

# Effect of nintedanib on progression of systemic sclerosis-associated interstitial lung disease (SSc-ILD) over 100 weeks: data from the SENSIS® trial

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## INTRODUCTION

- Interstitial lung disease (ILD) is the leading cause of death related to systemic sclerosis (SSc).<sup>1</sup>
- Decline in forced vital capacity (FVC) in subjects with SSc-ILD is associated with mortality.<sup>2,3</sup>
- The primary analysis of the randomised, placebo-controlled SENSIS trial showed that in subjects with SSc-ILD, treatment with nintedanib was associated with a significant reduction in the rate of decline in FVC (mL/year) over 52 weeks.<sup>4</sup>

## Aim

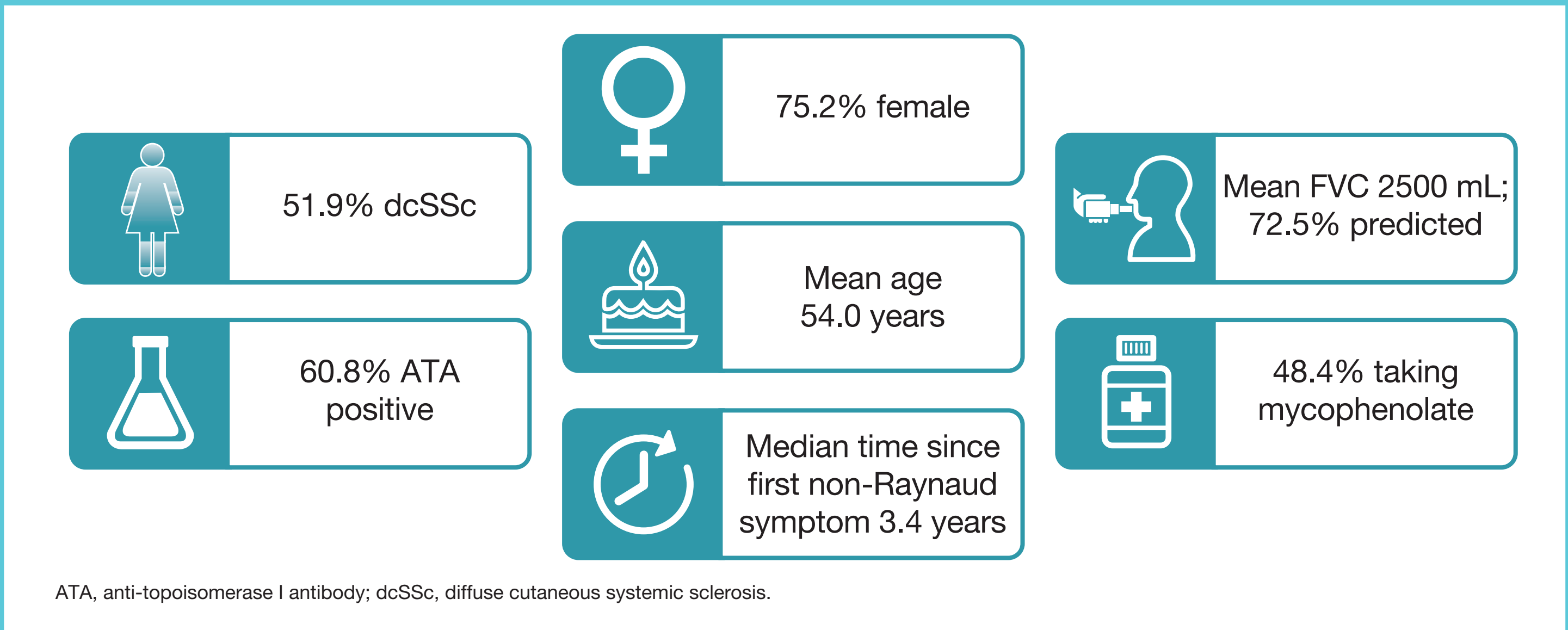
- To assess the effect of nintedanib on progression of ILD over the whole SENSIS trial.

