

Correlations between changes in FVC and imaging parameters in patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD): sub-study of the SENSIS trial

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INTRODUCTION

- In the SENSIS trial in patients with SSc-ILD, nintedanib reduced the rate of decline in forced vital capacity (FVC) (mL/year) over 52 weeks by 44% compared with placebo.¹
- In a sub-study, numerical non-significant trends towards less worsening in HRCT parameters were observed in patients treated with nintedanib versus placebo.²

AIM

- To assess correlations between changes from baseline in FVC and qualitative and quantitative imaging parameters in the SENSIS trial.

METHODS

The SENSIS trial

- Patients had SSc with onset of first non-Raynaud symptom ≤ 7 years before screening, extent of fibrotic ILD $\geq 10\%$ on HRCT (based on assessment of the whole lung), FVC $\geq 40\%$ predicted and DLco 30–89% predicted.
- Patients were randomized to receive nintedanib or placebo until the last patient had reached week 52 but for ≤ 100 weeks.

HRCT sub-study

- HRCT images were assessed visually by two independent radiologists at baseline and at week 52 or 60. Changes in the extent of regions with evidence of abnormalities (honeycombing and/or reticulation and/or ground glass opacity [GGO]) were categorized qualitatively from “much better” to “much worse”.
- Changes from baseline in the following parameters were assessed using data-driven texture analysis:³
 - Quantitative fibrosis score: extent (%) of reticular patterns with architectural distortion
 - Quantitative ILD score: sum of scores for extent (%) of reticulation, honeycombing and ground glass opacities.
- We analyzed associations between changes in qualitative imaging parameters and the rate of decline in FVC, and between changes in qualitative and quantitative imaging parameters, using Kendall’s τ -b correlation coefficients.

Assessment of qualitative changes in imaging parameters from baseline to week 52/60

Much better	Moderate decrease in honeycombing and/or reticulation and/or fibrotic GGO; decrease was $>10\%$
Better	Definite but mild decrease in honeycombing and/or reticulation and/or fibrotic GGO; decrease was $\leq 10\%$ Decrease in extent of fibrosis, including change from fibrotic GGO to pure GGO, was considered improvement
Same	No change in honeycombing and/or reticulation and/or fibrotic GGO
Worse	Definite but mild increase in honeycombing and/or reticulation and/or fibrotic GGO; increase was $\leq 10\%$ Increase in extent of fibrosis, including change from pure GGO to fibrotic GGO, was considered worsening
Much worse	At least a moderate increase in honeycombing and/or reticulation and/or fibrotic GGO; increase was $>10\%$

Any increase or decrease in coarsening or extent of honeycombing was considered worsening or improvement (even in the setting of a larger decrease or increase in reticulation or fibrotic GGO). A change in the extent of pure GGO by itself, without a change in the degree of fibrosis, was not considered as worsening or improvement. Disagreement between the radiologists in the categories “much better” or “better” and “worse” or “much worse” were considered “intermediate better” or “intermediate worse”. Where there was disagreement in other categorizations, a third radiologist adjudicated.

CONCLUSIONS

- In patients with SSc-ILD, weak to moderate correlations were observed between changes in qualitative and quantitative HRCT parameters, and weak correlations were observed between changes in qualitative HRCT parameters and the rate of decline in FVC over 52–60 weeks.
- These analyses were limited by the small number of patients with evaluable HRCT scans at follow-up.

RESULTS

Patients

- Of 576 patients in the SENSIS trial, 150 participated in the HRCT sub-study.

Baseline characteristics of patients in overall SENSIS trial and HRCT sub-study

	Overall population (n=576)	HRCT sub-study (n=150)
Age, years, mean	54.0	54.3
Female	75.2%	69.3%
ATA positive	60.8%	56.7%
Diffuse cutaneous SSc	51.9%	44.7%
Extent of fibrotic ILD*	36%	35%
FVC, % predicted	72.5%	73.9%
Taking mycophenolate	48.4%	50.7%

