







# Treatment and outcomes for early non-small-cell lung cancer: a retrospective analysis of a Portuguese hospital database

Marta Soares<sup>\*.1</sup> , Luís Antunes<sup>2</sup> , Patrícia Redondo<sup>3</sup> , Marina Borges<sup>3</sup> , Ruben Hermans<sup>4</sup>, Dony Patel<sup>4</sup>, Fiona Grimson<sup>4</sup>, Robin Munro<sup>4</sup>, Carlos Chaib<sup>5</sup>, Laure Lacoïn<sup>6,7</sup>, Melinda Daumont<sup>6</sup> , John R Penrod<sup>8</sup>, John C O'Donnell<sup>8</sup>, Maria José Bento<sup>2,9</sup>  & Francisco Rocha Gonçalves<sup>10</sup>

<sup>1</sup>Department of Medical Oncology, Portuguese Oncology Institute of Porto (IPO-Porto), 4200-072 Porto, Portugal

<sup>2</sup>Cancer Epidemiology Group, IPO Porto Research Center (CI-IPOP), Portuguese Oncology Institute of Porto (IPO-Porto), 4200-072 Porto, Portugal

<sup>3</sup>Outcomes Research Lab, Portuguese Oncology Institute of Porto (IPO-Porto), 4200-072 Porto, Portugal

<sup>4</sup>Real World Solutions, IQVIA, London, N1 9JY, UK

<sup>5</sup>R&D Medical Affairs, Bristol Myers Squibb, 28050 Madrid, Spain

<sup>6</sup>Worldwide Health Economics & Outcomes Research, Bristol Myers Squibb, 1420 Braine-l'Alleud, Belgium

<sup>7</sup>Epi-Fit, Bordeaux, Nouvelle-Aquitaine 33000, France

<sup>8</sup>Worldwide Health Economics & Outcomes Research, Bristol Myers Squibb, Princeton, NJ 08540, USA

<sup>9</sup>Department of Population Studies, Institute of Biomedical Sciences Abel Salazar, University of Porto (ICBAS-UP), 4050-313 Porto, Portugal

<sup>10</sup>MEDCIDS, Faculty of Medicine, University of Porto, 4200-450 Porto, Portugal

\*Author for correspondence: Tel.: +351 96176 0994; [martasoares@ipoporto.min-saude.pt](mailto:martasoares@ipoporto.min-saude.pt)

**Aim:** This observational study evaluated treatment patterns and survival for patients with stage I–IIIA non-small-cell lung cancer (NSCLC). **Materials & methods:** Adults newly diagnosed with NSCLC in 2012–2016 at IPO-Porto hospital were included. Treatment data were available for patients diagnosed in 2015–2016. **Results:** 495 patients were included (median age: 67 years). The most common treatments were surgery alone or with another therapy (stage I: 66%) and systemic anticancer therapy plus radiotherapy (stage II: 54%; stage IIIA: 59%). One-year OS (95% CI) for patients with stage I, II and IIIA NSCLC (diagnosed 2012–2016) were 92% (88–96), 71% (62–82) and 69% (63–75), respectively; one-year OS (95% CI) for treated patients with stage I–II or stage IIIA NSCLC (diagnosed 2015–2016) were 89% (81–97) and 86% (75–98) for non-squamous cell and 76% (60–95) and 49% (34–70) for squamous cell NSCLC. **Conclusion:** Treatment advances are strongly needed for stage I–IIIA NSCLC, especially for patients with squamous cell histology.

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**Keywords:** non-small-cell lung cancer • non-squamous cell carcinoma • overall survival • real-world evidence • squamous cell carcinoma • stage I–IIIA • treatment patterns

Most patients with lung cancer are diagnosed with advanced disease as the physical symptoms occur late in disease progression [1]. However, approximately 20–30% of lung cancers, including non-small-cell lung cancer (NSCLC), are diagnosed at earlier stages of the disease (stages I–IIIA); this proportion is expected to increase with implementation of lung cancer screening in Europe [2–7].

