

Table S1 Detailed information of study participants (section I)

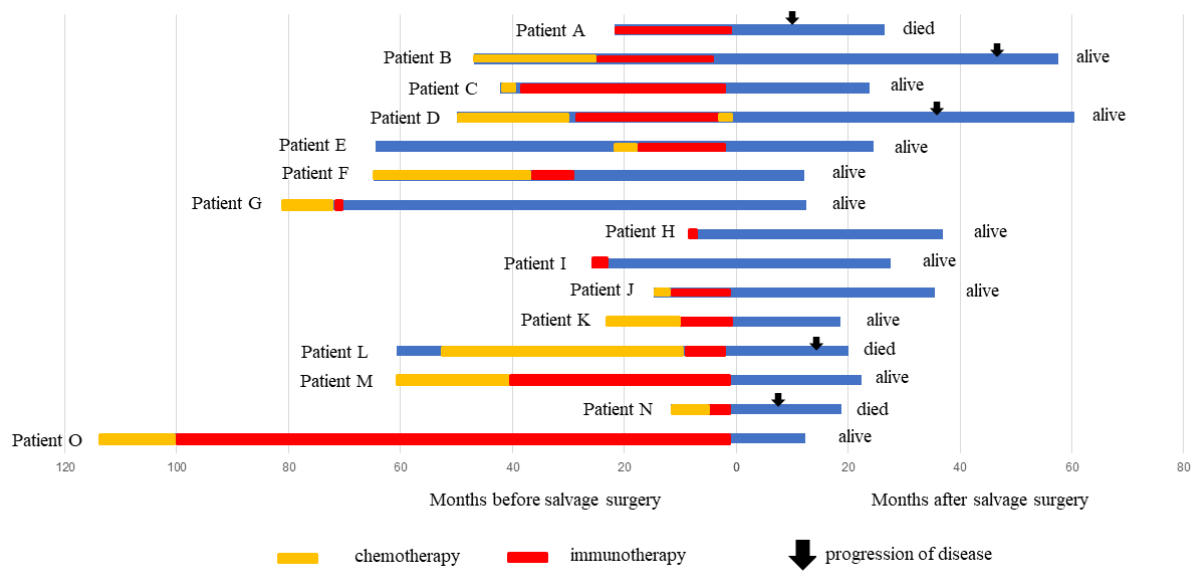
Patient	Age at salvage surgery	Gender	Charlson comorbidity index	Histology at initial biopsy	Initial stage	Initial PD-L1 expression	Stage prior to ICIs	First-line treatment prior to salvage surgery	Subsequent treatment
A	73	Male	6	Adenocarcinoma	2A	20-30%	3A	Thoracoscopic left upper lobectomy and adjuvant chemotherapy (cisplatin and vinorelbine)	Carboplatin and pemetrexed, followed by pembrolizumab (11 cycles)
B	70	Male	6	Adenocarcinoma	4A	Not measured	4A	Carboplatin + pemetrexed + avastin	Docetaxel, followed by nivolumab (19 cycles)
C	72	Male	5	Adenocarcinoma	4B	1-24%	4B	Stereotactic radiotherapy and resection (brain metastasis)	Carboplatin and nab-paclitaxel, followed by nivolumab (59 cycles)
D	66	Female	4	Adenocarcinoma	4A	Not measured	4A	Carboplatin + pemetrexed + avastin	Nivolumab (26 cycles)
E	53	Male	3	Adenocarcinoma	1A	10-20%	4B	Thoracoscopic right upper lobectomy and adjuvant tegafur-uracil	Carboplatin, paclitaxel, and avastin, followed by atezolizumab (39 cycles)
F	44	Male	3	Adenocarcinoma	4A	Negative	4A	Thoracoscopic right middle lobe wedge resection and talc pleurodesis	Carboplatin, pemetrexed, and avastin, followed by nivolumab (13 cycles)
G	70	Male	6	Adenocarcinoma	4A	Not measured	4A	Carboplatin + nab-paclitaxel	Afatinib, followed by nivolumab (4 cycles)
H	75	Female	3	Non-small cell lung cancer	3A (multiple mediastinal lymph node metastasis)	75%	3A	Pembrolizumab (1 cycle) only	Not applicable
I	71	Male	7	Adenocarcinoma	4B	75%	4B	Pembrolizumab (2 cycles) only	Not applicable
J	77	Female	3	Adenocarcinoma	3A (multiple mediastinal lymph node metastasis)	Negative	3A	Carboplatin, paclitaxel, and radiotherapy (60 Gy)	Durvalumab (20 cycles)
K	52	Female	3	Adenocarcinoma	4B	Unknown	4B	Cisplatin, pemetrexed, and atezolizumab	Pemetrexed and atezolizumab (32 cycles)
L	72	Female	6	Adenocarcinoma	4A	1%	4A	Thoracoscopic right lower lobectomy (cytology of pleural fluid positive for metastasis)	Cisplatin and pemetrexed, followed by carboplatin and nab-paclitaxel, docetaxel and ramucirumab, and nivolumab (11 cycles)
M	77	Male	5	Adenocarcinoma	4B	Not measured	4B	Carboplatin and nab-paclitaxel	Nivolumab (82 cycles)
N	56	Male	3	Adenocarcinoma	3B	60%	3B	Cisplatin, vinorelbine, and radiotherapy (60 Gy)	Atezolizumab (4 cycles)
O	66	Male	3	Squamous cell carcinoma	3C	Not measured	3C	Cisplatin and docetaxel	Nivolumab (111 cycles)