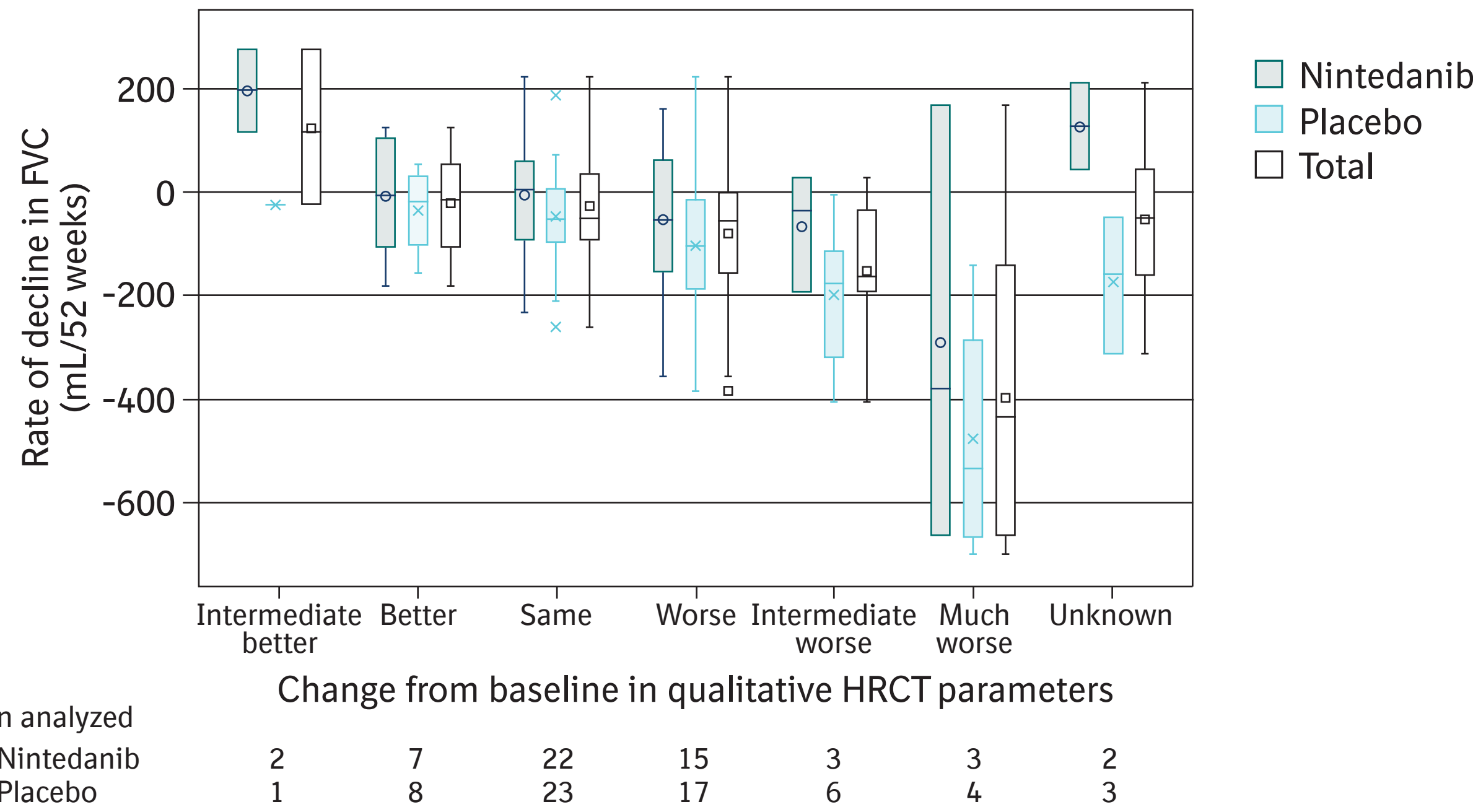
*Extent of fibrotic ILD was assessed visually in the whole lung to the nearest 5%. The assessment did not include pure (non-fibrotic) ground glass opacities. ATA, anti-topoisomerase I antibody.

- At week 52/60, 111 patients (nintedanib 52, placebo 59) had evaluable scans to determine changes in qualitative parameters and 54 patients (nintedanib 23, placebo 31) had evaluable scans to determine quantitative scores.

Associations between changes in qualitative HRCT parameters and rate of decline in FVC

- There were weak negative correlations between changes in qualitative HRCT parameters and the rate of decline in FVC (mL/year) over 52/60 weeks (Kendall’s τ -b correlation coefficients: placebo, -0.37 [95% CI: -0.51, -0.21]; nintedanib, -0.14 [-0.32, 0.04]).
- This suggests that worsening in qualitative HRCT parameters was associated with a greater rate of decline in FVC.

