Editorial Commentary

Optimizing adjuvant therapy in *EGFR*-mutated non-small cell lung cancer

Annemarie F. Shepherd[1,2], Isabel R. Preeshagul[3], Narek Shaverdian[1], Abraham J. Wu[1], Daphna Y. Gelblum[1], Daniel R. Gomez[1], Andreas Rimner[1], Charles B. Simone II[1,2]

[1]Department of Radiation Oncology, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Department of Radiation Oncology, New York Proton Center, New York, NY, USA; [3]Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA

Correspondence to: Charles B. Simone, II, MD. New York Proton Center, 225 East 126th Street, New York, NY 10035, USA.
Email: csimone@nyproton.com.

Comment on: Liang W, Cai K, Chen C, *et al.* Society for Translational Medicine consensus on postoperative management of EGFR-mutant lung cancer (2019 edition). Transl Lung Cancer Res 2019;8:1163-73.

Submitted May 15, 2020. Accepted for publication Jun 05, 2020.
doi: 10.21037/atm-20-3982
View this article at: http://dx.doi.org/10.21037/atm-20-3982

Lung cancer remains the leading cause of deaths from cancer worldwide. Of the 280,820 estimated patients to be diagnosed in the United States in 2020, two-thirds of those patients will be considered unresectable (1). Of the one-third of patients who are considered surgical candidates, many will relapse, with recurrence rates as high as 70% in the stage III setting (2). The significant risk of developing metastatic disease after curative resection necessitates the role for adjuvant therapy to treat potential micrometastases and reduce the chance of recurrence.

When the original practice-guiding adjuvant trials were designed, molecular features including tissue histology, the presence of actionable mutations like Epidermal Growth Factor Receptor (*EGFR*) mutation, and the expression of program death ligand-1 (PD-L1) were not yet known as essential tumor characteristics. Therefore, the role of immunotherapy and targeted therapy in the adjuvant setting has yet to be defined.

Targeted therapy, however, has revolutionized the treatment landscape for metastatic lung cancer patients who harbor a driver mutation. The most common of the actionable driver alterations is *EGFR* mutation, encoding a cell surface receptor of the tyrosine kinase family. The incidence of *EGFR* mutations varies worldwide, involving about 40% of lung cancer cases in Asia and 15% of lung cancer cases in the United States.

While targeted therapy with a tyrosine kinase inhibitor (TKI) is standard of care first-line treatment for patients with advanced *EGFR*-mutated non-small cell lung cancer (NSCLC), there is less consensus regarding their utilization in the adjuvant setting after radical surgical resection in patients with stage I-III *EGFR*-mutant NSCLC.

Consensus statements from the International Association for the Study of Lung Cancer (IASLC, published in 2016), American Society of Clinical Oncology (ASCO, published in 2017) and European Society for Medical Oncology (ESMO, published in 2017) all indicate that at the time of publication, there was insufficient evidence to support the routine use of *EGFR*-TKIs in the adjuvant setting (3-5). The previously published studies on this topic (BR-19 and RADIANT, published in 2013 and 2015, respectively) did not select for patients with activating *EGFR* mutations and, therefore, the results from these studies were inconclusive (6,7).

However, the results of the EVAN and ADJUVANT trials, published in 2018, indicated an improvement in disease free survival (DFS) for patients receiving adjuvant *EGFR*-TKI therapy for 2 years compared with adjuvant standard-of-care platinum doublet chemotherapy (8,9). These trials did not allow for adjuvant chemotherapy in the TKI arm or adjuvant radiation therapy in either arm. The SELECT trial, a single-arm study published in 2019 (10), demonstrated an impressive DFS rate (2-year: 88%, 5-year: 56%) with the use of adjuvant *EGFR*-TKI (erlotinib) for 2 years following standard platinum doublet adjuvant chemotherapy. The SELECT trial, unlike EVAN and ADJUVANT, permitted adjuvant radiation therapy. The

details of these trials are listed in *Table 1*.

