Early View

Invited review

ERS 2023 International Congress: Thoracic Oncology Assembly highlights

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ERS 2023 International Congress: Thoracic Oncology Assembly highlights

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Abstract

Lung cancer is the leading cause of cancer mortality in the world. It greatly affects the patients’ quality of life, being a challenge for the daily practice in Respiratory Medicine. Advances in the genetic knowledge of thoracic tumours mutational landscape, the development of targeted therapies and immune checkpoint inhibitors, led to a paradigm shift in the treatment of lung cancer and pleural mesothelioma. During the annual ERS Congress in Milan, Italy, experts from all over the world presented their high-quality research and reviewed best clinical practices. Lung cancer screening, management of early-stages of lung cancer, application of artificial intelligence and biomarkers were discussed and they will be summarised here.

1. INTRODUCTION

In recent times, there has been a significant evolution in the approach to patients with thoracic tumours. New scientific advances improved the quality of life of these patients and overall survival. The implementation of lung cancer screening has revolutionized the diagnosis of this disease, with a significant reduction in mortality. New challenges have arisen, particularly with regards to incidental findings and their management. Artificial intelligence started playing an uprising role in this field. Clinical trials have led to the approval of immunotherapy combined with chemotherapy in the neoadjuvant phase, as well as targeted therapy in the adjuvant phase for EGFR mutation and ALK rearrangement, constituting a significant improvement in resectable non-small cell lung cancer (NSCLC). Furthermore, new biomarkers could be useful tools for
predicting outcomes and treatment response in thoracic oncology. Regarding pleural malignancies, several promising clinical trials are underway that could change the prognosis of these patients. In this manuscript, we will provide an overview of the thoracic oncology highlights presented at the European Respiratory Society (ERS) International Congress 2023.

2. NEW CHALLENGES AND OPPORTUNITIES IN LUNG CANCER SCREENING

a. Implementing lung cancer screening in the real world

Previous clinical trials have demonstrated that lung cancer screening using low-dose CT scans (LDCT) reduces both lung cancer mortality and overall mortality (1, 2). Despite these results, lung cancer screening has not yet been widely implemented in Europe. In fact, its applicability in clinical practice remains a challenge. In 2022, the European Commission proposed that lung cancer should be included in the EU cancer screening recommendations (3). There are some pilot studies on the implementation of lung cancer screening in Europe. At the 2023 ERS congress, the final results of a French pilot study on lung cancer screening (DEP KP80) were presented (4). The aim was to assess the feasibility and effectiveness of a lung cancer screening pilot program with LDCT scans in a French department. Patients were prospectively recruited by general practitioners or pulmonologists from 2016 to 2020, using the same inclusion criteria as the National Lung Screening Trial (NLST), and three rounds of annual LDCT scans were planned. Out of 1369 participants, 75.1% underwent the first LDCT, 28.4% completed the second round and 28.4% completed the third round. The cumulative incidence of lung cancer was 2.5% and the false positive rate 2.74%. Most patients with lung cancer were in stage I-II (72.1%) and 81.4% were treated with surgery. This study demonstrated the feasibility of lung cancer screening in a real-life context and confirmed its efficacy but also raised awareness of the importance of participation in all rounds.

European lung cancer screening studies have set the ground for lung cancer screening implementation across Europe however significant challenges exist in real life clinical settings.

The ERS has addressed this as a key stakeholder in lung cancer screening and has recently launched SOLACE (Strengthening the screening of Lung Cancer in Europe) in collaboration with other stakeholders including patient organizations (5). SOLACE is a pioneering new EU4Health project that was launched under the Europe’s Beating Cancer Plan. A consortium of experts appointed by the European Society of Radiology and the ERS will work closely and will have continuous input from the European Lung Foundation and Lung Cancer Europe to ensure patient perspective is incorporated and considered throughout. The SOLACE project was presented during this year’s congress and it aims to facilitate implementation of lung cancer screening programmes across Europe with particular focus in breaking down the barriers to screening. It will ensure that all people from various social and economic backgrounds have equal access to lung cancer screening. In particular, it will focus on difficult to reach groups that are at higher risk for lung cancer due to health inequalities and unequal access to healthcare services and/or insurance cover.

