Is there a difference between the sexes in the rate of progression of systemic sclerosis-associated ILD (SSc-ILD)? Data from the SENSCIS® trial

Volkmann ER et al. Is there a difference between the sexes in the rate of progression of systemic sclerosis-associated ILD (SSc-ILD)? Data from the SENSCIS trial. Poster developed for Annual European Congress of Rheumatology, 2020.

Introduction

- In the SENSCIS trial in patients with SSc-ILD, nintedanib reduced the rate of decline in FVC (mL/year) over 52 weeks by 44% compared with placebo, with an adverse event profile characterised predominantly by gastrointestinal events[1]
- Previous studies have suggested that male sex may be associated with a greater rate of progression of SSc-ILD[2]

FVC, forced vital capacity.

1. Distler O et al. N Engl J Med 2019;380:2518–28; 2. Winstone TA et al. Chest 2014;146:422–36.
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Aim

- To assess the rate of decline in FVC, and the efficacy and safety of nintedanib, in male and female patients in the SENSCIS trial

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Methods

- Inclusion criteria included SSc with first non-Raynaud symptom <7 years before screening, fibrotic ILD of ≥10% extent on an HRCT scan, FVC ≥40% predicted and 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
- Subjects were randomised to receive nintedanib or placebo until the last patient had reached week 52 but for ≤100 weeks

DLco, diffusion capacity of the lung for carbon monoxide; HRCT, high-resolution computed tomography.

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Analyses

- We analysed the following over 52 weeks in subgroups by sex:
  - Rate of decline in FVC (mL/year)
  - Proportions of patients with categorical declines in FVC
  - Time to absolute decline in FVC ≥10% predicted or death
  - Change in modified Rodnan skin score (mRSS)
- Interaction p-values were calculated to assess potential heterogeneity in the treatment effect of nintedanib versus placebo between the subgroups. No adjustment for multiplicity was made
- Dose adjustments and adverse events were assessed descriptively

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Distribution of patients by sex

