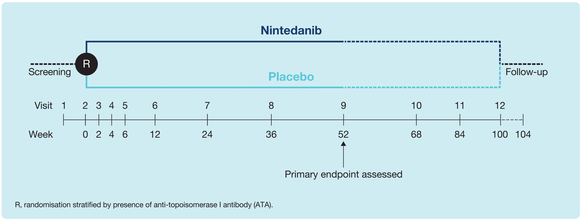
Does dose adjustment affect decline in forced vital capacity in patients treated with nintedanib? Data from the SENSCIS® trial

Maureen D. Mayes,[1] Oliver Distler,[2] Masataka Kuwana,[3] Virginia Steen,[4] Christian Stock,[5] Martina Gahlemann,[6] Veronika Kohlbrenner,[7] Susanne Stowasser,[8] Kristin B. Highland[9] on behalf of the SENSCIS trial investigators

[1]Division of Rheumatology and Clinical Immunogenetics, University of Texas McGovern Medical School, Houston, Texas, USA; [2]Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland; [3]Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan; [4]Division of Rheumatology, Georgetown University, Washington, D.C., USA; [5]Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany; [6]Boehringer Ingelheim (Schweiz) GmbH, Basel, Switzerland; [7]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, Connecticut, USA; [8]Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Germany; [9]Cleveland Clinic, Cleveland, Ohio, USA

Introduction

- In the SENSCIS trial, patients with systemic sclerosis-associated ILD were randomised to receive nintedanib 150 mg bid or placebo. Nintedanib reduced the rate of decline in forced vital capacity (FVC) (mL/year) over 52 weeks by 44% compared with placebo.[1]



R, randomisation stratified by presence of anti-topoisomerase I antibody (ATA).

- Dose reductions from 150 mg bid to 100 mg bid and treatment interruptions were permitted to manage adverse events.[1]

Aim

- To assess whether dose adjustments affected the rate of FVC decline in the SENSCIS trial.

Methods

Patients

- Inclusion criteria for the SENSCIS trial included: SSc with first non-Raynaud symptom ≤7 years before screening, fibrotic ILD of ≥10% extent on an HRCT scan, FVC ≥40% predicted and diffusion capacity of the lung for carbon monoxide (DLco) 30–89% predicted.
- Subjects on prednisone ≤10 mg/day and/or stable therapy with mycophenolate or methotrexate for ≥6 months prior to randomisation were allowed to participate.
- Dose reductions from 150 mg bid to 100 mg bid and treatment interruptions (≤8 weeks) were permitted to manage adverse events. After resolution of the adverse event, nintedanib could be reintroduced, or the dose increased back to 150 mg bid. Patients who had a dose reduction and/or treatment interruption were asked to attend all visits as planned.

Analyses

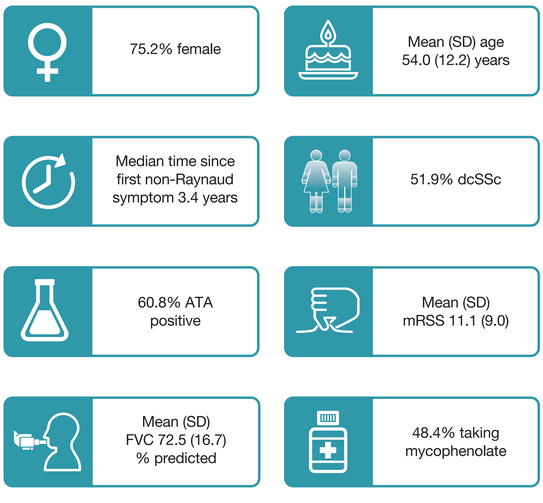
- In patients treated with nintedanib, we assessed the rate of decline in FVC (mL/year) over 52 weeks in patients who had:
  - ≥1 dose reduction
  - ≥1 treatment interruption
  - ≥1 dose reduction and/or treatment interruption
  - dose intensity of ≤90%. Dose intensity was defined as the amount of drug administered divided by the amount of drug that would have been received if 150 mg bid had been administered over 52 weeks or until permanent treatment discontinuation.
- Analyses were descriptive.

Results

Patients

- In total, 288 patients received ≥1 dose of nintedanib and 288 patients received ≥1 dose of placebo.

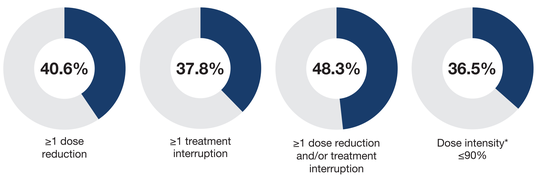
Baseline characteristics of patients in the SENSCIS trial (n=576)



ATA, anti-topoisomerase I antibody; mRSS, modified Rodnan skin score.

