between response to CS+GH and baseline protein levels ($p=0.007$) thus increasing the power of our prediction model (ROC up to 0.843). In the Celecoxib group, non parametric analysis showed increased levels only of TSP1 at baseline in responders compared to non-responders (R: 363.03 ± 104.83 ng/mL vs NR: 331.95 ± 92.59 ng/mL; $p=0.041$), while no statistically significant differences were found for this protein in the CS+GH group. When we include in the regression model 4 predictive variables (2 clinical and 2 analytical) and TSP1 as covariate, we found a specific interaction between response to Celecoxib and baseline protein levels ($p=0.045$) thus increasing the predictive power of this model (ROC up to 0.749).

Conclusions: Combining clinical and analytical parameters, we clinically validated (qualified) 2 panels of biomarkers that could efficiently predict OA patients' response to CS+GH with an accuracy of 84.3% or to Celecoxib with an accuracy of 74.9%.

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SAT0585 DECREASED SYNOVIAL LEVELS OF DICKKOPF-1 ARE ASSOCIATED WITH RADIOLOGICAL PROGRESSION IN KNEE OSTEOARTHRITIS PATIENTS

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Background: Dickkopf-1 (Dkk-1) is a direct inhibitory ligand of Wnt β -catenin signalling pathway that act through binding to low-density lipoprotein (LDL) related proteins (LRP5/6) receptors. Dkk-1 is considered an important mediator of cartilage homeostasis and skeletal remodelling.¹

Objectives: This study aimed to measure serum and synovial fluid (SF) levels of Dkk-1 in patients with early primary knee osteoarthritis (KOA) and to examine the relationship between these levels and the clinical and functional parameters as well as radiological progression of KOA

Methods: We measured Dkk-1 in the serum ($n=48$) and SF samples ($n=22$) from 48 early KOA patients and in the serum from healthy control ($n=30$). Body mass index (BMI), numerical rating scale of pain (NRS) and The Western Ontario Mc Master scale (WOMAC) were recorded. Plain radiographs using Osteoarthritis Research Society International (OARS) atlas to assess joint space narrowing (JSN)² and musculoskeletal ultrasound examination (MSUS) were performed at baseline and after 24 months to assess radiological progression. Radiological progression was considered if there is more than 2 points increase in JSN score or transition to higher grade in MSUS examination³ at the 24 months follow up period compared to baseline grade.

Results: SF Dkk-1 levels were significantly decreased (mean $\pm$ SD 115.05 $\pm$ 34.2 pg/ml) compared to their paired serum levels (mean $\pm$ SD 969.82 $\pm$ 365.72 pg/ml), $p<0.001$ in KOA patients. There was no significant difference in serum Dkk-1 levels between KOA patients and healthy controls (mean $\pm$ SD 988.77 $\pm$ 385.19 pg/ml and 1084.73 $\pm$ 408.38 pg/ml respectively), the SF concentrations of Dkk-1 significantly correlated with the baseline thickness of the cartilage on the medial condyle (0.53, $p<0.05$) but not on the lateral condyle of the femur ($r=0.11$, $p>0.05$). There was no significant correlation between serum Dkk-1 and baseline cartilage thickness on medial and lateral condyles ($r=-0.13$ and -0.09 respectively, $p<0.05$). Patients in the least quartile of SF Dkk-1 had an increased risk of radiological progression with plain radiography and MSUS (age, sex and BMI adjusted RR 2.1 and 3.4, 95% CI respectively).

Conclusions: Osteoarthritis patients have significantly lower synovial levels than serum levels of Dickkopf-1 that were obviously associated with radiological progression on plain radiography and MSUS suggesting that it could be a useful marker to reflect OA severity and implies a possible role in the pathogenesis of OA.

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SAT0586

RESULTS FROM A 52 WEEK RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PHASE 2 STUDY OF A NOVEL, WNT PATHWAY INHIBITOR (SM04690) FOR KNEE OSTEOARTHRITIS TREATMENT

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Background: Knee osteoarthritis (OA) is characterised by pain, disability and joint deformity due to articular cartilage degradation and bone remodelling. Wnt signalling is involved in these cellular processes. SM04690, a small molecule Wnt pathway inhibitor, is in development as a potential disease modifying OA drug (DMOAD) for knee OA.