Incidental findings are unexpected anomalies detected in LDCT, often unrelated to lung cancer but carrying significant clinical implications. Currently, radiologists lack a consensus on how to define, report, and manage these incidental findings. The Academy College of Radiology’s (ACR’s) quick reference guide for lung cancer screening CT incidental findings is available (6), but the need for international standardisation remains. This standardisation is crucial for
determining clinical relevance and healthcare costs. Studies like the NELSON trial found that only 7% of incidental findings were clinically relevant, with just 1% having clinical implications (7). The HANSE study shows a higher percentage of clinically significant incidental findings (8), emphasising the need for further research on clinical implications.

Interestingly, the data revealed that non-malignant conditions like cardiovascular and non-malignant lung diseases played a significant role in all-cause mortality in the lung cancer screening population, as demonstrated in the NELSON study (7). Artificial intelligence (AI) plays a potential role in lung cancer screening programs. Automated detection and segmentation of non-small cell lung cancer in CT images show promise in reducing the clinician's burden and improving accuracy. Trustworthiness and multidisciplinary collaboration will be essential in implementing AI effectively.

The discussion underlines the importance of transparent and empathetic communication with patients about incidental findings. It's crucial to inform patients about potential findings and guide them through the next steps. Primary care physicians play a significant role in this process, as they have a deep understanding of their patients' medical history and can relay results and recommendations effectively.

Detecting emphysema and interstitial lung abnormalities (ILA) during screening programs is clinically relevant (9, 10). Both conditions are valuable radiographic biomarkers for lung cancer risk. Screening programs for patients with chronic obstructive pulmonary disease (COPD) allow for the diagnosis of other comorbidities (9-15). Managing incidental findings effectively not only enhances the overall safety and effectiveness of these programs but also contributes to a more comprehensive approach to healthcare, extending beyond lung cancer to include the early diagnosis of other health conditions (9-15).

Another ongoing challenge in lung cancer screening (LCS) are indeterminate pulmonary nodules; and differentiating those which represent early malignancy from benign causes. Such indeterminate nodules are found in up to a quarter of baseline LDCTs (16), and whilst evidence from the NELSON study has demonstrated radiological surveillance with volumetric assessment of growth to be an effective approach (7), false positive, false negative and delays to definitive diagnosis remain an issue. A study by J. McCabe et al. evaluated the accuracy of exponential function in modelling the observed growth of early-stage lung cancer presenting as solid (volume) and subsolid (mass) nodules, particularly solid (volume) and subsolid (mass) nodules, by analysing the nodules of patients in the SUMMIT lung cancer screening study (17). This study concluded that volume growth of early-stage lung cancer presenting as solid nodules is well described by an exponential growth function. However, the mass growth of early-stage lung cancer presenting as subsolid nodules is less accurately modelled by an exponential growth function. These results support current guidelines that recommend longer-term surveillance for subsolid nodules due to their less predictable future growth. Furthermore, novel biomarkers and techniques could improve the diagnosis of indeterminate nodules.

b. Genomic analysis of bronchial and nasal epithelium and fluid specific microRNA-based signatures

Ideally, subsequent investigations for indeterminate pulmonary nodules should provide a definitive answer whilst minimising invasive investigations. One such approach involves genomic analysis of bronchial epithelial cells, looking for cancer-associated gene expression profiles. In the AEGIS-1 and AEGIS-2 trials (18), participants with suspected lung cancer who were undergoing bronchoscopy underwent collection of epithelial cells from the (normal-appearing) mainstem bronchus for genomic analysis. In patients with an indeterminate pre-test probability of cancer but a nondiagnostic bronchoscopy, the genomic classifier achieved a 91% negative
predictive value (NPV) (95% confidence interval (C.I) 75-98) and a 40% positive predictive value (PPV) (95% C.I. 27-55). Whilst these results offer insight into the potential additional utility of genomic analysis of (macroscopically normal) airway epithelium in suspected cancer, this approach still required bronchoscopy. Further analysis of samples collected in this trial found that gene expression alterations were shared between nasal and bronchial epithelium (19), opening the possibility for minimally-invasive samples collected via nasal swabs to guide management decisions. This has led to the development of the Percepta Nasal swab (Veracyte, USA); a trial to demonstrate the clinical utility of this test in the management of patients with lung nodules is currently recruiting (20).

