

# Effects of nintedanib in subgroups based on combined pulmonary fibrosis and emphysema (CPFE) index at baseline

Vincent Cottin,<sup>1</sup> Christopher J Ryerson,<sup>2</sup> Kevin R Flaherty,<sup>3</sup> Joyce S Lee,<sup>4</sup> Tamera J Corte,<sup>5</sup> Birgit Schinzel,<sup>6</sup> Leticia Orsatti,<sup>6</sup> Manuel Quaresma,<sup>6</sup> Athol U Wells<sup>7</sup>

<sup>1</sup>National Reference Center for Rare Pulmonary Diseases, Louis Pradel Hospital, Hospices Civils de Lyon, Claude Bernard University Lyon 1, Lyon, France; <sup>2</sup>Department of Medicine & Centre for Heart Lung Innovation, University of British Columbia, Vancouver, Canada; <sup>3</sup>University of Michigan, Ann Arbor, MI, USA; <sup>4</sup>Dept of Medicine, University of Colorado Denver, Aurora, CO, USA; <sup>5</sup>Royal Prince Alfred Hospital, Camperdown, New South Wales, Australia and University of Sydney, New South Wales, Australia; <sup>6</sup>Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Germany; <sup>7</sup>National Institute for Health Research Respiratory Biomedical Research Unit, Royal Brompton and Harefield NHS Foundation Trust, and National Heart and Lung Institute, Imperial College, London, UK.

## INTRODUCTION

- A greater extent of emphysema on high-resolution computed tomography (HRCT) may be associated with a smaller decline in forced vital capacity (FVC) in patients with idiopathic pulmonary fibrosis (IPF).<sup>1</sup>
- The combined pulmonary fibrosis and emphysema (CPFE) index estimates the extent of emphysema on HRCT in patients with IPF based on pulmonary function tests. The formula was developed in a cohort of 212 patients diagnosed with IPF between 1990 and 1996 and tested in 455 patients with IPF enrolled in two clinical trials and in a real-world cohort of 191 patients diagnosed with IPF between 2011 and 2014.<sup>2</sup>
- In the INPULSIS trials, nintedanib reduced the annual rate of decline in FVC (mL/year) in patients with IPF by 49% versus placebo.<sup>3</sup>

## Aim

- To assess the effect of nintedanib in subgroups by CPFE index at baseline in the INPULSIS trials.

## METHODS

### The INPULSIS trials<sup>3</sup>

- The INPULSIS trials enrolled patients with a diagnosis of IPF, FVC  $\geq 50\%$  predicted, forced expiratory volume in 1 second (FEV<sub>1</sub>)/FVC ratio of  $\geq 70\%$ , and diffusing capacity of the lung for carbon monoxide (DLco) 30-79% predicted. Patients with emphysema evident on an HRCT scan were eligible to participate.
- Patients were randomized to receive nintedanib 150 mg bid or placebo for 52 weeks.
- FVC was measured at baseline and at weeks 2, 4, 6, 12, 24, 36 and 52.

### Combined pulmonary fibrosis and emphysema (CPFE) index<sup>2</sup>

$$2.84 + (0.90 \times \text{FVC \% predicted}) - (0.60 \times \text{FEV}_1 \text{ \% predicted}) - (0.44 \times \text{DLco \% predicted}) = \text{CPFE index}$$

