NVALT 15 Study

Study Title:

Phase II study with oral fibroblast growth factor-1 inhibitor BIBF1120 as second line treatment in lung carcinoma patients harboring fibroblast growth factor receptor-1 gene amplification

Rationale: Array comparative genomic hybridization (aCGH) showed amplifications of the 8p11-p12 region including the FGFR1 locus in 40% of patients with squamous cell lung carcinoma. In 12 to 18% of the samples high copy number amplification region containing FGFR1 were observed. With FISH technique FGFR1 amplifications were detected in more than 20% of cases. This focal amplification associates with therapeutically tractable FGFR1 dependency in predominantly squamous cell lung cancer. BIBF1120 is a potent oral inhibitor of fibroblast growth factor receptor 1 and 3. We hypothesized that patients with an amplified FGFR1 gene in their tumor cells will show an improved PFS to BIBF1120.

Objective: The primary objective is 6 month progression-free survival (1/2-year PFS) of lung cancer patients who have an FGFR1 gene amplified in their tumor cells upon second line treatment with BIBF1120. The secondary objective is to assess tumor response rate, duration of tumor response, overall survival and safety.

Study design: A multicenter phase II study in squamous and large cell lung cancer with FGFR1 amplification will be performed. Patients will be treated with oral BIBF1120 200 mg bid. The FGFR1 amplification status should be available at the start of treatment. Because this amplification is most prevalent in squamous and large cell lung cancer patients this group of patients will be included. The anticipated 6 months PFS for low (> 2 but < 9 copies) and high (≥ 9 copies) amplified FGFR1 treated with BIBF1120 is 28 and 45%, respectively. In a historical control group treated with standard chemotherapy the 6 months PFS was 25%. The study has a one-stage design to elucidate any activity of BIBF1120.

Study population: Patients with FGFR1 positive FISH (>2 copies) and histologically confirmed squamous or large cell lung cancer, stage IV or recurrent disease with a life expectancy of at least 3 months and with Eastern Cooperative Oncology Group (ECOG) score of 0, 1 who have been treated previously with one line of chemotherapy.

Intervention: BIBF1120 soft gelatin capsule 200 mg bid.

Start date: unknown

Total number of patients:
To detect an improvement in 6-month PFS beyond 25% requires 80 patients. If this stage is successful then a large trial is considered. If unsuccessful the study will be terminated. All patients are required to deliver tumor biopsy for FGFR1 FISH evaluation and translational research.

Study Coordinator:
Prof.dr. H.J.M. Groen, UMCG Groningen

Centraal Data Management:
NVALT Data Center, Amsterdam