IIIA LUAD. We find it disconcerting that only 60% of patients in ADAURA received adjuvant chemotherapy and note an unusually high rate of recurrence in the placebo arm. There are too many unknowns to disregard the proven survival advantage of adjuvant chemotherapy for the unproven benefit of osimertinib.

Longer follow-up is required to see if ADAURA endures the test of time and adjuvant osimertinib confers a survival advantage. Regardless, we are certain that there is an imminent and inevitable paradigm shift toward targeted therapy in the treatment of resectable LUAD on the horizon.

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Commentary: Targeting our attention

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The expert opinion article by Jones and colleagues is an extremely well-written essay that describes and provides context to the recently published ADAURA trial, which demonstrated dramatic improvements in survival for patients with stage IB-IIIA epidermal growth factor receptor mutation–positive non–small cell lung cancer who received adjuvant osimertinib. Because of its clarity and efficiency presenting key results and background, we have little to add and recommend it highly as a review article.

Instead, we wish to emphasize how this article portends a front of rapidly changing paradigms for our specialty for which we need to prepare. A review of current protocols open for enrollment reveals an explosion of new studies using novel treatment combinations with different sequencing in resectable non–small cell lung cancer.

Central Message

Successful thoracic surgeons will need to adapt by studying targeted signaling pathways with immunotherapies and integrate them into their practices.

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2021 Surgical Intrinsic Trials*
adjuvant approach (S) to extend therapies for select early stages (see the legend of Figure 1 for details). Still others use local consolidative therapies for oligometastatic disease. The “Other” trial in Figure 1 involves a preoperatively implanted device that selectively elutes 19 chemotherapy drugs in the region of the primary tumor with the intent of determining (in vivo) adjuvant chemosensitivity. In addition, completely novel interventional approaches involving intratumoral administration of immunomodulatory therapies are being trialed. Such explorations will be necessary if we wish to approach the survival rates of less-virulent malignancies like breast and colon cancers.

What are the implications of these novel approaches to the practicing thoracic surgeon? First, thoracic surgeons need to be both aware of and comfortable with novel agents and their associated outcome data. If we are to remain disease managers, we should facilitate an informed discussion with patients regarding these approaches and agents. Second, we have to be engaged in the conduct and interpretation of these trials, lest surgery be underused and surgeons be left out of the conversations. Third, surgeons will need to understand the side effects of these drugs. For instance, tyrosine kinase inhibitors may affect the function of membrane-bound solute transporters, an understudied class of proteins, by preventing their phosphorylation. Perioperatively, this can affect the metabolism of our prescribed drugs, alter creatinine transport and change the need for insulin supplementation.

In summary, if we embrace such changes as opportunities, then we can engage with lung cancer biology with renewed vigor and enthusiasm.

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