Table 1. Clinical, laboratory and lung functions tests of patients treated with RTX-B. Data expressed as mean±SD. FVC=forced vital capacity(% predicted); TLC=total lung capacity(% predicted); DLCO=diffusion lung CO(% predicted); DAS28=disease activity score 28 (3 RTX-Bn, 3 RTX-Bs) patients with arthritis;ESR(mm/1h).

Overall	Time 0	6 Months	p value
mRSS	11.8±9.3	8.8±7.7	0.001
FVC	89.7±21.1	92.8±20.4	0.089
TLC	86.3±19.4	87.9±18.9	0.219
DLCO	62.3±21.0	60.7±18.8	0.542
DAS28	3.6±1.1	2.2±0.9	0.028
ESR	21.3±13.0	16.9±9.7	0.003
RTX-Bn			
mRSS	12.3±10.6	9.2±8.3	0.011
FVC	91.3±22.3	95.3±18.8	0.100
TLC	89.60	93.3±18.5	0.172
	±21.16		
DLCO	67.5±19.1	64.3±15.4	0.422
DAS28	4.3±0.4	2.1±1.1	0.109
ESR	21.9±14.8	17.4±11.2	0.017
RTX-Bs			
mRSS	11.0±7.8	8.2±5.9	0.046
FVC	87.6±20.4	89.4±23.1	0.546
TLC	82.1±17.4	80.1±18.0	0.750
DLCO	56.00	56.33	0.799
	±22.54	±22.49	
DAS28	3.0±1.3	2.4±0.9	0.109
ESR	20.5±11.0	16.2±7.8	0.066

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FRI0303 THE EFFECTS OF RIOCIQUAT ON RAYNAUD'S PHENOMENON AND DIGITAL ULCERS IN PATIENTS WITH DIFFUSE SYSTEMIC SCLEROSIS: RESULTS FROM THE PHASE IIB RISE-SSC STUDY

Dinesh Khanna¹, Yannick Allanore², Christopher Denton³, Masataka Kuwana⁴, Marco Matucci-Cerinic⁵, Janet Pope⁶, Janette de Oliveria Pena⁷, Kaisa Laapas⁸, Zhen Yao⁹, Melanie Hemmrich¹⁰, Oliver Distler¹¹. ¹University of Michigan, Ann Arbor, MI, United States of America; ²Cochin Hospital, Paris, France; ³University College London, London, United Kingdom; ⁴Nippon Medical School, Tokyo, Japan; ⁵University of Florence, Florence, Italy; ⁶University of Western Ontario, Ontario, Canada; ⁷Bayer US LLC, Whippany, NJ, United States of America; ⁸StatFinn Oy, Espoo, Finland; ⁹Bayer Healthcare Co. Ltd, Beijing, China; ¹⁰Bayer AG, Wuppertal, Germany; ¹¹University Hospital Zurich, Zurich, Switzerland

Background: Riociguat is a soluble guanylate cyclase stimulator approved for treatment of pulmonary arterial hypertension associated with connective tissue disease. Through its vasodilatory and anti-remodeling properties, it was predicted that riociguat might relieve Raynaud's phenomenon (RP) attacks and reduce net digital ulcer (DU) burden in patients with diffuse cutaneous systemic sclerosis (dcSSc).

Objectives: We present exploratory endpoints from the RISE-SSc study (NCT02283762) on the effects of riociguat on RP and DUs in early dcSSc patients.

Methods: RISE-SSc was a Phase IIb, multicenter, randomized, double-blind, placebo-controlled study. Inclusion criteria were: SSs fulfilling ACR/

EULAR criteria, diffuse cutaneous involvement, disease duration ≤18 months, and modified Rodnan skin score 10–22 units. Patients were assigned to placebo or riociguat individually adjusted from 0.5 mg up to 2.5 mg, 3 times daily. Exploratory efficacy endpoints included 1) change in Raynaud's attacks from baseline to Week 14, assessed by: Raynaud's condition score; patient/physician assessment of RP; attack symptoms, attack duration, and average number of attacks per day; and 2) change in net DU burden from baseline to Week 52, assessed by ulcer count, ulcer burden, and visual analog score for patient-reported severity. Blood samples for exploratory evaluation of biomarkers were taken on Day 0, Week 14 and for discontinuation before Week 14.

Results: 60 patients were treated with riociguat and 61 with placebo. None of the effects of riociguat on RP or DUs were statistically significant vs placebo. However, there was a greater relative reduction in attack duration, attack frequency, pain, numbness, tingling, and patient/physician global assessment in the riociguat group vs placebo, from baseline to Week 14. Reductions in net DU burden were -0.09 ± 0.50 for riociguat and -0.08 ± 1.47 for placebo (estimated treatment difference: -0.11 [95% CI: $-0.38, 0.17$; $p=0.44$]) at Week 52. At Week 14, 2 patients in the riociguat group and 6 in the placebo group had developed new DUs. At Week 52, 5 and 12 patients, respectively, had developed new DUs. The total numbers of new DUs were 4 and 6 with riociguat and placebo, respectively, at Week 14, and 12 and 65, respectively, at Week 52 (Figure). Riociguat was associated with reductions vs placebo in serum sPECAM-1 ($p=0.004$) and CXCL-4 ($p=0.008$), potentially indicating anti-vasculopathy properties of riociguat.

Conclusion: Riociguat did not produce statistically significant changes in DUs. Riociguat may reduce the development of new DUs in patients with early dcSSc and may favourably improve cytokine vasculopathy.

Figure. Development of new digital ulcers

Left: Number of patients with new digital ulcers

Right: Total number of new digital ulcers

New digital ulcers are defined as ulcers not existing at baseline.

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