PD-L1, programmed death-ligand 1; ICI, immune checkpoint inhibitor.

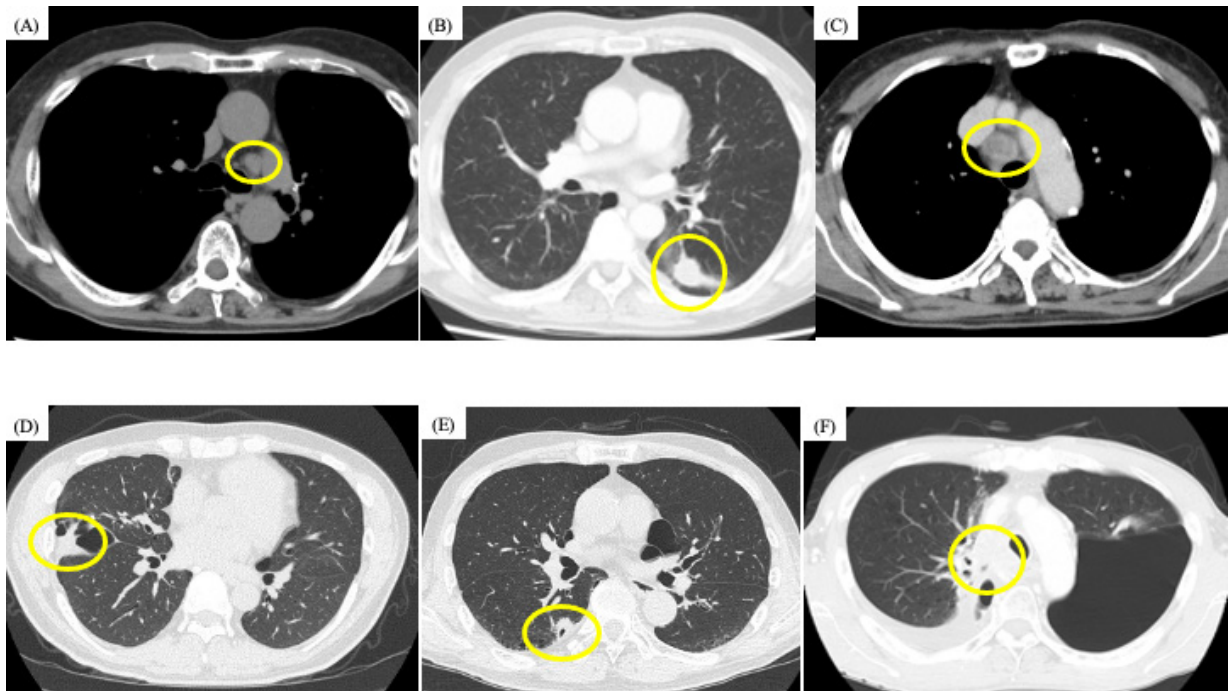
**Table S2** Detailed information of study participants (section II)

