

| <b>Supplementary Table S3. Phase I nintedanib dose reductions and exposure</b> |                                   |                                   |                                   |                                  |                                   |                                   |                                   |
|--|-----------------------------------|-----------------------------------|-----------------------------------|----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|
|  | <b>Group I</b>                    |                                   |                                   | <b>Group II</b>                  |                                   |                                   |                                   |
|  | <b>Nintedanib,<br/>100 mg bid</b> | <b>Nintedanib,<br/>150 mg bid</b> | <b>Nintedanib,<br/>200 mg bid</b> | <b>Nintedanib,<br/>50 mg bid</b> | <b>Nintedanib,<br/>100 mg bid</b> | <b>Nintedanib,<br/>150 mg bid</b> | <b>Nintedanib,<br/>200 mg bid</b> |
| Number of dose reductions, <i>n</i> (%)  |                                   |                                   |                                   |                                  |                                   |                                   |                                   |
| 0  | 6 (100)                           | 3 (100)                           | 2 (50.0)                          | 3 (100)                          | 4 (100)                           | 3 (75.0)                          | 6 (75.0)                          |
| 1  | 0                                 | 0                                 | 2 (50.0)                          | 0                                | 0                                 | 1 (25.0)                          | 0                                 |
| 2  | 0                                 | 0                                 | 0                                 | 0                                | 0                                 | 0                                 | 2 (25.0)                          |
| Median time to first dose reduction, days (range)                              | -                                 | -                                 | 306.5 (283–330)                   | -                                | -                                 | 15.0                              | 67.5 (32–103)                     |
| Median dose intensity  | 100%                              | 100%                              | 99.3%                             | 100%                             | 100%                              | 100%                              | 100%                              |
| Median duration of treatment, days (range)                                     | 214 (30–785)                      | 241 (226–483)                     | 559 (43–1,261)                    | 130 (93–456)                     | 68.5 (42–113)                     | 100.5 (20–336)                    | 74.5 (27–365)                     |