Additional file

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 6: Preclinical Tissue Distribution Study

Purpose: This tumor distribution study was aimed to confirm whether larotinib had a better distribution than other EGFR-TKIs in esophageal tumor tissues.

Methods: SD rats (males) were given as single daily dose of 5 mg/kg larotinib as well as other EGFR-TKIs (oral administration). Subsequently, the rats were anesthetized at 1, 4, and 8 h. Blood was collected via caudal vein and transferred into heparinized tubes immediately. The collected samples were centrifuged at 3000 rpm for 15 min, and the supernatant plasma was transferred into another tube and stored at −70 °C until analysis. Stomach, lung, liver, esophagus, colon, pancreas, rectum, galactophore and prostate were excised, rinsed with 0.9% (weight volume) saline, and gently blotted with absorbent paper to remove surface saline and blood. The obtained samples were labelled and stored at -70 °C until analysis.

Results: The mean concentration-time profiles of each tissue are summarized in Figure S2, indicating that larotinib was well absorbed after oral administration. This was attributed to the fact that all the tissue concentrations were kept at higher levels after administration at 1, 4 and 8 h. We also found that larotinib showed higher concentrations than other EGFR-TKIs, especially in esophageal tissues. The ratio of esophagus tissue/plasma was 61 times that of EGFR-TKI at 1 h after treatment (Fig. S2; Table S5).

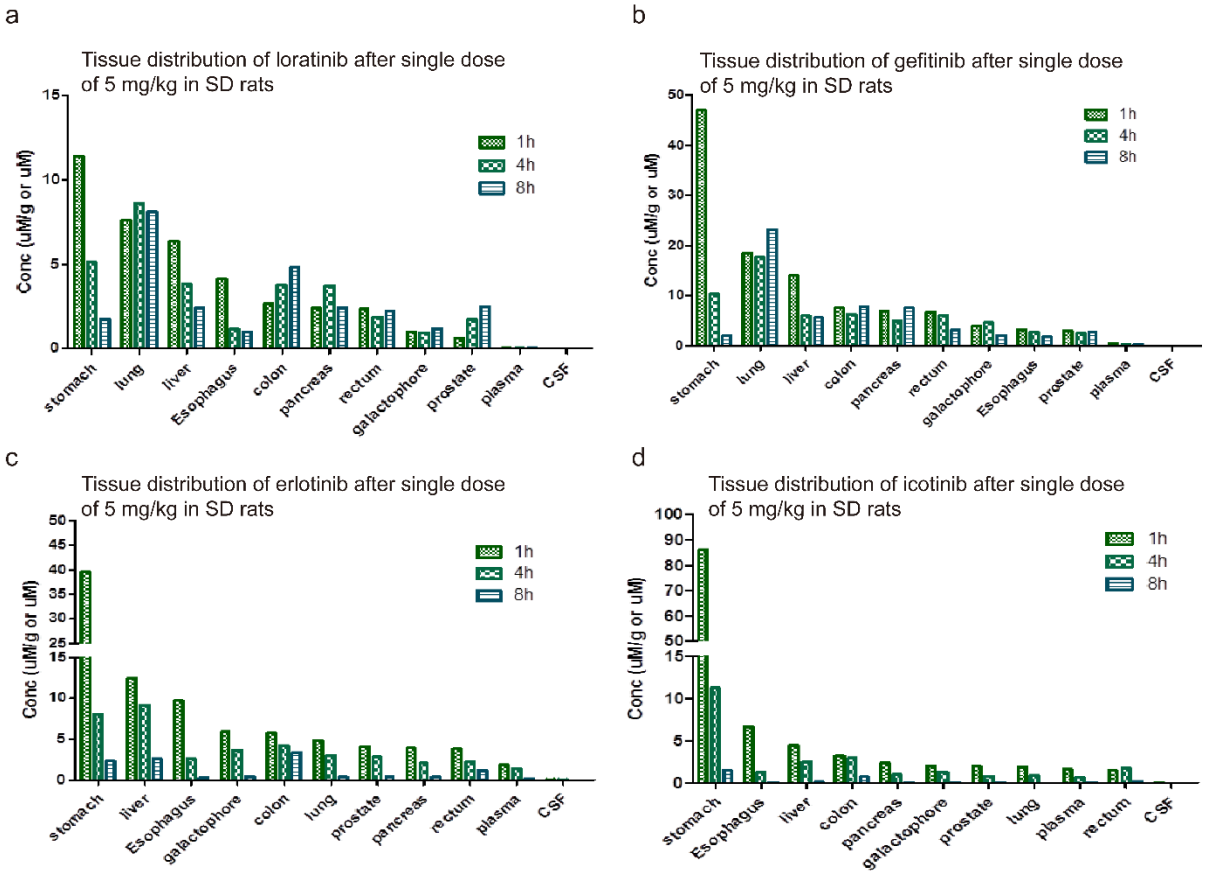

Fig. S2 The mean concentration-time profile of each tissue sample. a) larotinib; b) gefitinib; c) erlotinib; d) icotinib

Table S5 Ratio of esophageal /plasma of different EGFR-TKIs at different time points

Drugs/Time	Ratio of esophageal /plasma		
	1h	4h	8h
Larotinib	61	35	17
Gefitinib	7.6	13	5.5
Erlotinib	5.2	2	1.5
Icotinib	4.1	1.9	1.9