433 patients (75.2%) were female

143 patients (24.8%) were male

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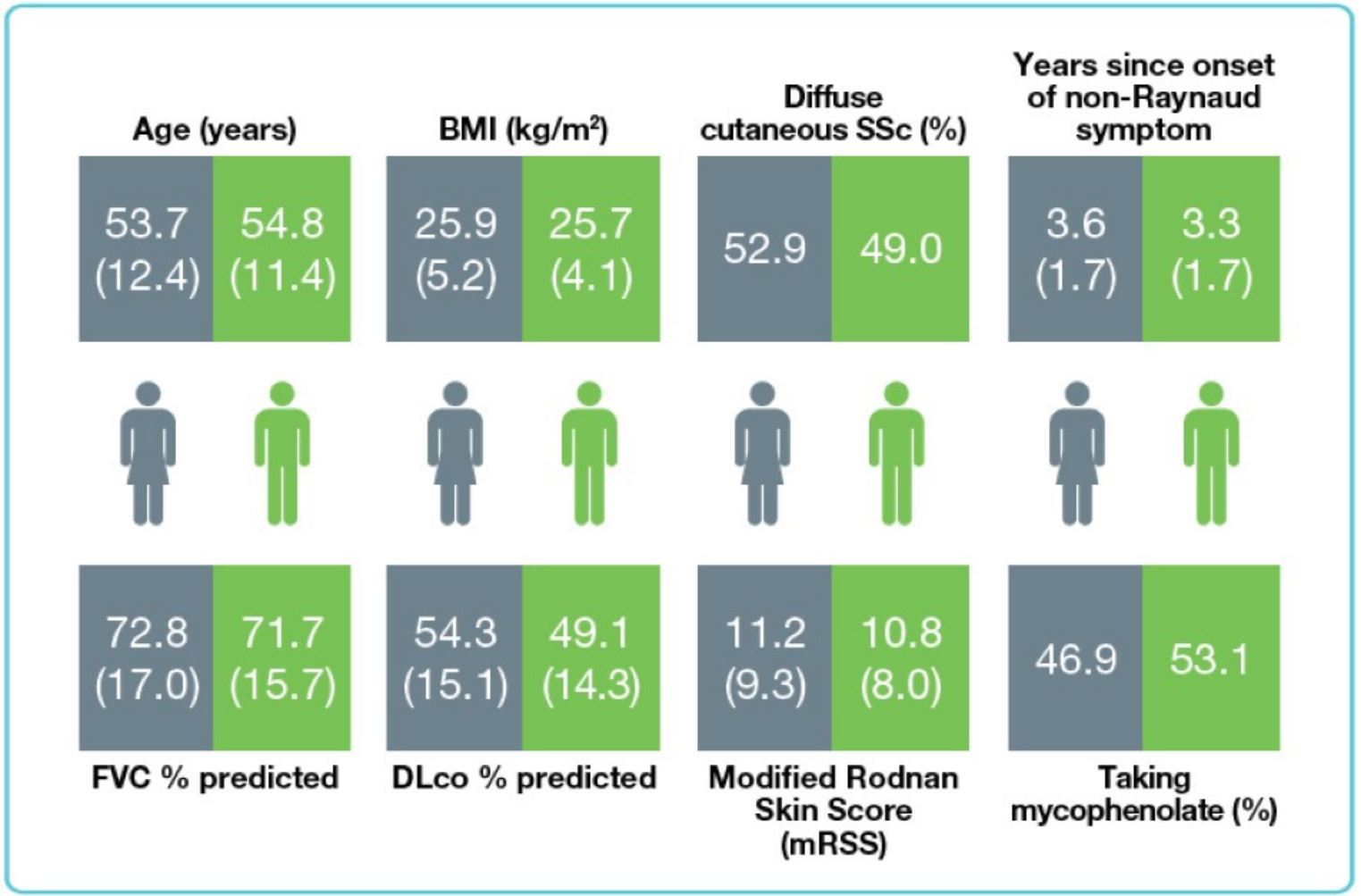
Baseline characteristics of subgroups by sex



Mean (SD) or % of patients.

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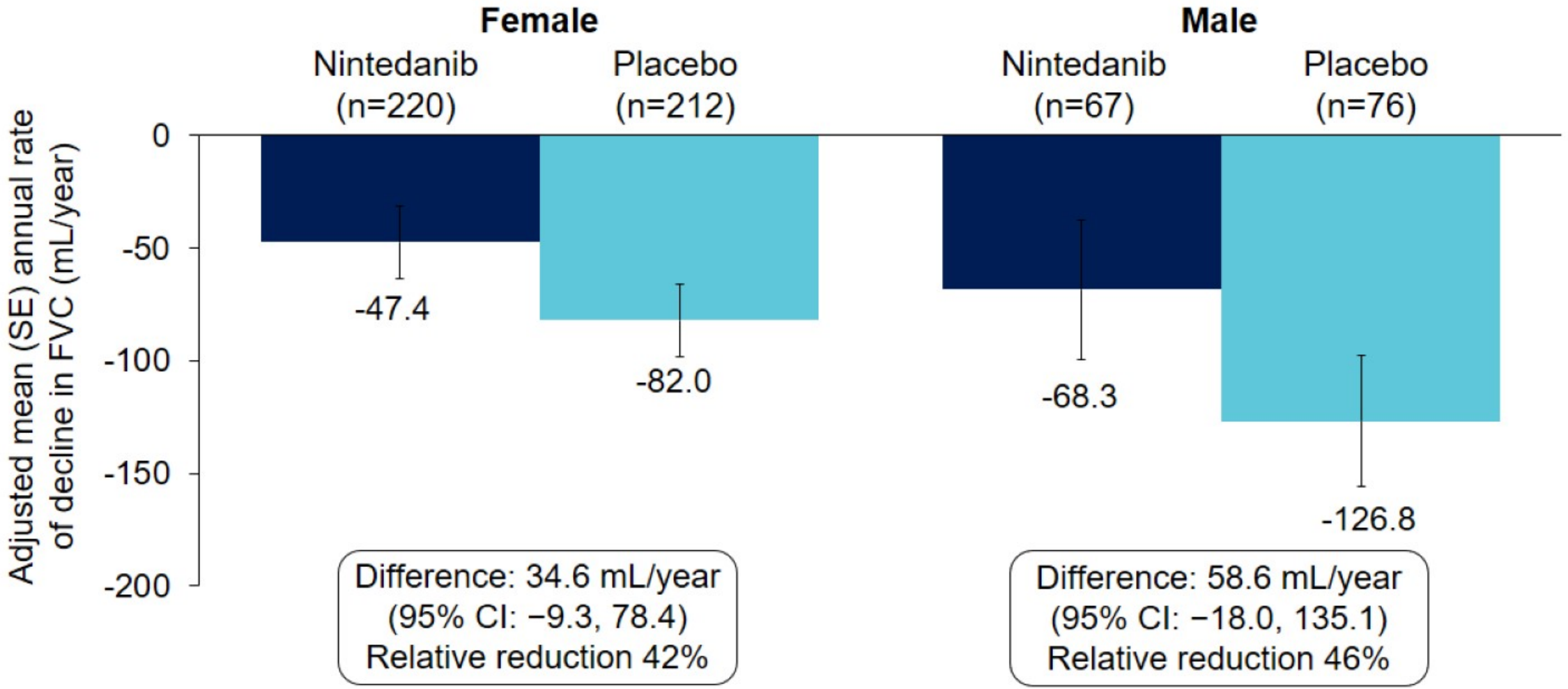
Rate of decline in FVC (mL/year) over 52 weeks in subgroups by sex



