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.

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OP0024 PATIENT DISCUSSIONS OF GLUCOCORTICOID-RELATED SIDE EFFECTS WITHIN AN ONLINE HEALTH COMMUNITY FORUM

Arani Vivekanantham, Maksim Belousov, Lamiece Hassan, Goran Nenadic, Will Dixon. *University of Manchester, Manchester, United Kingdom*

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 then 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.

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OP0025 FENEBRUTINIB COMPARED TO PLACEBO AND ADALIMUMAB IN PATIENTS WITH INADEQUATE RESPONSE TO EITHER METHOTREXATE THERAPY OR PRIOR TNF THERAPY: PHASE 2 STUDY

Stanley Cohen[1], Katie Tuckwell[2], Tamiko R. Katsumoto[3], Rui Zhao[2], Chin Lee[2], Alberto Berman[4], Nemanja Damjanov[5], Dmytro Fedkov[6], Sławomir Jeka[7], Mark C. Genovese[3]. *[1]Metroplex Clinical Research Center, Dallas, United States of America*; *[2]Genentech, Inc., South San Francisco, United States of America*; *[3]Stanford University, Stanford, United States of America*; *[4]Centro Médico Privado De Reumatología, Tucumán, Argentina*; *[5]University of Belgrade, Institute of Rheumatology, Belgrade, Serbia*; *[6]Bohomolets National Medical University, Kyiv, Ukraine*; *[7]University Hospital no 2 in Bydgoszcz, CM UMK, Bydgoszcz, Poland*

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

Objectives: This study evaluated the efficacy and safety of FEN compared with placebo (PBO) and adalimumab (ADA), in combination with background methotrexate (MTX), in patients (pts) with rheumatoid arthritis (RA).
Methods: This multicenter, randomized, double-blind Phase 2 study included pts with moderate-to-severe active RA with an inadequate response to MTX (MTX-IR, Cohort 1) or TNF inhibitors (TNF-IR, Cohort 2). Cohort 1 pts were randomized to FEN at 50 mg QD (FEN-50), 150 mg QD (FEN-150), 200 mg BID (FEN-200), 40 mg ADA injections SC Q2W, or PBO. Cohort 2 pts were randomized to FEN-200 or PBO. Key efficacy endpoints evaluated the proportion of pts with an ACR50 response at Week 12 (W12), comparing FEN doses to PBO (both cohorts) and to ADA (Cohort 1).
Results: Cohort 1 (FEN-50, n=40; FEN-150, n=109; FEN-200, n=110; PBO, n=110; ADA, n=111) and Cohort 2 (FEN-200, n=48; PBO, n=50) demographics and disease characteristics were balanced, and ~90% of pts per arm completed the study. In Cohort 1, ACR50 response rates increased with increasing FEN dose (18%, 28%, and 35% for FEN-50, FEN-150, and FEN-200, respectively). FEN-150 (28%, p=0.0164) and FEN-200 (35%, p=0.0003) were superior to PBO (15%), and numerically similar to ADA (36%). In Cohort 2, the response for FEN-200 was higher than PBO (25% vs. 12%) (Table 1). Adverse events (AEs) were generally balanced across Cohort 1; there were 9 serious AEs in 7 pts and one death in the FEN-200 group. In Cohort 2, more pts in the PBO arm reported AEs, and no serious AEs were reported.
Conclusion: FEN demonstrated higher efficacy rates than PBO for ACR50 at W12 in both MTX-IR and TNF-IR populations, and was similar to ADA in MTX-IR pts. The overall safety profile of FEN was acceptable.
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OP0026

A PHASE 3 STUDY OF THE EFFICACY AND SAFETY OF PEFICITINIB (ASP015K) IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO HAD AN INADEQUATE RESPONSE TO METHOTREXATE

Tsutomu Takeuchi[1], Yoshiya Tanaka[2], Sakae Tanaka[3], Atsushi Kawakami[4], Manabu Iwasaki[5], Mitsuhiro Rokuda[6], Hiroyuki Izutsu[6], Satoshi Ushijima[6], Yuichiro Kaneko[6], Teruaki Shiomi[6], Emi Yamada[6]. [1]*Keio University, Tokyo, Japan*; [2]*University of Occupational and Environmental Health, Kitakyushu, Japan*; [3]*University of Tokyo, Tokyo, Japan*; [4]*Nagasaki University, Nagasaki, Japan*; [5]*Yokohama City University, Yokohama, Japan*; [6]*Astellas Pharma, Inc., Tokyo, Japan*