## METHODS

- The SENSIS trial enrolled subjects with SSc-ILD with first non-Raynaud symptom ≤7 years before screening, extent of fibrotic ILD ≥10% 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 or equivalent and/or stable therapy with mycophenolate or methotrexate for ≥6 months prior to randomisation were allowed to participate.
- The SENSIS trial was designed to demonstrate a reduction in the rate of decline in FVC (mL/year) in subjects treated with nintedanib versus placebo over 52 weeks. However, subjects could remain on randomised blinded treatment until the last subject reached week 52 (but for ≤100 weeks), resulting in a variable length of follow-up.
- FVC was measured at baseline and at week 2, 4, 6, 12, 24, 36, 52, 68, 84 and 100. A post-treatment follow-up visit, at which FVC data were collected, was conducted 28 days after the end of treatment. Subjects who prematurely discontinued treatment were asked to continue to attend visits, including the post-treatment follow-up visit, until the end of the trial.
- The rate of decline in FVC (mL/year) over the whole trial was assessed in a descriptive and exploratory manner. Given the variable length of follow-up beyond week 52, three methods were used:

- At baseline, subjects had moderately impaired FVC; almost half were taking mycophenolate (Figure 2).

Figure 2. Baseline characteristics of subjects in the SENSIS trial



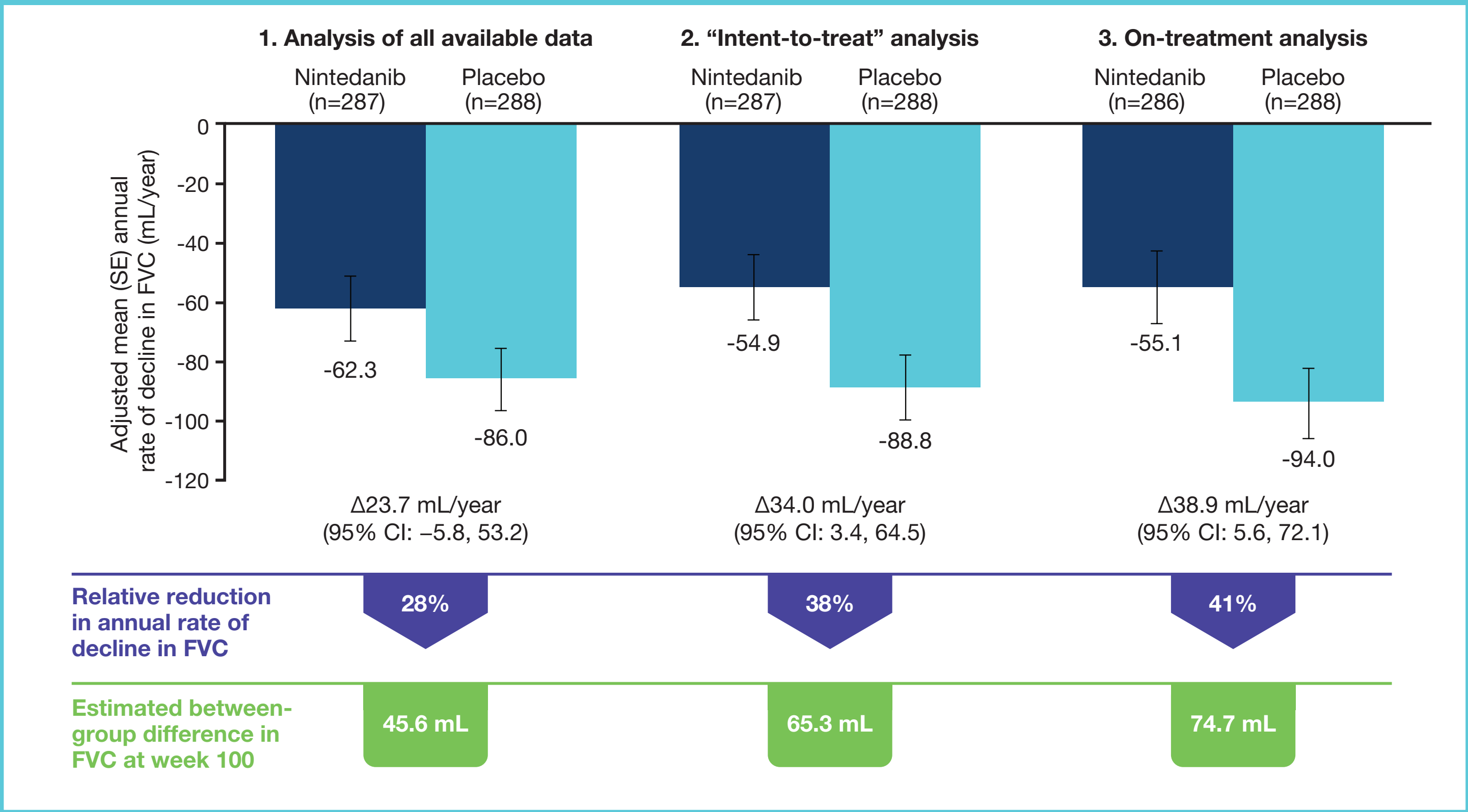
## Exposure

- Median exposure to trial drug was 15.4 months in the nintedanib group and 15.6 months in the placebo group. Maximum exposure was 23.2 and 23.8 months, respectively.

