Supplementary Tables Legend

Supplementary Table S1. Patient characteristics. Clinical characteristics for each patient are listed in this table, along with mean target coverage data for germline, pre-treatment, and resistant tumors (if available).

Supplementary Table S2. Mutations seen exclusively in resistant tumors. For patients with whole exome sequencing data on both pre-treatment and resistant tumors (n = 32), this table summarizes the complete set of non-synonymous mutations and short insertion/deletions called only in the resistant but not pre-treatment tumors. Alterations in this table met the additional criteria of at least 30X coverage in the tumor and an allelic fraction of at least 0.05. Each column is a patient, each row is a gene, and each non-blank entry denotes the protein change that results from the mutation.

Supplementary Table S3. Mutations seen in patients with tumors at one time point. For patients with whole exome sequencing data on either pre-treatment (for early resistance cases) or after relapse (for acquired resistance cases), this table summarizes the complete set of non-synonymous mutations and short insertion/deletions called. Alterations in this table met the additional criteria of at least 30X coverage in the tumor and an allelic fraction of at least 0.05. Each column is a patient, each row is a gene, and each non-blank entry denotes the protein change that results from the mutation seen.

Supplementary Table S4. Complete listing of all somatic mutations seen in all tumors. This table provides details on every non-synonymous mutation or short insertion/deletion observed in this cohort, with data on genomic coordinates, protein change, protein region affected, and read counts for each event. Many additional annotations are provided (e.g. cDNA change, RefSeq number).

Supplementary Table S5. PI3K pathway alterations. This table provides additional details on the PI3K pathway alterations observed in this cohort. Additional information regarding the time point, protein change, and appropriate reference are provided. Biopsy time point entries in gray denote situations where the tumor was unavailable for sequencing. Allelic fractions in bold denote situations where there is evidence for loss of the alternate allele between time points. (PMID = PubMed identification number). For activating or inactivating alterations, predicted function was derived by review of the published literature. The “likely” designation was reserved for alterations that occurred at the same amino acid residue as reported events but involved different changes at that site. For remaining missense mutations, “Probably Damaging” and “Possibly Damaging” designations were obtained from PolyPhen2 *in silico* predictions; alterations that met that criteria had PolyPhen2 scores between 0.9 and 1. Remaining nonsense mutations were considered “Probably Damaging”.