Objectives: A phase 2, multicenter, 52 week, placebo-controlled (PBO) trial was conducted to identify a target population, determine optimal dose and assess safety.

Methods: Knee OA subjects, Kellgren-Lawrence (KL) grades 2–3, received a single 2 mL injection of SM04690 0.03 mg, 0.07 mg, 0.23 mg or PBO in target (most painful) knee. WOMAC Pain and Function were assessed (Weeks 0, 4, 13, 26, 39, 52) and fixed flexion radiographs (QuAP positioned; Weeks 0, 26, 52) assessed medial joint space width (mJSW). Analysis of covariance adjusted for baseline was conducted using multiple imputation for missing data. Exploratory subgroups included: 1) unilateral symptomatic subjects (pre-specified; determined by history and examination) and 2) unilateral symptomatic subjects without comorbid pain (post-hoc; Widespread Pain Index ≤ 4 , Symptom Severity ≤ 2 [WP-]).

Results: 455 subjects (mean age 60.3 [± 8.7] years, BMI 29.9 [± 4.6] kg/m², female 58.9%, KL grade 3 [64.4%], unilateral symptomatic OA [36.0%]) were enrolled, 91% with radiographic bilateral OA. Seventeen serious adverse events, all unrelated to SM04690, were reported.

The primary endpoint of Week 13 change from baseline in WOMAC Pain was not met. In ITT, at all timepoints, minimal clinically important differences ($>10\%$ full range) in WOMAC Pain and Function compared to baseline were seen in all groups. In 0.07 mg unilateral symptomatic subjects, at 52 weeks, WOMAC Pain (4.4, $p=0.049$), and Function (17.5, $p=0.035$) were significantly improved compared to PBO. In 0.07 mg unilateral symptomatic WP- subjects at Weeks 26, 39, and 52, WOMAC Pain (4.6, $p=0.039$; 5.9, $p=0.042$; and 5.6, $p=0.025$, respectively) and Function (16.3, $p=0.027$; 19.7, $p=0.035$; and 22.8, $p=0.017$, respectively) were significantly improved compared to PBO (**Abstract SAT0586 – figure 1**).

At 26 and 52 weeks, 0.07 mg unilateral symptomatic (0.5 mm, $p=0.006$ and 0.4 mm, $p=0.021$, respectively) and 0.07 mg unilateral symptomatic WP- (0.5 mm, $p=0.016$ and 0.4 mm, $p=0.032$, respectively) subgroups demonstrated significant increases from baseline in mJSW compared to PBO (figure 1).

Abstract SAT0586 – Figure 1. Ladder plots depicting mean improvement (and 95% confidence intervals) of SM04690 over placebo adjusted for baseline.

Conclusions: A target subgroup of unilateral symptomatic knee OA subjects and potential optimal dose (0.07 mg) of SM04690 were identified. Clinical and radiographic outcomes suggested that SM04690 has potential as a DMOAD, especially in subjects with unilateral symptomatic WP- knee OA. Further studies are ongoing.

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Other orphan diseases

SAT0587 MAJOR SALIVARY GLANDS ULTRASONOGRAPHY IN DIFFERENTIAL DIAGNOSIS OF IGG4-RELATED DISEASE AND PRIMARY SJOGREN'S SYNDROME

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Background: IgG4-related disease (IgG4-RD) is a group of fibro-inflammatory immunomediated conditions with IgG4 overexpression in the serum and affected tissues in the majority of patients. Major salivary and lacrimal glands are the most frequently affected sites in IgG-RD. Moderate sicca symptoms can be present as well thus requiring differential diagnosis with primary Sjogren's syndrome (pSS). Major salivary glands ultrasonography (sUS) has been reported as an effective diagnostic tool in pSS.

Objectives: To evaluate the difference in sUS score in pSS and IgG4-RD patients

Methods: 15 patients with IgG4-related sialoadenitis consecutively admitted to our clinic and 28 with pSS underwent sUS. Parenchymal echogenicity, homogeneity, hypoechogenic and hyperechogenic areas and clearness of salivary gland border were scored according to the Hoyer scoring system (cut-off – 15 points). Statistical analyses were performed using MEDCALC program. Median values of the sUS score and Mann-Whitney U-test were used to evaluate differences in total ultrasound score between patients in two groups.