Treatment-by-time-by-subgroup interaction p=0.59.

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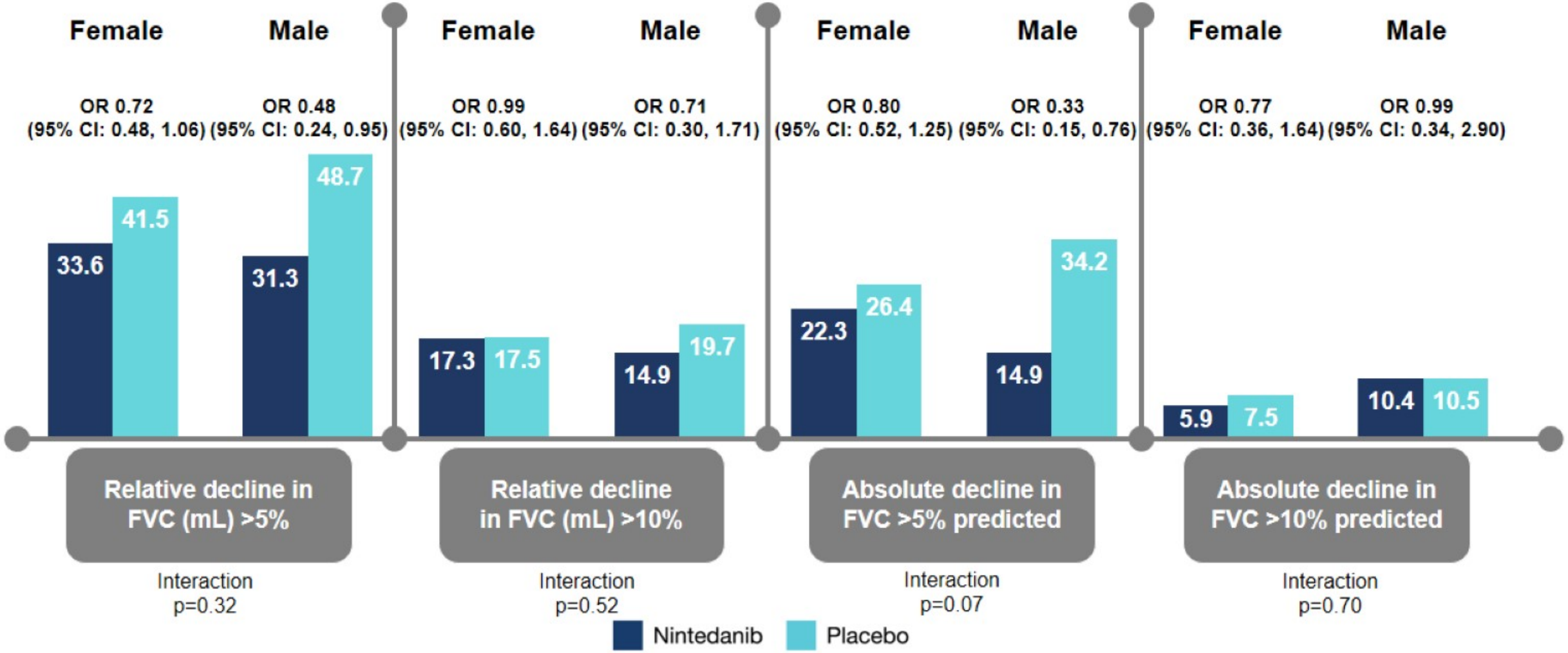
Proportions of patients with absolute and relative declines in FVC in subgroups by sex



