Managing Hodgkin Lymphoma

Overview of the 12th International Conference on Malignant Lymphoma

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Hello, my name is James Armitage. I am a professor of Medicine at University of Nebraska Medical Center. Today, I would like to share with you some of, what I think, are the most interesting things and most practical things for you to use as a clinician from the 12th International Conference on Malignant Lymphoma, often called the Lugano meeting, which is the biggest lymphoma meeting that occurs in the world. As the name suggests, it occurs in Lugano, Switzerland, and it occurs every other year, and I am at that meeting right now. What I would like to do is just highlight a few of the most practical papers from this meeting. There is one paper about CNS lymphoma that was provocative, I thought. The investigators from Italy took patients and divided them using their own system of high-risk and low-risk into those that were unlikely to have CNS relapse, usually meningeal relapse for a patient treated systematically, or those who they thought were at high risk. Then, they went back and looked at the patients and found an extremely interesting thing and that is those patients at high-risk, if they got intrathecal therapy, still had an increased risk compared to low-risk patients of relapse in the CNS. But those patients who received high-dose methotrexate or intermediate-dose methotrexate incorporated with the primary therapy, had no one with CNS relapse. It is a very interesting idea. An alternate approach that was discussed was doing spinal taps on patients and doing flow studies and identifying those people who already, by flow, you can find minimal disease in the spinal fluid, and then treating them specifically for CNS lymphoma. Of course, the problem here is that CNS relapse is really relatively rare particularly in the area of rituximab. If you can identify high-risk patients, it maybe that something other than a few dosage of intrathecal methotrexate would be a better approach. One other issue about CNS disease that was discussed at this meeting is a report using temsirolimus for patients who failed primary therapy which would be usually high-dose methotrexate perhaps with high-dose cytarabine perhaps with radiotherapy. They had an amazingly high response rate. Over half the patients who had failed standard upfront therapy still responded to temsirolimus, interesting idea.

Another issue that was addressed here is where radiotherapy fits today in the treatment of patients with lymphoma. You can hear people say in talks and you can read in papers that perhaps radiotherapy no longer has much of a place in treating patients with

lymphoma, but there were some papers here that would certainly dispute that idea. There was long-term followup from the team at Princess Margaret Hospital in Toronto, in patients with low-stage follicular lymphoma which showed a 10-year freedom from relapse of 48% including both stage 1 and stage 2 patients; that is pretty good outcome. Everybody responded. Almost everybody had complete remission and about half the patients remained in remission for over 10 years. So, maybe radiotherapy is not too old fashioned for localized follicular lymphoma. There were several papers that addressed the issue of radiotherapy as an adjunct in the patients with diffuse large B-cell lymphoma. There was a paper from the NCCN in United States and another from a German Hodgkin Lymphoma Study Group that both when they looked back on their data found that there seemed to be an advantage to patients with bulky disease even if they achieved the remission, they got radiotherapy after treatment. There was a very interesting paper from the team in Vancouver which showed that patients who at the end of therapy had a negative PET scan did quite well, had failure-free survival of about three quarters. The patients who had a positive PET scan at the end of therapy, if they receive no more treatment, only a third of them stayed well. However, those who got radiotherapy, four out of five stayed well. Now, this suggests that you can use a radiotherapy with an equivocal or positive PET scan at the end of treatment to assay the bulky mass and the patient can do well, but it also makes you wonder those patients who had a negative PET scan since their ultimate outcome was actually slightly worse than those who had a positive PET scan that got radiotherapy, if radiotherapy would have contributed there. So, at least, you should not completely give up on the idea.

There were data again about surveillance scanning presented here and showed once again that there is little evidence that surveillance scanning in patients with aggressive lymphoma contributes to outcome; that is, most patients would have been identified clinically and little difference if there is an improvement in survival. This applies to both Hodgkin lymphomas and aggressive non-Hodgkin lymphomas. However, there was one interesting paper from Denmark where the investigators looked back at the large number of patients with both Hodgkin lymphoma and non-Hodgkin lymphoma. They had a relatively higher number of people identified uniquely by surveillance imaging where about a quarter of relapses were identified by surveillance imaging. But they had a suggestion that the patients in the aggressive B-cell lymphoma, mostly diffused large B-cell lymphoma that patients in that group might have done better if they were asymptomatic and had their disease discovered by surveillance imaging. At the moment, the overwhelming data would suggest that there is no place for surveillance imaging and that is what I do. My colleagues and I do not do routine surveillance imaging, but I think this study and some other bits of data are enough of hint that really would be appropriate to identify very high-risk patients where we had effective salvage therapy like transplant for diffuse large B-cell lymphoma and do a randomized trial to

answer this question about whether or not this study that is a surveillance CT or PET CT which costs a lot of money, scares patients, and can lead to second malignancies, whether or not the net effect could be positive if we found the right group of patients.

There were a couple of really interesting papers about things that we do not usually think about. One from Worcester, Massachusetts, Chicago, and Duarte, looked at patients' exercise and diet and found that the patient who had a diet high in fruits and vegetables were more likely to have follicular lymphomas that had a micro-environment that we know is associated with good outcome; that is, perhaps what you are eating and somehow or the other affects your immune system and improves its ability to respond to the tumor. Pretty interesting, something we have not paid a lot of attention to. Another from the German High-grade Lymphoma Study Group looked at patients from a large study of CHOP-R, and what they found was that people who were vitamin-D deficient were more likely to relapse and live less long than those who had adequate levels of vitamin D. There have been other bits of data about this and this is actionable. Maybe, we should all be checking our patients' vitamin D level and replacing that routinely and especially replacing that in people who have lower than normal values. Maybe, it will make a difference. Again, something that we have not as a group paid a whole lot of attention to.

Finally, I will end with one last provocative thing. There have been studies presented at both ASCO and ASH over the last year that suggested that men do not do as well when given rituximab as women. There are studies from Europe showing that men excrete rituximab more rapidly than women. Data presented here confirm that in data from the NCCN men had a less good outcome with rituximab than women. Also, people with higher body surface area, that is, they got a higher dose of rituximab seem to do better. The German Hodgkin Study Group showed that men do excrete the rituximab, but their levels do not stay as high as women, but that seemed to be largely in elderly men. And in fact, elderly men treated with aggressive regimens for diffuse large B-cell lymphoma that include rituximab had a poorer outcome than in either younger men or women. So, I do not know the answer of this yet. Should you be giving guys higher dosage of rituximab, you probably would not get it paid for. But it may well be that one of the reasons that men today do not do quite as well being treated for high-grade lymphomas is that the rituximab does not benefit them as much as it does women. I want to thank you for listening. I hope you enjoyed these highlights, and I hope you watch other highlights from the 12th ICML, and if you are interested to attend this really excellent meeting, you get another chance in 2 years.

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