



CLL SOCIETY

BTKI RESISTANCE MUTATIONS

WHAT IS BTKI TREATMENT RESISTANCE AND WHY DOES IT MATTER?

Treatment resistance refers to a reduction in the effectiveness of a medication in treating a disease.

CLL is a chronic disease and although there are excellent treatments, for most there is no cure. Targeted therapies, such as BTK inhibitors, can often effectively manage CLL for years and even offer many a normal life expectancy. But there are several reasons a person may need to stop taking a BTK inhibitor. A common one is relapse. Relapse occurs because your cancer cells evolve and mutate to resist the treatment.

HOW DO I KNOW IF I DEVELOP A RESISTANCE MUTATION?

Mutations causing resistance precede disease progression by a median of 8.5 months. That means it can be a long time between detection of a resistance mutation and even longer before retreatment is needed. Progression can be observed by your physician through regular monitoring of your CLL and/or through a return of symptoms.

HOW DO MUTATIONS DEVELOP?

Our understanding of how and when these mutations develop is still very early and incomplete, but the hope is that as we learn more, we may be able in the future to guide patients as to their best sequence of medications to allow the longest total time that the CLL is kept in check.

WHAT IS THE DIFFERENCE BETWEEN PRIMARY AND ACQUIRED RESISTANCE?

Primary Resistance

- Pre-existing resistance; occurs with first exposure to a drug.
- In CLL, this can occur with chemo (CIT), especially in patients with deletion 17p or TP53 mutation.
- Not seen with BTK inhibitors. Almost all patients will respond initially, especially if your first line of CLL treatment is with a BTK inhibitor.

Acquired Resistance

- CLL develops a “resistant mutation” while on therapy- a response to the drug.
- Most often occurs after long periods of successful treatment, often measured in years.
- More common when a BTKi was not your first line of treatment.
- Each of the approved BTKi drugs has different propensities for mutation.