Table 1. Spearman Rho Correlation between timed function tests and MMT8, FI-2, patient and physician VAS

	Δ 30s rise from chair test	Δ 30s arm lift test	Δ 2min walk test
Δ MMT8	0.382	0.337	0.724**
Δ FI-2			
Hip flexion right	0.388	0.413	0.314
Hip flexion left	0.503*	0.416	0.422
Neck flexion	0.600**	0.590**	0.610**
Shoulder flexion right	0.183	0.300	0.239
Shoulder flexion left	0.393	0.222	0.207
Shoulder abduction right	0.236	0.222	0.348
Shoulder abduction left	0.182	0.236	0.273
Step test right	0.744**	0.489*	0.326
Step test left	0.840	0.500*	0.378
Heel rise	0.442	0.294	0.388
Toe rise	0.446	0.291	0.419
Δ Physician VAS	-0.508*	-0.506**	-0.215
Δ Patient VAS	-0.600**	-0.597**	-0.249

Δ → change from baseline to 3 months *→ Correlation is significant at the 0.05 level **→ Correlation is significant at the 0.01 level

Conclusion: Timed function tests correlated well with MMT 8 and parameters with in FI-2. Thus these tests are good alternatives in assessing disease activity and response assessment in inflammatory myositis.

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SAT0315

INHIBITION OF MICROSOMAL PROSTAGLANDIN E SYNTHASE-1 (mPGES-1) BY GS-248 REDUCES PROSTAGLANDIN E2 BIOSYNTHESIS WHILE INCREASING PROSTACYCLIN IN HUMAN SUBJECTS

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Background: Microsomal prostaglandin E synthase-1 (mPGES-1) catalyzes the formation prostaglandin (PG) E₂ from cyclooxygenase derived PGH₂^(1,2). Inhibition of mPGES-1 leads to reduction of pro-inflammatory PGE₂, while in vessels there is a concomitant increase of vasoprotective prostacyclin (PGI₂) via shunting of PGH₂^(3,4). Apart from relieving symptoms in experimental animal models of inflammation, inhibitors of mPGES-1 cause relaxation of human medium sized arteries⁽⁴⁾ and resistance arteries⁽⁵⁾. The prostaglandin profile following mPGES-1 inhibition, explains the anti-inflammatory effects and also opens for the possibility of treating inflammatory diseases with concomitant vasculopathies. GS-248 is a potent and selective inhibitor of mPGES-1 exhibiting sub-nanomolar IC₅₀ in human whole blood *ex vivo*.

Objectives: To evaluate safety, tolerability, pharmacokinetics and pharmacodynamics of GS-248.

Methods: Healthy males and females (age 18–73 years) were included in the study. Six cohorts were administered single oral doses of 1-300mg GS-248 (n=36) or placebo (n=12), three cohorts were administered once daily doses of 20-180mg GS-248 (n=18) or placebo (n=12) over ten days. In addition, 8 subjects were treated in a separate cohort with 200mg celecoxib bid for ten days. Blood samples were drawn for measurement of GS-248 exposure and production of PGE₂ after LPS incubation *ex vivo*. The content of PGE₂ and PGI₂ metabolites was measured in urine. All analyses were performed by LC-MS/MS.

Results: GS-248 was safe and well tolerated at all tested dose levels. Maximum plasma concentration was achieved 1 - 2.5 hours after dosing, and half-life was

about 10 hours. Induced PGE₂ formation *ex vivo*, catalyzed by mPGES-1, was completely inhibited for 24 hours after a single low dose (40mg) of GS-248. In urine, GS-248 dose-dependently reduced the excretion of PGE₂ metabolite by more than 50% whereas the excretion of PGI₂ metabolite increased more than twice the baseline levels. In the celecoxib cohort urinary metabolites of both PGE₂ and PGI₂ were reduced with approx 50%.

Conclusion: GS-248 at investigated oral doses was safe and well tolerated. There was a sustained inhibition of LPS induced PGE₂ formation in whole blood. In urine, there was a metabolite shift showing reduced PGE₂ and increased PGI₂, while celecoxib reduced both PGE₂ and PGI₂ metabolites. This suggests that selective inhibition of mPGES-1 results in systemic shunting of PGH₂ to PGI₂ formation, leading to anti-inflammatory and vasodilatory effects, while preventing platelet activation. The results warrant further evaluation of GS-248 in inflammatory conditions with vasculopathies such as Digital Ulcers and Raynaud's Phenomenon in Systemic Sclerosis.

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SAT0316

ANTI-PM/SCL ANTIBODIES IN SYSTEMIC SCLEROSIS: CLINICAL ASSOCIATIONS IN THE RESCLE COHORT

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Background: Anti-PM/Scl antibodies are associated to systemic sclerosis (SSc) but are not specific to SSc. The true prevalence of anti-PM/Scl antibodies in SSc is unknown, ranging from 2.5% to 12.5%. An association between anti-PM/Scl antibodies with muscular involvement, pulmonary fibrosis, calcinosis, and a relatively benign prognosis have been described.

Objectives: To compare the clinical manifestations and prognosis of SSc patients according the presence of anti-PM/Scl antibodies in the cohort of RESCLE (Spanish Scleroderma Registry).

Methods: From the Spanish Scleroderma Study Group database, we selected patients in whom anti-PM/Scl antibodies had been tested. We compared demographic features, clinical manifestations, laboratory characteristics, and survival data between patients according the anti-PM/Scl antibodies status.

Results: 72 out of 947 (7%) patients tested positive for anti-PM/Scl antibodies. As presenting SSc manifestations, patients with anti-PM/Scl antibodies had higher prevalence of puffy fingers (11% versus 2%; p=0.002) and arthralgias (11%