Current European Society for Medical Oncology (ESMO) guidelines for early-stage NSCLC recommend surgery for stages I and II with adjuvant chemotherapy recommended for stage II and considered for stage IB [1]. Radiotherapy is recommended as a nonsurgical option for stage I [1]. For resectable stage III disease, surgery with chemotherapy (adjuvant or induction) or induction concurrent chemoradiotherapy are recommended [1]; for unresectable stage III disease, concurrent or sequential chemoradiotherapy is recommended. These recommendations have not changed significantly from the previous 2013 guidelines [8]. With the availability of tyrosine kinase inhibitors and immune

checkpoint inhibitors, studies are underway to determine their potential use in early-stage NSCLC, predominantly as neoadjuvant or adjuvant therapy [9,10].

I-O Optimise is a multinational, observational research initiative providing valuable insights on the evolving lung cancer landscape based on established real-world data sources [11]. Through this initiative, treatment patterns and survival outcomes in stage I–IIIA patients with NSCLC in Northern Portugal are being assessed using real-world data from the Instituto Português de Oncologia do Porto Francisco Gentil, EPE (IPO-Porto) hospital.

## Materials & methods

IPO-Porto, a single-site oncology hospital treating approximately 40% of oncology patients in Northern Portugal, holds a research database capturing data on all cancer types. The IPO-Porto hospital and associated research database have been described previously [12].

This observational retrospective cohort study included adults ( $\geq 18$  years) newly diagnosed with NSCLC between January 2012 and December 2016 and followed up at IPO-Porto until June 2017. Inclusion and exclusion criteria are described in [Supplementary Table 1](#). This analysis focused on patients diagnosed with stage I–IIIA NSCLC (International Association for the Study of Lung Cancer 7th edition of the tumor, node and metastasis classification of lung cancer) [13]. Initial treatment includes patients diagnosed in 2015–2016, as systemic anticancer therapy (SACT) data were available since 2015, and was defined as the first treatment received within 6 months of diagnosis, including any other associated treatment received within a specified time period following first treatment, considering lung surgery, radiotherapy and SACT ([Supplementary Table 2](#)).

Patient characteristics and initial treatment were reported with descriptive statistics. Median time from diagnosis to first treatment received was calculated for treated patients. Overall survival (OS) was estimated by the Kaplan–Meier method from date of diagnosis (or from the treatment initiation date for analyses of treated populations) to death, loss to follow-up or end of study period. When sample sizes were limited, disease stages were combined. No imputation methods were used to handle missing data.

## Results

### Patients

Between 2012 and 2016, 1524 patients were diagnosed with NSCLC at IPO-PORTO and met the eligibility criteria with approximately a third (32.5%) diagnosed at stages I–IIIA ([Figure 1](#)). Although the number of patients diagnosed annually remained consistent, the proportion diagnosed at stages I–IIIA showed a modest increase from 30.9% in 2012 to 34.2% in 2016. In patients with stages I–IIIA NSCLC, median age was 67 years and 35.2% were diagnosed with stage I, 17.4% with stage II and 47.5% with stage IIIA ([Table 1](#)).

