BACKGROUND

Dysregulation of fibroblast growth factor receptor (FGFR) signaling by FGFR fusions is implicated in many cancers. Debio 1347 is a selective oral inhibitor of FGFR 1-3 tyrosine kinases. It exhibited high antitumor activity in vitro and in vivo tumor models with FGFR1-3 gene fusions. 1,2

Results from dose-escalation part of ongoing Phase 1 (NCT01948297) show efficacy and tolerability in patients harboring FGFR 1-3 fusion irrespectively of tumor type.3

Here we present the design for a multicenter, basket, 2-stage, adaptive single arm Phase 2 trial investigating Debio 1347 in patients with solid tumors harboring FGFR1-3 fusion/rearrangement.

ELIGIBILITY

Main Inclusion Criteria
- Cytologically or histologically confirmed advanced solid tumor
- Age ≥18 years
- Locally-advanced (unresectable) or metastatic disease harboring an FGFR1-3 gene fusion/rearrangement
- The subject must have received at least one prior line of standard therapy appropriate for tumor type and stage of disease (if available)
- Measurable disease according to RECIST criteria version 1.1
- Eastern Cooperative Oncology Group performance status 0 to 1
- Laboratory values:
  - Total bilirubin ≤ 2 x UNL
  - Creatinine clearance ≥ 30 mL/min
  - AST and ALT ≤ 2.5 x UNL (5 x UNL in the presence of liver metastases)
  - Serum Phosphate < 1.5 x UNL

Main Exclusion Criteria
- Chemotherapy, radiotherapy or small molecule anti-cancer agents within 2 weeks prior to initial dosing with Debio 1347
- Prior treatment with a FGFR1-3 selective inhibitor
- Known evidence of clinically significant corneal/retinal disorder confirmed by ophthalmologic examination
- History and/or current evidence of ectopic mineralization/calcification
- Symptomatic or unstable brain metastases < 1 month

STUDY OBJECTIVES

Primary
- Efficacy of Debio 1347 in terms of objective response rate (ORR)

Secondary
- Efficacy of Debio 1347 in terms of duration of response (DoR), DCR, PFS and OS
- To assess the safety of Debio 1347
- To assess exposure-response relationships vs efficacy & safety (notably QTcF)

Exploratory
- To assess the effects of intrinsic factors and extrinsic factors on the PK of Debio 1347
- Impact of biomarkers on Debio 1347 efficacy
- To assess patient-reported outcome - QOL questionnaire

STATUS

FUZE is a worldwide clinical trial with participating countries in blue
Recruitment started in February 2019
NCT03834220

STUDY DESIGN

Adaptive Phase-2, non-controlled, open-label, multicenter study (NCT03834220)

Subjects with solid tumors harboring FGFR1-3 gene fusion/rearrangement:

I. Cohort 1: biliary tract cancer
II. Cohort 2: urothelial cancer
III. Cohort 3: other solid tumor histologies (Non-Small Cell Lung Cancer (NSCLC), head and neck cancer, thyroid cancer, oral cancer, breast cancer, prostate cancer, and other malignancies but excluding primary brain tumors)

Debio 1347 will be administered at 80 mg once daily (in the morning), with each cycle consisting of 28 days of dosing administered on a continuous basis in 28-day cycles until progression of disease or unacceptable toxicity.

Subjects will be treated with Debio 1347 daily in 28-day cycles until the occurrence of disease progression or unacceptable toxicity.

An interim analysis for futility and homogeneity will be performed after 27 evaluable patients.