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Time to absolute decline in FVC ≥10% predicted or death in subgroups by sex

	Female		Male	
	Nintedanib (n=221)	Placebo (n=212)	Nintedanib (n=67)	Placebo (n=76)
Absolute decline in FVC ≥10% predicted or death, n (%)	30 (13.6)	43 (20.3)	10 (14.9)	19 (25.0)
Hazard ratio (95% CI)	0.68 (0.42, 1.08)		0.57 (0.27, 1.23)	
Interaction p-value	p=0.69			

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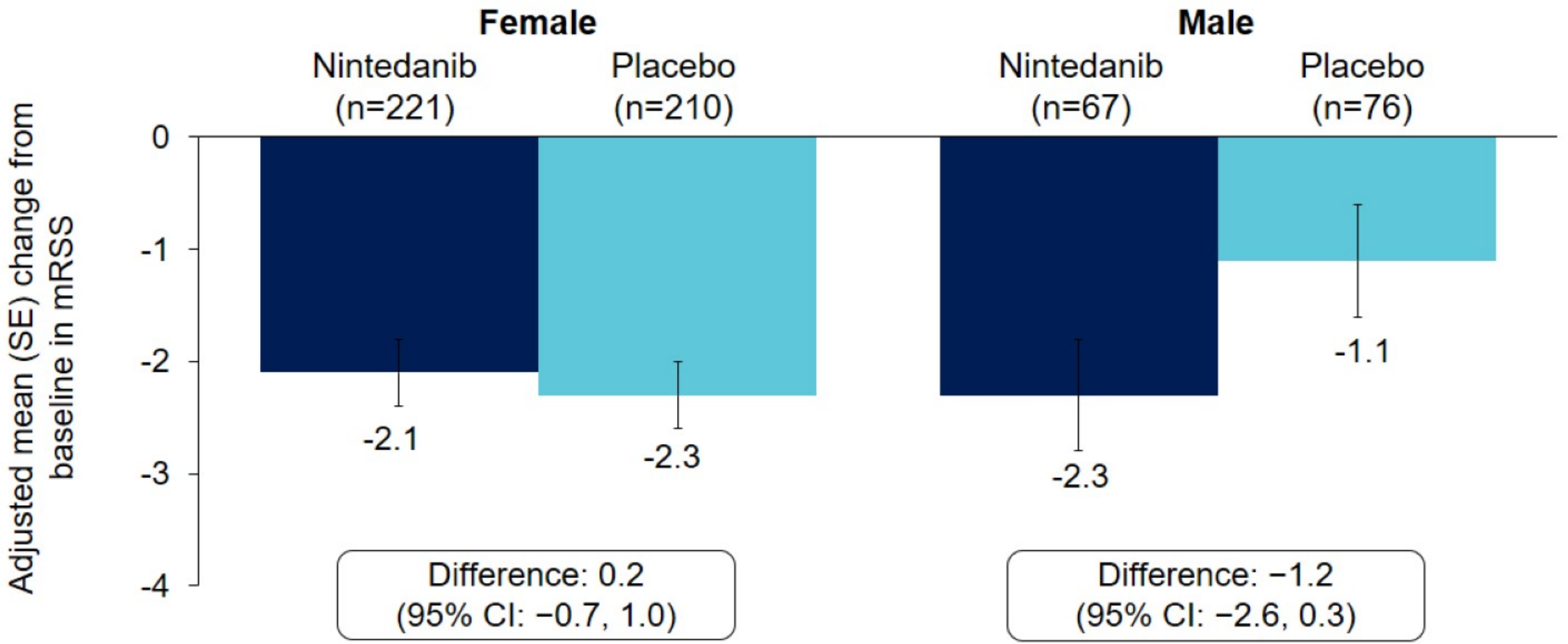
Change in mRSS at week 52 in subgroups by sex



