Human Papillomavirus (HPV) Advances; A Patient Education Program

Deintensification in HPV-Driven SCCHN

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Hello. I'm Jared Weiss. I'm a Professor of Medicine, and Sector Chief of Thoracic and Head and Neck Oncology at UNC's Lineberger Comprehensive Cancer Centre, and a volunteer Executive Board member here at Global Resource of Advancing Cancer Education. I'm pleased to speak to you today on the subject of treatment de-intensification in HPV-driven head and neck cancer. The interest in treatment de-intensification arises from two thoughts. One is that many of our patients who we cure with locally-advanced head and neck cancer, permanently suffer morbidities that harm quality of life. In particular, patients can have stiff necks, they can have dry mouths, they can have problems speaking or swallowing. For the chemotherapy, they can have problems hearing particularly the high frequency, and of hearing, ringing in the ears, neuropathy which is a numb tingling at the tips of fingers, it can even become painful, as well as decreased kidney function, probably even leaving some out. So which is to say that chemo-radiotherapy is a rough thing to go through. And so, we have an interest in decreasing the intensity of both the radiation and the chemo to ameliorate these effects. Our standard dose of radiation is 70Gy. And it's notable that between 50 and 70 Gy there is a steep difference in the expected morbidity. The differences in this realm might be clinically important for improving long-term quality of life. Of course, we want to improve quality of life in all of our patients, HPV-driven or smoking-driven, but the superior prognosis of HPV-driven cancer opens a window of opportunity to consider this. The data on the superior prognosis of HPV started in part from RTOB 0129. One of the things we learnt from this study was that, both is terms of cancer-control shown on right and in terms of overall survival from any cause from on left, the HPV-positive patient does much better than the HPV-negative patient. I apologise for the poor colour coding here. But this has been confirmed in multiple other studies. And when you talk about low-risk HPV-people, who have never smoked or who've had less than ten packs in their smoking history, and who are not very advanced stage and HPV-positive cancers, we are talking about more than 90% cure rates. So, a natural question arising in the minds of clinicians who are upset by how much we are hurting people in the long-run when we cure them is that can we decrease the intensity of the chemotherapy, the radiation therapy, or both, and preserve that high cure rate. So, many of these studies done had been kind of complicated and don't answer the question in a simple way. My colleague, Dr. Bhisham Chera, led an effort that in my mind was the simplest at both decreasing the intensity of the study. So patients go 60Gy of radiotherapy, down from the standard of 70. Most patients got cisplatin at 30mg per m^2, which is a decrease from the simple, most commonly used regiment of 40mg per m^2. And those with the earliest stage, T0 to 2, which refers to a small primary where it started; and 0 to 1, which means not a lot of nodal spread, got no chemotherapy at all in combination with this reduced dose of radiation. And when you're looking at the bottom, our curves looking at a variety of measures of interest to clinicians and I imagine our patients, every X-axis is time, and every Y-axis is the percent of patients with the N-point of interest. And whether you're looking at local regional control (meaning control in the head and neck), whether you're looking at distant metastasis-free survival (meaning absence of spread elsewhere), PFS (which takes down any time the cancer froze or a patient dies from any cause), or a total survival, the most objective of measures. The

outcomes were rather good. So the strength of this and similar efforts are that the data are very good. The major unmet need here is that this is not a randomised study. To have, what we call, Level 1 evidence, you would need to de-intensify the therapy of half the patients, provide standard of care in the other half, and show what statisticians call non-inferiority. And we may never really get quite that level of data because of the extraordinary number of patients that will be required with the good prognosis of this group. But I will share with you, in addition to this study, what we know.