Background: Peficitinib (ASP015K), a novel oral JAK inhibitor, demonstrated efficacy as once-daily monotherapy in patients with moderate-to-severe rheumatoid arthritis (RA) in a phase 2b study (NCT01649999)[1].
Objectives: To evaluate the efficacy and safety of peficitinib–methotrexate (MTX) combination in patients with RA who had an inadequate response to MTX.
Methods: This multicentre, randomised, double-blind, parallel-group, placebo (PBO)-controlled, phase 3 study (NCT02305849) was conducted in Japan. Patients had RA diagnosed within the past 10 years (1987 ACR or 2010 ACR/EULAR criteria), active disease (≥6 tender and painful joints and ≥6 swollen joints, using 68 and 66-joint assessment respectively; CRP ≥1.0 mg/dL; bone erosion; and ACPA or RF positivity) and inadequate response to MTX (administered for ≥90 days; ≥8 mg/week for ≥28 days prior to baseline). Patients were randomised 1:1:1 to 52-week MTX plus PBO, peficitinib 100 mg/day or peficitinib 150 mg/day. At week 12, inadequate responders in the PBO group (<20% improvement from baseline in tender and swollen joint counts) were switched (under blinded conditions) to peficitinib 100/150 mg until end of treatment. Remaining patients in the PBO group were switched (under blinded conditions) to peficitinib at week 28. Concomitant stable MTX dose (≤16 mg/week) was mandatory. Primary efficacy variables were ACR20 response rate at week 12/early termination (ET) and change from baseline in modified Total Sharp score (mTSS) at week 28/ET.

Table 1 Primary and selected secondary efficacy endpoints at week 12/ET

	Week 12/ET			Week 28/ET		
Result	**PBO**	**Peficitinib 100 mg/day**	**Peficitinib 150 mg/day**	**PBO**	**Peficitinib 100 mg/day**	**Peficitinib 150 mg/day**
ACR20, n/N (%)	37/170 (21.8)	102/174 (58.6)***	112/174 (64.4)***	50/170 (29.4)	129/174 (74.1)***	137/174 (78.7)***
ACR50, n/N (%)	13/170 (7.6)	52/174 (29.9)***	80/174 (46.0)***	19/170 (11.2)	88/174 (50.6)***	103/174 (59.2)***
ACR70, n/N (%)	4/170 (2.4)	21/174 (12.1)***	41/174 (23.6)***	10/170 (5.9)	47/174 (27.0)***	70/174 (40.2)***
Mean (SD) CRP change from baseline, mg/dL	-0.001 (2.038)	-1.499 (1.855)***	-1.421 (2.182)***	-0.041 (2.399)	-1.649 (2.165)***	-1.625 (2.236)***
Mean (SD) ESR change from baseline, mm/h	-2.42 (19.71)	-18.90 (19.85)***	-22.17 (22.79)***	-3.26 (22.68)	-24.51 (23.67)***	-26.21 (24.58)***
DAS28-CRP <2.6, n/N (%)	13/169 (7.7)	54/172 (31.4)***	60/171 (35.1)***	20/169 (11.8)	86/172 (50.0)***	86/171 (50.3)***
Mean (SD) DAS28-CRP change from baseline	-0.51 (1.10)	-1.70 (1.20)***	-2.09 (1.33)***	-0.64 (1.33)	-2.27 (1.31)***	-2.56 (1.38)***
Mean (SD) change from baseline in patient's assessment of pain, 100 mm VAS	-6.64 (25.22)	-21.09 (27.04)***	-26.87 (26.65)***	-7.61 (27.81)	-26.33 (28.22)***	-32.23 (27.59)***
SDAI remission (SDAI score ≤3.3), n/N (%)	1/169 (0.6)	12/172 (7.0)**	24/171 (14.0)***	6/169 (3.6)	36/172 (20.9)***	37/171 (21.6)***
	Week 28/ET			**Week 52/ET**		
	PBO	**Peficitinib 100 mg/day**	**Peficitinib 150 mg/day**	**PBO**	**Peficitinib 100 mg/day**	**Peficitinib 150 mg/day**
Mean (SD) mTSS change from baseline[a]	3.37 (5.46)	1.62 (4.23)***	1.03 (2.86)***	6.27 (10.18)	2.12 (5.83)***	1.54 (4.11)***
Patients achieving mean mTSS change from baseline ≤0.5[a], n/N (%)	70/153 (45.8)	110/164 (67.1)***	119/164 (72.6)***	65/153 (42.5)	105/164 (64.0)***	113/164 (68.9)***

