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NINTEDANIB REDUCED DECLINE IN FORCED VITAL CAPACITY ACROSS SUBGROUPS OF PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE: DATA FROM THE SENSIC TRL

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Background: In the SENSCIS trial, nintedanib reduced the progression of interstitial lung disease associated with systemic sclerosis (SSc-ILD) compared with placebo, as demonstrated by a significantly lower rate of decline in forced vital capacity (FVC) over 52 weeks (primary endpoint).

Objectives: To assess the effect of nintedanib on the rate of decline in FVC in the SENSCIS trial across pre-specified subgroups defined by baseline characteristics.

Methods: Patients with SSc-ILD with onset of first non-Raynaud symptom ≤7 years before screening and ≥10% fibrosis of the lungs on a high-resolution computed tomography scan were randomised to receive nintedanib 150 mg bid or placebo double-blind. The annual rate of decline in FVC (ml/year) assessed over 52 weeks (primary endpoint) was analysed in the overall population using a random coefficient regression model (with random slopes and intercepts) including anti-topoisomerase I antibody (ATA) status, age, gender and baseline FVC as covariates. Analyses by pre-specified subgroups by baseline characteristics included additional terms for treatment-by-subgroup and treatment-by-subgroup-by-time interaction.

Results: A total of 576 patients were treated (288 in each group). Most (75.2%) of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline. Mean ± SD age was 54.0 ± 12.2 years and 21.4% of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline. Mean ± SD age was 54.0 ± 12.2 years and 21.4% of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline. Mean ± SD age was 54.0 ± 12.2 years and 21.4% of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline. Mean ± SD age was 54.0 ± 12.2 years and 21.4% of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline.

Conclusions: Nintedanib is effective at reducing ILD progression in a broad range of patients with SSc-ILD.

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MIR-34A IS A POTENTIAL THERAPEUTIC TARGET IN OSTEOARTHRITIS

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Background: We have previously reported that microRNA-34a (miR-34a) is expressed at significantly higher levels in the synovial fluid of late-stage radiographic knee osteoarthritis (OA) compared to early-stage radiographic knee OA. Despite increased levels of miR-34a, its exact role in OA pathogenesis is largely unknown. The aim of this study was to comprehensively elucidate the role and therapeutic potential of microRNA-34a in OA.

Methods: Human plasma, cartilage and synovium were obtained from total knee replacement (TKR) patients. Chondrocytes and synovial fibroblasts were transfected with miR-34a mimic or inhibitor for qRT-PCR or Western blot. For in-vivo studies, mice were injected once with a vehicle or injected miR-34a defined as being a control. The synovia and joints were collected 8 weeks post-injection for histology. Mice were subjected to destabilization of the medial meniscus (DMM) to induce OA and injected 2, 4, and 6 weeks post-surgery with miR-34a inhibitor and joints were collected 10 weeks post-surgery for histology. Heterozygous miR-34a knock out...