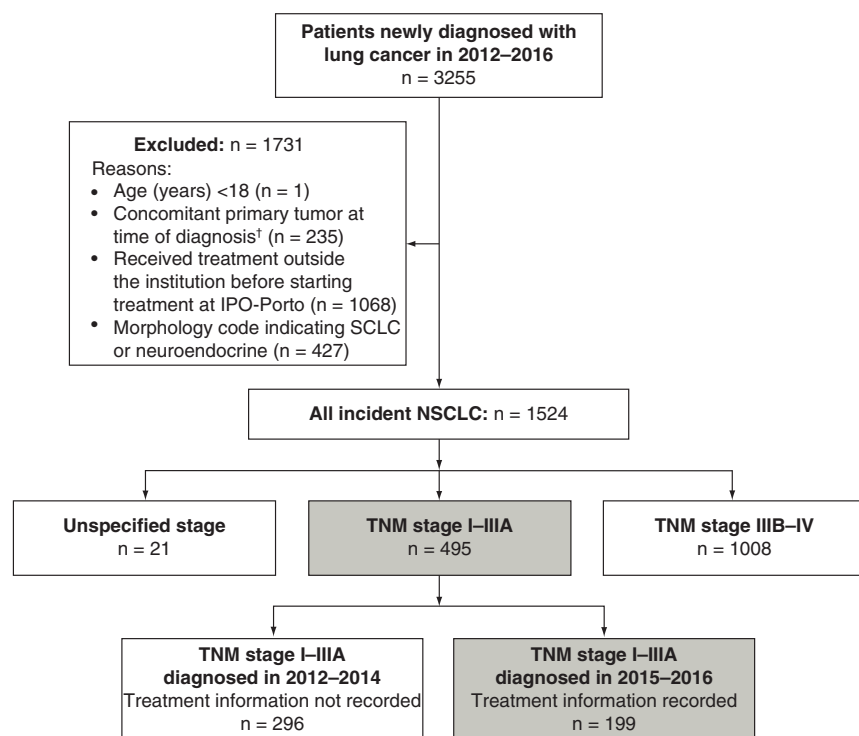
The most common histologies were non-squamous cell (NSQ) carcinoma (58.8%) and squamous cell (SQ) carcinoma (33.7%). Compared with patients with SQ carcinoma, a greater proportion of patients with NSQ carcinoma were diagnosed at stage I (43.0 vs 25.1%) and a lower proportion with NSQ carcinoma were diagnosed at stage IIIA (41.2 vs 55.1%). Characteristics of the 199 patients diagnosed at stages I–IIIA in 2015–2016, when treatment data was collected, were broadly similar to those diagnosed in 2012–2016 ([Table 1](#)).

### Initial treatments

Of the patients diagnosed in 2015–2016, 90.5% (180/199) were treated within 6 months of diagnosis, <1% (1/199) began treatment >6 months after diagnosis (i.e., not included in the treated population as per our protocol definition), 7.5% (15/199) were not treated (received best supportive care) and 1.5% (3/199) had data collected, but processing issues prevented assessment. Among treated patients, median (interquartile range [IQR]) time to first treatment was 67 days (45–95) for stages I–II and 39 days (28–59) for stage IIIA.

The proportion of treated patients declined marginally with advancing disease (stage I: 93.5% [72/77]; stage II: 90.9% [30/33]; stage IIIA: 87.6% [78/89]). Age at diagnosis also appeared to impact treatment decisions, with 96.4% (80/83) and 94.4% (67/71) of patients aged <65 years and  $\geq 65$  to <75 years, respectively, receiving treatment, compared with 75.6% (34/45) of patients aged  $\geq 75$  years and only 56.3% (9/16) of patients aged  $\geq 80$  years.

Initial treatment for patients diagnosed with stages I–IIIA NSCLC (NSQ or SQ carcinoma only) in 2015–2016 are presented in [Table 2](#). For stage I, 66.2% of treated patients received surgery, where 41.2% received surgery



**Figure 1. Flow diagram of patients diagnosed with lung cancer.** Grey shaded cohorts were included in the study analysis.

†Excluding nonmelanoma skin cancer (ICD-10 codes C44, C4A) and *in situ*/benign neoplasms.

NSCLC: Non-small-cell lung cancer; SCLC: Small-cell lung cancer; TNM: Tumor, node and metastasis.

**Table 1. Demographic and clinical characteristics of patients diagnosed with stage I–IIIa non-small-cell lung cancer.**

Parameter	2012–2016 cohort		2015–2016 cohort <sup>†</sup>	
	All n = 495	All n = 199	Treated patients <sup>‡</sup>	
			Diagnosed at stage I–II n = 102	Diagnosed at stage IIIa n = 78
Age at NSCLC diagnosis (years)				
Mean (SD)	66.5 (10.1)	66.5 (9.9)	66.8 (9.1)	64.0 (10.1)
Median (IRQ)	67 (59–74)	68 (59–74)	67 (60–73)	63 (57–72)
Range	34–88	34–86	34–85	38–83
Gender, n (%)				
Male	369 (74.5)	149 (74.9)	74 (72.5)	59 (75.6)
Female	126 (25.5)	50 (25.1)	28 (27.5)	19 (24.4)
TNM stage, n (%)				
I	174 (35.2)	77 (38.7)	72 (70.6)	–
II	86 (17.4)	33 (16.6)	30 (29.4)	–
IIIa	235 (47.5)	89 (44.7)	–	78 (100.0)
Histology, n (%)				
NSQ	291 (58.8)	119 (59.8)	68 (66.7)	41 (52.6)
SQ	167 (33.7)	68 (34.2)	28 (27.4)	33 (42.3)
NSCLC NOS	21 (4.2)	7 (3.5)	M	M
Other histologies	16 (3.2)	5 (2.5)	M	M

<sup>†</sup> Cohort with treatment data.