Last Observation Carried Forward imputation method was used, except for mTSS. Statistical testing was performed for peficitinib 100 mg, and 150 mg, compared with PBO.
**p<0.01 vs PBO; ***p<0.001 vs PBO, according to Fisher's Exact test for ACR20, ACR50, ACR70, DAS28-CRP <2.6, SDAI remission, and mTSS change from baseline ≤0.5; analysis of covariance for CRP, ESR, DAS28-CRP, and patient's assessment of pain; and rank analysis of covariance for mTSS change from baseline. Closed testing procedure was used for multiplicity adjustment in the primary analysis.
[a]For the calculation of mTSS, patients who discontinued at or before week 28 or were switched from PBO to peficitinib at week 12 due to lack of efficacy, week 28/ET mTSS was extrapolated using linear extrapolation method based on the mTSS at baseline and early termination or week 12 (day 85) (before switching). For patients who discontinued at or before week 52 or switched to receive peficitinib instead of placebo at week 12 or week 28, mTSS at week 52/ET was extrapolated using a linear extrapolation method based on mTSS at baseline and early termination, week 12 (Day 85) or week 28 (Day 197) (before switching).
mTSS=modified Total Sharp score; SD=standard deviation; SDAI=simplified disease activity index; VAS=visual analog scale.

Table 2 Treatment-emergent adverse events

	PBO (N=170)	**Peficitinib 100 mg/day (N=174)**	**Peficitinib 150 mg/day (N=174)**	**Peficitinib 100 mg/day + 150 mg/day (N=348)**
Event, n (%), Week 0–12				
Any AE	84 (49.4)	89 (51.1)	104 (59.8)	193 (55.5)
Drug-related AE[a]	47 (27.6)	57 (32.8)	80 (46.0)	137 (39.4)
Death	0	0	0	0
SAE	4 (2.4)	5 (2.9)	3 (1.7)	8 (2.3)
Drug-related SAE[a]	2 (1.2)	3 (1.7)	3 (1.7)	6 (1.7)
Grade ≥3 AE[b]	8 (4.7)	9 (5.2)	16 (9.2)	25 (7.2)
AE leading to permanent discontinuation of study drug	7 (4.1)	5 (2.9)	5 (2.9)	10 (2.9)
Serious infection	0	3 (1.7)	1 (0.6)	4 (1.1)
Herpes zoster-related disease	0	2 (1.1)	3 (1.7)	5 (1.4)
Malignancy	0	0	0	0
Incidence rate per 100 patient-years (95% confidence interval), overall study period[c]	**PBO (N=170)**	**Peficitinib 100 mg/day (N=174)**	**Peficitinib 150 mg/day (N=174)**	**Peficitinib total (N=496)[d]**
Serious infection[e]	0.0	3.8 (1.7, 8.4)	3.7 (1.7, 8.3)	3.4 (2.0, 5.8)
Herpes zoster-related disease	3.2 (0.8, 12.8)	8.3 (4.8, 14.3)	3.8 (1.7, 8.4)	5.7 (3.8, 8.6)
Malignancy	1.6 (0.2, 11.3)	0.6 (0.1, 4.4)	0.0	0.2 (0.0, 1.7)

[a]Possibly or probably related to study drug, as assessed by the investigator, or records where relationship is missing.
[b]Based on NCI-CTCAE grade: grade 3=severe or medically significant, grade 4=life threatening, grade 5=death related to AE.
[c]Patient-years covers from initial dose up to first incidence of AE for patients who had at least one event, otherwise, the duration of the patients are summed as from initial dose through follow-up. Incidence rate was calculated as (100 x number of patients who had at least one incidence / total patient-year).
[d]Includes AEs that occurred after initial peficitinib dosing, and after switching from PBO to peficitinib 100 mg/day or 150 mg/day.
[e]Defined as an AE belonging to the system organ class of 'Infections and infestations' and regarded as serious.
AE=adverse event; SAE=serious adverse event.

Results: 519 patients were treated: PBO (n=170), peficitinib 100 mg (n=175) and peficitinib 150 mg (n=174). At week 12, 75 PBO-treated patients were switched to peficitinib 100 mg (n=37) and 150 mg (n=38) due to inadequate response. At week 12/ET, peficitinib showed superior efficacy vs PBO with respect to symptoms and inflammatory markers (**Table 1**). At weeks 28 and 52, peficitinib significantly reduced the mean mTSS change from baseline vs PBO (**Table 1**). Week 0–12 safety results were similar for PBO and peficitinib (**Table 2**). For the overall study period, incidence rate of serious infections per 100 patient-years was higher with peficitinib 100 mg/150 mg than PBO (**Table 2**).
Conclusion: In patients with RA who had an inadequate response to MTX, peficitinib 100 mg/day and 150 mg/day demonstrated significant superiority vs PBO in reducing RA symptoms and suppressing joint destruction, according to primary efficacy variables (ACR response and change in mTSS). Peficitinib 100 mg and 150 mg showed acceptable safety and tolerability, with no new safety signals compared with other JAK inhibitors.