Supplementary Online Material

Exclusion criteria

Patients could not participate in the trial if they met any of the following exclusion criteria:

1. ALT, AST of >1.5-fold upper limit of normal (ULN) at Visit 1
2. Total bilirubin of >1.5-fold ULN at Visit 1
3. Underlying chronic liver disease (Child Pugh A, B, or C hepatic impairment). Laboratory parameter could be re-tested within the permitted timeframe, if found abnormal at Visit 1 and thought to be a measurement error or was the result of a temporary and reversible medical condition. It was not required that the Child Pugh classification was performed at screening
4. Relevant airways obstruction (i.e. pre-bronchodilator FEV1/FVC of <0.7 at Visit 1)
5. History of myocardial infarction within 6 months of Visit 1 or unstable angina within 1 month of Visit 1
6. Bleeding risk:
    a. Known genetic predisposition to bleeding
    b. Patients who required fibrinolysis, full-dose therapeutic anticoagulation (e.g. vitamin K antagonists, dabigatran, heparin, and hirudin) or high dose antiplatelet therapy
        i. Exceptions were prophylactic low dose heparin or heparin flush as needed for maintenance of an indwelling intravenous device (e.g., enoxaparin 4000 IU s.c. per day) and prophylactic use of antiplatelet therapy (e.g. acetyl salicylic acid up to 325 mg/d, or clopidogrel at 75 mg/d, or equivalent doses of other antiplatelet therapy)
    c. History of haemorrhagic central nervous system (CNS) event within 12 months prior to Visit 1
    d. History of haemoptysis or haematuria, active gastrointestinal bleeding or ulcers and/or major injury or surgery within 3 months prior to Visit 1
    e. International normalised ratio (INR) of >2 at Visit 1
    f. Prothrombin time (PT) and partial thromboplastin time (PTT) of >150% of institutional ULN at Visit 1
7. Planned major surgery during the trial participation, including lung transplantation, major abdominal or major intestinal surgery (per investigator judgement)
8. History of thrombotic event (including stroke and transient ischemic attack) within 12 months of Visit 1

9. Severe renal impairment (creatinine clearance of <30 mL/min calculated by Cockcroft–Gault formula at Visit 1) or end-stage renal disease requiring dialysis
10. Treatment with n-acetylcysteine, prednisone of >15 mg daily or of >30 mg every 2 days or equivalent dose of other oral corticosteroids or fluvoxamine within 2 weeks of Visit 2
11. Treatment with azathioprine, cyclophosphamide, cyclosporine as well as any other investigational drug within 8 weeks of Visit 2
12. Previous treatment with pirfenidone in the past 3 months prior to Visit 2 (Group 1)
13. Previous treatment with nintedanib in the past 14 days prior to Visit 2
14. Permanent discontinuation of nintedanib or pirfenidone in the past due to adverse events considered drug-related
15. Known hypersensitivity to nintedanib, pirfenidone, or their excipients; or to peanut or soya
16. A disease or condition which in the opinion of the investigator could have interfered with the testing procedures or put the patient at risk when participating in this trial
17. Alcohol or drug abuse, which in the opinion of the treating physician would have interfered with treatment
18. Women who were pregnant, nursing, or who planned to become pregnant
19. Women of childbearing potential not using highly effective methods of birth control per ICH M3 [R09-1400]. Highly effective methods of birth control were defined as those, alone or in combination, that resulted in a low failure rate of <1% per year when used consistently and correctly such as implants, injectables, combined oral contraceptives, some intrauterine devices (IUDs), sexual abstinence or vasectomised partner. Barrier contraceptives (e.g. male condom or diaphragm) were acceptable if used in combination with spermicides (e.g. foam, gel). Contraception had to be used for 28 days prior to and 3 months after nintedanib and pirfenidone administration. Women of childbearing potential were defined as any female who has experienced menarche and does not meet the criteria for ‘women not of childbearing potential’ defined as women who are postmenopausal (12 months with no menses without an alternative medical cause) or who are permanently sterilised (e.g. tubal occlusion, hysterectomy, bilateral oophorectomy, or bilateral salpingectomy)
20. Patients not able to understand and follow study procedures including completion of diaries without help
21. Current smoker (vaping and e-cigarettes were acceptable)

Safety evaluation

Adverse events were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 20.0; the intensity of diarrhoea, nausea, and vomiting events were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 4.03. Spirometry and ECG measurements were performed at regular intervals throughout the study. Any abnormalities at screening were captured as a baseline condition. Thereafter they were reported as an adverse event.

Concomitant disease diagnoses at baseline

System organ class/preferred term	**Group 1 n (%)**	**Group 2 n (%)**
Cardiac disorders	**8 (40.0)**	**4 (23.5)**
Vascular disorders	**5 (25.0)**	**4 (23.5)**
Respiratory, thoracic and mediastinal disorders	**5 (25.0)**	**4 (23.5)**

Concomitant therapies on-treatment

The majority of patients in Group 1 and Group 2 took at least 1 concomitant therapy on-treatment. On preferred name level, these primarily included lansoprazole, acetylsalicylic acid, metformin, paracetamol, and levothyroxine.