Reply to “EGFR Mutation in Patients with Lung Adenosquamous Cell Carcinoma”

Yosuke Morodomi, MD, PhD, Tatsuro Okamoto, MD, PhD, and Yoshihiko Maehara, MD, PhD

Department of Surgery and Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

TO THE EDITORS

We would like to thank Dr. Tamura, Dr. Kagohashi, and Dr. Satoh for their valuable observations. We appreciate this opportunity to address their comments.

Our study found somatic epidermal growth factor receptor (*EGFR*) mutations in specimens from 21.9% of patients (7/32) with histological diagnosis of adenosquamous cell carcinoma (ADSQCC).¹ Over the same period, we detected *EGFR* mutations in 45.6% of adenocarcinoma (AD) patients (327/717) who had specified *EGFR* gene mutation status. Therefore, the *EGFR* mutation rate in ADSQCC was approximately half that in AD. Additional analysis showed that relapse-free survival and overall survival in ADSQCC patients with higher ratios of AD components did not significantly differ from those with lower ratios.

As Dr. Satoh mentions, examining whether both cell types of ADSQCC harbored the identical mutation would confer not only clinical importance but also biological interest in non-small cell lung cancers. Unfortunately, as we did not perform microdissection procedures during DNA extraction from these tissue samples, separate evaluation of gene status between the AD and squamous cell carcinoma (SQCC) components was not possible.

Nonetheless, we suspect that the two histologic components in ADSQCC might be morphological alterations from a genetically monoclonal origin. A recent

investigation provided further profound evidence to support a monoclonal origin for this tumor.²

Furthermore, *EGFR* mutations have been observed in a certain percentage of SQCC lung cancers,³ which supports the validity of *EGFR* mutations in SQCC.

These findings suggest a possibility that mutated *EGFR* acts as a driver oncogene in the tumor initiation period, and then morphological changes to adenocarcinoma or SQCC develop in the tumor promotion period. As shown in Fig. 3 of our article,¹ the finding that *EGFR* mutations were widely dispersed in ADSQCC tumors irrespective of the proportion of adenocarcinoma also supports this possibility.

DISCLOSURE None.

REFERENCES

1. Morodomi Y, Okamoto T, Takenoyama M, et al. Clinical significance of detecting somatic gene mutations in surgically resected adenosquamous cell carcinoma of the lung in Japanese patients. *Ann Surg Oncol*. 2014;22:1–6.
2. Mather JP, Roberts PE, Pan Z, et al. Isolation of cancer stem like cells from human adenosquamous carcinoma of the lung supports a monoclonal origin from a multipotential tissue stem cell. Fields AP, ed. *PLoS ONE*. 2013;8(12):e79456.
3. Perez-Moreno P, Brambilla E, Thomas R, Soria J-C. Squamous cell carcinoma of the lung: molecular subtypes and therapeutic opportunities. *Clin Cancer Res*. 2012;18(9):2443–2451.