Table S1. Baseline characteristics at the start of TOMORROW period 1

| | **Placebo (n=85)** | **Nintedanib** | | | |
|---|---|---|---|---|---|
| | | **50 mg qd (n=86)** | **50 mg bid (n=86)** | **100 mg bid (n=86)** | **150 mg bid (n=85)** |
| Male, n (%) | 63 (74.1) | 65 (75.6) | 62 (72.1) | 65 (75.6) | 65 (76.5) |
| Age, years, mean (SD) | 64.8 (8.6) | 65.3 (9.4) | 64.9 (8.5) | 65.1 (8.6) | 65.4 (7.8) |
| Smoking history, n (%) | | | | | |
| Never smoked | 28 (32.9) | 27 (31.4) | 29 (33.7) | 32 (37.2) | 25 (29.4) |
| Ex/current-smoker | 57 (67.1) | 59 (68.6) | 57 (66.3) | 54 (62.8) | 60 (70.6) |
| Time since diagnosis, years, mean (SD) | 1.4 (1.5) | 1.4 (1.3) | 1.1 (1.2) | 1.2 (1.2) | 1.0 (1.2) |
| FVC, L, mean (SD) | 2.8 (0.8) | 2.8 (0.8) | 2.7 (0.7) | 2.9 (0.8) | 2.7 (0.8) |
| FVC, % predicted, mean (SD) | 81.7 (17.6) | 80.4 (17.8) | 79.8 (15.8) | 85.5 (19.2) | 79.1 (18.5) |
| $SpO_2$, %, mean (SD) | 95.3 (2.2) | 95.0 (2.7) | 95.4 (2.2) | 95.3 (2.0) | 95.6 (1.7) |
| DLco, % predicted, mean (SD) | 48.4 (12.9) | 46.2 (13.6) | 46.6 (12.7) | 48.7 (12.8) | 47.5 (11.0) |

Table S2. Summary of exposure to actual treatment dose received across TOMORROW periods 1 and 2 and the open-label extension trial

| **Randomised treatment in TOMORROW period 1** | **Actual treatment dose received** | **N** | **Duration of exposure (months)** | |
|---|---|---|---|---|
| | | | **Mean (SD)** | **Median (range)** |
| Placebo | Placebo | 85 | 10.6 (3.0) | 11.9 (0.3, 12.4) |
| Placebo | Nintedanib 50 mg qd | 53 | 12.7 (6.2) | 12.0 (2.6, 27.1) |
| Placebo | Nintedanib 50 mg bid* | 2 | 10.3 (2.8) | 10.3 (8.3, 12.3) |
| Placebo | Nintedanib 100 mg bid | 11 | 15.8 (15.8) | 13.3 (0.2, 52.6) |
| Placebo | Nintedanib 150 mg bid | 35 | 17.5 (18.2) | 8.3 (0.1, 55.8) |
| Placebo | Off-treatment† | 25 | 2.0 (1.3) | 2.0 (0.3, 6.0) |
| Nintedanib 150 mg bid | Nintedanib 150 mg bid | 85 | 21.4 (24.1) | 12.0 (0.1, 86.1) |
| Nintedanib 150 mg bid | Nintedanib 100 mg bid | 28 | 18.3 (21.2) | 6.8 (0.3, 68.9) |
| Nintedanib 150 mg bid | Off-treatment† | 24 | 2.4 (2.2) | 1.6 (0.4, 8.9) |

*Two patients were mistakenly marked as reduced dose at the end of TOMORROW period 1 and continued on 50 mg bid. †Duration off-treatment was calculated as the sum of all treatment interruptions. Of the 35 patients who increased their dose to nintedanib 150 mg bid, 11 had ≥1 dose reduction to 100 mg bid during the extension trial. Of the 35 patients in the nintedanib 150 mg bid group who entered the extension trial, three had ≥1 dose reduction to 100 mg bid in the extension trial.

