currently conducted. Other outcomes, of which health resource use and sick leave, will be assessed at the end of the program.

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Personalised medicine in rheumatic disease

OP0104

THE PRESENCE OF BLOOD IN THE JOINT AND THE IMMEDIATE MOLECULAR RESPONSE IN SYNOVIAL FLUID ARE INDEPENDENTLY ASSOCIATED WITH WORSE CLINICAL OUTCOMES AT 2 YEARS AFTER HUMAN KNEE INJURY

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Background: Knee injury increases the risk of knee osteoarthritis at least 7 fold. We have shown an immediate inflammatory response to acute knee injury which is measurable both in mouse joint tissues and also in human synovial fluid (SF).

Objectives: We set out to test whether the measured immediate inflammatory protein response in SF or plasma/serum was associated with knee symptoms at 2 years after knee injury.

Methods: 150 individuals were recruited within 8 weeks of a significant acute knee injury to the Knee Injury Cohort at the Kennedy (KICK; REC 10/H0805/39; NCT02667756) from 2011-2014. The primary outcome was the Knee Injury and Osteoarthritis Outcome Score (KOOS)-4 at 2 years (a composite measure of 4 KOOS domains, where 100 is normal knee health). Baseline covariates were sex, age, body mass index (BMI), clinical effusion, SF blood staining, radiographic Kellgren/Lawrence (KL) Grade. 14 SF and 4 plasma/serum biomarkers were defined based on our prior translational studies. Regression models assessed association of biomarkers with 2 year KOOS4, adjusting for significant covariates.

Results: 123/150 (82%) were male, mean age (SD) 27(8) years and BMI 26(4) kg/m². Mean KOOS4 increased from 38(18) at baseline to 70(18) at 2 years. 64 (43%) had KL 0/1, 24 (16%) KL 2 and 11 (7%) KL 3, 75 (50%) medium/large effusion and 50 (39%) moderate/severe SF blood staining.

Medium/large knee effusion (-7.2(-13.5,-0.9)P=0.025) and moderate/severe SF blood staining (-10.1(-18.6,-1.6)P=0.02) were significant. Significant biomarkers adjusted for these covariates are shown in Table. MCP-1 and IL-6 were each significantly associated with 2 year KOOS4 independently in the fully adjusted model and in the multivariable model.

SF biomarker (pg/ml)	Adjusted simple linear model (by baseline KOOS4)		Fully adjusted model (by baseline KOOS4, blood staining and effusion)	
	coef (95% CI)	P	coef (95% CI)	P
MCP-1	-0.020 (-0.029, -0.011)	0.00005	-0.015 (-0.027, -0.004)	0.01
FGF-2	-0.047 (-0.087, -0.007)	0.02	-0.021 (-0.059, -0.017)	0.28
IL-6	-0.0006 (-0.0010, -0.0003)	0.001	-0.0005 (-0.0009, -0.0001)	0.02
TGFβ	-0.0028 (-0.0053, -0.0003)	0.03	-0.0018 (-0.0042, 0.0006)	0.14
IL-18	-0.078 (-0.147, -0.008)	0.03	-0.02 (-0.11, 0.08)	0.75

Conclusion: Those with higher levels of SF MCP-1 and IL-6 at the time of injury had a significantly worse outcome at 2 years. The presence of haemarthrosis, clinical effusion and impairment/pain at the time of injury were also independent predictors of outcome. In contrast, no baseline plasma/serum markers were associated with outcome. Stratifying individuals at high risk of persistent symptoms after knee injury may enable clinical trials of interventions to prevent or treat PTOA.

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The riddle of adherence

OP0105-HPR

DO MOBILE APPS IMPROVE SHARED DECISION MAKING AND DISEASE MANAGEMENT IN THE RHEUMATIC DISEASES? AN EVALUATION OF APPS IN A SWISS RHEUMATOLOGY REGISTRY

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Background: From 2015 to 2018, the Swiss Clinical Quality Management in Rheumatic Diseases registry (SCQM) offered two mobile apps, iDialog and COM-PASS, allowing patients to track disease and health status between rheumatology visits. Both apps are linked to the registry database, providing patients and physicians extra information to guide disease management decisions.

