 posts were identified as containing information representing a sADR. After manual review of the 50 sampled sADRs, only 36% (18/50) of these posts contained a true ADR. Of the 50 sampled posts that included a mention of GCs and a health issue but were not a sADR, 28% (14/50) were found to contain true ADRs. Thematic analysis of the 32 posts containing true GC ADRs found the most frequently mentioned ADRs were fractures (n=6), infection (n=5), headaches (n=3) and weight gain (n=3). Posts included rich descriptions about the nature of side effects ("my weight tripled in size with steroids"). This included experiences of how side effects changed with time ("huge mood swings settles after a while"). Users also described how ADRs impacted on their quality of life ("with steroid induced diabetes, I lost a stone in three days, it was grim"), and their value judgements about the importance of side effects ("my taste buds are making everything taste strange, either salty, metallic, or plain awful ... but I cope with it, as hardly any pain with steroids.") Posts also described frustrations about how well informed they were about side effects ("I had two eye ops for cataracts, no one told me steroids caused cataracts"). Within posts where ADRs were discussed, patients also commented on the benefits of treatment ("my pain subsided with steroids") and the difficult balance between benefits and harms ("wonderful to not feel like I had RA in the first month of having [pred], but now I have more acne than when I was a teenager").

Conclusion: Current machine learning models for ADR detection in social media still need further improvements to identify sADRs in health forum data. Nonetheless, manual review shows there are important themes relating to patients' experiences and perceptions of using GC that may not be obtained using traditional methods such as analysis of health records or spontaneous pharmacovigilance. With improved automated ADR detection, this rich data source may be useful to identify ADRs most important to patients and the impact on quality of life.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.2446

OP0025

FENEBRUTINIB COMPARED TO PLACEBO AND ADALIMUMAB IN PATIENTS WITH INADEQUATE RESPONSE TO EITHER METHOTREXATE THERAPY OR PRIOR TNF THERAPY: PHASE 2 STUDY

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Background: Fenebrutinib (GDC-0853, FEN) is a small molecule inhibitor of Bruton's Tyrosine Kinase (BTK) that is orally administered, highly selective, non-covalent, and reversible.

Table 1. Endpoints

	Cohort 1, MTX-IR				Cohort 2, TNF-IR		
	FEN-50 50 mg QD (n=40)	FEN-150 150 mg QD (n=109)	FEN-200 200 mg BID (n=110)	PBO (n=110)	ADA 40 mg Q2W (n=111)	FEN-200 200 mg BID (n=48)	PBO (n=50)
ACR50 responders at W12	7 (18%)	30 (28%)	38 (35%)	16 (15%)	40 (36%)	12 (25%)	6 (12%)
95% confidence interval (CI)	(6%, 29%)	(19%, 36%)	(26%, 43%)	(8%, 21%)	(27%, 45%)	(13%, 37%)	(3%, 21%)
Weighted difference vs. PBO	8.0%	12.9%	20.0%	-	21.6%	13.9%	-
95% CI of weighted difference*	(-6%, 22%)	(2%, 23%)	(9%, 31%)	-	(11%, 33%)	(-1%, 29%)	-
P-value**	0.2503	0.0164	0.0003	-	0.0001	0.0650	-
Weighted difference vs. ADA	-17.8%	-8.6%	-1.5%	-21.6%	-	-	-
95% CI of weighted difference*	(-34%, -2%)	(-21%, 4%)	(-14%, 11%)	(-33%, -11%)	-	-	-
P-value**	0.0268	0.1694	0.8132	0.0001	-	-	-
DAS28-CRP at W12							
Change from baseline							
Pts (n) completing W12	36	95	95	99	104	47	44
Adjusted mean*	-1.74	-1.96	-1.96	-1.33	-2.11	-1.96	-1.20
95% CI of weighted difference*	(-0.93, -0.11)	(-1.00, -0.25)	(-1.00, -0.24)	-	(-1.15, -0.41)	(-1.14, -0.37)	-
P-value vs. PBO**	0.1674	0.0002	0.0002	-	<0.0001	0.0002	-
Safety							
AEs	15 (37.5)	45 (41.3)	56 (50.9)	50 (45.5)	50 (45.0)	11 (22.4) [^]	22 (44.9) [^]
Pts with ≥1 event, n (%)							
Serious AEs:	-	1 (0.9)	3 (2.7)	1 (0.9)	2 (1.8)	-	-
Pts with ≥1 event, n (%)							
Deaths, n (%)	-	-	1 (0.9)***	-	-	-	-

*Adjusted for geographic region (Eastern Europe, Latin America, and USA) for Cohort 1, and geographic region and prior exposure to a non-TNF biologic for Cohort 2

**Not adjusted for multiplicity

***Death was due to myocardial infarction

[^]One PBO pt was treated with FEN-200 in error