

The research methodology utilized a comprehensive approach to understand drug resistance in chronic myeloid leukemia (CML), with a specific focus on elucidating the impact of BCR-ABL kinase mutations. Beginning with a meticulous data collection phase, relevant literature, including the study conducted by Redaelli et al., was reviewed to compile a comprehensive dataset encompassing known mutations associated with TKI resistance in CML. Structural analyses were then conducted to elucidate the structural alterations induced by these mutations within the BCR-ABL kinase domain.

Utilizing computational tools such as PyMOL, three-dimensional models of the protein were constructed to visualize and analyze the impact of mutations on protein conformation. Molecular imaging and simulations further explored the spatial relationships between mutations and the TKI binding pocket, with distances graphed using Prism software to provide insights into drug binding interactions. While the IC50 values were not directly calculated by the researcher, they were obtained from the study conducted by Redaelli et al. These values served as a crucial metric for assessing TKI efficacy in inhibiting BCR-ABL activity. A one-way ANOVA test was then employed to compare the distances measured for different mutations, facilitating the identification of mutations associated with varying degrees of spatial alterations.

Microsoft Excel and PRISM played a pivotal role in organizing and interpreting the data generated throughout the study. Its functionalities were utilized for data management, statistical analyses, and visualization purposes, enabling the construction of graphs and charts to present findings effectively. Through this interdisciplinary approach, the research aimed to provide valuable insights into the molecular mechanisms underlying TKI resistance in CML. By integrating computational techniques with experimental data, the study sought to contribute to the development of more effective therapeutic strategies for managing CML and overcoming drug resistance challenges.