Background
Glioblastoma (GBM) is the most aggressive and common adult primary malignant brain tumor. GBM has an incidence rate of 3.2 per 100,000 in the US and a median overall survival of 14.6 months once diagnosed. Researching the mutations in GBM is critical to understanding and working towards a potential cure.

The basis for my research focused on patients’ overall survival as a result of the most common alterations, including amplification, splice variants, and missense mutations. An "amplification" occurs when a gene mutates, leaving multiple copies of itself. In GBM, the most common amplification is on the epidermal growth factor receptor (EGFR) gene. A "splice variant" is a type of mutation that results in a deletion of a part of a sequence of DNA. The most common, EGFRvIII, has a deletion of exons 2-7 on the EGFR gene, making the receptor incapable of binding to another ligand. Finally, "missense" mutations contain a mistake in the DNA resulting in the wrong amino acid. The most common missense mutations for GBM are A289D/T/V, R108G/K, and G598V. The A289D/T/V missense mutation results in increased invasiveness increased proliferation and decreased patient survival.

Methods
To investigate EGFR mutations’ relationship with GBM patients’ overall survival, I analyzed patients’ records from the University of Pennsylvania from the year 2012 to 2020 using GraphPad, a statistical software program. Using the log-rank test, I also produced a p-value for each comparison to determine whether each population had a statistically significant difference.

Results

Figure 1: IDH1 WT 1° De-novo EGFR amplified vs. non-amplified. The red survival curve is the amplified population, where the median survival is 16 months. The blue survival curve is the non-amplified population, where the median survival is 13 months.

Figure 2: IDH1 WT 1° De-novo positive EGFRvIII vs. negative EGFRvIII. The red survival curve is the positive EGFRvIII population, where the median survival is 13 months. The blue survival curve is the negative EGFRvIII population, where the median survival is 12 months.

Figure 3: IDH1 WT 1° De-novo A289D/T/V vs. R108G/K vs. G598V. The red survival curve is the A289D/T/V population, where the median survival is 9 months. The blue survival curve is the R108G/K population, where the median survival is 16 months. The green survival curve is the G598V population, where the median survival is 15 months.

Discussion
For the first comparison in Figure 1, the red and blue curves almost align perfectly. Its p-value of 0.5035 further confirms that there is no significant difference between the overall survival of the amplified and non-amplified populations.

In the second comparison in Figure 2, the red line lies slightly above the blue line the whole time. Its p-value of 0.1049, however, indicates that there is no significant difference between the overall survival of the positive and negative EGFRvIII populations.

In the third comparison in Figure 3, the red line, the A289D/T/V population, appears below both other populations. This data conveys that an A289D/T/V mutation correlates with decreased patient survival in GBM. For all three curves, its p-value of 0.0317 demonstrates that there is a significant difference. In order to determine where this difference lies, I applied the test to each. For A289D/T/V vs. R108G/K, the p-value of 0.0206 indicates that there is a significant difference. Similarly, for A289D/T/V vs. G598V, the p-value of 0.0177 indicates that there is a significant difference. Conversely, for R108G/K vs. G598V, the p-value of 0.1355 indicates that there is not a significant difference, as these curves overlap.

Significance
GBM is the most aggressive and invasive form of a tumor. Studying EGFR mutations provides valuable insight into designing clinical trials for EGFR-targeted therapies in GBM, thus providing the best opportunity towards working towards a potential cure for GBM.

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