



Human Papillomavirus (HPV) Advances; A Patient Education Program

Reduction of Post-Operative Adjuvant Intensity

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So, the radiation dose in de-intensification clearly went well. We are looking at a different study here, looking at elimination of the chemotherapy, of the Cisplatin; and that did not go as well. In particular, at the bottom left. Local region failure was quite a bit higher in patients for whom the chemotherapy was omitted. That was not clearly reflected in the survival curve shown at top right, but may be a consequence of salvage. When chemo-radiotherapy or radiotherapy alone, for half of the patients, doesn't cure people, you can come back and salvage a cure with surgery. The problem is, those surgeries are dramatic and brutal compared to what you would have done if surgery was the upfront curative modality. And so, the upper regional failure here is a big deal, and you can see here a trend in the wrong the direction for progression-free survival shown at top left. And so, we are more hesitant about eliminating or reducing the dose of chemotherapy than we are about reducing the radiation dose. This is a more complicated study (I apologise for that), it is ECOG3311. But, in editorialising which of the many important studies to share with you, this is actually a very important one. So, I'll walk you through the design. Basically what happened here was that the lowest risk patients, after surgery, were observed. The highest risk patients got standard adjuvant chemotherapy and radiation, at very standard doses. And those with an intermediate risk were were randomised to either the standard adjuvant radiation dose, 60Gy, or a dose reduction of 50Gy. I want to comment here on surgery before moving forward because I think that if we've focused here on quality of life, we need to not lump all surgery together because not head and neck cancer surgery harms quality of life to the same extent. Happily, over the decades, chemotherapy-supportive care has improved, particularly for nausea control and amelioration of renal problems. Happily, radiation has improved. The ability to focally deliver has improved, and I want to acknowledge that surgical standard of care has improved as well. More specifically is the advent of transoral surgeries. So these are just what they sound like. Instead of splitting the jaw and coming from outside to in, transoral surgery (be it transoral laser or transoral robotics), goes from the inside to out for the oral cavity and the oropharynx, meaning the tonsil and the base of tongue, and sometimes even high hypopharynx cancers. I'm not the surgeon, but I do admire these surgeries. They have a whole lot less blood loss, typically on par with a blood-draw and not with one of the old-school surgeries. The cosmetic defect from the removal of the primary tumour is zero. And the functional outcomes are quite good compared to the older surgeries. As well, the recovery time is faster, hospital stays are shorter. So these are better surgeries. As a medical oncologist, I kind of vaguely think of transoral surgeries as de-intensified surgery in terms of the risk performed to the patient. And these are really the kinds of surgery that are the most relevant in the HPV-positive cancer patient. Overwhelming majority of cancers here are the oropharynx, and the base of tongue and tonsils, which are very minimal to these kinds of surgeries. So, onto the data. Of course, Arm A, the low-risk patients, did the best. This is not necessarily reflective that people do better if you leave out radiation. This is reflective that this is a low-risk population. And like the first study did I showed you, de-intensification here still had a positive outcome. In orange, we we see that the highest-risk patients did the worst. Of course the highest-risk patients do the worst. But what's really interesting here, to me



most instructed, is how similar these green and red curves are. It's the same curve, they cross over each other a few times. There's no different between these curves other than what random noise gives us, suggesting (this wasn't a phase 3 study) that it may be safe to reduce the adjuvant radiation dose in these patients from 60 to 50, and the decrease from 60 to 50 is meaningful just like in the first study I showed you, it was meaningful going from 70 to 60.