Supplementary Methods

RNAseq

RNA sequencing was performed on available tumor tissue. Isolated RNA was subjected to library construction using the TruSeq RNA Access Library Prep Kit Rev B and sequenced on an Illumina NextSeq 500 using paired 75 bp reads. Raw FastQ files were quality-trimmed using cutadapt (cutadapt-1.9.1) and aligned using GSNAP (1) (v2013-11-27, command line parameters -B 5 -A sam -N 1 -t 8 -s splicesites --quality-protocol=sanger --gunzip --sam-multiple-primaries --maxsearch=1000 --npaths=100) to build 37.p5 of the human genome. Read counts were quantified using a custom Perl script and summarized at the gene level (NCBI h37.p13 annotation) and quantile-normalized using a custom R script, requiring a minimum of 7.5M reads for inclusion in the analysis and reported as log2 of mean exon reads. Samples from patients whose biopsy was obtained outside the 2-weeks (before Day 13 or after Day 15) window of study treatment or from patients who went off study treatment (>4 days) before biopsy at the 16-week timepoint were also excluded for analysis.

MODAplex Analysis

Extracted RNA was reverse-transcribed using Superscript Vilo III (Invitrogen). The cDNA was then pre-amplified using Taqman 2x Preamp Master Mix (Thermo Fisher). For gene expression, qPCR was performed on the MODAplex platform (Qiagen). Twenty-eight cell cycle-related genes (GoI) were analyzed, along with 3 reference genes; TBP, PGK1, and PPIB. The MODAplex software generated Ct values for each gene of interest, as well as the reference genes. The relative expression was calculated for each gene of interest using the average of the reference genes based on modification of the standard delta Ct (2). The expression was calculated as follows: 2^(20-Ct GoI + Ave Ct Reference Gene)/1000.

Staining and quantification of tumor-infiltrating lymphocytes (TILs)

The scoring of the stroma TILs was determined histopathologically on hematoxylin-and-eosin stained FFPE section and given a category of A, B, or C according to the Bloom–Richardson method (3). Category A indicated a tumor stroma with no or minimal cells (0%-to-10%); Category B represented an intermediate/heterogeneous infiltrate in tumor stroma (10%-to-40%), and Category C exhibited a high immune infiltrate in tumor stroma (40%-to-90%).

References for supplementary methods:

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3. Salgado R, Denkert C, Demaria S, Sirtaine N, Klauschen F, Pruneri G*, et al.* The evaluation of tumor-infiltrating lymphocytes (TILs) in breast cancer: recommendations by an International TILs Working Group 2014. *Ann Oncol* **2015**;26(2):259-71. doi 10.1093/annonc/mdu450.

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