Objectives: To investigate the effect of SCQM app use on shared decision making (SDM) and disease management.

Methods: Patients were administered a cross sectional survey about satisfaction with SDM [1], disease management, and app use (February-December 2018). Patients' demographic data and longitudinal data on disease status, health status, and medication use was extracted from the SCQM database.

Analyses included patients diagnosed with rheumatoid arthritis (RA), psoriatic arthritis (PsA), or axial spondyloarthritis (axSpA) who had 1) used an SCQM app for at least 6 months and discussed app data with their physician (app + discussion group), 2) used an SCQM app for at least 6 months and did not discuss app data with their physician (app only group), or 3) did not use any SCQM app (non-app users).

We compared the 3 groups by conducting logistic regressions for the following dichotomized outcomes: maximum satisfaction with SDM and physician following the evolution of the disease, low disease activity at the most recent SCQM visit, disease activity improvement in the last year of followup, and treatment intensification (adding/increasing the dose of a disease-modifying antirheumatic drug) in the last 6 months of followup. Regressions were weighted using multinomial propensity scores to balance differences in baseline characteristics between the 3 groups.

Results: 1924 patients were included in the analyses. App users were younger than non-app users (Table 1). In adjusted analyses (Table 2), satisfaction rates were higher in the app + discussion group (p<0.05) compared to non-app users, but not for the app only group. The app only group had higher rates of treatment intensification in the last 6 months of followup (p=0.02) compared to non-app users. Although the app only and app + discussion groups had higher adjusted rates of other disease management outcomes compared to non-app users, the effects were not statistically significant.

Conclusion: App users who communicated with their rheumatologist about their app data were more satisfied with their physicians than app users who did not communicate about their app data and non-app users. Provision of apps that increase the frequency of disease monitoring may have limited impact on patient satisfaction with care and disease management processes without integration of app use into existing care processes.

REFERENCES:

[1] Elwyn G, et al. Developing CollaboRATE: A fast and frugal patient-reported measure of shared decision making in clinical encounters. Patient Education and Counseling 2013;93:102-107.
[2] Coates LC, et al. Defining minimal disease activity in psoriatic arthritis: a proposed objective target for treatment. Ann Rheum Dis 2010;69:48-53.

Table 1. Baseline characteristics

	Mean (standard deviation) or %			
	App use (n=128)	App use + discussion (n=158)	No app use (n=1638)	P-value ^a
Age in years	42.44 (12.11)	43.62 (13.15)	47.77 (13.21)	<0.001
% Male	44.5%	45.9%	42.0%	0.572
Diagnosis				0.030
% RA	35.9%	38.2%	43.8%	
% PsA	21.1%	16.6%	21.6%	
% axSpA	43.0%	45.2%	43.8%	
Disease duration in years	16.10 (4.28)	16.49 (4.19)	16.55 (4.69)	0.596
Low disease activity at baseline	35.8%	40.3%	34.3%	0.356

#Test of difference between groups

*Low disease activity was defined as DAS28 < 3.2 in RA and BASDAI ≤ 4 in axSpA. In PsA, it was defined as fulfilling at least 5 of 7 criteria for minimal disease activity [2].

Table 2. Association of app use with patient satisfaction and disease management

Outcome	Odds Ratio (95% CI) (reference group: no app use)	
	App use only	App use + discussion
Satisfaction with shared decision making ^a	0.79 [0.53, 1.17]	1.74 [1.14, 2.66]
Satisfaction with following evolution of disease ^a	0.73 [0.48, 1.09]	2.07 [1.36, 3.14]
Low disease activity at last visit ^a	1.08 [0.85, 1.32]	1.39 [0.82, 2.30]
Improved disease activity ^a	1.30 [0.88, 1.76]	1.54 [0.98, 2.40]
Treatment intensification ^a	1.82 [1.16, 3.01]	1.08 [0.60, 1.95]

^aTotal=1924 (app use only=128, app use + discussion=158, no app use=1638) & Total=1141 (app use only=106, app use + discussion=114, no app use=921)

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From the cradle to the grave – what does paediatric disease teach us about adult disease?___

OP0106

A NOVEL KNOCK-IN MOUSE MODEL OF CAPS THAT DEVELOPS AMYLOIDOSIS: THERAPEUTIC EFFICACY OF PROTON PUMP INHIBITORS

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Background: Cryopyrin associated periodic syndromes (CAPS) are a group of autoinflammatory diseases linked to gain-of-function mutations in the NLRP3

gene that cause uncontrolled IL-1β secretion. CINCA syndrome is the most severe CAPS disease characterized by central nervous system disabilities with a long-term risk of secondary amyloidosis.