Treatment-by-visit-by-subgroup interaction p=0.12.

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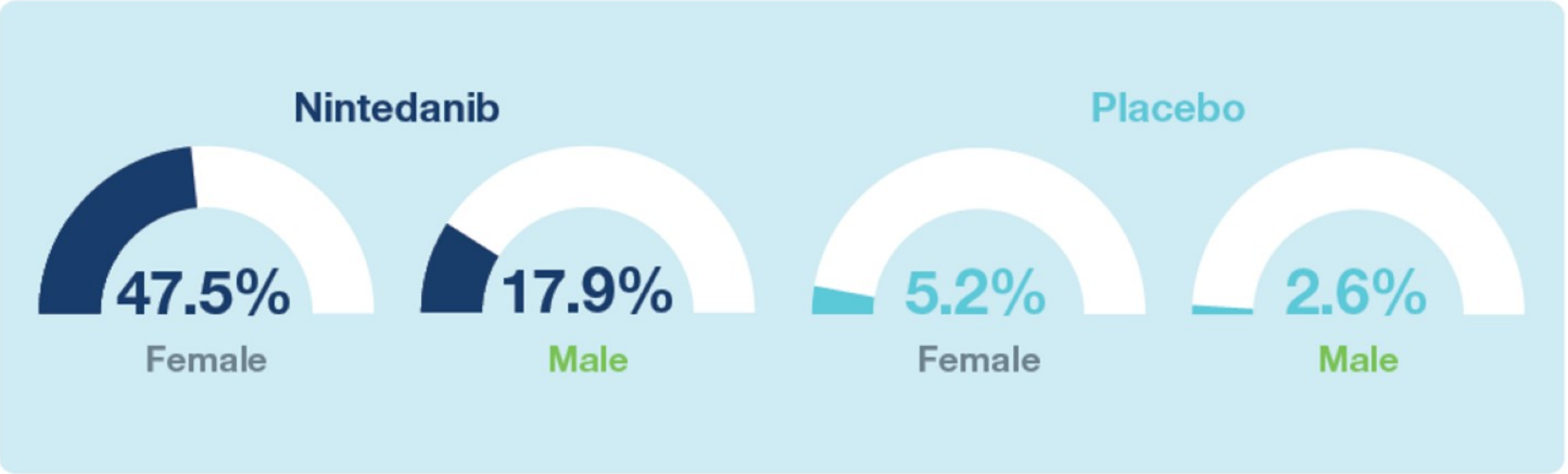
Patients with ≥1 dose reduction over 52 weeks in subgroups by sex



