**SUPPLEMENTARY METHODS**

**Sanger sequencing**

The MSH6 genomic region surrounding the c.3438+1G>A\* mutation was amplified using AmpliTaq Gold (Applied Biosystems, Foster City, CA, USA), with the following primer pair: forward, 5′- GCAGGAAAATGGCAAAGCCT-3′ and reverse, 5′- CAGGGAGTAATTTCCCTTTGCTTC-3′. Upon agarose-gel quality control, PCR products (215 bp) were purified with Illustra ExoSAP-IT ExoProStar (GE Healthcare, Buckinghamshire, UK) and underwent Sanger sequencing on the ABI 2720 thermal cycler (Applied Biosystems). Amplicons were sequenced using BigDye Terminator Cycle Sequencing Kit v1.1 on the ABI Prism 3730xl DNA Analyzer (Applied Biosystems) in both directions.

**IDH1/2 mutations**

Sanger sequencing of IDH1 and IDH2 genes (exon 4) was performed to identify all mutations at codon 132 and 172, respectively.

**Fluorescence in situ hybridization (FISH)**

FISH was performed on 4 μm paraffin-embedded sections with ZytoLight SPEC EGFR/CEN 7 dual color probe (ZytoVision, Bremerhaven, Germany) following standard procedures. Analyses were carried out with a fluorescence Zeiss microscope AxioImager Z2 (Zeiss, Göttingen, Germany) and TissueFISH software (Metasystems, Germany) in one hundred non-overlapping nuclei. Amplification of EGFR was defined as ratio EGFR/CEP7 ≥ 2 or average of EGFR copy number ≥ 6 copies/nucleus. In the presence of heterogeneous pattern, a case was considered amplified if the population of amplified cells was greater than 10% of the whole tumour.