Managing Hodgkin Lymphoma Expert Interview Series

An Update on the Current State of Hodgkin Lymphoma Care in Europe

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Editor's Note:
The treatment of patients with Hodgkin lymphoma (HL) is one of the major success stories in oncology. Currently between 70–90% of treatment-naïve patients are cured of their malignancy depending on clinical stage and risk factors.[1] In patients with refractory or relapsed disease, high-dose chemotherapy (HDCT) followed by autologous hematopoietic stem cell transplant (HSCT) is the standard of care, and can lead to a cure in ~50% of patients.[2] However, current combined modality treatment regimens for first diagnosed HL patients can induce severe, life-threatening treatment-related side effects, which include secondary cancers and cardiovascular disease. Despite success in both treatment-naïve patients and patients with refractory or relapsed disease, new treatment options are needed. On behalf of ManagingHodgkinLymphoma.com (MHLC), George Davatelis, PhD, spoke with Franco Cavalli, MD, FRCP, scientific director of the Oncology Institute of Southern Switzerland, Bellinzona, Switzerland, to discuss the latest advances and current state of science in HL treatment in Europe.

MHLC: *Could you tell us about the standard of care in Switzerland specifically and in the EU in general on Hodgkin lymphoma?*

Dr. Franco Cavalli: First, we have to consider that there are two schools of thought in Europe. For early stages there is consensus where we combine chemotherapy, mostly ABVD (Adriamycin [doxorubicin], bleomycin, vinblastine and dacarbazine),[3] and radiotherapy and, based on the result of the German studies, there is a widespread tendency to reduce the number of courses which are given. However, in advanced Hodgkin lymphoma the standard of treatment is ABVD, as in the United States, and I would say that the majority of the Latin countries — Portugal, Spain, Italy, etc. — belong to this approach, while in the rest of Europe, there is a more pronounced German influence and there is more dependency of using the BEACOPP (bleomycin, etoposide, Adriamycin, cyclophosphamide, Oncovin, procarbazine and prednisone), the German-devised national chemotherapy regimen as the first treatment of choice in the patients with advanced Hodgkin lymphoma. I think we have both components in Switzerland.

We have the German-speaking area and the French- and Italian-speaking area in which I would say that we have this difference, where the German-speaking party is more prone to use BEACOPP and the rest of region is more used to treat patients with advanced Hodgkin lymphoma with ABVD being the first line of treatment.

MHLC: *What do you think are the biggest treatment challenges in the EU?*

Dr. Franco Cavalli: There are, I would say, three major challenges. One is the fact that we have to further minimize the late side effects of the treatment, mainly cardiac and pulmonary ones, that are more frequent in relapses. So although we have succeeded in the last 15 years to decrease the percentage of secondary tumors and have also somewhat decreased the percentage of occurrence of cardiac and pulmonary late side effects, we still have further to go to decrease the side effects since net toxicity is becoming a bigger problem as we cure the vast majority of the patients. Besides that, there are two more specific challenges. The first one is to find the treatment for somewhere between 5% and 10% of patients who are primarily resistant to the current treatment and the patients who have very bad prognosis. And the second challenge is how to treat patients who perhaps relapse mainly after high-dose chemotherapy and the autologous transplantation, because it is generally accepted that for patient relapsing after first-line treatment, the treatment of choice in any case is high-dose chemotherapy plus treatment with autologous stem cells. But about roughly half of these patients will further relapse as a second relapse and how to treat those patients is the second, let's say, more specific challenge related to the management of the patients with Hodgkin lymphoma.