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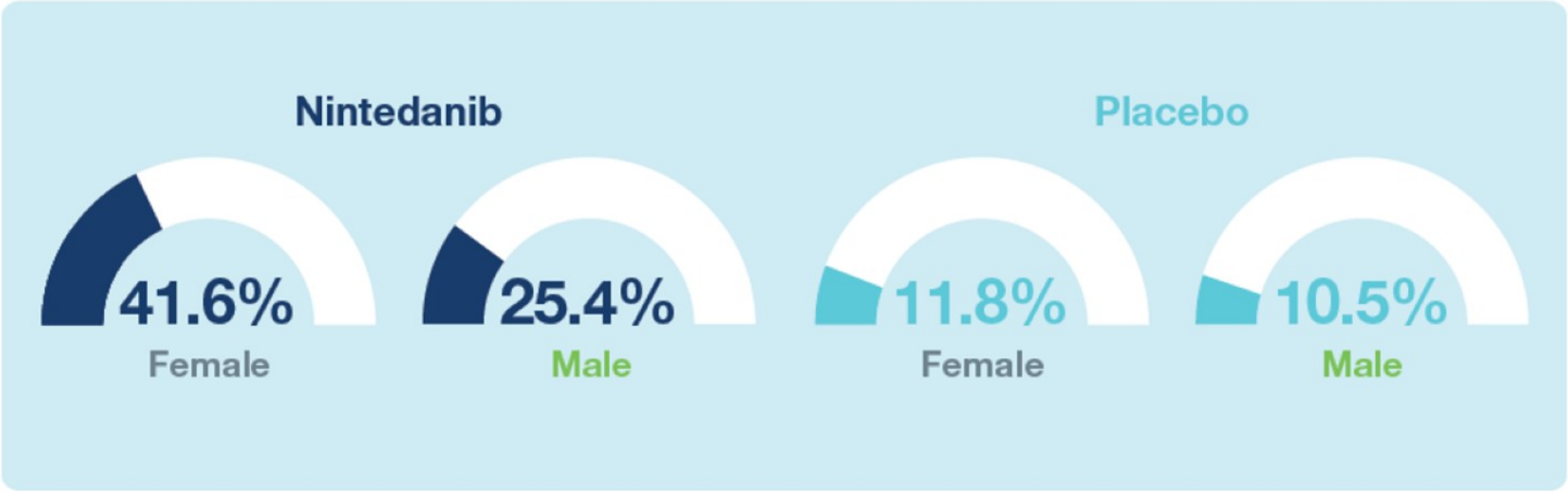
Patients with ≥1 treatment interruption over 52 weeks in subgroups by sex



