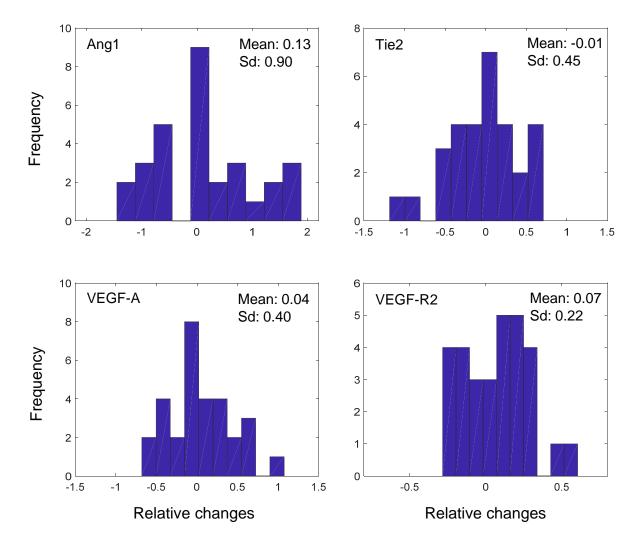


## sFigure 1. Study Design

A study CONSORT diagram showing patient enrolment in CIRCCa and in the associated translational biomarker study. There were six treatment naïve stage IVb patients in the CIRCCa trial who were not included in the translational study due to a lack of longitudinal samples.



## sFigure 2. Pre-treatment variation of plasma biomarkers

Variation of plasma biomarker concentrations were estimated as log2 transformed ratio of two pretreatment measurements. Thirty-two out of the total 52 patients contributed to this analysis due to availability of samples. Histograms of the observed variations were demonstrated with the maximum and minimum variation values excluded to remove potential outliers. The mean and standard deviation of variation were annotated.