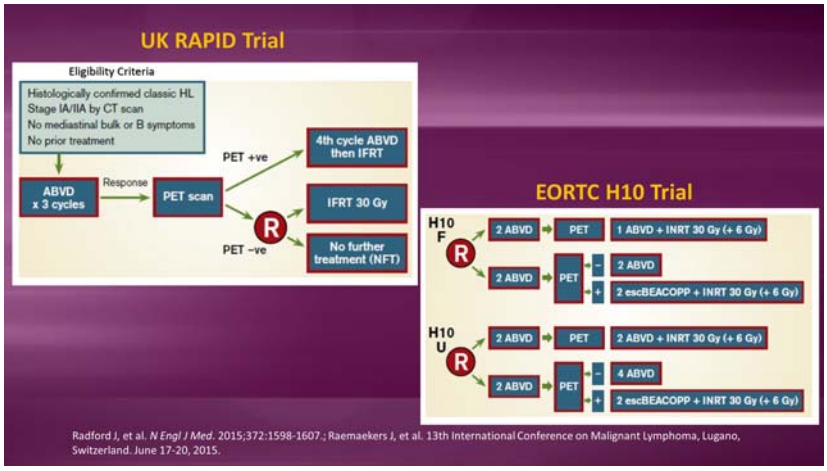
Martin Hutchings, MD, PhD
Department of Hematology
The Finsen Centre, National Hospital
Copenhagen University Hospital
Copenhagen, Denmark

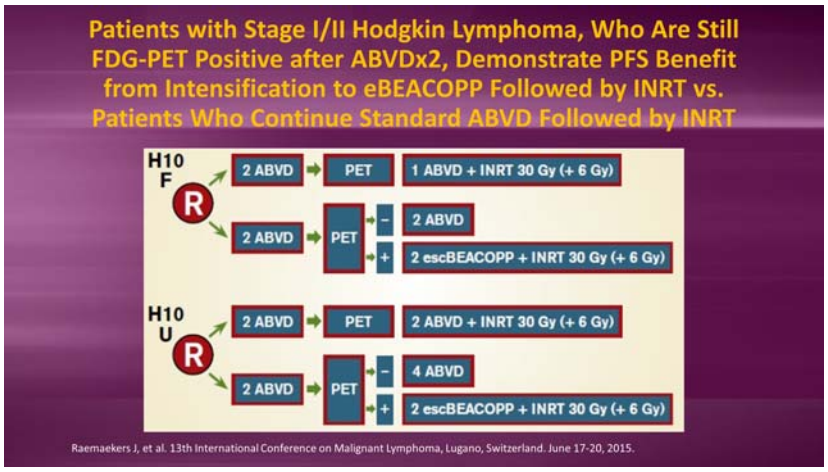
Welcome to *Managing Hodgkin Lymphoma*. My name is Martin Hutchings. I am Senior Consultant at the Department of Hematology at Rigshospitalet which is in Copenhagen, Denmark. I would like to take the next few minutes to provide you an overview of the data which were presented at the early stages session. The session was divided into two parts. Part one included three talks, and in the second part there were presentations of three submitted abstracts. In the first talk, I had the privilege to talk about the pros and cons of PET response-adapted therapy of early favorable stage Hodgkin lymphoma. The talk was mainly based on the results from two recently published randomized trials.

One, the UK RAPID trial, including patients with early-stage disease stage 1 and 2A non-bulky. As well as the EORTC French/Italian H10 study where the final analysis has very recently been made. The main result of both studies is actually a negative one. There was not any proven non-inferiority for patients who offer an early interim PET which was negative had omission of radiotherapy. In other words, there was a loss of disease control in both studies for patients who had omission of radiotherapy after negative PET as compared to patients who were treated with standard combined modality treatment. On the other hand, the conclusions are not perhaps so clear because in the experimental arms where patients did not receive radiotherapy if they had an early negative PET, survival, progression free and overall, were both excellent even in the experimental arm, even if the criteria for non-inferiority were not met.



Much of the discussion was based on the patient tailored therapy because there are patients where combined modality treatment is desirable, and there are patients where perhaps it is particularly important to avoid the perils of radiotherapy and the risk of late effects. For example, young women where you would like to avoid irradiation of the breast, and in those instances, perhaps chemotherapy alone treatment would be desirable, even if there is a slight loss of disease control. The second talk was given by my colleague from the EORTC Lymphoma Group, John Raemaekers, who focused on recent data in early-stage unfavorable patients.