With this additional data, the "Society for Translational Medicine consensus on postoperative management of *EGFR*-mutant lung cancer" was recently published in *Translational Lung Cancer Research*, aiming to provide treatment recommendations in the adjuvant setting. This important consensus addresses the need to routinely test for driver mutations, the use and duration of adjuvant therapy, surveillance imaging, and the work-up and management for relapsed disease (11). A panel of Chinese experts reached consensus on eight topics and scored each consensus statement based upon the level of evidence (Category 1 = high-level evidence; Category 2A = lower-level evidence, but uniform consensus that the intervention is appropriate; Category 2B = lower-level evidence, but some consensus that the intervention is appropriate; Category 3 = major disagreement that the intervention is appropriate) and the strength of recommendations [strong *vs.* weak, according to the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system]. All eight consensus statements were Category 1-2B and "strong" recommendations.

To obtain a more comprehensive consensus, 11 experts outside China were invited to comment on four controversial topics: the need for *EGFR* mutation profiling after curative-intent resection, whether an *EGFR*-TKI can replace chemotherapy in patients requiring adjuvant therapy, the necessity for regular surveillance for brain and bone metastases in patients with *EGFR* mutations after radical resection, and the role of osimertinib in the relapsed setting. Interestingly, the only consensus opinion (with 10 of the 11 experts agreeing) was regarding the superiority of osimertinib as the TKI of choice, given the findings of the FLAURA trial (12). Consensus was lacking (with only 5 or 6 of the 11 non-Chinese experts agreeing) on the other three questions.

The role of frontline osimertinib for patients with stage IV NSCLC harboring an *EGFR* sensitizing mutation is clear. The FLAURA trial, a large phase III double blind prospective trial, randomized 556 patients with treatment naive, *EGFR* mutation-positive NSCLC to receive osimertinib *vs.* gefinitib or erlotinib. The investigators found that the osimertinib arm had improved progression free survival (PFS) as well as overall survival (OS) with similar safety profiles (12). This benefit in PFS was also demonstrated in the subset analysis of patients enrolled at Asian sites (13).

Additionally, a recent press release on the ADAURA trial (NCT02511106), a large randomized phase III study evaluating adjuvant osimertinib *vs.* placebo in completely resected (R0) patients with an activating *EGFR* mutation, announced early unblinding of the study due to "overwhelming efficacy" in the adjuvant osimertinib arm (14). The ADAURA trial, importantly, is using osimertinib as the adjuvant *EGFR*-TKI of choice for up to 3 years, is allowing adjuvant chemotherapy, and is including both Asian and non-Asian patients. The results are eagerly awaited.

Comments on each consensus statement

Consensus Statement #1: regarding the need for *EGFR* mutation profiling after radical resection, if resources allow, *EGFR* mutation profiling should be considered after radical resection to risk-stratify patients, provide more information on tumor biology, help guide adjuvant therapy decisions and plan treatment options in the case of a future recurrence. The resources for testing likely vary by country and center. However, since the result of *EGFR* mutation profiling can offer more insight for treatment planning, it should be considered.

Consensus Statement #2 indicates that the decision for adjuvant therapy should be made based on risk-stratification. While risk-stratification is an integral part of the discussion, there are many other factors that contribute to offering adjuvant therapy and this important question warrants a multidisciplinary shared decision-making process involving the patient. For patients with earlier stage disease (Stage IA–IB), it is unclear if patients benefit from adjuvant TKI therapy due to their relative lower risk for recurrence given their early pathologic stage. Although the SELECT and ADAURA trials included stage I patients, the ADJUVANT and EVAN trials did not. Until adjuvant *EGFR*-TKI therapy is specifically studied in patients with early-stage resected disease, the use of adjuvant *EGFR*-TKI therapy in these early-stage patients is not routinely recommended.

Consensus Statement #3 indicates that there is level 1 evidence for the use of adjuvant *EGFR*-TKI to achieve longer DFS compared to chemotherapy. For patients with a poor expected tolerance to chemotherapy, the use of adjuvant *EGFR*-TKI alone is reasonable. For patients who are good candidates for chemotherapy, the impact of replacing adjuvant chemotherapy with an *EGFR*-TKI *vs.* treatment with adjuvant chemotherapy followed by *EGFR*-TKI is unclear. ADJUVANT and EVAN, both published 2018, evaluated chemotherapy *vs.* TKI in the adjuvant setting;

Table 1 List of adjuvant EGFR-TKI trials in patients with completely resected EGFR mutant non-small cell lung cancer

