Tracks 1-9

Track 1  Advances in understanding the biology of myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML)

Track 2  Evaluation and initial treatment for patients with MDS

Track 3  Selection of hypomethylating agent — azacitidine or decitabine — for the treatment of MDS

Track 4  Monitoring and management of treatment-related neutropenia and anemia during early cycles of hypomethylating agents

Track 5  Schedule and duration of administration with hypomethylating agents in MDS

Track 6  Lenalidomide in MDS with or without del(5q)

Track 7  Novel markers for risk stratification and treatment approach for older patients with AML

Track 8  Induction chemotherapy/all-trans retinoic acid (ATRA) with arsenic trioxide consolidation therapy as up-front treatment of acute promyelocytic leukemia (APL)

Track 9  High early death rate in APL despite ATRA

Select Excerpts from the Interview

Track 3

DR LOVE: How do you choose between the hypomethylating agents, azacitidine and decitabine, when treating myelodysplastic syndromes (MDS)?

DR FENAUX: It’s difficult. At least 1 study has shown a survival advantage with azacitidine (Fenaux 2009a; [3.1]), but that’s not yet been shown with decitabine. This might be related to a difference between the agents, but it may also be that the schedule used in the decitabine trials was not optimal. Since those data were presented, a new schedule of 20 mg/m² per day for 5 days every month has been approved by the FDA. This may be more active than the schedule evaluated in the initial trials, and it’s used in most centers in the United States.

Another reason why the decitabine studies were not conclusive for a survival advantage may be that the number of cycles administered was not adequate. It
appears that prolonged treatment is key. The azacitidine trial that reported a survival improvement had a median number of 9 cycles overall and 15 cycles in responders, which is probably significant in terms of outcome.

**Track 4**

- **DR LOVE:** What common side effects and toxicities are seen with hypomethylating agents?

- **DR FENAUX:** The most significant problem is related to cytopenias during the first cycles. Hypomethylating agents lead to fewer cytopenias compared to chemotherapy, but MDS occurs in patients who are typically older than those who would receive chemotherapy, so it remains an issue in these patients. Protracted neutropenia also occurs in many of these patients, in addition to defects in neutrophil function. These patients are prone to infections, and patients must be carefully monitored during the first cycles.

  When necessary, we transfuse the patients or administer prophylactic antibiotics. Oncologists need to be aware in advance that these agents are associated with cytopenias and treat accordingly. Otherwise, the risk may be stopping too early, lowering the dose too rapidly or increasing the interval too quickly between cycles.

**Track 6**

- **DR LOVE:** What are your thoughts on lenalidomide for patients with MDS and 5q deletions?

- **DR FENAUX:** The MDS-003 and MDS-004 trials (List 2006; Fenaux 2009b; [3.2]) demonstrated that a sufficient dose of lenalidomide initially — 10 mg rather than 5 mg daily — is necessary to achieve transfusion independence. More patients who received the higher dose achieved cytogenetic responses, which is associated with fewer cases of progression from MDS to acute myeloid leukemia (AML). This analysis showed that the more you eradicate the disease in terms of cytogenetic response, the longer the remissions are and the fewer the cases of progression to AML.
Track 8

DR LOVE: What’s new in acute promyelocytic leukemia (APL)?

DR FENAUX: APL can be cured in the majority of patients. Combination chemotherapy/all-trans retinoic acid (ATRA) leads to an 80% event-free survival and a 90% disease-free survival (Powell 2010; [3.3]). Arsenic trioxide (ATO) can also be used as consolidation to reduce the risk of mortality in remission. Some physicians use ATO up front without chemotherapy, in combination with ATRA, but this approach can be potentially dangerous due to significant differentiation syndrome. I believe the Intergroup trial used a wise approach in keeping the anthracycline/ATRA combination for induction and using arsenic derivatives for consolidation and/or maintenance.

SELECT PUBLICATIONS


Fenaux P et al. RBC transfusion independence and safety profile of lenalidomide 5 or 10 mg in pts with low- or int-1-risk MDS with del5q: Results from a randomized Phase III trial (MDS-004). Proc ASH 2009b; Abstract 944.