Another potential useful biomarker is the microRNA pattern of liquid biopsies. A study presented by G. Casagrande showed that there are fluid-specific microRNA signatures in plasma and sputum that can potentially be employed in lung cancer screening programs to guide the selection of high-risk subjects for early detection of lung cancer, which may reduce the healthcare system costs associated with lung cancer screening (21).

c. Exhaled breath condensate

An alternative minimally-invasive approach for indeterminate pulmonary nodules is analyzing patterns of volatile organic compounds (VOCs) in exhaled breath condensate. Exhaled breath contains a complex mixture of thousands of VOCs, and changes in the patterns of these may reflect pathological processes, allowing diagnoses to made via a non-invasive approach (22). A multi-centre study using the aeoNose device (the eNose company) aimed to develop and validate a risk-prediction model to identify patients with NSCLC based on exhaled breath patterns (23). A model combining clinical and exhaled breath parameters achieved a sensitivity of 95%, specificity of 49%, NPV 94% and area under the receiver operating curve (AUROC) of 0.86 in the validation cohort. A further study used the BreathCloud cohort (a multi-centre observational study using eNose analysis in patients with chronic respiratory disease (24) to explore whether this approach could detect early lung cancer in patients with COPD (25). Lung cancer was developed within 2 years after inclusion in 37 of 682 patients with COPD in the study. Significant differences in VOC patterns at baseline test were identified between those patients with COPD who did and did not go on to subsequently develop lung cancer (p<0.01, AUROC 0.9). Another study, presented by K. Zwijsen, showed that the analysis of VOCs from exhaled breath sampling using multi-capillary ion-mobility spectrometry (MCC-IMS) may be useful in distinguishing between benign and malignant pulmonary nodules. However, none of the selected VOCs showed a significant correlation with nodule size (26).

Whilst these results are exciting, it remains to be seen how this technology may complement current screening programmes. As a cheap, feasible, point-of-care test, eNose may have a role in lung cancer detection in less economically advanced settings with limited access to CT scans. Within Europe and the United States, exhaled breath analysis could have a role in risk-stratification prior to low-dose CT screening, used in combination with CT, or to predict malignancy risk in CT-detected indeterminate nodules.

3. NOVEL BRONCHOSCOPIC TECHNIQUES FOR SMALL PULMONARY NODULES

Despite the increasing evidence for minimally or non-invasive approaches for identifying malignancy in pulmonary nodules, histopathological confirmation remains the only way cancer can be definitively diagnosed or excluded. Pre-resection diagnosis can reduce false-positive surgical resection rates and can be obtained via conventional bronchoscopy for proximal endobronchial lesions or percutaneous image-guided biopsy for peripheral nodules. However,
the associated risk of pneumothorax (15-40% (27)) with percutaneous biopsy, of particular concern in patients with emphysema, may preclude this approach. Electromagnetic navigation bronchoscopy (ENB) is a minimally invasive technology that uses electromagnetic guidance to accurately direct a bronchoscope to pulmonary lesions. Further imaging techniques including radial EBUS, fluoroscopy or cone-beam CT ensure the biopsy are accurately obtained.