## Decline in FVC

- The adjusted mean (SE) annual rate of decline in FVC over 100 weeks was consistently lower with nintedanib versus placebo across all three analyses (Figure 3).

Figure 3. Annual rate of decline in FVC (mL/year) over 100 weeks and estimated between-group difference in FVC (mL) at week 100



- Smaller proportions of subjects treated with nintedanib than placebo had categorical declines in FVC (Table 1).

	Nintedanib (n=288)	Placebo (n=288)
Absolute decline in FVC >5% predicted, n (%)	130 (45.1)	150 (52.1)
HR (95% CI)	0.83 (0.66, 1.05)	
p-value	0.12	
Absolute decline in FVC >10% predicted, n (%)	52 (18.1)	67 (23.3)
HR (95% CI)	0.79 (0.55, 1.13)	
p-value	0.19	
Relative decline in FVC (mL) >5%, n (%)	171 (59.4)	201 (69.8)
HR (95% CI)	0.80 (0.65, 0.99)	
p-value	0.04	
Relative decline in FVC (mL) >10%, n (%)	103 (35.8)	117 (40.6)
HR (95% CI)	0.88 (0.67, 1.14)	
p-value	0.33	

## Adverse events

- Consistent with previous studies, diarrhoea was the most frequently reported adverse event (Table 2).

Table 2. Most frequently reported adverse events

	Nintedanib (n=288)	Placebo (n=288)
Diarrhoea	220 (76.4)	94 (32.6)
Nausea	96 (33.3)	41 (14.2)
Vomiting	78 (27.1)	33 (11.5)
Skin ulcer	57 (19.8)	56 (19.4)
Nasopharyngitis	43 (14.9)	56 (19.4)
Cough	41 (14.2)	63 (21.9)
Upper respiratory tract infection	39 (13.5)	44 (15.3)
Weight decreased	39 (13.5)	15 (5.2)
Abdominal pain	36 (12.5)	21 (7.3)

Data are n (%) of subjects with ≥1 such adverse event. Adverse events reported in >12% of subjects in either treatment group are shown. Adverse events were reported irrespective of causality and coded by preferred terms in the Medical Dictionary for Regulatory Activities (MedDRA).

- Serious adverse events were reported in 30.6% and 27.4% of subjects treated with nintedanib and placebo, respectively.
- Adverse events led to permanent discontinuation of trial drug in 17.4% and 10.1% of subjects treated with nintedanib and placebo, respectively. Diarrhoea was the adverse event that most frequently led to discontinuation of trial drug (Table 3).

Table 3. Adverse events that most frequently led to permanent discontinuation of trial drug

	Nintedanib (n=288)	Placebo (n=288)
Diarrhoea	22 (7.6)	1 (0.3)
Nausea	6 (2.1)	0
Vomiting	4 (1.4)	1 (0.3)

Data are n (%) of subjects with ≥1 such adverse event. Events reported in >1% of subjects in either treatment group are shown.

