Managing Hodgkin Lymphoma Expert Interview Series

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

George Davatelis, PhD – Moderator/Writer
with
Won Seog Kim, MD, PhD
Division of Hematology-Oncology
Department of Medicine
Samsung Medical Center
Sungkyunkwan University
Seoul, Republic of Korea

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 Dr. Won Seog Kim of the Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University, Seoul, Republic of Korea, to discuss the latest advances and current state of HL treatment in Asia.

MHLC: *Compared with west, Hodgkin lymphoma in eastern Asian countries is characterized by a lower incident rate, but a higher proportion of mixed cellular histology, can you tell us a little bit about this?*

Dr. Won Seog Kim: Hodgkin lymphoma makes up 4.6% of all the lymphomas in Korea.[3] So, it is lower than on the western side and I think it is a general phenomenon in Asian countries like Japan. Unfortunately, we have very little information from China, but based on the experience from Hong Kong or Singapore, I think they have very similar epidemiologic characteristic, so it is a little lower comparing with western side. We have a little higher incidence of mixed cellularity, but in general, I have no idea why we have some difference in the epidemiologic side.[4] I think it is a kind of ethnic difference, but we have no backup data for that.

MHCL: *What is the standard of care for Hodgkin lymphoma in Korea?*

Dr. Won Seog Kim: The standard of care is quite similar to western side. Because of the rarity of the disease, we did not do any front-line clinical trial targeting Hodgkin lymphoma. So, if you see the paper published in *Annals of Hematology* by our group's Hodgkin lymphoma survey, you can see our treatment/care pattern. We are just following the ideas from the western side, so ABVD will be the front line. Very rarely, they used BEACOPP, but right now in my understanding, more than 90% of the institutes are using ABVD as the front-line treatment as the standard care.

MHCL: *What do you believe are the challenges in treating Hodgkin in Korea, and how do you think they might differ from other areas, say EU or the US?*

Dr. Won Seog Kim: From the front-line treatment, ABVD is giving us very nice outcomes. Almost 80% will be cured with just ABVD or short-course ABVD with lower dose of radiation. The challenging area is the primarily refractory cases and also the relapse cases. For that kind of patients, we usually prefer the platinum-based salvage chemo regimen for the non-Hodgkin lymphoma like ICE (ifosfamide, carboplatin, and etoposide) or DHAP [dexamethasone, cytosine arabinoside (Ara-C), and cisplatin].[5]
If the patient is young, we prefer autotransplantation for the chemosensitive patient. The problem is, the failure after autotransplantation or refractory to salvage chemo regimen. Brentuximab is available right now, but it is not reimbursed from the Korean Health Insurance System. So, the cost is a big issue to use brentuximab. We know that it is a very nice drug, it is very efficient, but at the same time, it is quite expensive. After the failure of the autotransplant or after three-line failure, I usually recommend brentuximab vedotin. If they have to pay from their pockets, around 70% of patients agree to use that one. So, the situation is much better, but I feel they are feeling a little financial burden to use brentuximab vedotin. If the patients are maintaining good response, I usually stop after 6 cycles because of the financial reason.

MHLC: *What do you see as opportunities for treating Hodgkin's in Korea?*

Dr. Won Seog Kim: If they can get the reimbursement, we have more chance to use brentuximab earlier. You have to understand the health insurance system of Korea. We have only one health insurance system under the government. We are waiting for the outcome of phase III trials, ABVD versus AVD and brentuximab. So, if the trial is positive, our lymphoma society will discuss again with the health insurance system under the government to getting reimbursed, and I think we can have a better chance to use more and more brentuximab.

MHLC: *Do you think that western clinical trials in Hodgkin lymphoma, whether it is in Europe or the US, are really relevant to Asian clinical practice?*

Dr. Won Seog Kim: Yes, actually, the Korean government and the Korean FDA is quite flexible getting the ideas from the western side. If the FDA or EMA approve some drugs and they have phase III trials, the Korean government approves the drug quite easily. So, two criteria are very important based on phase III trial and approval of EMA or FDA. Japan and China have very different policies, especially Japan. For every drug they want phase I trial from only Japanese population. In their ideas, the Japanese population is ethnically different from the western side, so they have to confirm the safety issues. I am told that China has very similar policies.

MHLC: *We know that approximately 80% of Hodgkin's patients are cured using standard of care treatment, but that the treatment side effects are becoming more and more of a problem. Can you tell us a little bit about the thinking in your practice and then maybe in Korea in general, of how you are addressing those concerns about treatment-related side effects?*

Dr. Won Seog Kim: The big issues right now are the second malignancies in the late toxicity. We are trying to reduce the number of cycles and reduce the dose of radiation and reduce the field of radiation. So, right now, I am using more and more PET-CT scans. So if the PET-CT gives us a response, and also if the patient has a favorable risk group, I try to reduce the number of cycles. So, right now especially, the second malignancies in the late toxicity are bigger than the acute toxicity.

MHCL: *What do you think about some of these new drugs coming out, and do you see any of them looking particularly promising?*

Dr. Won Seog Kim: Right now, brentuximab vedotin is giving us the best outcome, so, it will be more and more frontline. We have no data on HDAC inhibitors and mTOR inhibitors. The one problem is gathering the patients for the trials is very difficult because 80% will be cured with just the standard of cares and another group will be getting good response with brentuximab vedotin. So I think in the future we need a trial to test the HDAC inhibitors or mTOR inhibitor or other small molecules to see if it is really effective or not. If they are giving us some good positive signs, we can have a chance to make another very kind of combination treatment even with brentuximab vedotin. I am doing the pilot study of ruxolitinib to see the efficacy in very refractory Hodgkin lymphomas and the interim data will be presented at the ASH meeting this year. I think the JAK-1 & 2 inhibitor will be one of the good agents in Hodgkin lymphoma in the future. So, I think one thing I really wanted to test in the next step will be the combination with ruxolitinib with brentuximab vedotin.

MHLC: *A lot more older patients are being diagnosed with Hodgkin lymphoma. How do you think physicians in Korea should be treating elderly patients?*

Dr. Won Seog Kim: The question is related to the toxicity. Now, we are having more and more elderly patients, some of them are very old, 80 or even 90. I found a very interesting presentation from an Italian group at the EHA meeting this year. They are giving the two cycles of brentuximab vedotin first and then moved to chemo. I think that kind of approach is really interesting. The elderly patients are very vulnerable to toxicity. Adriamycin is toxic to the heart, and bleomycin has toxicity to lung. So, I think if we can move more and more to use of brentuximab as a frontline treatment, we can reduce the number of cytotoxic chemotherapy.

MHLC: *What do you think are the educational needs of your colleagues in Korea and the rest of Asia?*

Dr. Won Seog Kim: Education is the very important, especially for the clinicians. Inside Korea we have meetings dealing with many new compound and new information and update the clinical trial outcomes. I have been involved in many education programs in Asian. I found that the knowledge level of the Asian country is very heterogeneous. Hong Kong, Singapore, Korea, and Japan are very well developed, and the knowledge level is almost same with the European or the US countries. In the other countries like Myanmar, Cambodia, Vietnam, Philippines, some of the lymphoma clinicians never used the rituximab, and they are not doing the immunohistochemical staining for diagnosis of lymphoma. One of the hurdles is if I can teach them and educate them, they have no chance to use very expensive new compound. In China, most of the young doctors have no chance to go outside to attend ASH or ASCO, or EHA meetings, so young doctors are very eager to getting the information from other experts, other investigators from western side or from other countries. So, I think still, the education need is really, really big in most of the Asian countries.

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