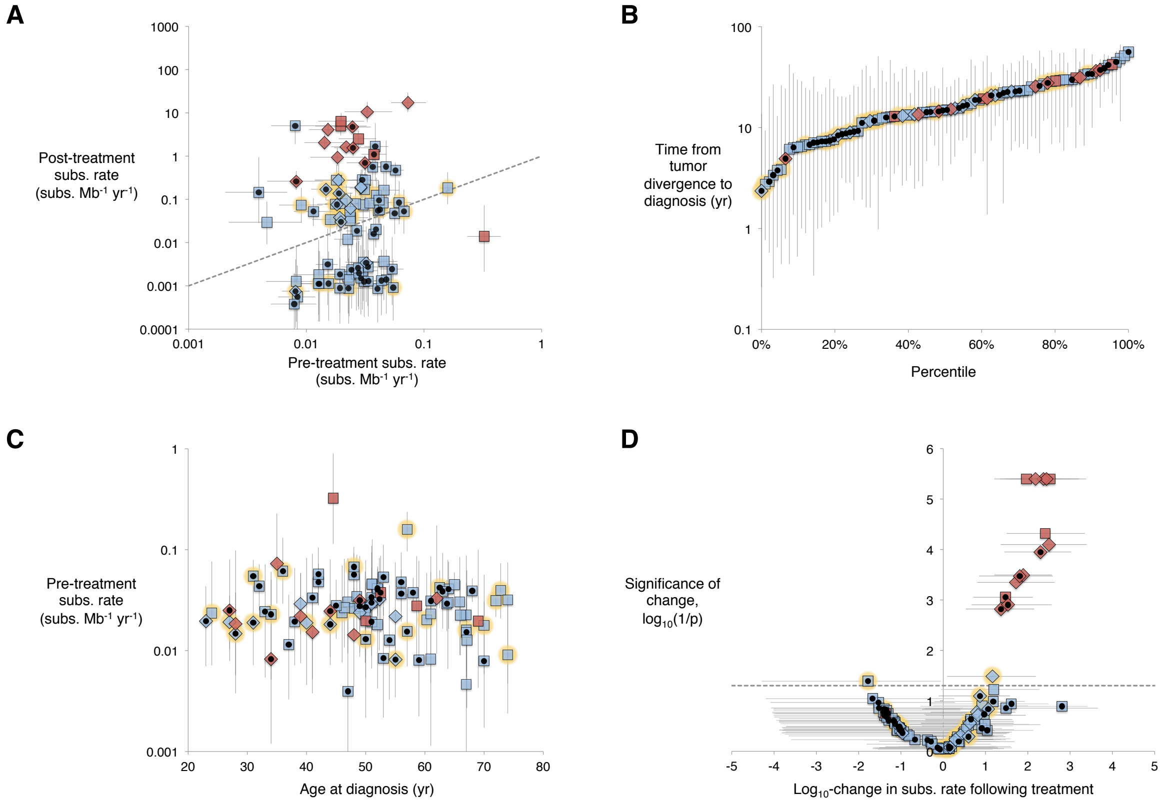

Additional Figure M1. Evolutionary model analysis, using mutant cellular frequency ≥0.92 as clonality cutoff. (A) Relationship between estimated substitution rates before and after treatment, as in Figure 3C. Dashed line shows diagonal (pre- and post-substitution rates equal). (B) Distribution of estimated time before diagnosis when the intial and recurrent lineages diverged, as in Figure 3D. (C) Relationship between pre-treatment substitution rate and diagnosis, as in Supplementary Figure 8. (D) Volcano plot of fold-change in substitution rate following treatment, as in Supplementary Figure 9. Horizontal dashed line shows p=0.05. (A, B, C, D) Each symbol shows median estimate for a patient; error bars show interquartile range (A) or 95% credible interval (B, C, D). Hypermutated tumors shown in red, non-hypermutated tumors in light blue. Primary GBM diagnoses shown as squares, secondary GBM diagnoses as diamonds. Black dot in center of symbol shows patients who fit the model well (see Methods). Yellow halo shows patients with TP53 mutated in both the initial and recurrent samples.