Minimal Residual Disease (MRD) in CML

Dr. M. Mauro - Memorial Sloan Kettering - NYC

Dr. Mauro reminded us of the treatment milestones of CML as outlined in the NCCN and the ELN guidelines. He pointed out that there is controversy over whether the 3 month PCR result is as important as the 6th month PCR result. Regarding the controversy of the 3 or 6 month response levels, he referred to this as Early Molecular Response (EMR). He then presented trial information where the 3 month and 6 month response levels were monitored. In these studies we could see that knowing the early molecular response was helpful in providing information on knowing who was responding and who would be at a higher risk of progression. However, Dr. Mauro said that EMR should be used very cautiously and not necessarily be used as the trigger to switch a patients treatment as the side effects profiles with some drugs are more toxic and these toxicities and complications need to be carefully weighed against the benefits. So, he says Dr's should exercise a bit of patience for their patients.

The second part of his talk was about Complete Cytogenetic response (CCyR) and Major Molecular response (MMR)

Dr. Mauro highlighted that CCyr is still a very important milestone of treatment to achieve and does confer a benefit of improved overall survival, versus not achieving CCyR. MMR offers a benefit as well, but he stressed that deeper faster molecular response does not always equal improved overall survival (when compared to CCyR)

CCyR and MMR are both appropriate milestones to achieve, but both of them have a different agenda. For example patients with MMR and better and are well sustained can potentially be considered for a stopping TKI trial. This will not be offered to patients who have only achieved CCyR.

Dr. Mauro stated that the Ultimate goal to achieve is MR 4.5 or ' stable deep response'

He asked if we can get more patients to achieve this level of response and indeed according to results of some clinical trials, i.e. ENEST (patients were switched from IM to NIL if they had not achieved treatment milestones as per guidelines). Based on current data from clinical trials, Mauro believes that deeper molecular response does offer a benefit (less likelihood of disease relapse, as long as patient continues to be adherent to therapy and monitored every 3 months with molecular BCR ABL) and optimizes patients outcomes.

Mauro suggests that if a sustainable deeper molecular response is achieved that may suggest that drug therapy time may be limited and this would offset the concerns of the toxic effects of the newer TKI's. So, in cases where the patient is diagnosed in CP CML and may have a low sokal risk score, the toxic side effects of some of the newer drugs could be better managed and perhaps well worth the risk if it allows the patient to eventually stop treatment safely.

He then tackled the interesting subject of Treatment Free Remission (TFR). Looking at the results form clinical trials that are on-going and will be further updated at this meeting, we can see a 60% of success on TFR without loss of MMR. As we know, the European studies do not restart the drug unless you have a loss of MMR.. He presented the Eurooski trial requirements, which will be covered later at this meeting.

Mauro pointed out the concern of whether patients who stop treatment and experience a molecular relapse will be able to regain their prior good response and he says concerns in this area have not increased. He knows of only one case where a patient did not regain their prior good response once the drug was restarted