Tracks 1-12

Track 1  **Case discussion:** A 51-year-old man with chronic-phase chronic myeloid leukemia (CML) with disease progression on dasatinib is found to harbor a rare F317L mutation and receives ponatinib

Track 2  Mitigating ponatinib-related side effects with dose reductions or discontinuation

Track 3  Rational placement of omacetaxine in the treatment algorithm for CML

Track 4  **Case discussion:** A 48-year-old man with hydroxyurea-resistant polycythemia vera (PV) receives ruxolitinib

Track 5  Duration and rapidity of response with ruxolitinib in PV versus myelofibrosis (MF)

Track 6  Activity and toxicities of novel JAK inhibitors — pacritinib, momelotinib — in myeloproliferative disorders

Track 7  Approach to ruxolitinib dosing in patients with anemia and thrombocytopenia

Track 8  Diagnostic and prognostic roles of JAK and other mutations in MF

Track 9  **Case discussion:** A 95-year-old woman with intermediate-2 myelodysplastic syndrome with abnormal karyotype experiences a prolonged complete cytogenetic response to azacitidine

Track 10  SORAML: Results of a Phase II trial of sorafenib versus placebo in addition to standard therapy for younger patients with newly diagnosed acute myeloid leukemia (AML)

Track 11  Activity and incidence of tumor lysis syndrome with the novel second-generation Bcl-2 inhibitor venetoclax (ABT-199) in AML

Track 12  **Case discussion:** A 25-year-old woman with high-risk acute promyelocytic leukemia receives gemtuzumab ozogamicin on a compassionate use program

Select Excerpts from the Interview

**DR LOVE:** What is your approach to the choice of tyrosine kinase inhibitor (TKI) for first-line therapy in chronic myeloid leukemia (CML)?

**DR JABBOUR:** Imatinib, nilotinib and dasatinib are available for front-line therapy. For patients with low-risk disease, I would recommend imatinib because the advantage of the second-generation TKIs dasatinib or nilotinib is marginal and yields no effect on survival. I start with imatinib and switch therapy at 3 to 6 months if the response is not good.

For patients who are young and have high-risk features, I would consider dasatinib or nilotinib up front. My choice would be based on comorbidities. I would avoid dasatinib for patients who are at risk for pleural effusion and offer them nilotinib instead. In contrast, for patients with diabetes or cardiovascular issues, I would opt for dasatinib.
In the future, the cost of these agents will also dictate our choice of therapy, especially when generic imatinib becomes available.

**DR LOVE:** Ponatinib is a potent TKI used for patients who are resistant/intolerant to dasatinib or nilotinib or those with the T315I mutation. What is known about the cardiovascular side effects with ponatinib?

**DR JABBOUR:** Ponatinib is associated with a higher incidence of cardiovascular events compared to other TKIs. Arterial events are observed at a rate of approximately 13% per year of therapy. This does not increase with time on therapy. Both venous and arterial events are observed. When these events occur, the drug must be discontinued. Based on the PACE trial, patients with certain risk factors at baseline, such as cardiac disease, diabetes or advanced age, are at higher risk of developing vascular events (Cortes 2013). We try to optimize risk factors before starting patients on ponatinib. Because the agent is potent and you can minimize side effects by reducing the dose, in our practice we administer 30 mg per day and reduce to 15 mg.

**DR LOVE:** What are your thoughts on the role of omacetaxine, another drug approved for CML?

**DR JABBOUR:** Omacetaxine inhibits protein translation and has shown activity in patients who are resistant or intolerant to multiple TKIs and those with the T315I mutation. In a pivotal trial that led to the approval in chronic phase, 23% of patients achieved a major cytogenetic response (Cortes 2012). For patients in blast phase, the combination of omacetaxine and a TKI is attractive. It can be considered off label with a TKI in patients for whom you want to stop therapy.

As induction therapy, the drug is administered subcutaneously twice daily for 2 weeks. It can now be administered at home, which is more practical for patients. In my practice, I administer it for 1 week at the start and then for 3 days later to minimize the risk of myelosuppression.

**Tracks 5-7**

**DR LOVE:** What is your clinical experience with ruxolitinib for polycythemia vera (PV)?

**DR JABBOUR:** The main goal is to achieve hematocrit control and improve symptoms in patients with PV. The response to ruxolitinib in PV is rapid because myelosuppression is not as much of a concern as it is with myelofibrosis (MF). I have found it to be a well-tolerated agent. The blood counts must be closely monitored early on and the dose adjusted if necessary. Patients usually receive 10 mg BID and experience a dramatic improvement in quality of life. In the RESPONSE trial, assessing ruxolitinib versus best available therapy in patients with PV who had an inadequate response to or unacceptable side effects from hydroxyurea, the probability that a response to ruxolitinib would be maintained for 1 year was approximately 90% (Vannucchi 2015; [3.1]).

**DR LOVE:** How do you approach dosing of ruxolitinib in patients with anemia and thrombocytopenia?

**DR JABBOUR:** For patients who have platelet counts on the order of 100 or 110 x 10⁹/L, I usually start with a 10-mg dose and titrate upward. A dose of 10 mg BID or higher is necessary to have an effect on the spleen. I will monitor blood counts on a
The goal is to avoid discontinuing therapy. If therapy is stopped, the benefits are lost within 7 days and patients start experiencing symptoms again. Drugs like danazol can be used in combination with ruxolitinib to manage the anemia.

**DR LOVE:** What do we know about the novel agent pacritinib in the treatment of myeloproliferative neoplasms?

**DR JABBOUR:** Pacritinib is a JAK2 inhibitor that has similar efficacy to ruxolitinib. The main advantage of pacritinib versus ruxolitinib is that it doesn’t cause as much myelosuppression. If pacritinib were available, I would consider it for patients who have baseline anemia or thrombocytopenia. The main side effects are gastrointestinal toxicities like diarrhea, nausea and vomiting, which can be managed with dose reductions. The drug is promising and is also being evaluated in patients with low counts compared to best available therapy, including ruxolitinib.

**DR LOVE:** What other novel agents are being investigated in MF?

**DR JABBOUR:** A number of new agents are being evaluated. They include histone deacetylase inhibitors and antifibrotic agents. With histone deacetylase inhibitors, more side effects are encountered. A promising therapy for patients who have the mixed syndrome of myelodysplastic syndrome/myeloproliferative neoplasm is the combination of azacitidine and ruxolitinib, which can be considered sequentially instead of concurrently to improve outcomes and reduce the risk of side effects.

**Track 10**

**DR LOVE:** Would you discuss the results of the SORAML trial of sorafenib in addition to standard therapy for younger patients with newly diagnosed acute myeloid leukemia (AML)?

**DR JABBOUR:** In the SORAML study, an advantage was observed overall with sorafenib versus placebo among patients with AML in the front-line setting, independent of FLT3-ITD status (Rollig 2014; [3.2]). It cannot be determined from the study...
if sorafenib increases overall survival. Although sorafenib has not been approved in this setting, it can be considered in combination with chemotherapy for patients with AML who have the FLT3-ITD mutation.

**SELECT PUBLICATIONS**