Trials	N	Patient population	Design, Arms, Endpoint	Duration of TKI	Country	EGFR mutation	Toxicity	DFS	OS
ADJUVANT, published 2018	222; enrolled from 2011–2014	- Stage: II-IIIA (N1–N2) Resection - Resection status: R0 - No adjuvant chemotherapy or radiation therapy allowed	- Phase III, randomized, open-label - Arms: Gefitinib *vs.* chemotherapy (vinorelbine + cisplatin) - Primary endpoint: DFS	2 years	100% China	EGFR exon 19 or L858R confirmed for all patients	- Grade ≥3 toxicity: 12% with TKI *vs.* 48% with chemo - SAE: 7% with TKI *vs.* 23% with chemo	Median DFS: 28.7 months with TKI *vs.* 18 months with chemo (P=0.005)	Not mature
EVAN, published 2018	102; enrolled from 2012–2015	- Stage: IIIA - Resection - Resection status: R0 - No adjuvant chemotherapy or radiation therapy allowed	- Phase II, randomized, open-label - Arms: Erlotinib *vs.* chemotherapy (vinorelbine + cisplatin) - Primary endpoint: DFS	Median was 2 years	100% China	EGFR exon 19 or L858R confirmed for all patients	Grade ≥3 toxicity: 12% with TKI *vs.* 26% with chemo	2-yr DFS: 81.4% with TKI *vs.* 44.6% with chemo (p=0.005)	Not mature, but initial results indicate OS improved with TKI (HR 0.165, P=0.002)
SELECT, published 2019	100; enrolled from 2008–2012	- Stage: IA-IIIA (30% were IIIA) - Resection status: R0 + adjuvant chemotherapy + radiation therapy allowed	- Phase II, open-label, single arm - Erlotinib - Primary endpoint: DFS	2 years after adjuvant chemotherapy	100% United States	EGFR exon 19 or L858R confirmed for all patients	No grade ≥4 toxicity	- 2-yr DFS: 88% with TKI - 5-yr DFS: 56%	5-yr OS: 86%
ADAURA, (not yet published)	682; enrolled from 2015–2020	- Stage: IB–IIIA - Resection status: R0 - Adjuvant therapy: adjuvant chemotherapy was allowed - No radiation therapy allowed	- Phase III, randomized, double-blind - Arms: Osimertinib *vs.* placebo - Primary endpoint: DFS	Up to 3 years	- 60% Asian - 40% non-Asian	- EGFR exon 19 or L858R confirmed - For all patients	Not published	Pending; however, 4/10/2020: Press release stated that an Independent Data Monitoring Committee recommended unblinding of the trial due to "overwhelming efficacy."	Not mature
ALCHEMIST, (still accruing)	2014–current	- Stage: IB–IIIA - Resection status: R0 - Adjuvant therapy: adjuvant chemotherapy and radiation therapy are allowed	- Phase III, randomized, double-blind (now unblinded) - Arms: erlotinib *vs.* placebo - Primary endpoint: OS	Up to 2 years	100% United States	EGFR exon 19 or L858R confirmed - For all patients	Pending	Pending	Pending

EGFR, Epidermal Growth Factor Receptor; TKI, tyrosine kinase inhibitor.

however, the study cohorts were limited to the Chinese population and they did not permit radiation. While the reported 2-year DFS benefit is exciting, it is not a surrogate for OS, for which the data is not mature. We eagerly await these results. Adjuvant chemotherapy improves overall survival in high-risk patients with resected NSCLC and is considered standard of care (15). Therefore, the potential detriment of omitting adjuvant chemotherapy in these high-risk patients needs to be considered. To gain further clarity on this question, we must await the results of the ADAURA trial as well as the ALCHEMIST trial (NCT02193282) randomizing erlotinib *vs.* observation in patients with completely resected (R0) stage IB to IIIA *EGFR*-mutant NSCLC after standard postoperative therapy (14,16).

Consensus Statement #4 indicates that all three adjuvant systemic therapy options (chemotherapy alone, *EGFR*-TKI, or chemotherapy plus *EGFR*-TKI) are reasonable in patients requiring adjuvant therapy. The question of whether an *EGFR*-TKI can replace chemotherapy is a controversial topic as noted above.