**CPFE index**

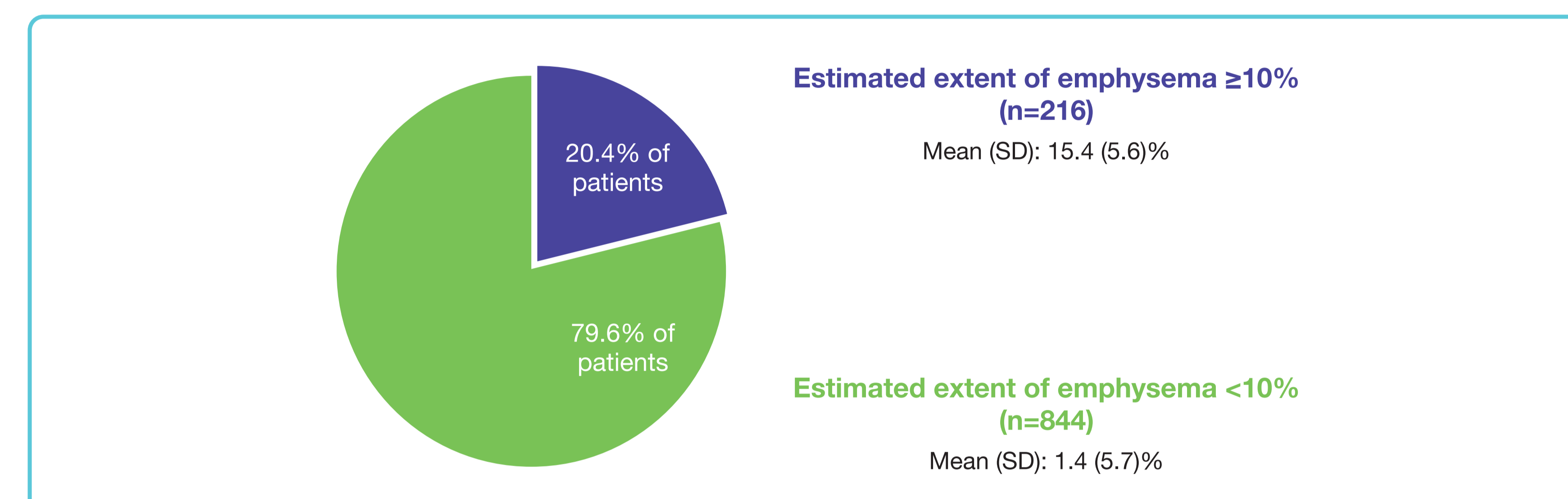
(estimate of extent of emphysema on HRCT)

### Analysis

- In post-hoc analyses, we analyzed the following in subgroups by CPFE index-estimated extent of emphysema <10% versus  $\geq 10\%$  at baseline:
  - Annual rate of decline in FVC (mL/year)
  - Change from baseline in St George's Respiratory Questionnaire (SGRQ) total score at week 52
  - Time to absolute decline in FVC  $\geq 5\%$  predicted or death over 52 weeks
  - Time to absolute decline in FVC  $\geq 10\%$  predicted or death over 52 weeks.
- 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.

