**Supplementary file for:**

**Rationale, design and objectives of two phase III, randomised, placebo-controlled studies of GLPG1690, a novel autotaxin inhibitor, in idiopathic pulmonary fibrosis (ISABELA 1 and 2)**

## Authors

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## *Dissemination*

No datasets have been generated or analysed at this time; all available information regarding the studies to date has been included in the article.

Protocol amendments will be submitted to the Independent Ethics Committee (IEC)/Institutional Review Board (IRB) for review and approval prior to implementation (unless an immediate modification is necessary to avoid a hazard to subjects). The IEC/IRB will receive a progress report from the investigator at least once a year. Study reports will be written upon completion of the studies and the results will be reported in a peer-reviewed publication. An independent quality assurance representative, regulatory authorities and/or IECs/IRBs may review the study; auditors/inspectors will have access to data from the studies, source documents and subjects’ files.

Table 1. Schedule of assessments

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Event** | **Screening period** | | | **First 52 weeks of study treatment** | | | | | | | | | | **After 52 weeks of study treatment** | | | | |
| **Study visit** |  | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** | **Every 12 weeks up to EoST/**  **EoSA**  **±7d** | **Every 24 weeks up to EoST/**  **EoSA**  **±7d** | **ETD** | **EoST/**  **EoSA** | **FU** |
| **Study days (D) or weeks (W) ± visit window** |  | **D–28 to  D–1** | | **D1** | **W2 ±2d** | **W4**  **±2d** | **W8**  **±4d** | **W12**  **±4d** | **W18**  **±4d** | **W26**  **±4d** | **W34**  **±4d** | **W42**  **± 4d** | **W52**  **±4d** |  |  | **4 weeks after EoST/EoSA ±7d** |
| Informed consent |  | ✓ |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| FSH (if applicable) and serology |  | ✓ |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| HRCT/LB sent for central review |  | ✓ |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Inclusion/exclusion criteria |  | ✓ | ✓ |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Demographics and medical history |  | ✓ |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Alcohol consumption and smoking habits |  | ✓ |  | ✓ |  |  |  |  |  | ✓ |  |  | ✓ | ✓ |  | ✓ | ✓ |  |
| Physical examination and vital signs |  | ✓ |  | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |  | ✓ | ✓ |  |
| ECG triplicate recording |  | ✓ |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| ECG triplicate recording before and 2–3 h after IMP intake |  |  |  | ✓ | ✓ |  |  |  |  |  |  |  |  |  |  |  |  |  |
| ECG single recording before IMP intake |  |  |  |  |  | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |  |  |  |  |
| ECG single recording 2–3 h after IMP intake |  |  |  |  |  | ✓ |  | ✓ |  |  | ✓ |  |  |  |  |  |  |  |
| ECG single recording |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | ✓ | ✓ |  |
| Pregnancy test (serum) |  | ✓ |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pregnancy test (urine) |  |  |  | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |  | ✓ | ✓ |  |
| Clinical laboratory tests |  | ✓ |  | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |  | ✓ | ✓ |  |
| Spirometry |  | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |  | ✓ | ✓ |  |
| DLCO |  | ✓ |  | ✓ |  |  |  |  |  | ✓ |  |  | ✓ |  | ✓ |  |  |  |
| Oxygen saturation test |  | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |  | ✓ | ✓ |  |
| 6MWT and Borg scale |  | ✓ | ✓ | ✓ |  |  |  |  |  | ✓ |  |  | ✓ |  | ✓ |  |  |  |
| Randomisation |  |  |  | ✓ |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Dispense IMP |  |  |  | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |  |  |  |  |
| Collect IMP/perform drug accountability |  |  |  |  | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |  | ✓ | ✓ |  |
| Diary card collection for drug accountability |  |  |  | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |  | ✓ | ✓ |  |
| EQ-5D, SGRQ, LCQ K-BILD questionnaire, VAS Cough and Urge to Cough |  | ✓ |  | ✓ |  |  |  |  |  | ✓ |  |  | ✓ |  | ✓ | ✓ | ✓ |  |
| Intake P and N at clinical study centre |  |  |  | ✓ |  |  |  |  |  | ✓ |  |  | ✓ |  |  |  |  |  |
| PK blood samples 2–4 h, and 5–10 h after N intake |  | ✓ |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| PK blood samples before IMP and P or N intake |  |  |  | ✓ |  |  |  |  |  | ✓ |  |  | ✓ |  |  |  |  |  |
| PK blood samples before IMP but after P or N intake |  |  |  |  |  |  |  | ✓ |  |  | ✓ |  |  |  | ✓ |  |  |  |
| PK blood samples 2–5 h after N intake and before IMP |  |  |  |  | ✓ | ✓ | ✓ | ✓ | ✓ |  | ✓ | ✓ |  | ✓ |  |  |  |  |
| PK blood samples 2–3 h after IMP intake |  |  |  |  |  |  |  | ✓ |  |  | ✓ |  |  |  |  |  |  |  |
| PK blood samples |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | ✓ | ✓ |  |
| Target biomarker/PD blood samples (LPA) |  | ✓ |  |  |  |  |  |  |  |  |  |  |  |  |  | ✓ | ✓ |  |
| Target biomarker/PD blood samples (LPA) before IMP intake |  |  |  | ✓ |  |  |  | ✓ |  | ✓ | ✓ |  | ✓ |  | ✓ |  |  |  |
| Target biomarker/PD blood samples (LPA) 2–3 h after IMP intake |  |  |  |  |  |  |  | ✓ |  |  | ✓ |  |  |  |  |  |  |  |
| Disease-specific biomarker blood samples |  | ✓ |  |  |  |  |  |  |  |  |  |  |  |  |  | ✓ | ✓ |  |
| Disease-specific biomarker blood samples before IMP intake |  |  |  | ✓ |  |  |  | ✓ |  | ✓ |  |  | ✓ |  | ✓ |  |  |  |
| Blood sample for genotype analysis |  |  |  |  | ✓ |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Vital status |  |  |  |  |  |  |  |  |  |  |  |  | ✓ |  |  | ✓ | ✓ | ✓ |
| Study medication intake |  |  |  | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |  |  |  |
| AE assessment, concomitant medication assessment and documentation |  | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |

6MWT, 6-Minute Walk Test; AE, adverse event; DLCO, diffusing capacity of the lung for carbon monoxide; ECG, electrocardiogram; EQ-5D, EuroQoL 5-Dimensions Questionnaire; EoSA, end-of-study assessment; EoST, end-of-study treatment; ETD, early treatment discontinuation (i.e. before the EoST/EoSA visit); FSH, follicle-stimulating hormone; FU, follow-up; HRCT, high-resolution computer tomography; IMP, investigational medicinal product; K-BILD, King’s Brief Interstitial Lung Disease; LB, lung biopsy; LCQ, Leicester Cough Questionnaire; LPA, lysophosphatidic acid; N, nintedanib; P, pirfenidone; PD, pharmacodynamics; PK, pharmacokinetic; SGRQ, St. George’s Respiratory Questionnaire; VAS, Visual Analogue Scale