Patient	Initial response to ICIs	Interval days between last ICI and salvage surgery	Adverse events associated with ICIs	Indication for salvage surgery	Procedures	Operative time (minutes)	yc stage	Genetic mutation	yp stage	PD-L1 expression of surgical specimens	Live status	Recurrence
A	Progressive disease	264	Grade 3 skin eruption	Metastatic	Open mediastinal LN (4L) resection	216	0	None	3A	Negative	Died at 23 months	A mediastinal lymph node at 9 months (treated with stereotactic radiotherapy)
B	Partial response	744	Grade 3 skin eruption	Primary	Thoroscopic left lower lobectomy	212	1A	None	1A	≥75%	Alive at 57 months	Right lung at 47 months (treated with radiotherapy)
C	Partial response	24	Grade 3 hypothyroidism	Primary	Robotic-assisted right upper lobectomy	291	1A	KRAS G12C (primary lesion)	1A	Not measured	Alive at 23 months	None
D	Complete response	463	Grade 3 interstitial pneumonitis	Metastatic	Thoroscopic mediastinal lymph node (4R) resection	153	0	None	3A	1-24%	Alive at 60 months	Lung and a hilar lymph node at 35 months (treated with thoroscopic resection)
E	Partial response	51	Grade 3 skin eruption	Metastatic	Thoroscopic right lower lobe wedge resection	117	4B	None	4B	1-24%	Alive at 24 months	None
F	Complete response	1137	None	Metastatic	Open pleural metastasectomy	240	0	None	4A	Negative	Alive at 12 months	None
G	Complete response	2179	Grade 3 hypoadrenalism and grade 1 interstitial pneumonitis	Metastatic	Robotic-assisted right superior segmentectomy	245	0	*EGFR (primary lesion)	4A	50-75%	Alive at 12 months	None
H	Complete response	248	Grade 3 skin eruption	Primary	Robotic-assisted right upper lobectomy	276	1A	None	1A	Not measured	Alive at 36 months	None
I	Complete response	497	Grade 2 interstitial pneumonitis	Metastatic	Robotic-assisted mediastinal lymph node (2L) resection	121	0	None	3B	Not measured	Alive at 27 months	None
J	Complete response	46	Grade 2 hypothyroidism	Primary	Open left lower lobectomy	340	0	None	2B	Not measured	Alive at 35 months	None
K	Complete response	15	Not applicable	Primary	Robotic-assisted left upper lobectomy	322	0	None	1A	Not measured	Alive at 18 months	None
L	Progressive disease	60	Grade 2 paronychia	Metastatic	Thoroscopic left upper lobe anterior segmentectomy	157	4A	None	4A	1%	Died at 20 months	Brain at 14 months (managed with best supportive care)
M	Partial response	25	Grade 2 skin eruption	Primary	Thoroscopic left upper lobectomy	255	1A	None	1A	Not measured	Alive at 18 months	None
N	Progressive disease	64	None	Primary	Open ex-vivo right upper extended sleeve lobectomy and auto-transplantation	818	3B	None	3B	Not measured	Died at 19 months	A mediastinal lymph node and adrenal gland at 7 months, treated with cytotoxic chemotherapy
O	Partial response	42	Grade 3 skin eruption	Primary	Open right upper sleeve lobectomy	423	2B	Not examined	2B	Not measured	Alive at 12 months	None

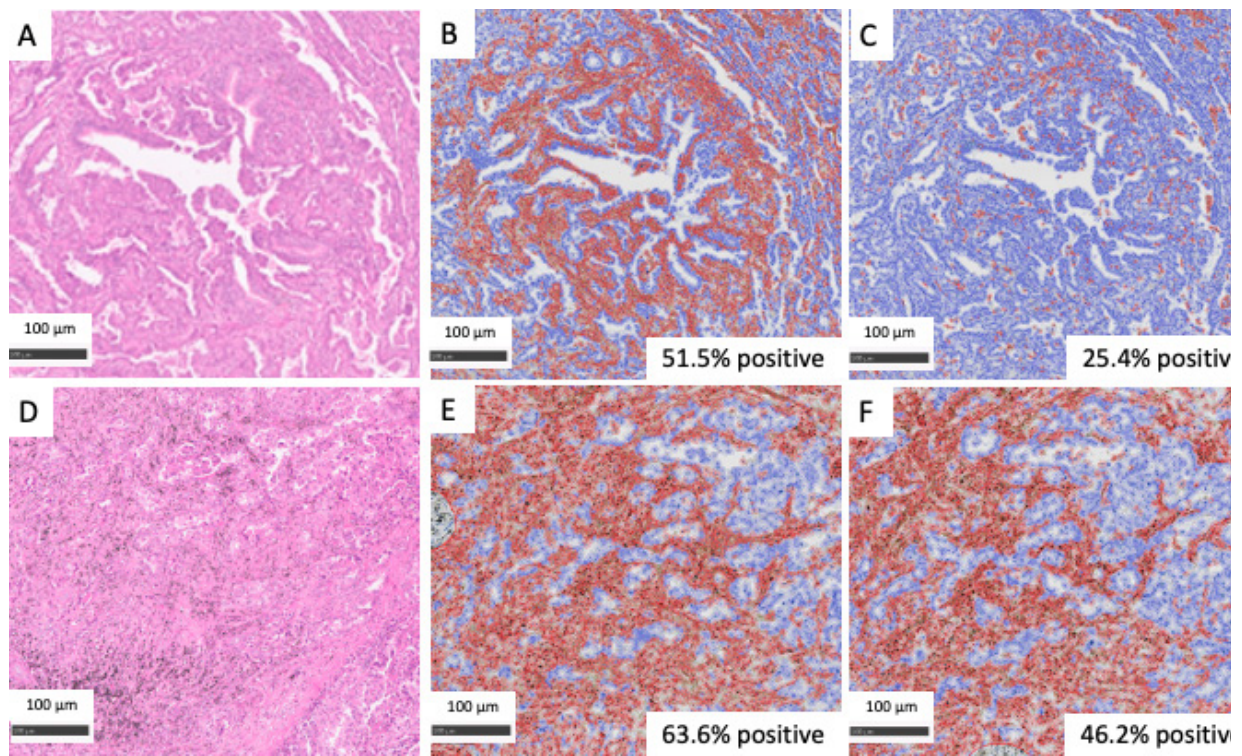
\*, EGFR mutation was not investigated in the metastatic lesion that was resected in salvage surgery. ICI, immune checkpoint inhibitor; PD-L1, programmed death-ligand 1.



