



The CLL Bloodline March 2019

MONTHLY QUIZ: Having deletion 17p confirms a poor prognosis. Choose all that are correct about this prognostic marker.

1. It is detected by “FISH” testing.
2. It refers to missing the short arm of the 17th chromosome that should contain the important anti- cancer gene, TP53.
3. It is associated with resistance to traditional chemotherapy, but less so with most novel agents.
4. It interferes with the cells ability to commit suicide even when it is badly damaged.
5. It can lead to increased genetic instability.
6. It is common at time of diagnosis but becomes rarer as the CLL progresses.

Answer: All are true, but the last.

Deletion 17p is detected by a fancy prognostic test called FISH testing (fluorescent in-situ hybridization) that probes the inside of the cells to look for missing or even extra genetic material. The short or the **p**etit arm of the 17th chromosome contains P53, a potent anti-cancer gene that has been called the guardian of the genome. P53 tries to repair damaged DNA and if it can't repair the damage, it starts the process for the cell to die. Without P53, damaged cancer cells, such as those ravaged by chemotherapy, are not killed, but instead continue to reproduce and may become even more mutant and resistant to therapy.

Deletion 17p is only detectable in some 5% of patients at diagnosis but is found in about 30% of patients at time of relapse after chemotherapy. It can also develop without treatment. That is why we recommend FISH testing before starting any therapy, as traditional chemo will not be helpful for patients with deletions 17p. This deletion is less important with the new targeted therapies such as ibrutinib, idelalisib, duvelisib, and venetoclax that work well for patients with or without functional P53.

NEWS:

1. CMS (Centers for Medicare & Medicaid Service) approves CAR-T therapy payment. CMS is the government agency that decides what gets paid for and what doesn't by Medicare and Medicaid. How willing hospitals are to do CAR-T will depend on the rate of reimbursement and how burdensome are the reporting requirements demanded by CMS.
2. Venetoclax (Venclexta®) will be added to Australian Pharmaceutical Benefits Scheme (PBS) starting March 1, 2019. Venetoclax was developed in Australia and though it has been approved for use since 2017, this announcement means that it will now be paid for by the government insurance in the country of its birth.

THE BASICS: When is treatment needed?

The decision to start treatment should never be based on blood counts alone, but by looking at the whole patient. Consider initiating therapy when there is the presence of:

1. B Symptoms
 - Weight loss >10% of body weight in previous 6 months
 - Severe fatigue (*ambulatory and capable of all self-care but unable to carry out any work activities*)
 - Fevers >38°C for at least 2 weeks without evidence of infection
 - Drenching night sweats for more than a month without evidence of infection
2. Evidence of progressive bone marrow failure manifest by low blood counts (cytopenias) including anemia (low red blood cells) or thrombocytopenia (low platelets).
3. Massive or symptomatic splenomegaly (enlarged spleen).



CLL SOCIETY

4. Massive lymph nodes or clusters of nodes (>10 cm) or progressive or symptomatic lymphadenopathy (enlarged lymph nodes).
5. Autoimmune Hemolytic Anemia (AIHA where the body attacks its own red cells) and/or Immune Thrombocytopenic Purpura (ITP where the body attacks its own platelets) that is poorly responsive to steroids or other standard therapy.
6. Rising ALC with an increase of more than 50% over a 2-month period or a lymphocyte doubling time (LDT) <6 months. If ALC is <30,000, LDT should not be used as the only criterion for beginning treatment.

See <http://cillsociety.org/2016/03/cil-watch-wait-start-treatment/> for more discussion of this important topic and the related subject of watch and wait.

WORD/ACRONYM OF THE MONTH: Tumor Lysis Syndrome (TLS). TLS is a complication of treatment caused by the rapid killing of the cancer cells that can result in dangerous metabolic abnormalities including too high levels of potassium and uric acid that can lead to fatal heart and kidney problems. It can occur with both oral (such as venetoclax) and IV treatments when the leukemia cells are lysed (killed) too fast and they spill out their inner contents into the blood stream and can overwhelm the body's ability to cope.

If the CLL Society has helped you or a loved one, please consider making a donation.