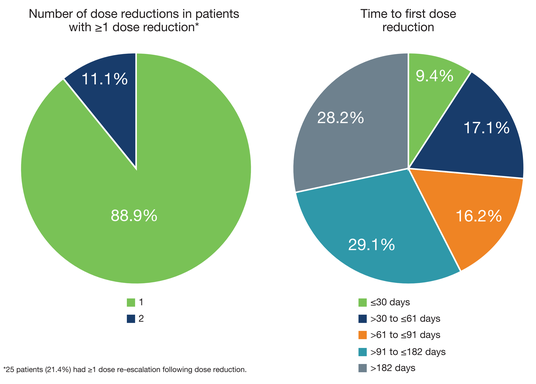
Dose adjustments

Dose adjustments over 52 weeks in nintedanib-treated patients in the SENSCIS trial



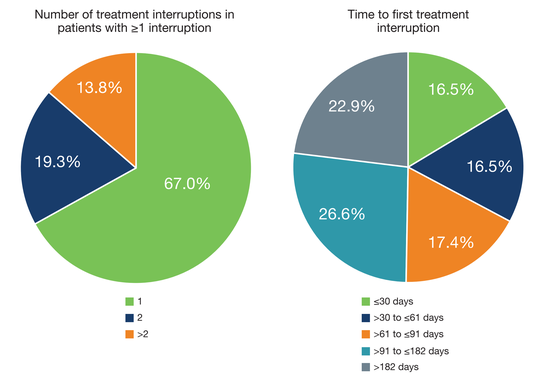
*Defined as amount of drug administered divided by the amount of drug that would have been received if 150 mg bid had been administered over 52 weeks or until permanent treatment discontinuation. 56 patients (19.4%) permanently discontinued nintedanib before week 52.

Nintedanib dose reductions over 52 weeks



*25 patients (21.4%) had ≥1 dose re-escalation following dose reduction.

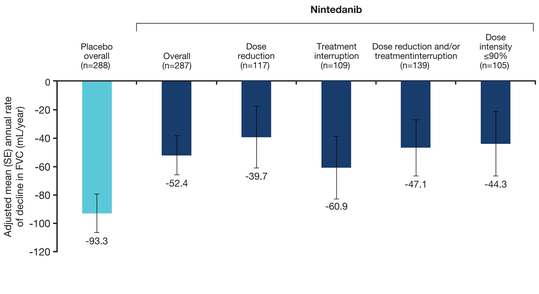
Nintedanib treatment interruptions over 52 weeks



- Over 52 weeks, 59.2% of dose reductions and 41.2% of treatment interruptions were due to diarrhoea.
- Mean (SD) total duration of treatment interruptions was 23.1 (17.4) days.

Annual rate of decline in FVC

Rate of decline in FVC (mL/year) over 52 weeks by dose adjustment



Conclusions

- **In the SENSCIS trial in patients with SSc-ILD:**
  - **almost half of patients had a nintedanib dose reduction and/or treatment interruption over 52 weeks.**
  - **the estimated rate of decline in FVC was similar in nintedanib-treated patients irrespective of whether they had dose adjustments to manage adverse events.**
- **Management of adverse events using symptomatic therapies and dose adjustment is important to help patients with SSc-ILD remain on nintedanib.**

Reference

1. Distler O et al. N Engl J Med 2019;380:2518–28.

Acknowledgements

The SENSCIS trial was funded by Boehringer Ingelheim. Editorial and formatting assistance, supported financially by Boehringer Ingelheim, was provided by Julie Fleming and Wendy Morris of FleishmanHillard Fishburn, London, UK during preparation of this poster. The authors were fully responsible for all content and editorial decisions, were involved at all stages of poster development and have approved the final version. The authors received no direct compensation related to the development of this poster. Boehringer Ingelheim was given the opportunity to review the poster for medical and scientific accuracy as well as intellectual property considerations. Maureen Mayes reports grants from Boehringer Ingelheim, Corbus, CSL Behring, Eicos and Galapagos and has served as a consultant for BI, Eicos, Galapagos. Kristin Highland reports grants and personal fees from Actelion Pharmaceuticals, BI and United Therapeutics; personal fees from Bayer; and grants from Genentech, Eiger BioPharmaceuticals and Reata Pharmaceuticals.

INTERACTIVE

https://www.globalmedcomms.com/respiratory/SSWC2020

https://www.globalmedcomms.com/respiratory/SSWC2020/mayes

Boehringer Ingelheim

Poster developed for the 6th Systemic Sclerosis World Congress, 12–14 July 2020.