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What Is the Rationale for the Use of Neoadjuvant and Adjuvant Immunotherapy to Treat Patients With Resectable Lung Cancer?

Announcer:
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Dr. Forde:
Hello, my name is Dr. Patrick Forde from Johns Hopkins University. In this session, I am going to discuss the rationale for the use of neoadjuvant and adjuvant immunotherapy to treat patients with resectable lung cancer.

In the US today, we see that approximately 22% of men and women who die from cancer die from lung cancer. And this is more than from other common cancers, including prostate and colon cancer for men and breast cancer and colon cancer for women.

We are thankfully seeing an impact from the use of novel systemic therapies on lung cancer mortality. This paper from Dr. Howlader and colleagues showed that in the earlier part of the previous decade, there had been a yearly 6.3% reduction in lung cancer mortality. Some of this is due to a reduction in incidents perhaps related to reduced smoking. However, the remainder is felt to be due to the many new drug approvals we have seen for advanced cancer.

We are also seeing, however, that this novel therapy development for earlier-stage resectable lung cancer has been relatively slow and this is despite a very clear unmet need. The five-year survival for patients with clinical stage IIA non-small cell lung cancer is only 60%. And when you go up to higher stage disease, which is still resectable, stage IIIA, this drops down to 36%. And this makes up almost 500,000 people worldwide who have potentially curable surgically resectable lung cancer. However, many of whom experience relapse and death from their cancer. When we are talking about systemic therapy for resectable cancer, what patients are we speaking about? Well, in terms of neoadjuvant or adjuvant chemotherapy we speak mainly about those tumors which are four centimeters or greater in diameter and/or have lymph node positivity.

We know from the LACE meta-analysis published now almost 15 years ago that there is a benefit from perioperative platinum-based chemotherapy showing a 5% improvement in survival at five years. However, this standard of care in 2008 was still the standard of care up until a couple of years ago despite many, many advances for advanced lung cancer in terms of immunotherapy and targeted therapy.

We know that neoadjuvant or preoperative chemotherapy followed by surgery delivers a very similar benefit when compared to surgery alone, approximately a 13% improvement in five-year survival.

So, what are the considerations we take into view when considering either neoadjuvant or adjuvant immunotherapy? Well, neoadjuvant therapy provides the earliest opportunity to eradicate micrometastatic disease, which is the major cause of death from cancer. More patients will commence neoadjuvant therapy, and more patients will complete the planned course if it is given preoperatively. And two key points that have arisen recently in terms of the use of neoadjuvant immunotherapy include the use of pathological response, so the

degree of tumor regression after neoadjuvant chemo-immunotherapy. And this may be a potential early indicator of the benefit of therapy. And also, the fact that when you administer immunotherapy prior to the surgery, the draining lymph nodes where the immune response is driven from are still in place and this could augment long-term anti-tumor immunity. In contrast, in the adjuvant setting patients can get straight to curative surgery. There is no risk of presurgical complications from the systemic therapy and patients can receive a longer duration of treatment. So, it is possible that both treatments, neoadjuvant and adjuvant immunotherapy, have a role in the management of patients with resectable lung cancer.

Back in 2018, we looked at the use of neoadjuvant anti-PD-1 nivolumab in patients with resectable non-small cell lung cancer, and this study showed rather surprising findings. Almost half of the patients had a major pathological response, or NPR, to just two doses of nivolumab. In long-term follow-up of those patients, we have seen that the patients who did have a major pathologic response have done remarkably well with no patients with active cancer at five-year follow-up. And this and other studies have driven a rapid increase in the use of neoadjuvant and adjuvant immunotherapy. You will see in this slide an increase from only two or three or four studies in 2014 up to over 250 trials now active worldwide looking at either neoadjuvant or adjuvant anti-PD-1. In the other studies, in the other segments of this CME activity, we will discuss some of these studies and some of the current applications to practice. Thank you for your attention.

Announcer:
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