Adjuvant Systemic Therapy and Adjuvant Radiation Therapy for Stage I-IIIA Completely Resected Non–Small-Cell Lung Cancer: ASCO Guideline Rapid Recommendation Update

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ASCO Rapid Recommendations Updates highlight revisions to select ASCO guideline recommendations as a response to the emergence of new and practice-changing data. The rapid updates are supported by an evidence review and follow the guideline development processes outlined in the ASCO Guideline Methodology Manual. The goal of these articles is to disseminate updated recommendations, in a timely manner, to better inform health practitioners and the public on the best available cancer care options.

BACKGROUND

In 2017, ASCO with Ontario Health—Cancer Care Ontario published a guideline on adjuvant therapy in resected stage I-III non–small-cell lung cancers (NSCLCs).[1] Two randomized control trials (RCTs)[2,3] were published in 2020[2] and 2021[3] and prompted this amendment to the 2017 guideline.

METHODS

A targeted electronic literature search to identify RCTs of osimertinib and atezolizumab in this patient population was conducted. No additional randomized trials were uncovered. Members from the original Expert Panel reconvened to assess key evidence from the Wu and Felip trials and to create and approve the revision to the recommendations.

EVIDENCE REVIEW

In the Wu et al[2] targeted therapy trial, patients with completely resected *EGFR* (Ex19 del or L858R) mutation–positive stage IB-IIIA (7th edition, AJCC Cancer Staging Manual),[4] NSCLC were randomly assigned to receive either osimertinib (80 mg once daily) or placebo for 3 years or until disease recurrence or fulfillment of a criterion for discontinuation. Administration of postoperative chemotherapy before random assignment was allowed but not mandatory (given in 26% and 75% of stage IB and II-IIIA patients, respectively). The benefit of postoperative osimertinib was not affected by the use of postoperative chemotherapy. The primary end point was disease-free survival (DFS) according to investigator assessment among patients with stage II-IIIA disease. A total of 682 patients were randomly assigned; 60% received adjuvant chemotherapy. At 24 months, 90% of stage II-IIIA patients receiving osimertinib (95% CI, 84 to 93) versus 44% receiving placebo (95% CI, 37 to 51) were alive and disease-free (overall hazard ratio [HR] for primary study end point 0.17; 99.06% CI, 0.11 to 0.26; $P < .001$). In the stage IB-IIIA population, 89% of the patients receiving osimertinib versus 52% receiving placebo were alive and disease-free at 24 months (95% CI, 85 to 92 *v* 95% CI, 46 to 58; overall HR 0.20; 99.12% CI, 0.14 to 0.30; $P < .001$). Overall survival data, a secondary end point, are immature, and it is unknown whether there is an overall survival benefit.

In the Felip et al[3] immunotherapy trial, patients with completely resected stage IB (≥ 4 cm)-IIIA (7th edition, AJCC Cancer Staging Manual)[4] NSCLC were randomly assigned to receive adjuvant atezolizumab (1,200 mg every 21 days for 16 cycles or 1 year) or best supportive care (BSC) after adjuvant cisplatin-based chemotherapy. The primary end point was investigator-assessed DFS in patients with stage II-IIIA NSCLC with at least 1% programmed death-ligand 1 (PD-L1) expression. A total of 1,005 patients were randomly assigned and included in the intent-to-treat population. At 32 months median follow-up, DFS was greater for patients with stage II-IIIA, PD-L1–positive with atezolizumab versus BSC (HR, 0.66; 95% CI, 0.50 to 0.88; $P = .0039$) and also for all patients with stage II-IIIA with atezolizumab versus BSC (HR, 0.79; 95% CI, 0.64 to 0.96; $P = .020$).

The quality of the evidence of these studies was assessed using the GRADE tool. Wu et al had a high certainty of evidence, whereas Felip et al had a moderate certainty of evidence.

2021 UPDATED RECOMMENDATION

Recommendation 1.2

Stage IB (3 < T ≤ 4 cm, N0M0): Adjuvant osimertinib is recommended for patients with sensitizing *EGFR* (Ex19del or L858R) mutations (Type: evidence based;

ASSOCIATED CONTENT

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Author affiliations and support information (if applicable) appear at the end of this article.

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Evidence quality: high; Strength of recommendation: strong).

Recommendation 1.2.1

Adjuvant cisplatin-based chemotherapy and/or atezolizumab are not recommended for routine use in this patient group. A postoperative multimodality evaluation, including a consultation with a medical oncologist, is recommended to assess benefits and risks of adjuvant therapies for each patient. Factors to consider other than tumor stage when making a recommendation for adjuvant therapy are outlined after the adjuvant systemic therapy section of the 2017 guideline (Type: evidence based and panel consensus, benefits outweigh harms, especially in patients with larger tumors; Evidence quality: intermediate; Strength of recommendation: moderate).

Recommendation 1.3

Stages IIA, IIB, and IIIA: Adjuvant cisplatin-based chemotherapy is recommended for all patients. Adjuvant osimertinib is recommended after chemotherapy for patients with tumors with sensitizing *EGFR* mutations, regardless of the PD-L1 status. Adjuvant atezolizumab is recommended for all patients with PD-L1 $\geq$ 1% after cisplatin-based chemotherapy except for patients with sensitizing *EGFR* mutations (Type: evidence based and panel consensus; Evidence quality: high; Strength of recommendation: strong).

Note: the guideline recommendations are based on the 7th edition staging system used in the studies as opposed to the current 8th edition staging system for lung cancer.[5]

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GUIDELINE AND CONFLICTS OF INTEREST

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EDITOR'S NOTE

This ASCO Clinical Practice Guideline Recommendation Update provides a recommendation update, with review and analysis of the relevant literature for the recommendation. Additional information, including links to patient information at www.cancer.net, is available at www.asco.org/thoracic-cancer-guidelines.

EQUAL CONTRIBUTION

K.P. and L.E.G. were the Expert Panel co-chairs.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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