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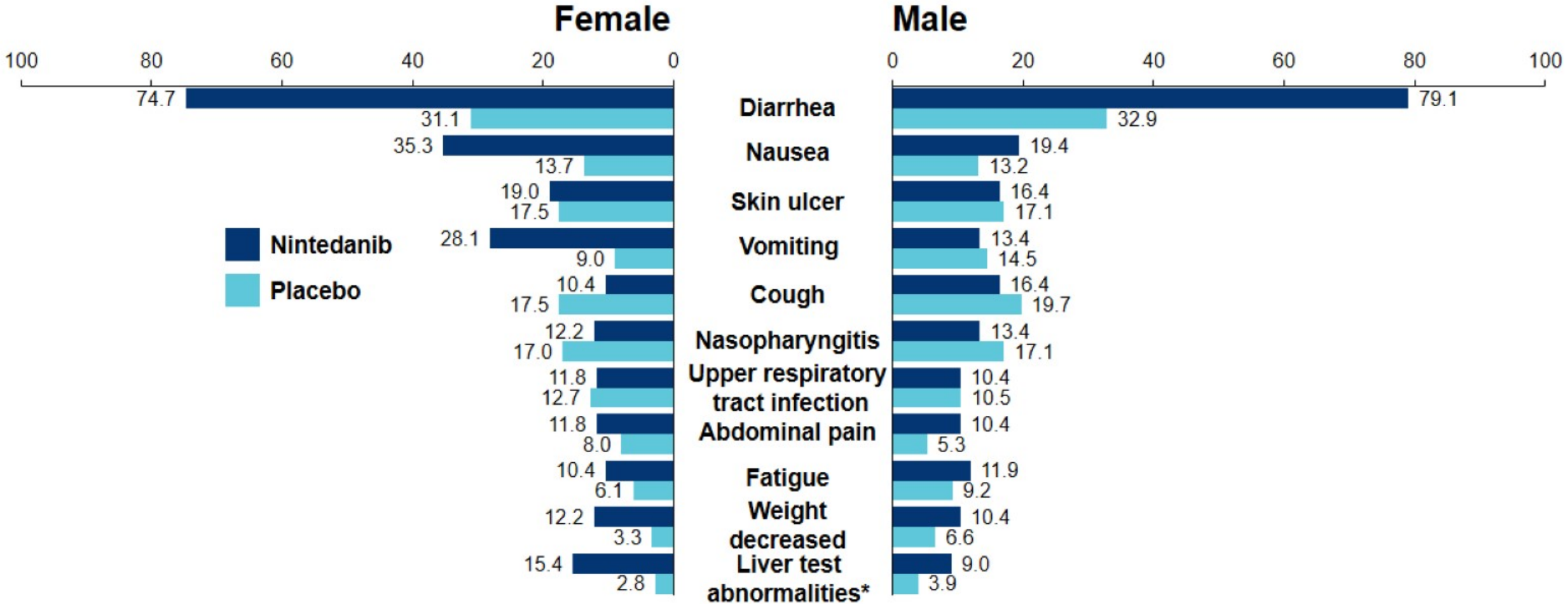
Most frequent adverse events in subgroups by sex



Data are % of patients with ≥1 such AE reported over 52 weeks (or until 28 days after last trial drug intake in subjects who discontinued trial drug before week 52). AEs reported in >10% of patients in either treatment group in the overall population are shown. AEs were based on preferred terms in the Medical Dictionary for Regulatory Activities (MedDRA) except that "liver test abnormalities" was based on the standardised MedDRA query "liver related investigations, signs and symptoms" (broad definition).

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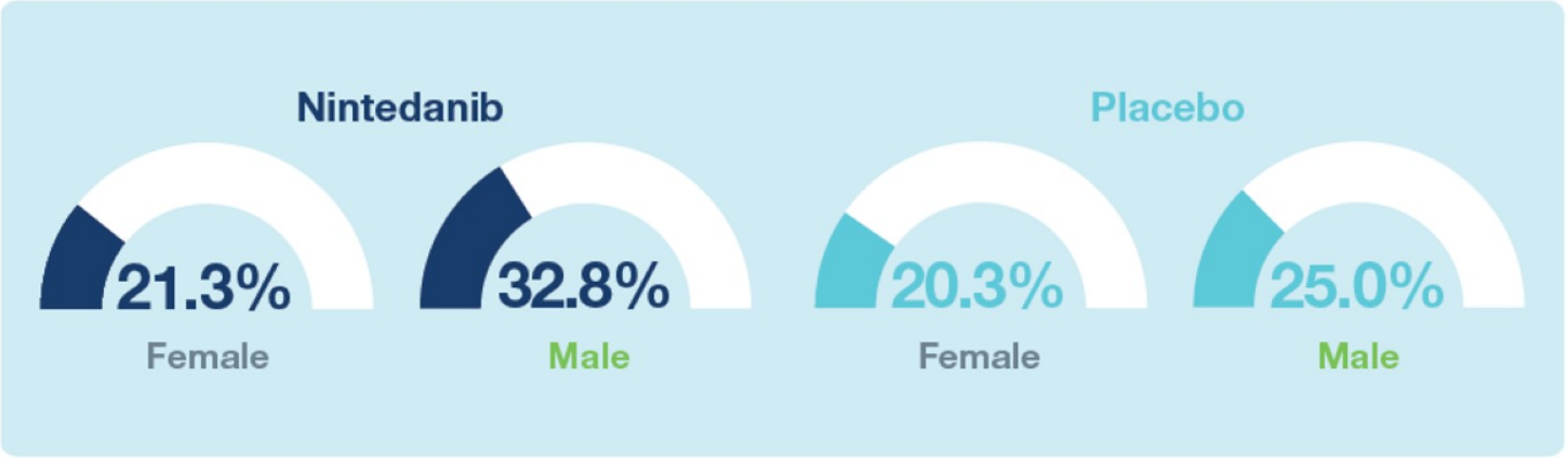
Serious adverse events in subgroups by sex