## CONCLUSIONS

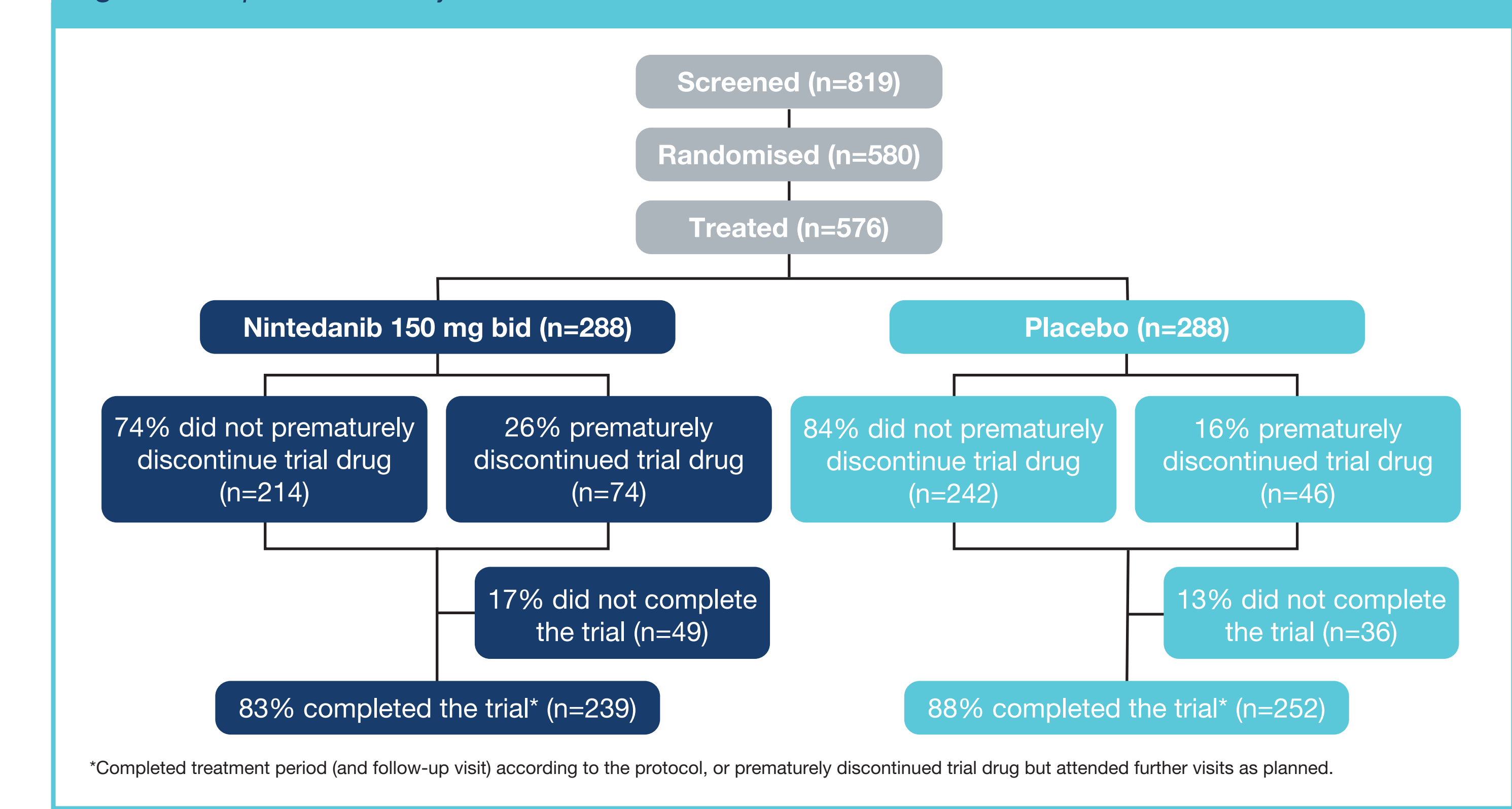
- Overall, data from the SENSIS trial suggested that the effect of nintedanib on slowing the progression of SSc-ILD observed over 52 weeks persists over at least 100 weeks.
- The adverse event profile of nintedanib over 100 weeks was consistent with that reported over 52 weeks and characterised mainly by diarrhoea.
- These findings suggest that nintedanib provides a clinically meaningful benefit on slowing the progression of SSc-ILD, with side-effects that are manageable for most patients.

## RESULTS

### Subjects

- The disposition of subjects over the trial is shown in Figure 1.

Figure 1. Disposition of subjects over the SENSIS trial



## References

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## Acknowledgements

The SENSIS 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. Boehringer Ingelheim was given the opportunity to review the poster for medical and scientific accuracy as well as intellectual property considerations. The authors received no direct compensation related to the development of this poster. Shervin Assassi reports grants, personal fees and other remuneration from Boehringer Ingelheim; grants from Bayer, Biogen Idec, and Momenta; and personal fees from Medscape, Integrity Continuing Education, and Corbus. Toby M Maher reports grants and personal fees from GlaxoSmithKline and UCB; and personal fees from Apellis, Bayer, Biogen Idec, Blade, Boehringer Ingelheim, Bristol-Myers Squibb, Galapagos, Galeco, Indalo, Novartis, RespiVent, Roche, and Trevi.