Consensus Statement #5 advises that adjuvant *EGFR*-TKI treatment should be delivered for at least 2 years. This is appropriate as all published studies aimed for patients to receive treatment for at least this duration. Additionally, in the ADJUVANT and SELECT studies, there were concerns for a downward trend in DFS later than 2 years that could potentially be related to stopping the *EGFR*-TKI therapy (9,10). For cases of poor tolerance, efforts to adjust the dose of the *EGFR*-TKI should be considered before discontinuing the therapy.

Consensus Statement #6, which advocates for annual brain MRI scans and annual bone scans, is controversial. While CNS recurrence is commonly seen in patients with an activating *EGFR* mutation, present National Comprehensive Cancer Network (NCCN) Guidelines for NSCLC recommends surveillance imaging after completion of definitive therapy with CT chest only (17). Brain MRI, PET scans, and bone scans are not routinely recommended. Additionally, the recently published ASCO guidelines on lung cancer surveillance after definitive curative-intent therapy do not recommend brain MRI or PET or bone scans for routine surveillance in patients with stage I-III NSCLC who have undergone curative-intent treatment (18). Neither of the guidelines, however, consider the difference in failure patterns in patients harboring *EGFR* mutations. In the ADJUVANT study, patients underwent surveillance MRI brain every 6 months and bone scans every 12 months. These scans revealed that, 50% (29/58) of recurrences in the *EGFR*-TKI arm occurred in the brain and 10% (6/58) occurred in the bone (19). In the chemotherapy arm, 37.5% (21/56) of recurrences occurred in the brain and 16% (9/56) occurred in the bone. Due to the relatively low rate of bone metastases, routine bone scans should not be performed in the surveillance setting. While routine brain MRI surveillance is not recommended after definitive-intent therapy, for *EGFR* mutant patients, clinicians should have a low threshold for performing CNS imaging when clinically warranted. The early detection of brain metastases could have implications in the radiotherapeutic management of brain metastases, as patients with a limited number of brain metastases are more likely to be candidates for stereotactic radiosurgery techniques.

Consensus Statements #7 and #8 recommend *EGFR*-TKI therapy as the treatment of choice for salvage therapy and obtaining genetic testing from the prior surgical specimen, re-biopsy, or alternatively, liquid-biopsy when tissue samples are not available, in the setting of recurrent disease. While this is appropriate, it is important to consider the nature and timing of the relapse. If patients relapse while on *EGFR*-TKI therapy such as gefitinib or erlotinib, then a liquid and tissue biopsy would help to evaluate for other driver mutations, transformations or resistance mutations, such as the well documented T790M resistance mutation status to determine the utility of osimertinib as salvage therapy. If patients relapse after the discontinuation of *EGFR*-TKI therapy, then retreatment with *EGFR*-TKI therapy should be considered, as the SELECT trial indicated that recurrences are likely still sensitive to *EGFR*-TKI therapy (10).

Finally, the Society for Translational Medicine consensus paper aimed to discuss postoperative management of NSCLC for patients with sensitizing *EGFR*-mutations, however, adjuvant radiation therapy was not discussed. Adjuvant radiation therapy with modern radiation therapy techniques should be considered in NSCLC patients with pathologic N2 disease or positive surgical margins due to a local control and survival benefit (20-25). The impact of adjuvant radiation therapy specifically in NSCLC patients with activating *EGFR*-mutations is less clear, but small, retrospective series indicate that this specific patient population similarly benefits from adjuvant radiation therapy (26). As radiotherapy techniques continue to improve the therapeutic ratio and reduce toxicities with more conformal modalities, including proton therapy, adjuvant radiation therapy should continue to be considered in

appropriate patients with NSCLC to optimize survival (27).

In conclusion, the "Society for Translational Medicine consensus on postoperative management of *EGFR*-mutant lung cancer (2019 edition)" is a much-needed updated consensus that highlights important topics on the postoperative management of completely resected (R0) *EGFR* mutant lung cancers. The areas of continued controversy will hopefully become clearer as the overall survival results of the ADJUVANT and EVAN trials mature, and when the DFS results of the ADAURA and ALCHEMIST trials are known.