## RESULTS

### CPFE index-estimated extent of emphysema at baseline

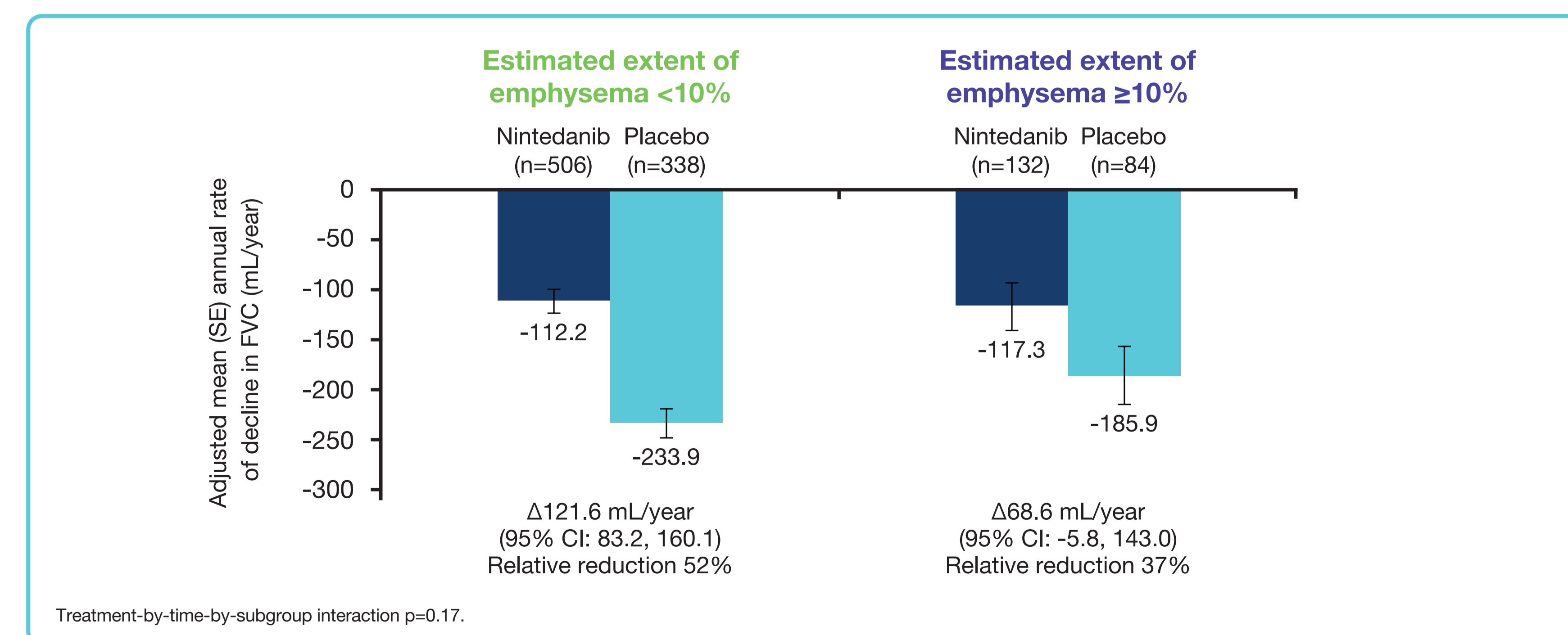


### Baseline characteristics by CPFE index-estimated extent of emphysema at baseline

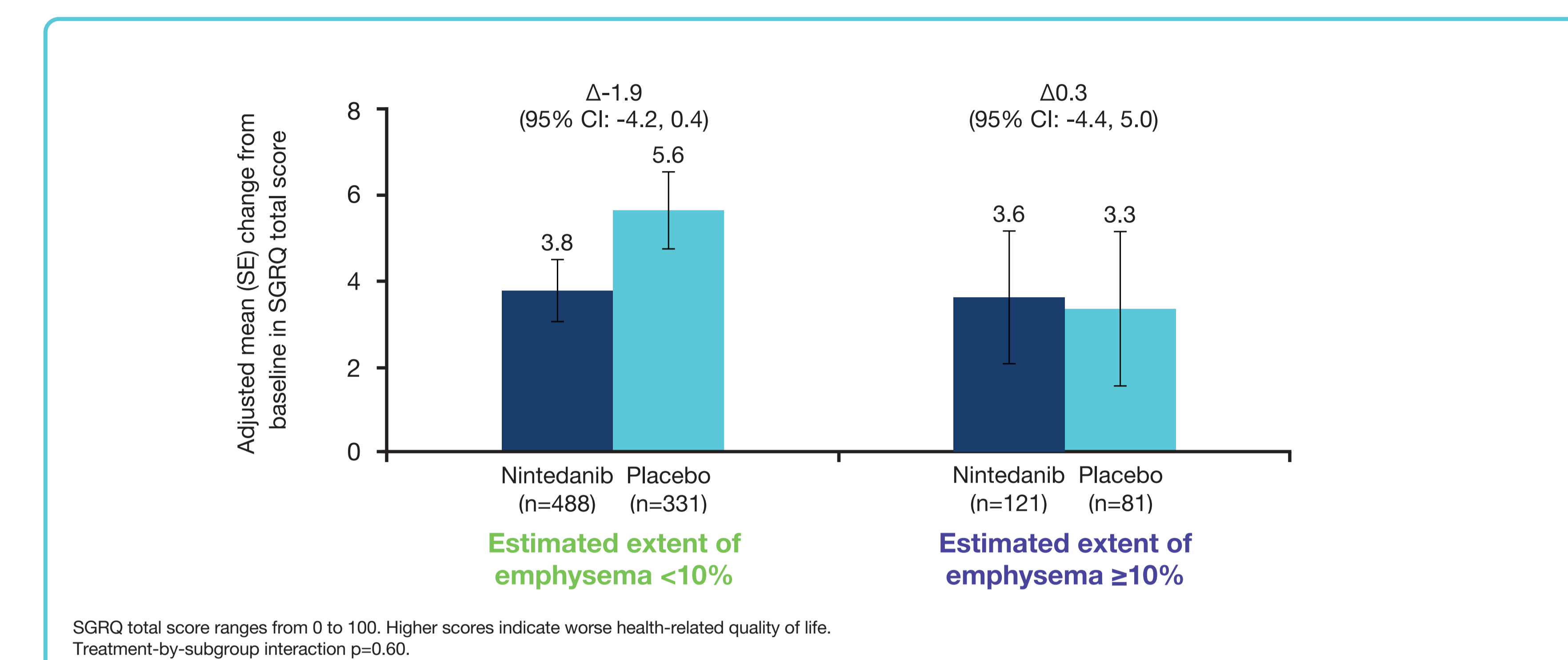
| Characteristic            | Estimated extent of emphysema <10% (n=844) | Estimated extent of emphysema $\geq 10\%$ (n=216) |
|---------------------------|--------------------------------------------|---------------------------------------------------|
| Age (years)               | 66.5 (8.1)                                 | 67.8 (7.6)                                        |
| Male                      | 82.0%                                      | 69.0%                                             |
| Former/current smoker     | 71.7%                                      | 74.1%                                             |
| FVC (mL)                  | 2614 (710)                                 | 3136 (883)                                        |
| FVC % predicted           | 75.1 (15.2)                                | 97.2 (16.4)                                       |
| Presence of emphysema*    | 34.7%                                      | 58.8%                                             |
| FEV <sub>1</sub> /FVC (%) | 83.0 (5.3)                                 | 76.5 (5.0)                                        |
| DLco % predicted          | 48.6 (13.7)                                | 42.1 (10.9)                                       |
| SGRQ total score          | 40.5 (19.0)                                | 35.6 (18.0)                                       |