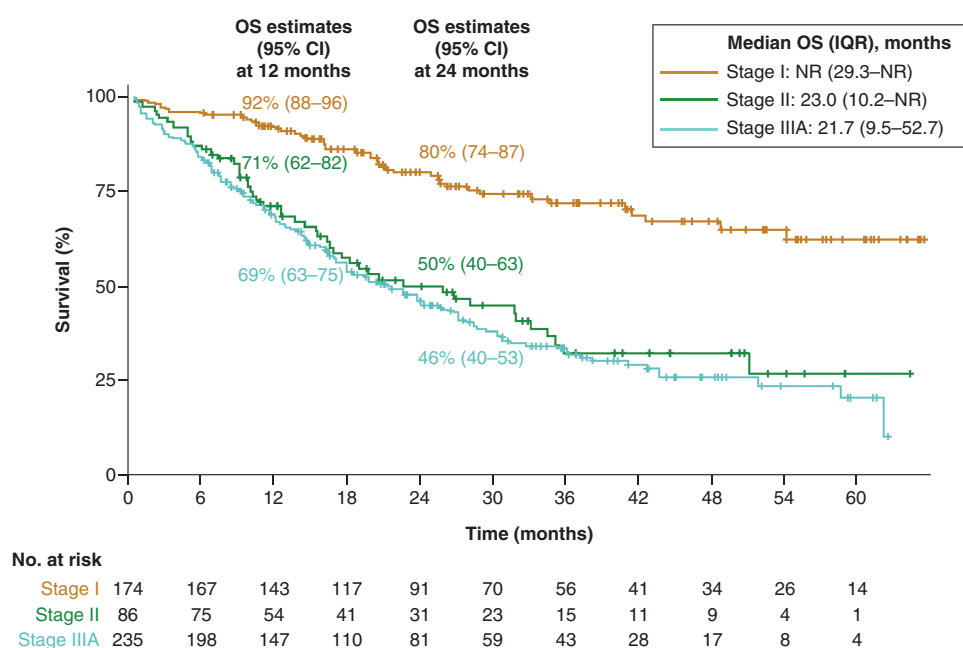
<sup>‡</sup> Includes patients treated within 6 months of diagnosis.

IRQ: Interquartile range; M: Masked; NOS: Not otherwise specified; NSCLC: Non-small-cell lung cancer; NSQ: Non-squamous cell; SD: Standard deviation; SQ: Squamous cell; TNM: Tumor, node and metastasis.

**Table 2. Initial treatments for patients diagnosed with stage I–IIIA NSQ or SQ non-small-cell lung cancer in 2015–2016.**

Treatment, n (%)	Treated patients with NSQ/SQ NSCLC <sup>†</sup> N = 170		
	Stage I n = 68	Stage II n = 28	Stage IIIA n = 74
Surgery	45 (66.2)	6 (21.4)	13 (17.6)
Surgery alone	28 (41.2)	M	M
Surgery + neoadjuvant or adjuvant SACT (with or without radiotherapy) <sup>‡</sup>	17 (25.0)	6 (21.4)	M
Radiotherapy alone	22 (32.4)	M	M
SACT plus radiotherapy	M	15 (53.6)	44 (59.5)
SACT alone	M	M	17 (23.0)

Data were masked if there were five or fewer patients.  
<sup>†</sup> There were six, five or fewer, and nine untreated patients with stage I, II and IIIA NSQ/SQ, respectively.  
<sup>‡</sup> For patients with NSQ and SQ NSCLC, five patients with stage II or IIIA received neoadjuvant SACT; five or fewer patients with stage I, and 10 patients with stage II or stage IIIA received some radiotherapy following surgery.  
M: Masked; NSCLC: Non-small-cell lung cancer; NSQ: Non-squamous cell; SACT: Systemic anticancer therapy; SQ: Squamous cell.