Table S3. Patient characteristics at the start of the open-label extension trial

| | **Nintedanib 150 mg bid (n=35)** | **Comparator (n=37)** |
|---|---|---|
| Male, n (%) | 28 (80.0) | 23 (62.2) |
| Age, years, mean (SD) | 67.2 (7.0) | 66.2 (7.3) |
| Smoking history, n (%) | | |
| Never smoked | 12 (34.3) | 14 (37.8) |
| Ex/current-smoker | 23 (65.7) | 23 (62.2) |
| Time since diagnosis, years, mean (SD) | 2.9 (1.1) | 3.5 (1.6) |
| FVC, L, mean (SD) | 2.7 (0.9) | 2.4 (0.7) |
| FVC, % predicted, mean (SD) | 77.1 (21.4) | 73.0 (17.9) |
| DLco, % predicted, mean (SD) | 40.1 (14.4) | 38.9 (10.5) |

Data based on information collected at visit 1 in the open-label extension trial. Patients in the comparator group received placebo in period 1 of the TOMORROW trial and nintedanib 50 mg qd in period 2. Patients entered the extension trial on the dose that they were receiving at the end of period 2, but had the option to increase dose to nintedanib 150 mg bid. Dose reduction from 150 mg bid to 100 mg bid and treatment interruption were permitted for the management of adverse events.

Table S4. Exposure over TOMORROW periods 1 and 2 and the open-label extension trial

| | **Nintedanib 150 mg bid (n=85)** | **Comparator* (n=85)** |
|---|---|---|
| Exposure, months | | |
| Mean (SD) | 27.6 (26.5) | 28.1 (23.1) |
| Minimum, maximum | 0.1, 86.1 | 0.3, 92.8 |
| Exposure by category, n (%) | | |
| ≤3 months | 10 (11.8) | 6 (7.1) |
| >3 to ≤6 months | 10 (11.8) | 2 (2.4) |
| >6 to ≤12 months | 16 (18.8) | 20 (23.5) |
| >12 to ≤13 months | 2 (2.4) | 3 (3.5) |
| >13 months | 47 (55.3) | 54 (63.5) |

*Patients in the comparator group received placebo in TOMORROW period 1 and nintedanib 50 mg qd in period 2. Patients entered the extension trial on the dose that they were receiving at the end of period 2, but had the option to increase dose to 150 mg bid. Dose reduction from 150 mg bid to 100 mg bid and treatment interruption were permitted for the management of adverse events.

Table S5. Exposure by trial and treatment

| Trial(s) | Treatment | N | Duration of exposure (months) | |
|---|---|---|---|---|
| | | | Mean (SD) | Median (range) |
| TOMORROW period 1 | Placebo | 85 | 10.6 (3.0) | 11.9 (0.3, 12.4) |
| | Nintedanib 150 mg bid | 85 | 9.5 (3.7) | 11.7 (0.1, 12.8) |
| TOMORROW period 2 | Nintedanib 50 mg qd | 54 | 6.9 (4.9) | 5.9 (0.5, 18.0) |
| | Nintedanib 150 mg bid | 48 | 5.1 (2.9) | 5.2 (0.8, 10.0) |
| TOMORROW periods 1 and 2 | Comparator | 85 | 16.8 (7.8) | 18.2 (0.3, 32.9) |
| | Nintedanib 150 mg bid | 85 | 14.2 (7.8) | 16.1 (0.1, 26.0) |
| TOMORROW periods 1 and 2 and open-label extension trial | Comparator | 85 | 28.1 (23.1) | 21.6 (0.3, 92.8) |
| | Nintedanib 150 mg bid | 85 | 27.6 (26.5) | 16.1 (0.1, 86.1) |
| TOMORROW periods 1 and 2 and open-label extension trial, including only patients who entered the open-label extension trial | Comparator | 37 | 48.5 (20.7) | 43.4 (19.6, 92.8) |
| | Nintedanib 150 mg bid | 35 | 54.0 (21.7) | 43.3 (25.4, 86.1) |

Data from patients randomised in TOMORROW period 1 unless otherwise stated. Patients in the comparator group received placebo in period 1 of the TOMORROW trial and nintedanib 50 mg qd in period 2. Patients entered the extension trial on the dose that they were receiving at the end of period 2,

but had the option to increase dose to nintedanib 150 mg bid. Dose reduction from 150 mg bid to 100 mg bid and treatment interruption were permitted for the management of adverse events.