Data are mean (SD) unless otherwise stated.  
\*Determined by qualitative assessment of HRCT scans by an expert radiologist.

### Annual rate of decline in FVC (mL/year) by CPFE index-estimated extent of emphysema at baseline



### Change from baseline in SGRQ total score at week 52 by CPFE index-estimated extent of emphysema at baseline



### Absolute decline in FVC predicted or death over 52 weeks by CPFE index-estimated extent of emphysema at baseline

|                                                            | Estimated extent of emphysema <10% |                 | Estimated extent of emphysema $\geq 10\%$ |                |
|------------------------------------------------------------|------------------------------------|-----------------|-------------------------------------------|----------------|
|                                                            | Nintedanib (n=506)                 | Placebo (n=338) | Nintedanib (n=132)                        | Placebo (n=84) |
| Absolute decline FVC $\geq 5\%$ predicted or death, n (%)  | 250 (49.4)                         | 237 (70.1)      | 80 (60.6)                                 | 65 (77.4)      |
| Hazard ratio (95% CI)                                      | 0.59 (0.49, 0.70)                  |                 | 0.69 (0.49, 0.95)                         |                |
| Treatment-by-subgroup interaction                          | p=0.46                             |                 |                                           |                |
| Absolute decline FVC $\geq 10\%$ predicted or death, n (%) | 129 (25.5)                         | 142 (42.0)      | 44 (33.3)                                 | 33 (39.3)      |
| Hazard ratio (95% CI)                                      | 0.56 (0.44, 0.71)                  |                 | 0.79 (0.50, 1.24)                         |                |
| Treatment-by-subgroup interaction                          | p=0.20                             |                 |                                           |                |

## CONCLUSIONS

- In the INPULSIS trials in patients with IPF:
  - The annual rate of decline in FVC in patients who received placebo appeared to be lower in patients who, at baseline, had a CPFE index-estimated extent of emphysema of  $\geq 10\%$  versus <10%.
  - Nintedanib reduced the annual rate of decline in FVC both in patients with a CPFE index-estimated extent of emphysema <10% and  $\geq 10\%$  at baseline.

## References

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- Wells A et al. Poster presented at the American Thoracic Society International Conference, 2019.
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INTERACTIVE

