



## **HPV Advances: A Patient Education Program**

### **Identifying Candidates for De-Escalation**

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I think we have some very promising treatment de-escalation for HPV-associated cancers, but our major barrier remains as to how do we choose the appropriate patients for de-escalation with the goal of maintaining cure and decreasing morbidity. And currently, we're using just the size of the tumour of the number of lymph nodes, and whether or not somebody is a smoker, or we're treating patients with induction chemotherapy or with surgery; and then based on their response or the pathology, determining who can be de-escalated. And I think we need better markers for de-escalation. So there are some markers that are currently being validated in a prospective trial, and I'll just tell you about a couple of those. There's some genomic markers that predict outcome. There's two genes in particular, called TRAF3 and CYLD, that are regulators of inflammatory signalling. And they're currently undergoing validation. I'll just show you a little of the data that led to this trial. This is from TCGA, and it shows that tumours in red, and mutations in these two genes, had better survival than HPV-associated tumours that lacked mutations in these genes. Without getting into a lot of details, basically defects in these genes identify two separate subtypes of HPV-associated cancers with many many differences molecularly, as well as the survival difference. And so, the idea now is can these markers identify patients that can be de-escalated? So I'd like to just summarise about de-escalation therapy for HPV-associated head and neck cancer. I really think it holds great promise and we need to do something to have our patients' quality of life improved after treatment. We want to decrease the morbidity of therapy, we want to maintain good cure rates, and something I hadn't mentioned is we want to improve cure rates for patients who are not going to do well with standard therapy, which may mean new therapies are needed. And we want to improve quality of life for our patients. So we want to take this and turn it into this; smaller radiation, smaller chemotherapy, minimal surgery, or perhaps new drugs. The challenge still remains how to appropriately identify patients who will do well with this de-escalated therapy. So with that, I'll close, and I appreciate the time to explain a little bit about where we're headed with de-escalated therapy for HPV-associated head and neck cancers.