Data are % of patients with ≥1 such AE reported over 52 weeks (or until 28 days after last trial drug intake in subjects who discontinued trial drug before week 52). Serious AEs were events that resulted in death, were life-threatening, resulted in hospitalisation or prolongation of hospitalisation, resulted in persistent or clinically significant disability or incapacity, were a congenital anomaly or birth defect, or were deemed to be serious for any other reason.

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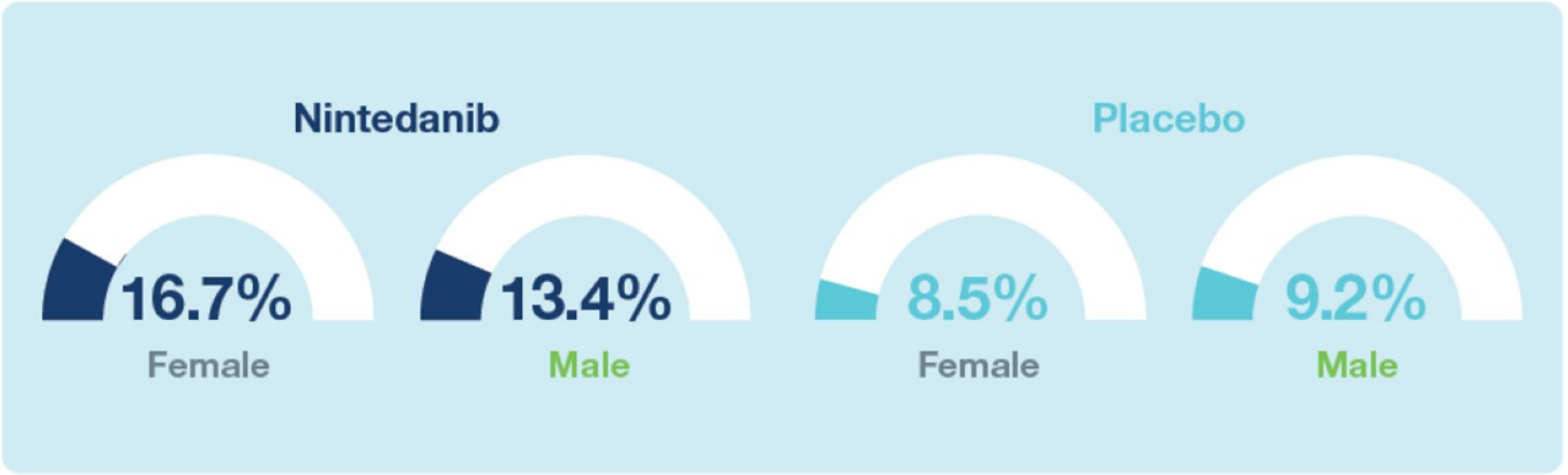
Adverse events leading to permanent treatment discontinuation in subgroups by sex



Data are % of patients with ≥1 such AE reported over 52 weeks.

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Conclusions

- In the SENSCIS trial in patients with SSc-ILD:
  - the rate of decline in FVC in the placebo group was numerically greater in male than female patients
  - nintedanib had a consistent effect in reducing the rate of decline in FVC between males and females
  - the safety profile of nintedanib was generally similar between male and female patients. Nintedanib dose adjustments were more common in female than male patients

- Differences between the male and female subgroups at baseline (related to their SSc, comorbidities, and other factors) may have influenced our findings

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