MHLC: *Can you expand on what you think is the latest thinking about the side effects related to the standard of care right now?*

Dr. Franco Cavalli: Well, I mean the overall research tendency for treatment-related side effects is to try to minimize the intensity of the treatment without jeopardizing the response rate and the immediate cure rate. In that sense, researchers are trying to establish criteria in which we can predict patients who will have problems in responding to the current treatment strategies. Of course, we have the clinical criteria, but they are of very limited usefulness in order to be able to spot those patients that will not have a compete response. So, the avenue of research today is to try to find out biomarkers or biological parameters which might predict the outcome. There have been a few publications either on some surface antigens or on some genetic signatures which might be predictive, but the data are, for the time being, not very consistent. So, it remains an avenue of research. But there is some hope that in the near future we will be able to personalize the treatment to avoid both over- and undertreatment. Also, current studies

are evaluating different approaches based on PET outcome to answer the question as to whether patients in early stages could be spared radiotherapy and likely decrease the rate of cardiac and pulmonary side effects and also decrease the rate of secondary tumors.

MHLC: *What is your impression of the new agents that are currently being tested or have made it to the market, and are any of them looking particularly promising in your view?*

Dr. Franco Cavalli: HDAC (histone deacetylase) inhibitors[4] are very efficacious and the response rate is very good, but the problem is the myelosuppression and thrombocytopenia side effects, mainly in some relapsing patients after bone marrow transplantation, which often tends to lower platelets and sometimes even granulocyte count and represents a real problem, especially for elderly patients. So, I think that for the time being the most promising group in my opinion are the anti-CD30 antibody drug conjugates[5] which have generated spectacular results we have never seen before. Ongoing studies are trying to find out which is the best way to combine them with the standard chemotherapy because early attempts to combine the anti-CD drug conjugate with bleomycin has shown importantly increased lung toxicity. So, although they have a manageable toxicity, they might not be combined with every cytotoxic agent we have been using in the past. In my opinion, this will be resolved, and moreover, there are other antibody drug conjugates which are now in the pipeline, and I really believe that this is a category of drugs which will help us tackle the remaining challenges in the treatment of Hodgkin lymphoma.

MHLC: *What do you believe has the greatest potential to impact and improve outcomes in the EU right now?*

Dr. Franco Cavalli: In my opinion, there are two weapons. The first one is to routinely use PET-CT (positron emission tomography-computed tomography),[6] either staging of patient with Hodgkin lymphoma or summarizing the treatment of patients based on the PET outcome after having given two or three courses of chemotherapy. The second one is to be able to find out an intelligent and feasible way to include the anti-CD30 antibody drug conjugate in the primary treatment of patients with Hodgkin lymphomas as well as in the treatment of relapsed patients. I am convinced that in the next 5 to 10 years, thanks to the intelligent use of the anti-CD30 drug conjugate, we will be able to bring down the rate of primarily resistant cases, and also to improve the outcome in the relapsing patients, and in both approaches, contribute to a further decrease in the intensity of the overall treatment and help us to further decrease the percentage of late toxicity.

MHLC: *What do you see being the key educational needs of physicians and clinicians in Switzerland and in the EU in general?*

Dr. Franco Cavalli: Well, in my opinion, there is a good level of knowledge in terms of education in medical oncologist or hemato-oncologist community about treatment of Hodgkin lymphoma. Hodgkin lymphoma is one of the diseases of the neoplastic disease where the patients are generally referred either to referral centers or to specialists who have knowledge of the disease. But I think the new challenges which I have described to you (ie, PET technology and the intelligent use of antibody drug conjugate) are not so simple. I think that there is a need to have a better knowledge about the PET technology and the correct use of PET. For instance, we just learned that PET is absolutely necessary in the treatment phase but might be of no value in the follow-up situation. So, people must know how to optimize the use of this technology, and probably, we need also to increase the knowledge of specialized physicians about new drugs because the nuances of the different new drugs are not really well known by most people. In many congresses, ASCO, EHA, or ASH, people did not go to the sessions where new drugs are discussed but mainly to sessions where phase III studies are discussed. So, I think that we need a better effort to integrate the use of the PET technology in the treatment of Hodgkin lymphoma and to better disseminate the knowledge about new agents.

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