**Figure 2. Overall survival in patients diagnosed with stage I–IIIA non-small-cell lung cancer in 2012–2016.** Patients were censored at the date of loss to follow-up or at the end of the study period, whichever occurred first. IQR: Interquartile range; NR: Not reached; NSCLC: Non-small-cell lung cancer; OS: Overall survival.

alone and 25.0% received surgery with an adjuvant SACT regimen, and 32.4% received radiotherapy alone. For those with stage II, 53.6% received SACT plus radiotherapy and 21.4% were treated with surgery with SACT (all patients had NSQ carcinoma; more than 80% of those received adjuvant SACT). Among patients with stages I–II, the median (IQR) age of patients treated with surgery and radiotherapy alone was 66 years (59–72) and 74 years (69–78), respectively. For stage IIIA, 59.5% of patients received SACT plus radiotherapy and 23.0% received palliative SACT only.

### Overall survival

Among patients diagnosed in 2012–2016, the 1-year OS estimate (95% CI) was highest in those diagnosed with stage I NSCLC (92% [88–96]) and estimates were relatively similar among those diagnosed with stage II or IIIA disease (71% [62–82] and 69% [63–75], respectively; Figure 2). This trend continued through the 2-year OS

analysis with 2-year OS estimates of 80% (74–87), 50% (40–63) and 46% (40–53) for stages I, II and IIIA, respectively.

Among patients diagnosed with stage I or II NSCLC in 2015–2016 and receiving treatment, the 1-year OS estimates were 89% (81–97) for those with NSQ carcinoma and 76% (60–95) for those with SQ carcinoma. In patients diagnosed with stage IIIA NSCLC in 2015–2016 and receiving treatment, the 1-year OS estimates were 86% (75–98) for those with NSQ carcinoma and 49% (34–70) for those with SQ carcinoma.

## Discussion

Epidemiological studies on early-stage NSCLC are limited, with much of the focus directed toward advanced disease. Treatment patterns in patients with stage I NSCLC at IPO-Porto (2015–2016) were generally reflective of ESMO guidelines with approximately two-thirds of patients with stage I NSCLC treated with surgery (alone or with another therapy) and a third treated with radiotherapy (elderly patients) [8]. However, even in this early-stage population, 7.5% of patients with stage I–IIIA NSCLC did not receive treatment.

The OS estimate (95% CI) for patients diagnosed with stage I disease in our study was high, with 92% (88–96) alive 1 year after diagnosis. In a study in Chinese patients with NSCLC (2011–2015), the survival profile for patients diagnosed at stage I were similar to those observed in this study (1-year OS, 97% [94–99]) [14]. Comparable OS in stage I has also been reported over similar time frames (2010–2014), such as in a Danish observational study conducted as part of the I-O Optimise initiative (1-year OS: NSQ carcinoma, 92% [90–93], SQ carcinoma, 85% [82–88]) [15].

Among patients diagnosed with stage II and IIIA NSCLC, less than 20% received surgery; surgery was mostly associated with an SACT regimen (mainly adjuvant treatment) and patients primarily had NSQ histology. The main treatment in stages II and IIIA was SACT plus radiotherapy; unfortunately, it was not possible to differentiate chemoradiation from SACT followed by palliative radiotherapy. In line with the similarities in initial treatment, patients with stage II or IIIA disease showed similar survival profiles with just under three-quarters alive after 1 year (OS estimates [95% CI]: stage II, 71% [62–82]; stage IIIA, 69% [63–75]). In the aforementioned Chinese study, OS for patients with stage II and IIIA NSCLC was higher than observed in our study (1-year, 89% [83–95] and 79% [74–84], respectively); however, in the Chinese cohort, 86.6% of patients with stage II and 59.0% of patients with stage IIIA disease had surgery [14]. In the Danish observational study, 1-year OS estimates for patients diagnosed in 2010–2014 were similar to those observed here (stage II: NSQ carcinoma, 86% [83–88]; SQ carcinoma, 69% [66–73]; stage IIIA: NSQ carcinoma, 72% [69–75]; SQ carcinoma, 60% [57–64]); in the Danish cohort, more than 60% of patients with stage II and around 30% with stage IIIA disease had surgery [15].

