Managing Hodgkin Lymphoma

Responses and Chemotherapy Dose Adjustment Determined by PET-CT: RATHL Study

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Hello, my name is Dr. Peter Johnson. I am from the Cancer Research UK Center in Southhampton in the UK, and I am reporting to you live from the 12th International Conference for Malignant Lymphoma in Lugano, Switzerland. I would like to take this opportunity to give you a brief overview of the talk that I have presented about the international RATHL study covering responses in chemotherapy dose adjustment according to PET CT imaging for patients with advanced Hodgkin lymphoma. This is a large international collaborative study conducted by the UK, groups in Italy, the Nordic countries, and Australasia looking at whether we can use FDG-PET imaging after two cycles of conventional therapy to determine the intensity of subsequent treatment, so the plan of the protocol was as follows. All patients with advanced Hodgkin lymphoma received two cycles of conventional ABVD and then had FDG-PET scan carried out at that point compared to a baseline scan done as part of the staging investigations. Patients who were judged to be PET negative went on to continue ABVD or to be randomized to drop the bleomycin and receive early AVD for the remainder of their treatment. Patients who scans showed up positive FDG avid disease went on to escalated treatment with either the escalated BEACOPP regimen or the BEACOPP 14-day regimen, both of which have been developed by the German Hodgkin Study Group. We included 1,200 patients from this international collaborative study over a period of just over 4 years, and when we looked at the results of the PET scans after two cycles of treatment, we found that 85% of patients had become PET negative. Now the way that these PET scans were analyzed is very important. There was central reading of all the PET scans by core labs in each country trained to the exact same standards and reporting all the scans according to a 5-point scale, so-called the Deauville scale, which gives us highly reproducible and highly accurate assessments of the FDG uptake in residual lymph nodes and other sites of disease. So all the scans in this study were prospectively read by the core labs and all the randomizations and all the judgements about subsequent treatment were made according to the central review of the scans, not according to the local review. We had 85% of patients who became PET negative and were randomized to either continue ABVD or to deescalate to AVD, and we had 15% of patients who went on to receive escalated treatment with one of the BEACOPP regimens. When we looked to the baseline characteristics of the patients in the study and compared them to the PET scan results, we found that patients with bulky disease and with a high international prognostic score were slightly more likely to be PET

positive after two cycles than those without those adverse features. When we looked at the final responses according to the PET score and compared conventional response outcomes with the PET outcomes in the PET negative group, we found that the actual PET score between 1 and 3, which were all counted as negative in this trial, correlated to the likelihood of achieving a complete response according to conventional CT criteria, so the lower the PET score at cycle two the higher the probability of achieving a conventional CR. When we looked at the outcomes in the PET positive group, the 15% of patients who went on to have BEACOPP treatment, we found that although they were all PET positive at the time they started the BEACOPP, at the end of the BEACOPP, we had 75% who were PET negative at that point. So we think that the BEACOPP is capable of salvaging a substantial proportion of those patients for whom ABVD appears to be failing early on. The protocol specified that patients who were PET negative after two cycles of treatment should not receive consolidation radiotherapy, although some discretion was allowed by the local treating clinicians in this respect. What we found was that less than 5% of patients who had a negative PET scan after two cycles went on to receive any consolidation radiotherapy indicating a high level of compliance with the protocol and also of course a substantial reduction in the proportion of patients with advanced Hodgkin lymphoma who are now receiving consolidation radiotherapy in this protocol.

To summarize the findings from this trial, we found that standardized central reporting of PET scans is practicable, is feasible, and works very well. We get very high and reproducible standards of reporting of the PET scans. We also found that the PET score is reflective of both some of the baseline characteristics and also to extent predictive of the conventional outcomes to subsequent conventional chemotherapy. We found that those patients who were PET positive and went on to escalated treatment had a high rate of salvage with escalation to BEACOPP, but of course we are going to require much longer follow up to know whether this is truly a valuable result and to know whether the long-term results of treatment are an improvement on what we have done previously.

I hope that you found this information useful and informative and thank you for joining us from this session at the 12th International Conference for Malignant Lymphoma.