



Positive Quality Intervention: CLL and Del17P

Description of PQI:

Chronic Lymphocytic Leukemia (CLL) diagnosis with the chromosomal abnormality of 17p Deletion is associated with a poor prognosis. The 17p deletion is found 3-10% of the time at diagnosis, but 30- 50% at relapse. Testing rates at diagnosis and especially relapse are low. Venetoclax is approved in patients who have relapsed after one therapy and have the 17p deletion. **This PQI is to ensure patients are tested (FISH) both at diagnosis of CLL and also at relapse of CLL.** This will allow those patients who are appropriate for Venetoclax to have access to a successful drug in a patient with a poor prognosis.

Background:

Chronic Lymphocytic Leukemia (CLL) is associated with mutations that have unfavorable outcomes. Chromosomal abnormality, Deletion 17p, is a proven predictor of poor response to therapy and shorter progression free survival. This abnormality can cause the loss of function of the TP53 protein which creates chemotherapy resistant cells. The thought is that during first line treatment, this cell line is able to survive which would explain the higher number at relapse. Del 17p is a common test ordered at diagnosis for patients with CLL. Only 9% of CLL patients present at diagnosis with this deletion. After initial treatment, many of these patients will have disease recurrence with few options for retreatment. Molecular testing at diagnosis and at relapse is very important in CLL. **Although only 9% of patients present with del17p, up to 50% of patients present at recurrence with del17p.** Unfortunately the testing rates at relapse are only 35-40%. NCCN guidelines recommend reevaluating FISH and karyotype at relapse.

Venetoclax is FDA approved in CLL in patients with 17p Deletion after one prior therapy. Venetoclax is a BCL-2 inhibitor which by its inhibition restores apoptosis in cells that overexpress BCL-2. CLL cells that are resistant to chemotherapy are found to over express the BCL-2 protein. A phase II trial was done, which studied 158 relapsed/refractory CLL patients with 17p deletion who were given Venetoclax. Overall Response Rate (ORR) was 77% and 20% CR/Cri with a median time to first response being 1 month and time to CR/Cri being 9.8 months. Majority of patients experienced one Adverse Drug Event with 17% needing dose reduction and 40% having their dose interrupted. Most common ADE was neutropenia, but was not attributed to any discontinuations. This produced a durable response for majority of patients, in a population where there is limited treatment.

PQI process:

- **Patients diagnosed with CLL, must have the proper cytogenetic testing (FISH) initially and at relapse.**
- Patients who have the 17p deletion or discover it at relapse are eligible to receive Venetoclax single agent.
- Building a reminder to test at diagnosis and at progression in the electronic medical record would be a very important step to confirm patients have the proper diagnosis and treatment.

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Patient Centered Activities:

- Use Starter Pack for first 4 weeks due to ramp up dosing schedule
- TLS: Start Allopurinol 2-3 days prior to starting Venetoclax (Rasburicase may be considered for high risk patients with elevated uric acid)
- Hydration: drink 6-8 glasses of water each day starting 2-3 days prior to starting Venetoclax
- Labs: Chemistries should be drawn at baseline, 6-8 hours, and 24 hours after each ramp up in dose.

References:

1. Strati P et al. Haematologica. 2014;99(8):1350-1355
2. Stigenbauer S et al. Venetoclax in Relapsed/Refractory CLL with 17p deletion: Outcome and Minimal Residual Disease from the full population of the pivotal M13-982 Trial. Poster presented at XVII International workshop on CLL 5/12/17-5/15/17

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