**Figure S1** Swimmer's plot of the study patients.

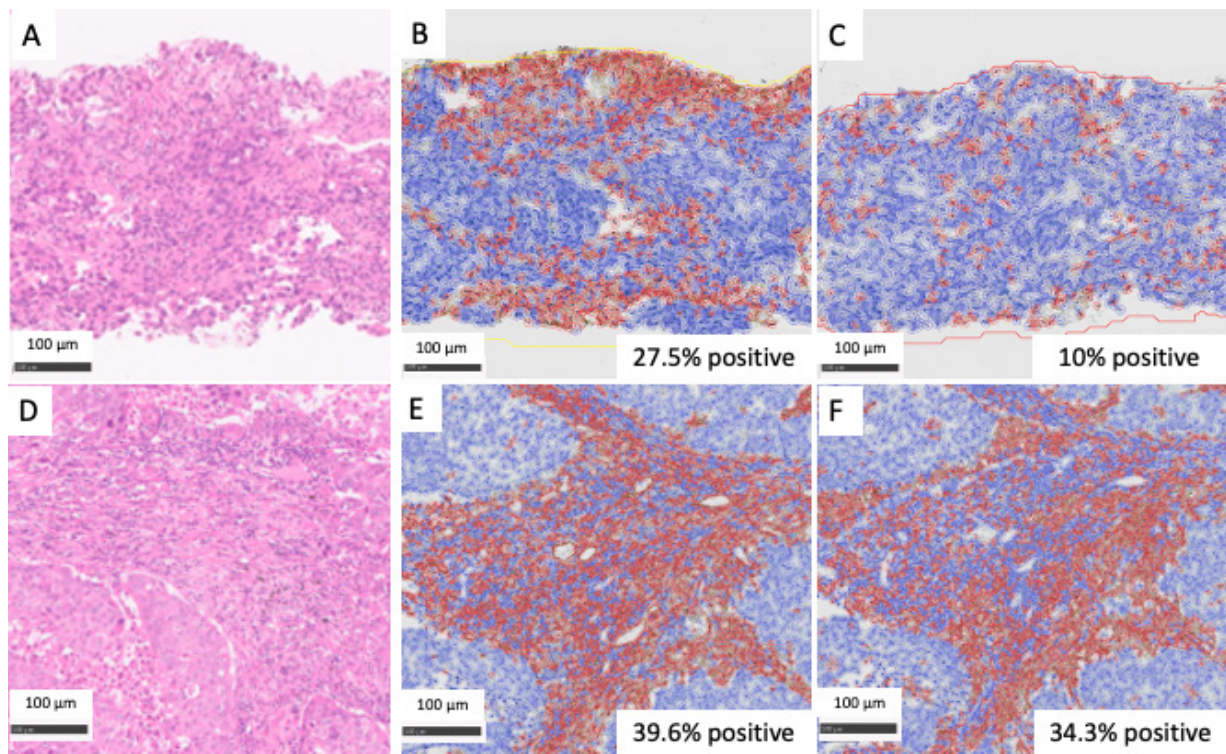


**Figure S2** Preoperative images of computed tomography (lesions indicated by yellow circles) in Patient A (A), Patient B (B), Patient D (C), Patient F (D), Patient G (E), and Patient N (F).