Results: All patients with IgG4-related sialadenitis and pSS had some sUS abnormalities. The most frequent feature in IgG4-RD were: the presence of hypoechotic lesions in major salivary glands (53% of patients) or diffuse salivary gland parenchyma hypoechogenicity (27% of patients) and multiple intraglandular lymph nodes (66.7% of patients). Median value of sUS score in IgG4-RD group was 12 points and in pSS group – 22 points. The difference was significant (Mann-Whitney U-test 60.5, $p < 0.05$).

Conclusions: Although different US-changes are frequently seen in IgG4-RD patients, sUS Hoyer score seems to be a rather reliable tool to differentiate IgG4-related sialoadenitis and pSS.

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SAT0588 RHEUMATOLOGIC IMMUNE-RELATED ADVERSE EFFECTS OF CHECKPOINT INHIBITOR THERAPY: A SINGLE CENTRE COHORT OF 29 PATIENTS

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Background: Immune checkpoint inhibitors for advanced malignancy are associated with a wide range of autoimmune phenomena known as immune-related

adverse effects (irAEs).¹ Knowledge of irAEs resembling rheumatologic diseases is limited to case reports and small case series, and there are currently no specific guidelines on how to diagnose or manage these patients.

Objectives: To describe the prevalence, clinical presentation, and management of patients with rheumatologic irAEs from checkpoint inhibitor therapy.

Methods: We retrospectively studied all patients who received a checkpoint inhibitor for any malignancy at Mayo Clinic Rochester, Minnesota between January 1 st, 2011 and November 1 st, 2017. From these patients we identified those with possible rheumatologic irAEs using diagnostic codes, search terms, and the presence of specific laboratory testing.

Results: Of the 1216 patients who received any checkpoint inhibitor, we identified 29 who were clinically diagnosed with a rheumatologic irAE. The diagnosis was confirmed by a rheumatologist in all but 3 cases. Mean follow up time from irAE diagnosis was 1.5 years (± 1.1). Seven patients had a pre-existing autoimmune disease with one of these being a rheumatologic disease (Giant-cell arteritis). irAEs included inflammatory arthritis,¹⁵ sicca syndrome,³ systemic sclerosis,³ myositis,³ vasculitis,³ spondylitis,¹ and polymyalgia rheumatica.¹ Only one irAE represented a disease flare. Mean time from initiation of checkpoint inhibitor therapy to onset of irAE symptoms was 15.0 weeks (± 10.8). 24 patients (83%) were treated with corticosteroids and 8 patients (28%) received additional therapy with disease modifying drugs. Mean treatment duration for these 24 patients was 19.5 weeks (± 21.7), and 8 patients (33%) had complete symptom resolution within the study period. Rheumatologic irAEs resulted in discontinuation of checkpoint inhibitor therapy in 7 patients (24%).

Abstract SAT0588 – Table 1. Clinical Features

Rheumatologic irAEs	29 total
Inflammatory arthritis	15
Sicca syndrome	3
Systemic sclerosis	3
Myositis	3
Vasculitis	3
Spondylitis	1
Polymyalgia rheumatica	1
Treatment	
Prednisone only	16
Prednisone plus biologics	8
No treatment	5
Starting prednisone dose, MG, mean (St. Dev)	47 (26)
Weeks on prednisone, mean (St. Dev)	15 (11)
Weeks to symptom onset, mean (St. Dev)	15 (11)
Sedimentation rate, mean (St. Dev)	39 (30)
C-reactive protein, mean (St. Dev)	49 (57)
Diagnosed by rheumatologist	26 (90%)
Positive autoimmune serologies	4 (14%)
Flare of existing autoimmune disease	2 (7%)
Comorbid non-rheumatologic irAEs	19 (66%)

Conclusions: Our study represents one of the largest cohorts of rheumatologic irAEs to date. Most patients required long courses of treatment with only a minority achieving complete symptom resolution. Prospective, multicenter studies are necessary to determine the optimal management of these emerging disorders.

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