Managing Hodgkin Lymphoma

An Overview of New Trials in HL

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Hi, my name is Andreas Engert. I am professor of internal medicine, hematology, and oncology at the University Hospital of Cologne, Germany, and I am chairman of the German Hodgkin Study Group.

I want to discuss with you some of the more recent trials in the area of Hodgkin's, a few ongoing trials and trials that are being reported this year in major meeting such as EHA and ASH. So, the first trial I want to discuss with you is our trial called HD13 that was a trial done in patients with early favorable Hodgkin's, so the best risk group, and here the standard of care in terms of chemotherapy is ABVD, and most centers add radiation to ABVD. The question we addressed in this trial after having shown that just 2 cycles of ABVD plus 20-Gy involved field is enough for these patients. The question is then can we go further and delete drugs from ABVD from this backbone, drugs such as dacarbazine or bleomycin, because these drugs are associated with some toxicity. In particular, bleomycin has always been questioned as if this drug is really needed. So, we did a large trial with 1,500 patients or so comparing four different chemotherapy regimens, ABVD as a standard of care, and then variants were either bleomycin or dacarbazine or both were deleted. And what we observed rather early in the arm where both drugs were deleted was more event, so we had to stop this arm with 160 patients or so. The same was true then for the arm in which dacarbazine only was deleted with 200 patients stopped, so clearly dacarbazine deleting from ABVD does not work, even if you just use 2 cycles in the best risk group, and then, the question remained how the impact of bleomycin was. And for that, we increased the number of patients to more than 600. The final analysis shows that even bleomycin is needed even if you delete this drug, you get more events, and this is the major result of HD13. A surprise though was that if we looked at overall survival with these major differences in tumor control between these arms, particularly between the weakest or two weakest and the standard, with overall survival, there was no difference whatsoever. That means that if these patients relapse or progress, treatment given at that stage such as BEACOPP or high-dose chemotherapy could still rescue these patients. So, this trial HD13 means that 2 cycles of ABVD should still be given, doctors could discuss if they want to enter the risk for their patients by deleting bleomycin in frail patients. That is an issue in elderly patients. Certainly, that is

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a medical indication then, but you should be aware that if you deleted, then this regimen is less effective than it is with bleomycin.

Other very interesting trials at this stage include brentuximab vedotin, that is a drug that was registered for relapsed Hodgkin's, relapsed after high-dose chemotherapy or at least two chemotherapy regimens. So, the question now is on about maintenance, and that is AETHERA trial that will be reported at ASH this year. There are other trials in first line. A registration trial where ABVD or an ABVD variant without bleomycin is combined with brentuximab and compared to the standard that is ABVD. That is an ongoing worldwide trial and aimed certainly at showing superiority of this new combination. Our group, the German Hodgkin Study Group, has used this drug, brentuximab vedotin, to improve on BEACOPP escalated, so we replaced drugs from this regimen and added brentuximab. We have just run a phase II randomized trial showing that both these variants worked very nicely, and we will run a large randomized trial starting later this year termed HD21 where 6 cycles of BEACOPP escalated, the current standard, will be compared with this new variant including brentuximab vedotin.

On other hand, there are quite a few reports on results taken from the so-called named patient program with brentuximab vedotin. This was initiated in many countries worldwide after the registration of this drug in the US. Registration in the Europe was a year later, and there are a number of publications from Europe and other countries, I think there are 21 programs overall. One was reported at EHA with 60 patients or so, and the results of these observations I should say because these were not clinical trials, these were patients treated and then looked at the data. The results confirmed efficacy and safety of this drug, brentuximab vedotin, although the responses were a little bit less as compared to the pivotal studies. This might be due to the fact that these were patients that would not qualify, not all qualify for these trials. These included very sick frail patients, patients that would not qualify for high-dose chemotherapy for instance or elderly patients, so that is not a surprise that when treating all these patients their outcome is a little bit less as compared to the pivotal data. However, it is confirming, and reconfirming really that the efficacy with this drug is very good also in these patients.

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