Acknowledgments

Funding: Supported by NIH/NCI Memorial Sloan Kettering Cancer Center Support Grant/Core Grant No. P30-CA008748, period: 1/1/19 - 12/31/23.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Annals of Translational Medicine*. The article did not undergo external peer review.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/atm-20-3982). AFS reports personal fees from ASCO, from null, outside the submitted work. IRP reports other from AstraZeneca, from null, outside the submitted work. Dr. Shaverdian reports grants from Novartis, from null, outside the submitted work. AJW reports grants from CivaTech Oncology, Inc., personal fees from AstraZeneca, personal fees from AlphaTau Medical, outside the submitted work. Dr. Gomez reports grants from Boehringer-Ingelheim, grants from Varian Medical Systems, grants from AstraZeneca, grants from Merck, grants from Bristol Myers Squibb, outside the submitted work. AR reports grants and personal fees from Varian Medical Systems, grants from Boehringer Ingelheim, grants from Pfizer, grants and personal fees from AstraZeneca, grants and personal fees from Merck, personal fees from Research to Practice, personal fees from Cybrexa, personal fees from MoreHealth, non-financial support from Phillips/Elekta, from null, outside the submitted work. Dr. Simone serves as an unpaid editorial board member of *Annals of Translational Medicine* from Dec 2018 to Nov 2020, and he reports personal fees from Varian Medical Systems, outside the submitted work. The other author has no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. American Cancer Society. Facts and Figures 2020. Available online: https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/cancer-facts-figures-2020.html
2. Goldstraw P, Crowley J, Chansky K, et al. The IASLC Lung Cancer Staging Project: proposals for the revision of the TNM stage groupings in the forthcoming (seventh) edition of the TNM Classification of malignant tumours. J Thorac Oncol 2007;2:706-14.
3. Kris MG, Gaspar LE, Chaft JE, et al. Adjuvant Systemic Therapy and Adjuvant Radiation Therapy for Stage I to IIIA Completely Resected Non-Small-Cell Lung Cancers: American Society of Clinical Oncology/Cancer Care Ontario Clinical Practice Guideline Update. J Clin Oncol. 2017;35:2960-74.
4. Postmus PE, Kerr KM, Oudkerk M, et al. Early and locally advanced non-small-cell lung cancer (NSCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2017;28:iv1-21.
5. Tan DS, Yom SS, Tsao MS, et al. The International Association for the Study of Lung Cancer Consensus Statement on Optimizing Management of EGFR Mutation-Positive Non-Small Cell Lung Cancer: Status in 2016. J Thorac Oncol 2016;11:946-63.
6. Kelly K, Altorki NK, Eberhardt WE, et al. Adjuvant Erlotinib Versus Placebo in Patients With Stage IB-IIIA Non-Small-Cell Lung Cancer (RADIANT): A Randomized, Double-Blind, Phase III Trial. J Clin Oncol 2015;33:4007-14.
7. Goss GD, O'Callaghan C, Lorimer I, et al. Gefitinib versus placebo in completely resected non-small-cell lung