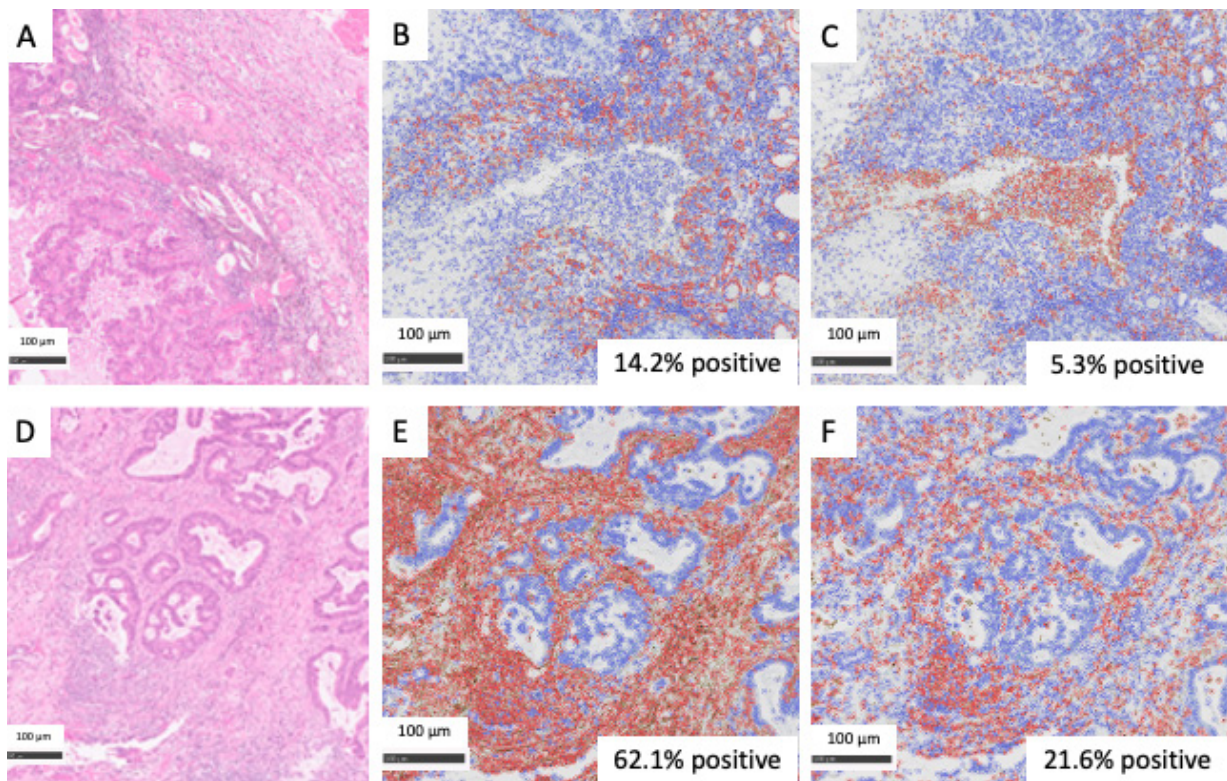


**Figure S3** Histopathological findings and immunohistochemical staining in comparison of before and after ICI therapy in Patient A. Hematoxylin and eosin staining (A), immunohistochemical staining with CD39 (B), and immunohistochemical staining with TIM-3 (C) before ICI therapy. Hematoxylin and eosin staining (D), immunohistochemical staining with CD39 (E), and immunohistochemical staining with TIM-3 (F) at salvage surgery. ICI, immune checkpoint inhibitor; CD, cluster of differentiation; TIM-3, T-cell immunoglobulin and mucin domain-containing molecule 3.





**Figure S4** Histopathological findings and immunohistochemical staining in comparison of before and after ICI therapy in Patient B. Hematoxylin and eosin staining (A), immunohistochemical staining with CD39 (B), and immunohistochemical staining with TIM-3 (C) before ICI therapy. Hematoxylin and eosin staining (D), immunohistochemical staining with CD39 (E), and immunohistochemical staining with TIM-3 (F) at salvage surgery. ICI, immune checkpoint inhibitor; CD, cluster of differentiation; TIM-3, T-cell immunoglobulin and mucin domain-containing molecule 3.



**Figure S5** Histopathological findings and immunohistochemical staining in comparison of before and after ICI therapy in Patient C. Hematoxylin and eosin staining (A), immunohistochemical staining with CD39 (B), and immunohistochemical staining with TIM-3 (C) before ICI therapy. Hematoxylin and eosin staining (D), immunohistochemical staining with CD39 (E), and immunohistochemical staining with TIM-3 (F) at salvage surgery. ICI, immune checkpoint inhibitor; CD, cluster of differentiation; TIM-3, T-cell immunoglobulin and mucin domain-containing molecule 3.