In the Danish observational study, OS differed between patients with NSQ and SQ histology, with the greatest differences observed among those diagnosed at stage II or IIIA. This was also apparent in our analysis, where the difference was most evident in patients with stage IIIA disease. In other real-world studies investigating NSCLC (all stages), some found that SQ histology was linked to a poorer prognosis [14]; however, others did not [3,16]. The poor outcomes in patients with stage II and IIIA disease further emphasizes the need for more effective therapies for early-stage NSCLC.

Limitations of this study included the use of a single center; although IPO-Porto is a large oncology hospital, it is not necessarily representative of clinical practice across Portugal. Additionally, performance status and comorbidity data were not available and treatment data were limited to patients diagnosed in 2015–2016.

## Conclusion

This observational study on treatment patterns and outcomes for patients with early-stage NSCLC in Northern Portugal adds to the established literature highlighting a need for diagnostic and therapeutic advances for this population. At present, there are a number of ongoing trials of neoadjuvant and/or adjuvant use of immune checkpoint inhibitors designed to investigate novel approaches that could prevent or reduce postoperative recurrence in patients with early-stage NSCLC, thereby possibly improving long-term survival [9,10]. In addition, recent data with targeted therapies in the early-stage setting have been disclosed [17]. With a greater chance of successful outcomes among patients with early-stage NSCLC [9], such treatment advancements have the potential to greatly improve outcomes for this patient population.

### Summary points

- This observational study evaluated treatment patterns and overall survival (OS) for patients newly diagnosed with stage I–IIIA non-small-cell lung cancer (NSCLC) between January 2012 and December 2016 at IPO-Porto, one of Portugal's largest oncology hospitals, with follow-up until June 2017.
- In total, 495 patients were diagnosed with stage I–IIIA NSCLC between January 2012 and December 2016; of these, 199 patients were diagnosed in 2015 and 2016 when treatment data were collected.
- Most patients who were diagnosed in 2015 and 2016 (90.5%) received treatment within 6 months of diagnosis, with median time to first treatment being slightly longer for those with stage I or II disease (67 days [IQR: 45–95]) than for those with stage IIIA disease (39 days [IQR: 28–59]).
- The most common initial treatments were surgery (alone or with another treatment) for stage I, and systemic anticancer therapy plus radiotherapy for both stage II and IIIA.
- As expected, OS increased with earlier diagnosis, with the highest OS estimates observed for stage I patients. However, there remained room for improvement among treated patients at all stages, particularly among those with squamous cell carcinoma.
- The findings of this single-center study align with real-world data for patients with stage I–IIIA NSCLC from other countries in Europe and worldwide, and add to the literature highlighting a need for treatment advances in this patient population.
- With results of clinical trials investigating neoadjuvant and/or adjuvant immunotherapy for the treatment of early-stage NSCLC expected in the near future, the use of 'baseline' pre-immunotherapy data, such as that reported herein, will help contextualize any associated real-world benefits.

### Supplementary data

To view the supplementary data that accompany this paper please visit the journal website at: [www.futuremedicine.com/doi/suppl/10.2217/lmt-2020-0028](http://www.futuremedicine.com/doi/suppl/10.2217/lmt-2020-0028)

### Ethical conduct of research

This study was conducted according to International Society for Pharmacoepidemiology Guidelines for Good Epidemiology Practices and the ethical principles described in the Declaration of Helsinki. The study followed the laws and regulatory requirements of Portugal. The Institutional Review Board (Ethics Committee of the Portuguese Oncology Institute of Porto) approved the protocol. As this was a retrospective observational study using anonymized patient data, informed consent was not required.

### Author contributions

M Soares, D Patel, R Munro, C Chaib, L Lacoïn, M Daumont, JR Penrod, JC O'Donnell, MJ Bento and FR Gonçalves worked on the conceptualization; methodology; writing (review and editing) and L Antunes, P Redondo, M Borges, R Hermans and F Grimson worked on the conceptualization; methodology; formal analysis; writing (review and editing) of this study.

