



Detection of pseudoprogression with [¹⁸F]-FDG-PET in a patient with pulmonary large cell neuroendocrine carcinoma who received anti-PD-1 treatment

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Abbreviations

CT	Computed tomography
FDG	Fluorodeoxyglucose
FDG-PET	Fluorodeoxyglucose positron emission tomography
ICI	Immune checkpoint inhibitor
LCNEC	Large cell neuroendocrine carcinoma
SUVmax	Maximum standardised undervalue
SUVmean	Mean standardised undervalue
TLG	Total lesion glycolysis
MTV	Metabolic tumour volume
ProGRP	Pro-gastrin-releasing peptide

It remains unknown whether pseudoprogression-related immune checkpoint inhibitors could occur in patients with large cell neuroendocrine carcinoma (LCNEC). Moreover, little is known about the detailed information to distinguish pseudoprogression from tumour progression by [¹⁸F]-FDG-PET [1].

A 72-year-old woman with smoking history was diagnosed with stage IV LCNEC (cT3N3M1b) (Fig. 1a). Carboplatin plus etoposide was initiated as the first-line treatment. Subsequently, she was treated with amrubicin as the second-line treatment. As she experienced marked recurrence in the mediastinal lymph nodes, nivolumab was

chosen as the third-line treatment. Four weeks after nivolumab administration, progressive mediastinal lymphadenopathy was observed (Fig. 1b). However, his general condition was gradually getting better without exacerbation of laboratory findings; moreover, there was a marked decrease in ProGRP. Considering the potential of pseudoprogression, nivolumab continued to be administered. Reduced [¹⁸F]-FDG accumulation and tumour shrinkage were observed 9 weeks after nivolumab treatment (Fig. 1b); therefore, a definite diagnosis of pseudoprogression was established. In this case, the degree of SUVmax and SUVmean on [¹⁸F]-FDG uptake almost did not change 4 weeks after nivolumab treatment, but that of total lesion glycolysis (TLG) and metabolic tumour volume (MTV) clearly increased. At 9 weeks after nivolumab treatment, all indices of [¹⁸F]-FDG uptake markedly decreased.

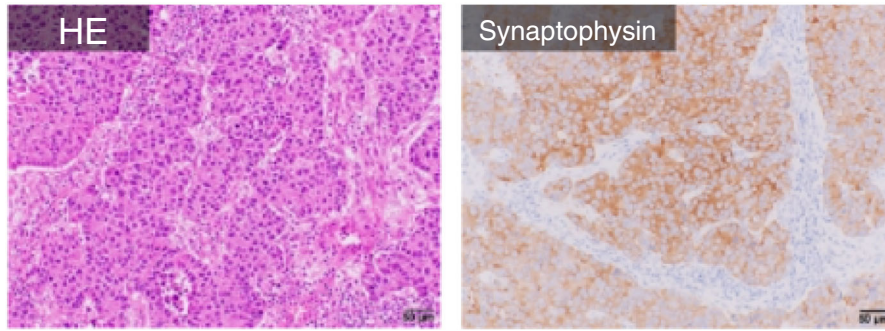
Our results documented that [¹⁸F]-FDG uptake by SUVmax and SUVmean did not increase despite morphological expansion, whereas metabolic tumour volume by TLG or MTV correlates with tumour diameter. As SUVmax on [¹⁸F]-FDG uptake closely correlated with tumour progression and survival in lung cancer, no increase in SUVmax or SUVmean under ICI administration may be suggestive of the potential of pseudoprogression. Our PET imaging of pseudoprogression is expected to be useful for the clinical practice of immunotherapy.

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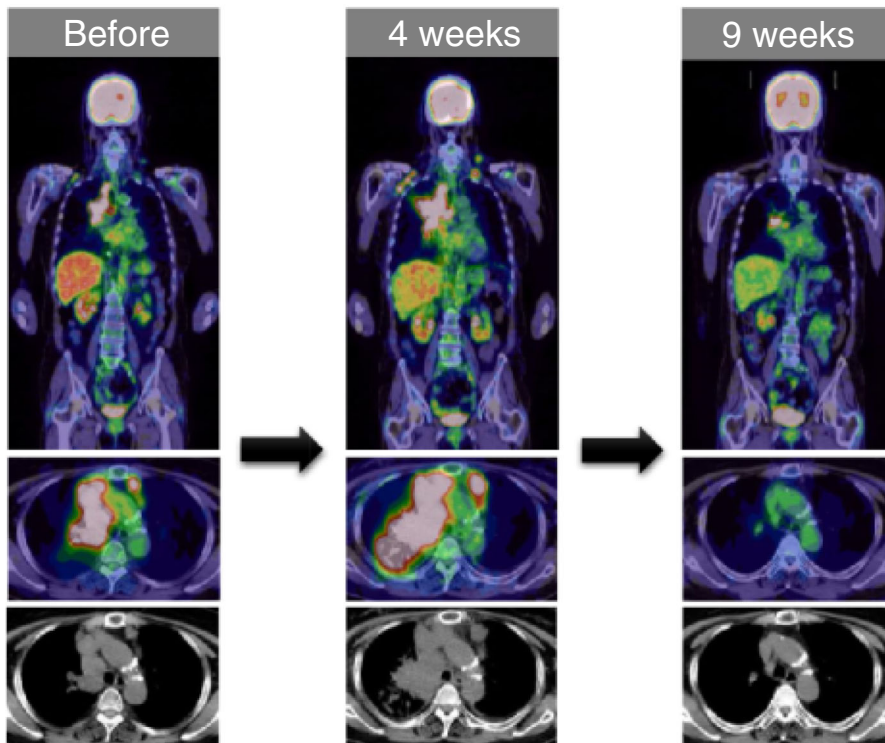
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a



b



MTV	93.70	→	267.55	→	11.15
TLG	605.29	→	1570.86	→	46.98
SUV_{max}	9.94	→	10.59	→	7.33
SUV_{mean}	6.46	→	5.87	→	4.22
ProGRP	1422.9	→	230.3	→	252.7

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Authors' contributions OY, KK, and HK: conception of the study; drafting and critical revision of the article.

KH: Acquisition, analysis, and interpretation of the data; critical revision of the article.

Compliance with ethical standards

Conflict of interest OY has received speaker honoraria from Ono Pharmaceutical Co., Ltd., Bristol-Myers Squibb. KK has received speaker honoraria from Ono Pharmaceutical Co., Ltd., Bristol-Myers Squibb. HK has received research grants from Ono Pharmaceutical Co. Ltd. HK has received speaker honoraria from Ono Pharmaceutical Co., Ltd., Bristol-Myers Squibb Co. KH has declared no conflicts of interest.

Ethics statement All procedures were in accordance with the ethical standards of the institution, the National Committee, and the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent The patient provided informed consent for publication of this Image of the Month.

Reference

1. Travis WD, Brambilla E, Nicholson AG, Yatabe Y, JHM A, Beasley MB, et al. The 2015 World Health Organization classification of lung tumors: impact of genetic, clinical and radiologic advances since the 2004 classification. *J Thorac Oncol.* 2015;10:1243–60. <https://doi.org/10.1097/JTO.0000000000000630>.

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