**Supplementary Fig. S1.** Baseline (A, B) and week 8-12 (C,D) CT in two patients treated with regorafenib. A,B: the arrow highlights single tumor metastases with cavitation. C, D: cavitation in multiple lung metastases.

**Supplementary Fig. S2.** Kaplan–Meier estimates of (A) progression-free survival and (B) overall survival in patients with lung and/or liver lesions (full analysis set). Blue solid line: positive cases of changes on imaging in the absence of post-regorafenib chemotherapy. Blue dotted line: negative cases of changes on imaging in the absence of post-regorafenib chemotherapy. Red solid line: positive cases of changes on imaging following post-regorafenib chemotherapy. Red dotted line: negative cases changes on imaging following post-regorafenib chemotherapy.

**Supplementary Fig. S3.** Forest plots of hazard ratios for (A) progression-free survival and (B) overall survival in patients with lung metastases.