



CLL SOCIETY

Test Before Treat

Once we know that our CLL needs treatment, we need to know how to treat it.

Current NCCN and iwCLL guidelines tell us that it is critical to get appropriate predictive testing before the first and every subsequent therapy. Results of these tests give us information about the biology of our disease, which in turn, gives us the ability to make a reasonable prediction as to which therapies offer us the best chance of success.

Simply put, depending on what the tests show, some commonly prescribed CLL therapies likely will work for us and others may not!

While there are many tests that might help CLL patients needing treatment to make their most informed decision, these three tests are essential:

1. **FISH** (Interphase fluorescence in situ hybridization) test looks for common chromosomal abnormalities that predict the likelihood that various CLL treatments will be effective and durable. For example, if FISH testing finds there is a deletion of the short arm of the 17 chromosome or del(17p) we know that traditional chemo-immunotherapy (CIT) such as fludarabine, cyclophosphamide and rituximab (FCR) or the combination of bendamustine and rituximab known as BR, will not be effective and should be avoided.
2. Additionally, it is important to test **IgVH** mutation status. IgVH mutation status almost never changes over time, so it is generally not recommended that it be retested. It is important because we know that patients with a “mutated” IgVH immunoglobulin do much better with FCR based therapies than those who are unmutated. Generally only patients who have mutated IgVH should consider FCR based therapies.
3. The 3rd and newest predictive factor is genetic testing for mutation of the **TP53** gene. TP53 is the gene on the short arm of the 17th chromosome that helps chemo to work and suppress cancer growth. It has been called the “guardian of the genome” because it tries to repair damaged genetic material in the CLL cells and if can’t repair what’s broken by chemo or any other cause, it signals the cell to commit programmed cell death or apoptosis. You can see how handy TP53 would be in suppressing cancer or helping chemo to work. However, if it’s missing as in del(17p) or mutated, and therefore dysfunctional, as discovered by genetic testing, generally chemotherapy will not work and the CLL can be harder to manage.

If you know the status of these 3 tests before your 1st and every subsequent treatment you can best map out your treatment strategy. FISH and TP53 need to be checked and rechecked before the first and any subsequent treatments as they can change over time, usually for the worse. IgVH mutation status is considered stable over time.

Test Before Treat

- **Test FISH and TP53 Mutation before every treatment**
- **Test IgVH mutation status before the 1st treatment**
- **Deletion 17p or del(17p) = NO CHEMOTHERAPY**
- **TP53 mutation = NO CHEMOTHERAPY**
- **IgVH unmutated = NO FCR**
- **IgVH mutated = possible FCR**