

SUPPLEMENTARY FILE**Treatment patterns and survival outcomes for patients with non-small cell lung cancer in the United Kingdom in the pre-immunology era: a REAL-Oncology database analysis from the I-O Optimise initiative**

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SUPPLEMENTARY APPENDIX**Appendix****Table S1.** ICD-O-3 morphology codes for NSCLC.

Morphology code	Type of NSCLC
	Adenocarcinoma (non-squamous NSCLC)
81403	Adenocarcinoma UNS
81443	Enteric adenocarcinoma
82303	Solid adenocarcinoma with mucin production
82443	MANEC mixed adenoneuroendocrine carcinoma
82500	Atypical adenomatous hyperplasia
82502	Adenocarcinoma in situ, non-mucinous
82503	Adenocarcinoma, bronchiolo-alveolar (BAC), bronchiolar carcinoma, (incl pathologic in situ-variant)
82523	Bronchiolo-alveolar carcinoma
82532	Adenocarcinoma in situ, mucinous
82533	Adenocarcinoma, mucinous bronchiolo-alveolar (BAC)
82543	Bronchiolo-alveolar carcinoma, mixed mucinous and non-mucinous

Morphology code	Type of NSCLC
82553	Adenocarcinoma, mixed with other types of carcinoma incl. squamous cell and small-cell carcinoma
82563	Minimally invasive adenocarcinoma, non-mucinous
82573	Minimally invasive adenocarcinoma, mucinous
82603	Papillary adenocarcinoma, NOS
82653	Micropapillary adenocarcinoma
83103	Clear cell adenocarcinoma
83333	Fetal adenocarcinoma
84703	Mucinous cystadenocarcinoma
84803	Mucinous adenocarcinoma
84903	Signet ring cell carcinoma
85503	Acinar cell carcinoma
85513	Acinar adenocarcinoma
<hr/> Squamous cell carcinoma	
80523	Papillary squamous cell carcinoma
80702	Squamous cell carcinoma in situ
80703	Squamous cell carcinoma

Morphology code	Type of NSCLC
80713	Keratinizing squamous cell carcinoma
80723	Non-keratinizing squamous cell carcinoma
80733	Squamous cell carcinoma, small cell non-keratinizing
80833	Basaloid squamous cell carcinoma
80843	Squamous cell carcinoma, clear cell type

NSCLC NOS

80103	Carcinoma, NOS
80203	Carcinoma, undifferentiated NOS
80213	Carcinoma, anaplastic NOS
80463	Carcinoma, non-small cell unspecified

Large cell carcinoma (non-squamous NSCLC)

| 80123 | Large-cell carcinoma, unspecified |

Neuroendocrine NSCLC carcinoma (other specified NSCLC carcinoma)

| 80133 | Large cell neuroendocrine carcinoma |
| 82463 | Neuroendocrine carcinoma, NOS |

Other miscellaneous NSCLC (other specified NSCLC carcinoma)

Morphology code	Type of NSCLC
80143	Large cell carcinoma with rhabdoid phenotype
80223	Sarcomatoid carcinoma, pleomorphic
80233	NUT carcinoma
80303	Spindle cell and giant cell carcinoma
80313	Giant cell carcinoma
80323	Spindle cell carcinoma, NOS
80333	Pseudosarcomatous carcinoma
81233	Basaloid carcinoma
82003	Adenocystic carcinoma
84303	Mucoepidermoid carcinoma
85603	Adenosquamous carcinoma
85623	Epithelial-myoepithelial carcinoma
89723	Blastoma, pulmonary (pneumoblastoma)
89803	Carcinosarcoma, NOS
89823	Myoepithelial carcinoma

ICD-O-3, *International Classification of Diseases for Oncology*, 3rd Edition; NOS, not otherwise specified; NSCLC, non-small cell lung cancer; UNS, unspecified.

Table S2. Initial treatment algorithm. Initial treatment was defined as the first treatment received within 6 months of diagnosis, associated with any other treatment received within a certain time period following first treatment as defined in the table below.

Initial treatment category	Definitions
A. Surgery	Sum of all A sub-groups
A0. Surgery only	Surgery + no SACT or RT within 12 weeks after surgery
A1. Surgery + adjuvant SACT (only) – no RT within 6 months of SACT start	Surgery + identification of SACT only (start) within 84 days (12 weeks) after surgery
A2. Surgery + adjuvant RT (only) – no SACT within 6 months of RT start	Surgery + identification of RT only (start) within 84 days (12 weeks) after surgery
A3. Surgery + adjuvant RT and SACT	Surgery + identification of RT [or SACT] (start) within 84 days (12 weeks) after surgery + identification of SACT [or RT] (start) within 180 days (6 months) after RT [or SACT]

A4. Neoadjuvant SACT + surgery	SACT + identification of surgery within 120 days (4 months) after first SACT regimen start + no RT identification prior to surgery AND:
A5. Neoadjuvant RT + surgery	RT + identification of surgery within 90 days (3 months) after first RT treatment start + no SACT identification prior to surgery AND:
A6. Neoadjuvant SACT and RT + surgery	RT and SACT + identification of surgery within 3 months after start + identification of SACT and RT prior to surgery Note: Neoadjuvant SACT and RT corresponds to RT within 6 weeks of SACT start
B. Radiotherapy alone	RT + no SACT nor surgery within 90 days (3 months) after RT
C. SACT + Radiotherapy	Sum of C1, C2 and C3
C1. RT followed by SACT	RT + identification of SACT within 90 days (3 months) after first SACT regimen start + no surgery within 6 months after first SACT start