Associations between changes in qualitative HRCT parameters and rate of decline in FVC (mL/year) over 52/60 weeks

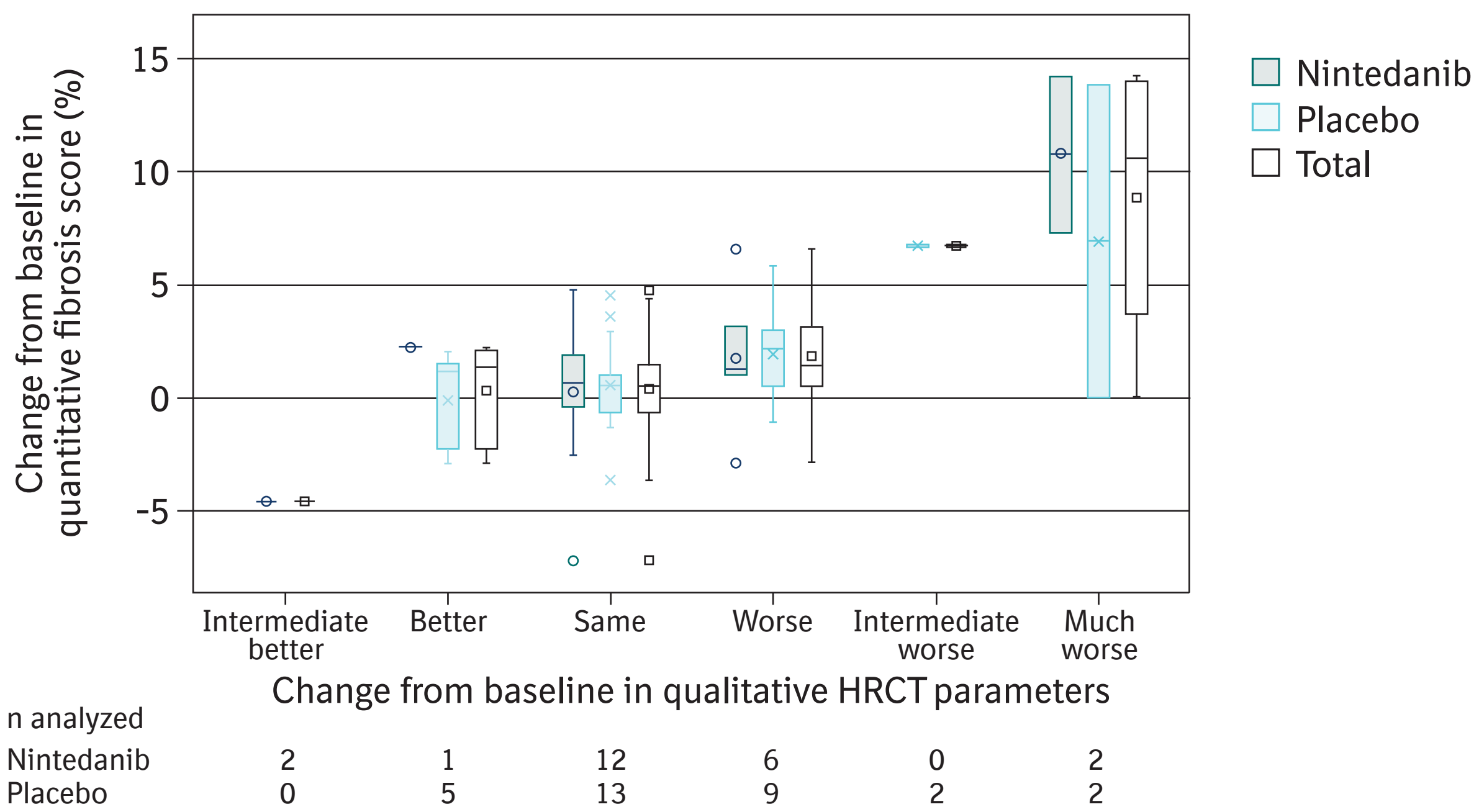


The markers within the boxes denote the means, the mid-line of the boxes the medians, and the boundaries of the boxes the 25th and 75th percentiles. The upper whiskers denote the values 1.5x the interquartile range above the 75th percentile, the lower whiskers the values 1.5x the interquartile range below the 25th percentile and the markers outside the boxes values that fell outside the range of the whiskers.

