**Supplementary**

*Tissue selection, DNA extraction and sequencing*

For DNA isolation, the area of interest was marked on H&E stained tissue slides and then macrodissected by scratching. The DNA was isolated using the Maxwell DNA purification kit according to the manufacturer’s protocol. The DNA concentration was quantified using the Qubit® dsDNA HS Assay Kit (ThermoFisher Scientific). The Ion AmpliSeq Library Kit V.2.0 (ThermoFisher Scientific) was used to prepare the libraries from 10-20 ng of DNA. The Ion Ampliseq HiFi Master Mix (ThermoFisher Scientific) was used to prepare the amplicons that were digested with FUPA reagent in order to remove primer-specific sequences and tagged with the IonCode Barcode Adapters. Finally, the amplified products were purified by performing a two-step cleanup using the Agencourt AMPure XP PCR purification system (Beckman Coulter, California, USA) at a bead to sample ratio of 1.15X and 1.0X, respectively. The Ion Library Equalizer Kit method was used to normalize the library concentration at ~100 pM. Finally, equal volumes of normalized DNA library were combined and amplified on Ion Sphere particles (ISP; ThermoFisher Scientific) by emulsion PCR using the Ion PI HiQ OT2 200 Kit (both ThermoFisher Scientific). Quality control was performed using the Ion Sphere Quality Control kit (ThermoFisher Scientific) to ensure that 10%–30% of template positive ISP were generated in the emulsion PCR. The template-positive Ion PI ISP were loaded on an Ion PI Chip and sequenced on an Ion S5TM XLSequencer (ThermoFisher Scientific) with the Ion PI HiQ Sequencing 200 Kit (ThermoFisher Scientific) according to the manufacturer’s instructions.

*Data analysis*

Raw data was processed automatically on the Torrent Server™ and aligned to the reference hg19 genome. NGS data analysis was performed on Ion Reporter Analysis Software (ThermoFisher Scientific) using the AmpliSeq Colon-Lung single sample workflow. QC was performed manually for each sample based on the following metrics; number of reads per sample >500’000 on-target reads > 90%, read uniformity > 90%, mean read coverage > 2000. The sequencing data of the QC passing samples was then uploaded in BAM format to the Ion Reporter™ Analysis Server for variant calling and annotation.Variants were filtered based on Phred score > 50, allele coverage > 500, and a minimum allele frequency of 2%. Furthermore, polymorphisms were filtered against UCSC common SNP, ExAC, 1000 Genomes, and 5000Exomes databases.

*Sequencing panel*

Oncomine™ Solid Tumour DNA Panel (22 Gene, exon analyzed in bracket): AKT1(3), ALK(22,23,25), BRAF(11,15), CTNNB1(3), DDR2(5,8,12,13,14,15,17), EGFR(12,18,19,20,21), ERBB2(19,20,21), ERBB4(3,4,6,7,8,9,15,23), FBXW7(5,8,9,10,11), FGFR1(4,7), FGFR2(7,9,12), FGFR3(7,9,14,16,18), KRAS(2,3,4), MAP2K1(2), MET(2,14,16,19), NOTCH1(26,27), NRAS(2,3,4), PIK3CA(10,14,21), PTEN(1,3,6,7,8), SMAD4(3,5,6,8,9,10,11,12), STK11(1,4,5,6), TP53(2,4,5,6,7,8,10)

*Sanger sequencing*

*FGFR1* (exon 7) and *TRPV4* (exon 12) mutations were screened by Sanger sequencing. Primers were designed using Primer3 online software (http://bioinfo.ut.ee/primer3-0.4.0/). Primer sequences used for the amplification of *FGFR1* (exon7) and *TRPV4* (exon 12) were respectively: (Forward) 5’ GCTTGTCCATTTTGCTTCCGT 3’, (Reverse) 5’ GCAGGACATCGAGAGGAGAA 3’ and (Forward) 5’ CGAGACCTTCAGCACCTTCC 3’, (Reverse) 5’ GCTTCCAGATGTGCTTGCTC 3’. PCR products were bidirectionally sequenced on an ABI 3130XL Genetic Analyzer (Applied Biosystems, USA) and resulting chromatograms were visualized using ABI Prism 3130 Genetic Analyzer (Applied Biosystems, USA). PCR conditions are available upon request.