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## References

Papers of special note have been highlighted as: ● of interest; ●● of considerable interest

1. 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.* 28(Suppl. 4), iv1–iv21 (2017).
- **Latest European guidance on management of patients with early or locally advanced non-small-cell lung cancer (NSCLC).**
2. Hespanhol V, Parente B, Araujo A *et al.* Lung cancer in Northern Portugal: a hospital-based study. *Rev. Port. Pneumol.* 19(6), 245–251 (2013).
3. Debieuvre D, Locher C, Asselain B *et al.* Evidence of slight improvement in five-year survival in non-small-cell lung cancer over the last 10 years: results of the French KBP-CPHG real-world studies. *Bull. Cancer* 106(4), 283–292 (2019).
4. Vergnenegre A, Carrato A, Thomas M, Jernigan C, Medina J, Cruciani G. Real-world healthcare resource utilization in a European non-small cell lung cancer population: the EPICLIN-Lung study. *Curr. Med. Res. Opin.* 30(3), 463–470 (2014).
5. Horeweg N, van der Aalst CM, Thunnissen E *et al.* Characteristics of lung cancers detected by computer tomography screening in the randomized NELSON trial. *Am. J. Respir. Crit. Care Med.* 187(8), 848–854 (2013).
6. Oudkerk M, Devaraj A, Vliegenthart R *et al.* European position statement on lung cancer screening. *Lancet Oncol.* 18(12), e754–e766 (2017).
7. Balata H, Evison M, Sharman A, Crosbie P, Booton R. CT screening for lung cancer: are we ready to implement in Europe? *Lung Cancer* 134 25–33 (2019).
- **Review of the recent status of lung cancer screening programs in Europe and related challenges.**
8. Vansteenkiste J, De Ruysscher D, Eberhardt WE *et al.* Early and locally advanced non-small-cell lung cancer (NSCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann. Oncol.* 24(Suppl. 6), vi89–98 (2013).
- **Earlier European guidance on management of early or locally advanced NSCLC. Useful to compare with [1] to gauge advances over previous decade**
9. Sandler JE, D’Aiello A, Halmos B. Changes in store for early-stage non-small cell lung cancer. *J. Thorac. Dis.* 11(5), 2117–2125 (2019).
10. Bai R, Li L, Chen X, Chen N, Song W, Cui J. Neoadjuvant and adjuvant immunotherapy: opening new horizons for patients with early-stage non-small cell lung cancer. *Front. Oncol.* 10, 575472 (2020).
- **Recent review of ongoing studies of neoadjuvant and/or adjuvant immunotherapy for patients with early-stage NSCLC.**
11. Ekman S, Griesinger F, Baas P *et al.* I-O Optimise: a novel multinational real-world research platform in thoracic malignancies. *Future Oncol.* 15(14), 1551–1563 (2019).
- **Background on the conceptualization and establishment of the I-O Optimise initiative.**
12. Soares M, Antunes L, Redondo P *et al.* Real-world treatment patterns and survival outcomes for advanced non-small cell lung cancer in the pre-immunotherapy era in Portugal: a retrospective analysis from the I-O Optimise initiative. *BMC Pulm. Med.* 20(1), 240 (2020).
- **Additional research from the IPO-Porto NSCLC population with a focus on advanced disease.**
13. Detterbeck FC, Boffa DJ, Tanoue LT. The new lung cancer staging system. *Chest* 136(1), 260–271 (2009).
14. Fan H, Shao ZY, Xiao YY *et al.* Incidence and survival of non-small cell lung cancer in Shanghai: a population-based cohort study. *BMJ Open* 5(12), e009419 (2015).
15. Sørensen JB, Ekman S, Horvat P *et al.* Initial treatment in patients (pts) diagnosed with non-small cell lung cancer (NSCLC) in Denmark from 2005–2015: the SCAN-LEAF study. Presented at: *European Society for Medical Oncology (ESMO) 2018 Congress*. Munich, Germany (2018). Poster number: 1483P.
16. Kocher F, Hilbe W, Seeber A *et al.* Longitudinal analysis of 2293 NSCLC patients: a comprehensive study from the TYROL registry. *Lung Cancer* 87(2), 193–200 (2015).
17. Wu YL, Tsuboi M, He J *et al.* Osimertinib in resected EGFR-mutated non-small-cell lung cancer. *N. Engl. J. Med.* 383(18), 1711–1723 (2020).