

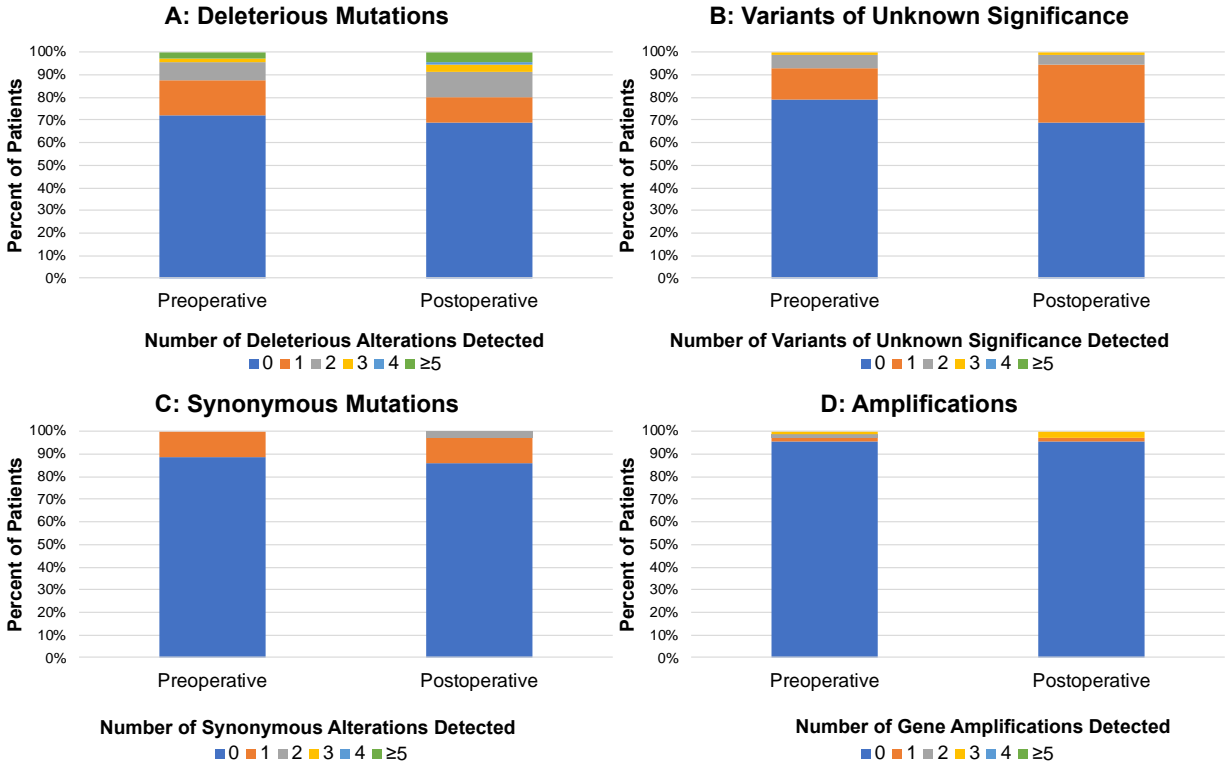
**Supplemental Table 1: Sequential Variable Analysis for Progression-Free Survival**

<b>Model Number</b>	<b>Variables</b>	<b>HR (95% CI)</b>	<b>p-value</b>
1	Preoperative high MSVAF alone	3.73 (2.06-6.77)	<b>&lt;0.001</b>
2	Model 1 + Age and sex	4.93 (2.54-9.6)	<b>&lt;0.001</b>
3	Model 2 + Cancer and treatment	4.54 (2.29-8.99)	<b>&lt;0.001</b>
4	Model 3 + Postoperative high VAF	3.8 (1.79-8.03)	<b>&lt;0.001</b>

Table depicting a mediation analysis using a sequential variable analysis. Groups of variables were added sequentially to the base model (preoperative high MSVAF) while observing the effect on the HR for high preoperative ctDNA. Though high preoperative ctDNA tended to have an increased effect when correcting for age, sex, cancer, and treatment covariates, the degree to which the postoperative ctDNA mediated its effect appeared to be marginal.

**Abbreviations:** PFS = progression-free survival, ctDNA = circulating tumor DNA, MSVAF = maximum somatic variant allele fraction, HR = hazard ratio, ctDNA = circulating tumor DNA, high MSVAF = MSAF  $\geq$ 0.25%.

## Supplemental Figure 1: Characterization of detected alterations in pre and postoperative circulating tumor DNA



Stacked bar plots representing the distribution of patients with **A.** characterized deleterious alterations detected **B.** variants of unknown significance detected **C.** synonymous mutations detected **D.** Amplifications detected. There were 4 patients with a detected deletion (1 preoperative only, 3 postoperative only), 3 patients with detectable gene fusions (all detected both pre and postoperatively), and no patients with detected gene insertions.