C2. SACT followed by RT	SACT + identification of RT within 90 days (3 months) after first SACT regimen start + no surgery within 6 months after first SACT start
C3. Concurrent chemoradiation	SACT + [start RT within 6 weeks of SACT] + no surgery within 3 months after chemoradiation
D. SACT alone	SACT + no RT nor surgery within 90 days (3 months) after first SACT regimen start
E. Not treated	No SACT, surgery or RT identified over entire follow-up period

RT, radiotherapy; SACT, systemic anticancer therapy

Table S3: OS in patients diagnosed with NSCLC in 2007–2012 and 2013–2017 by stage and pathological subtype

Substratification	N	Median OS (months)	Q1–Q3 (months)	1-year		3-year		5-year	
				n	OS (95% CI)	n	OS (95% CI)	n	OS (95% CI)
Stage I									
NSQ 2007–2012	64	55.27	24.8–98.5	58	0.91 (0.84–0.98)	37	0.58 (0.47–0.71)	25	0.43 (0.32–0.57)
NSQ 2013–2017	159	NA	34.2–NA	123	0.90 (0.86–0.95)	44	0.72 (0.64–0.81)	<6	0.51 (0.37–0.72)
SQ 2007–2012	58	37.28	18.5–66.8	46	0.79 (0.70–0.90)	29	0.50 (0.39–0.65)	16	0.28 (0.18–0.42)
SQ 2013–2017	69	51.13	32.6–NA	55	0.85 (0.77–0.94)	24	0.73 (0.61–0.86)	<6	0.32 (0.13–0.81)
CDUP 2007–2012	128	16.72	5.8–33.1	76	0.59 (0.51–0.69)	25	0.20 (0.14–0.28)	11	0.09 (0.05–0.16)
CDUP 2013–2017	189	20.90	8.0–40.3	97	0.66 (0.60–0.74)	17	0.27 (0.19–0.38)	<6	0.10 (0.04–0.28)
Stage II									
NSQ 2007–2012	61	34.27	10.6–80.0	41	0.68 (0.58–0.81)	27	0.45 (0.34–0.60)	18	0.31 (0.21–0.46)
NSQ 2013–2017	51	26.43	10.2–58.0	30	0.72 (0.60–0.85)	12	0.42 (0.30–0.61)	0	–
SQ 2007–2012	58	17.20	8.6–58.2	36	0.62 (0.51–0.76)	18	0.31 (0.21–0.46)	14	0.24 (0.15–0.38)
SQ 2013–2017	74	19.87	7.2–53.9	45	0.66 (0.55–0.77)	15	0.42 (0.31–0.57)	0	–
CDUP 2007–2012	81	8.93	2.9–16.8	27	0.33 (0.24–0.45)	11	0.14 (0.08–0.24)	7	0.09 (0.04–0.18)
CDUP 2013–2017	55	11.33	5.4–26.9	25	0.50 (0.38–0.65)	<6	0.09 (0.03–0.31)	0	–

Stage IIIA									
NSQ 2007–2012	51	9.93	6.5–38.6	23	0.45 (0.33–0.61)	14	0.27 (0.18–0.43)	9	0.18 (0.10–0.32)
NSQ 2013–2017	57	23.97	10.6–NA	35	0.74 (0.63–0.87)	<6	0.35 (0.22–0.58)	0	–
SQ 2007–2012	91	10.73	4.4–21.1	41	0.45 (0.36–0.57)	12	0.13 (0.08–0.22)	10	0.11 (0.06–0.20)
SQ 2013–2017	72	14.50	8.4–36.0	29	0.54 (0.43–0.68)	<6	0.21 (0.10–0.42)	0	–
CDUP 2007–2012	77	5.77	1.5–11.0	16	0.21 (0.13–0.32)	<6	0.05 (0.02–0.13)	0	–
CDUP 2013–2017	57	5.00	1.9–7.5	7	0.20 (0.12–0.36)	0	–	0	–
Stage IIIB–IV									
NSQ 2007–2012	345	4.07	1.3–10.5	68	0.20 (0.16–0.25)	19	0.06 (0.04–0.09)	11	0.03 (0.02–0.06)
NSQ 2013–2017	321	5.00	1.7–12.9	72	0.26 (0.21–0.31)	8	0.06 (0.04–0.11)	0	–
SQ 2007–2012	229	5.33	2.2–12.0	56	0.24 (0.19–0.31)	12	0.05 (0.03–0.09)	8	0.04 (0.02–0.07)
SQ 2013–2017	167	4.80	2.4–11.9	37	0.25 (0.19–0.32)	6	0.08 (0.04–0.15)	0	–
CDUP 2007–2012	370	1.23	0.4–3.2	30	0.08 (0.06–0.11)	8	0.02 (0.01–0.05)	<6	0.01 (0.00–0.02)
CDUP 2013–2017	323	1.23	0.4–3.4	14	0.06 (0.04–0.09)	<6	0.01 (0.00–0.04)	0	–

CDUP, clinically diagnosed with unknown pathology; NSCLC, non-small cell lung cancer; NSQ, non-squamous cell carcinoma; OS, overall survival; SQ, squamous cell carcinoma