cancer: results of the NCIC CTG BR19 study. J Clin Oncol 2013;31:3320-6.
8. Yue D, Xu S, Wang Q, et al. Erlotinib versus vinorelbine plus cisplatin as adjuvant therapy in Chinese patients with stage IIIA EGFR mutation-positive non-small-cell lung cancer (EVAN): a randomised, open-label, phase 2 trial. Lancet Respir Med 2018;6:863-73.
9. Zhong WZ, Wang Q, Mao WM, et al. Gefitinib versus vinorelbine plus cisplatin as adjuvant treatment for stage II-IIIA (N1-N2) EGFR-mutant NSCLC (ADJUVANT/CTONG1104): a randomised, open-label, phase 3 study. Lancet Oncol 2018;19:139-48.
10. Pennell NA, Neal JW, Chaft JE, et al. SELECT: A Phase II Trial of Adjuvant Erlotinib in Patients With Resected Epidermal Growth Factor Receptor-Mutant Non-Small-Cell Lung Cancer. J Clin Oncol 2019;37:97-104.
11. Liang W, Cai K, Chen C, et al. Society for Translational Medicine consensus on postoperative management of EGFR-mutant lung cancer (2019 edition). Transl Lung Cancer Res 2019;8:1163-73.
12. Ramalingam SS, Vansteenkiste J, Planchard D, et al. Overall Survival with Osimertinib in Untreated, EGFR-Mutated Advanced NSCLC. N Engl J Med 2020;382:41-50.
13. Cho BC, Chewaskulyong B, Lee KH, et al. Osimertinib versus Standard of Care EGFR TKI as First-Line Treatment in Patients with EGFRm Advanced NSCLC: FLAURA Asian Subset. J Thorac Oncol 2019;14:99-106.
14. Wu YL, Herbst RS, Mann H, et al. ADAURA: Phase III, Double-blind, Randomized Study of Osimertinib Versus Placebo in EGFR Mutation-positive Early-stage NSCLC After Complete Surgical Resection. Clin Lung Cancer 2018;19:e533-6.
15. Pignon JP, Tribodet H, Scagliotti GV, et al. Lung adjuvant cisplatin evaluation: a pooled analysis by the LACE Collaborative Group. J Clin Oncol 2008;26:3552-9.
16. Govindan R, Mandrekar SJ, Gerber DE, et al. ALCHEMIST Trials: A Golden Opportunity to Transform Outcomes in Early-Stage Non-Small Cell Lung Cancer. Clin Cancer Res 2015;21:5439-44.
17. NCCN Guidelines Version 2. 2020 Non-Small Cell Lung Cancer. Available online: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf
18. Schneider BJ, Ismaila N, Aerts J, et al. Lung Cancer Surveillance After Definitive Curative-Intent Therapy: ASCO Guideline. J Clin Oncol 2020;38:753-66.
19. Xu ST, Xi JJ, Zhong WZ, et al. The Unique Spatial-Temporal Treatment Failure Patterns of Adjuvant Gefitinib Therapy: A Post Hoc Analysis of the ADJUVANT Trial (CTONG 1104). J Thorac Oncol 2019;14:503-12.
20. Herskovic A, Mauer E, Christos P, et al. Role of Postoperative Radiotherapy in Pathologic Stage IIIA (N2) Non-Small Cell Lung Cancer in a Prospective Nationwide Oncology Outcomes Database. J Thorac Oncol 2017;12:302-13.
21. Lally BE, Zelterman D, Colasanto JM, et al. Postoperative radiotherapy for stage II or III non-small-cell lung cancer using the surveillance, epidemiology, and end results database. J Clin Oncol 2006;24:2998-3006.
22. Douillard JY, Rosell R, De Lena M, et al. Impact of postoperative radiation therapy on survival in patients with complete resection and stage I, II, or IIIA non-small-cell lung cancer treated with adjuvant chemotherapy: the adjuvant Navelbine International Trialist Association (ANITA) Randomized Trial. Int J Radiat Oncol Biol Phys 2008;72:695-701.
23. Billiet C, Peeters S, Decaluwé H, et al. Outcome after PORT in ypN2 or R1/R2 versus no PORT in ypN0 Stage III-N2 NSCLC after Induction Chemotherapy and Resection. J Thorac Oncol 2016;11:1940-53.
24. Robinson CG, Patel AP, Bradley JD, et al. Postoperative radiotherapy for pathologic N2 non-small-cell lung cancer treated with adjuvant chemotherapy: a review of the National Cancer Data Base. J Clin Oncol 2015;33:870-6.
25. Billiet C, Decaluwé H, Peeters S, et al. Modern post-operative radiotherapy for stage III non-small cell lung cancer may improve local control and survival: a meta-analysis. Radiother Oncol 2014;110:3-8.
26. Zhu Y, Fu L, Jing W, et al. Radiotherapy for patients with completely resected pathologic IIIA(N2) non-small-cell lung cancer: a retrospective analysis. Cancer Manag Res 2019;11:10901-8.
27. Remick JS, Schonewolf C, Gabriel P, et al. First Clinical Report of Proton Beam Therapy for Postoperative Radiotherapy for Non-Small-Cell Lung Cancer. Clin Lung Cancer 2017;18:364-71.

Cite this article as: Shepherd AF, Preeshagul IR, Shaverdian N, Wu AJ, Gelblum DY, Gomez DR, Rimner A, Simone CB 2nd. Optimizing adjuvant therapy in *EGFR*-mutated non-small cell lung cancer. Ann Transl Med 2020;8(23):1613. doi: 10.21037/atm-20-3982