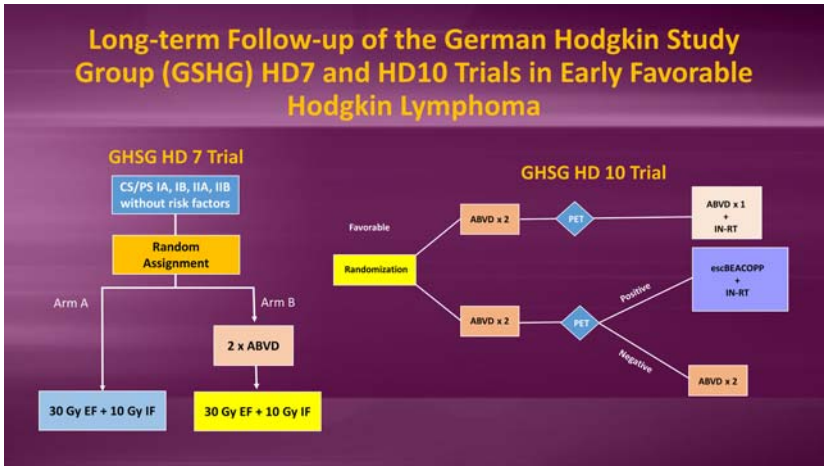
John Raemaekers mainly talked about the recent results from the EORTC French/Italian H10 study. In patients with unfavorable disease which is the majority of patients from that study, there was, just like in early favorable disease, there was not non inferiority of the main scope of the study which was to show whether you could omit safely radiotherapy in patients with an early negative PET. There was a loss of disease control if you omitted radiotherapy, but surprisingly, perhaps, the loss of disease control was less in the unfavorable group of patients than in the favorable group of patients. It seems as though you can omit radiotherapy in early PET negative patients if they are with unfavorable risk factors and lose less disease control than if they have favorable risk factors, perhaps because we are looking at two biologically slightly different situations. Another part of the H10 trial looked at escalation of therapy to those patients who are still PET positive after 2 cycles of therapy. A positive result from the H10 study was in fact that both in terms of progression-free survival and, albeit not statistically significant in terms of overall survival, there seems to be an improvement in efficacy if treatment is escalated to BEACOPP plus radiotherapy after 2 cycles of ABVD when the PET is positive.



In other words, outcomes are better for patients with an early positive PET if treatment is escalated from ABVD to BEACOPP. This analysis was not made separately for patients with

unfavorable risk factors and favorable risks factors. It was one big analysis, but the difference, the improvement in progression-free survival was mainly due to patients in the unfavorable risk groups. After these two talks which gave the most recent available data on the treatment of patients with early-stage Hodgkin lymphoma, there was an interesting presentation on the long-term results from the German Hodgkin Study Group on the treatment of patients with nodular lymphocyte-predominant Hodgkin lymphoma of early stages, a relatively rare disease which is treated and studied separately from classical Hodgkin lymphoma.

After these three talks, we looked at the three submitted abstracts, which were all interesting. The first one was a presentation given by Stephanie Sasse, a representative of the German Hodgkin Study Group. She gave a presentation providing data from a long-term followup of the German HD7 and HD10 trials, both trials in early favorable stage Hodgkin lymphoma. This was followup data for 1,817 patients with a very long median followup of 98 months in HD7 and 120 months in HD10. What Stephanie Sasse showed was that in the HD7, the long-term followup still shows that combined modality treatment is more effective than radiotherapy alone, and in the HD7, it was extended-field radiotherapy, a technique which has been abandoned since then. Still, there is no significant difference in overall survival between the treatment arms of the HD7 due to of course effective subsequent therapies for those patients who relapse. The HD10, which is still the trial that defines the standard of care for early-stage favorable disease, we saw a 10-year progression-free survival which is still non-inferior to the other arms of the preferred arm which is 2 cycles of ABVD followed by as little as 20 Gy involved-field radiation. This is minimal therapy highly effective with a 10-year progression-free survival of 86% and an overall survival high in the 90s, so still the standard of care for early-stage favorable disease.



The next abstract was a very interesting talk given by Kateřina Dědečková from Prague of the Czech Republic. She presented a single-institution experience of using proton therapy for mediastinal Hodgkin lymphoma. This was a very interesting, well-received, and much debated abstract where 33 evaluable Hodgkin lymphoma patients had undergone mediastinal proton therapy. She presented the techniques which are still relatively novel for most of the audience and focused on the differences between proton therapy and more conventional highly conformal photon therapy which is what we generally understand by radiotherapy. The big difference is that you can irradiate effectively the mediastinal masses without irradiating at high or low doses, healthy organs where you would like to avoid radiotherapy, what we call the thoracic path. Hopefully, this will result in fewer long-term undesirable effects of radiotherapy, particularly heart disease, lung disease, and second tumors.

Of course, they do not have followup to demonstrate this advantage. What was focused on were the acute toxicities which were markedly less frequent in this series in the patients who were treated with photon therapy than what you would expect if the patient has been given conventional radiotherapy.

The last abstract was given by Dr. David Straus from Memorial Sloan Kettering Cancer Center in New York. He presented an update of the U.S. Intergroup Trial CALGB/Alliance 50406 Study which was a single-arm study that already had data presented at the American Society of Hematology conference in December 2015. So, this was an update. It was a single-arm study for patients with stage 1 or 2 Hodgkin lymphoma non-bulky disease. Again, this study was a PET response adapted approach. All patients received 2 cycles of ABVD followed by a PET scan. If that PET scan was negative, they would continue with another 2 cycles of ABVD and no further treatment. Again, a radiotherapy-free approach for early PET-negative patients, and those patients who were still PET positive

after 2 cycles of ABVD would, just like in the H10 experimental arm, receive 2 cycles of BEACOPP escalated followed by radiotherapy. The new data that was presented basically confirmed what has already been shown from that trial and that is a very good disease control in the PET-negative patients who received chemotherapy alone. I believe they had an estimated 3-year progression-free survival of 92%, so confirming the data that we had already seen from the RAPID study and the H10 study, and in the PET-positive group, there was a failure rate of 31%. A little over two-thirds of the patients who were PET positive still went into long-term progression-free survival, of course, not as good as the PET negative groups, so confirming the prognostic value of an early PET. It was all in all a very productive and interesting session like so many other sessions here at the International Symposium of Hodgkin Lymphoma in Cologne.

Thank you very much for viewing this activity. For additional resources, please be sure to view the other educational activities on *ManagingHodgkinLymphoma.com*.