Proton pump inhibitors (PPIs), commonly used as inhibitors of gastric acid production, also display anti-inflammatory properties, making them promising drugs in sepsis and in inflammatory disorders.

Objectives: To develop a novel NLRP3 knock-in (KI) mouse model of CAPS to evaluate amyloid deposition and to test alternative therapeutic approaches.

Methods: We generated KI mice by engineering N475K mutation associated with CAPS phenotype into mouse *Nlrp3* gene. KI and Wild Type (WT) mice received PPIs or PBS intraperitoneally and were analyzed for survival, inflammation, cytokine secretion, and amyloidosis development. Cytokines secretion from bone marrow derived dendritic cells (BMDCs) and peritoneal macrophages (PMs) was evaluated by ELISA. Hystological analysis of all organs was evaluated by hematoxylin and eosin staining. Amyloid deposition was quantified through Congo Red staining.

Results: Mutant NLRP3 KI mice displayed features that recapitulates the immunological and clinical phenotype of CAPS. These mice had systemic inflammation, with high levels of serum pro-inflammatory cytokines compared to WT controls. Hystological analysis revealed the presence of acute and chronic inflammatory cell infiltrates and amyloid deposits in spleen, liver and kidneys. As in CAPS monocytes, BMDCs and PM from KI mice showed a strong increase in IL-1β, IL-18, and IL-1α secretion and decreased levels in interleukin-1 receptor antagonist (IL-1Ra), the naturally occurring IL-1b inhibitor.

PPIs treatment of KI mice showed a clear clinical impact with improvement of inflammatory conditions and regression of amyloid deposits. Remarkably, BMDCs and PMs from PPI-treated mice presented reduced secretion of pro-inflammatory cytokines and re-established the levels of IL-1RA.

Conclusion: NLRP3 KI mice display a CAPS phenotype with many characteristics of autoinflammation, including amyloidosis. The therapeutic effectiveness associated with lack of toxicity indicates that PPIs could represent relevant adjuvants to the anti-IL-1 drugs in IL-1 driven diseases.

REFERENCES:

[1] Gattorno M, Martini A. Beyond the NLRP3 inflammasome: autoinflammatory diseases reach adolescence. Arthritis Rheum. 2013;
[2] Brydges SD, Mueller JL, McGeough MD, Pena CA, Misaghi A, Gandhi C Putnam CD, et al. Inflammasome-mediated disease animal models reveal roles for innate but not adaptive immunity. Immunity. 2009;
[3] Balza E, Piccioli P, Carta S, Lavieri R, Gattorno M, Semino Cet al. Proton pump inhibitors protect mice from acute systemic inflammation and induce long-term cross-tolerance. Cell Death Dis. 2016.

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I perform consultancy activities on behalf of the Gaslini Institute for the companies listed below:

AbbVie, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, EMD Serono, Janssen, Novartis, Pfizer, R-Pharm.

The money received for these activities are directly transferred to the Gaslini Institute's bank account. Before March 2016, I was the head of the Pediatric Rheumatology Department at the G. Gaslini Hospital, where the PRINTO Coordinating Centre is located. For the coordination activity of the PRINTO network, the Gaslini Hospital received contributions from the industries listed in this section. This money has been reinvested for the research activities of the hospital in fully independent manners besides any commitment with third parties., Isabella Ceccherini: None declared, Marco Gattorno Grant/research support from: MG has received unrestricted grants from Sobi and Novartis, Anna Rubartelli: None declared, Sabrina Chiesa: None declared

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