Additional file 2

Article title: Larotinib in Patients with Advanced and Previously Treated Esophageal Squamous Cell Carcinoma with Epidermal Growth Factor Receptor Overexpression or Amplification: An Open-Label, Multicenter Phase 1b Study

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Additional file 2: Supplementary Materials and Methods

Protocol revisions

The study was originally designed as a randomized, open-label, multi-center clinical trial, the treatment groups were 350 mg and 300 mg. After enrolling 10 patients, there were 4 patients (3 of 5 patients in the 350 mg group and 1 of 5 patients in the 300 mg group) required dose reduction due to intolerability. A protocol amendment was made with the dose groups adjusted to 300 mg and 250 mg to ensure subject safety. However, when more safety and efficacy data were collected (one patient in 250 mg group, 15 patients in each 300 mg and 350 mg group), we re-evaluated the safety and efficacy of these three doses, and determined 350 mg to be the effective dose. Therefore, the study was ultimately designed as a single-arm, open-label study at 350 mg dose.