Associations between changes in qualitative and quantitative HRCT parameters

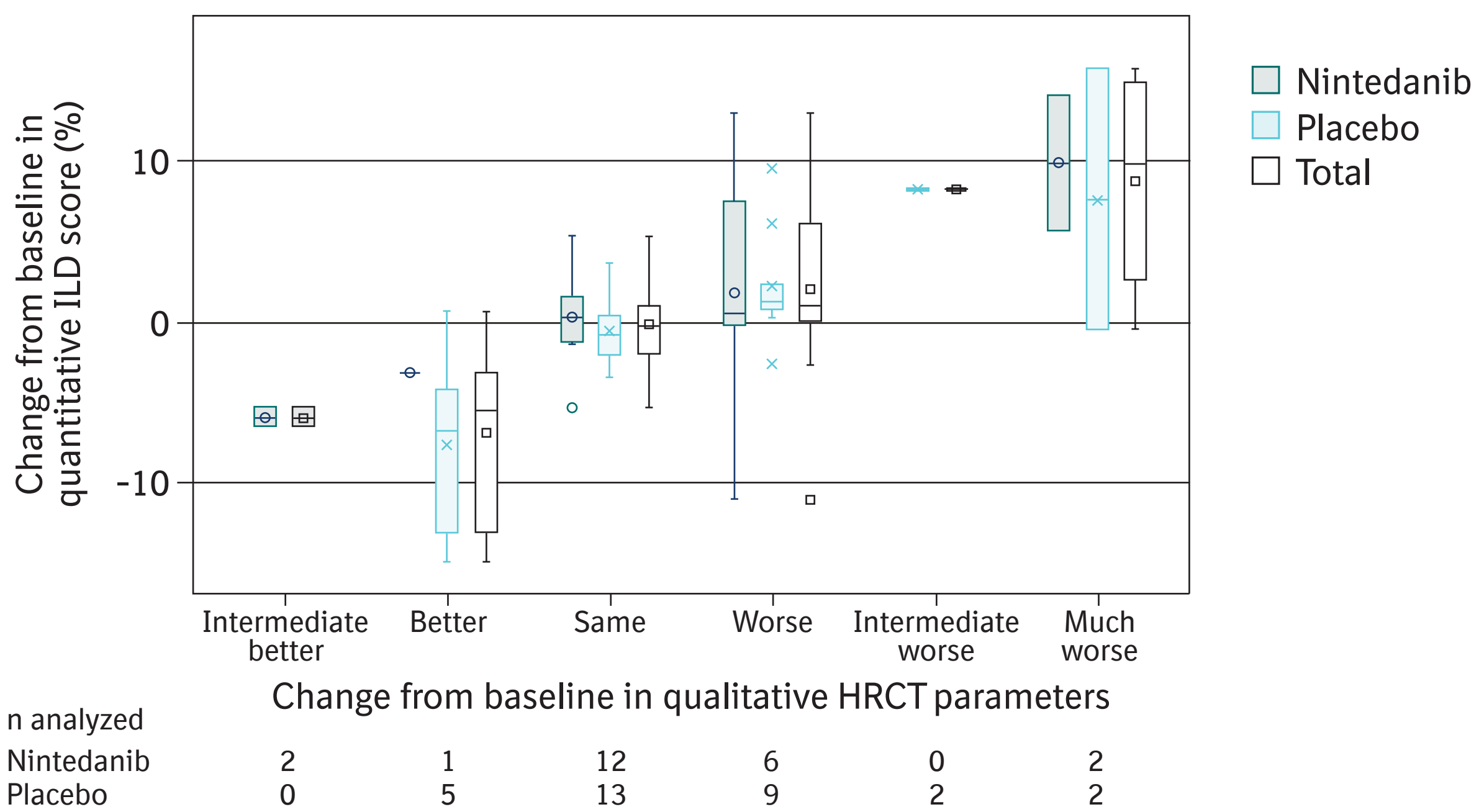
- Overall changes in quantitative HRCT parameters over 52/60 weeks were small. There were weak to moderate positive correlations between changes in qualitative HRCT parameters and changes in quantitative fibrosis score (Kendall’s τ -b correlation coefficients: placebo, 0.31 [95% CI: 0.08, 0.52]; nintedanib, 0.44 [0.18, 0.65]) and quantitative ILD score (placebo, 0.55 [0.36, 0.70]; nintedanib, 0.47 [0.21, 0.67]). These findings suggest that worsening in qualitative parameters was associated with worsening in quantitative parameters.

Associations between changes in qualitative HRCT parameters and changes in quantitative fibrosis score at week 52/60



The markers within the boxes denote the means, the mid-line of the boxes the medians, and the boundaries of the boxes the 25th and 75th percentiles. The upper whiskers denote the values 1.5x the interquartile range above the 75th percentile, the lower whiskers the values 1.5x the interquartile range below the 25th percentile and the markers outside the boxes values that fell outside the range of the whiskers.

Associations between changes in qualitative HRCT parameters and change in quantitative ILD score at week 52/60



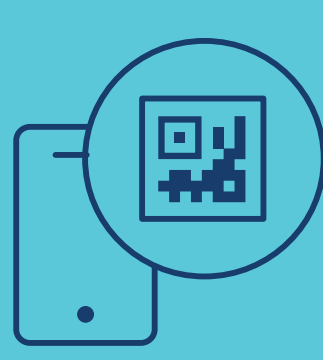
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