Although many retrospective single-centre studies of experience with ENB have been published, multi-centre studies with long-term follow up of diagnostic accuracy and safety were lacking. NAVIGATE is a prospective, multi-centre cohort study examining the diagnostic yield and safety of ENB in pulmonary nodules (28). In NAVIGATE, ENB achieved sensitivity of 69%, specificity 100%, PPV 100% and NPV 56%. Pneumothoraxes requiring either admission or chest tube placement occurred in 2.9%. Diagnostic yield was higher in lesions of 20mm or greater (77.6% vs 67.3%) and those in upper lobe location (76.5% vs 67.9%). Adequate tissue for molecular testing was obtained in 86.2% of the 87 lung lesions where testing was attempted. As experience and availability of ENB expands in Europe, this approach is likely to lead to further benefits for patients with indeterminate pulmonary nodules detected at lung cancer screening.

4. THE ONGOING CHALLENGE OF GROUND GLASS OPACITIES IN THE LUNG

Ground Glass Opacities (GGOs) or Sub-Solid Nodules (SSNs) represent a frequent radiological finding, usually detected incidentally or during screening programs or during chest CT scans offered to investigate other unrelated conditions. They may be neoplastic or not. There is currently no consensus between different guidelines regarding management and follow-up (29-31). GGOs include Ground Glass Nodules (GGNs) or Non-Solid Nodules (NSNs), which are pure ground glass lesions with a consolidation tumor ratio (CTR) = 0, and Part-Solid nodules (PSNs), in which we find a solid component (CTR > 0) (32). Histologically, the majority of lepidic pattern corresponds to lepidic predominant nonmucinous adenocarcinoma (LPA) followed by minimal invasive adenocarcinoma (MIA) and adenocarcinoma in situ (AIS), figure 1. The survival by MIA and AIS reaches 100%, which suggests that a conservative approach may be more suitable as long as no growing solid component is detected (33).

In screening programmes, the frequency of SSN varies between 10 and 20% mainly depending on the duration of the follow-up. In the NLST trial, the frequency of SSN was 9.4% (34), in the NELSON study it was 3.3% at baseline and 0.7% new SSN were detected at follow-up (35, 36), in the I-ELCAP study 4.2% NSN and 5.0% PSN at baseline with 0.7% NSN and 0.8% PSN at follow-up (37, 38) while the BioMILD trial (39) showed a frequency of 18.4%. The follow-up of GGOs showed the majority of them remain stable or regress. At 3 month, 37.6% of pure GGOs and 48.7% of mixed GGOs disappear (40). Only 5.4% of pure GGOs develop a solid component during a 4 year follow-up (41). The MILD trial showed a 2% progression of SSNs (including those <5mm) to lung cancer, 89% of them were stage I and no deaths were recorded (42). The BioMILD trial showed that in 4.4% of SSNs were diagnosed as lung cancer, 98% of them were in stage I and one case of stage III (39). Moreover, this trial also demonstrated that the incidence of SSNs was higher during the first 5 years but continued also up to 10 years (39). Knowing that GGOs are the most frequent non fibrotic CT abnormality observed in COVID-19 (43), the priority during the pandemic was not to differentiate if they were related to lung cancer. Actually, GGOs are described in 80% of the patients during the acute phase (44), and persist later among other radiological abnormalities (45, 46). Control CTs after a COVID-19 infection show GGOs in 49% at 3 months (47), a decrease of the prevalence at 5 to 7 months (47-50), reaching
24% at 1 year (49, 51, 52) and 11% at 18 months (48, 51-54). Until now it is unclear how long does the radiological clearance take (55).

The available research studied patients with a severe disease or persistent symptoms and many of the studies in the meta-analyses were retracted. Therefore, more consistent research is needed to produce consensual follow-up guidelines and the role of multidisciplinary teams is here crucial. It is suggested to perform a CT-scan at 3 months after discharge for severe cases and at a longer interval to control radiological clearance or in patients with new or progressive respiratory manifestations (55-57). The characteristics that help differentiate GGO in COVID-19 from early stage lung cancer is depicted at table 1. Furthermore, the development of a predictive AI module would be a helpful tool in the decision-making process (58).

5. EVOLVING CONCEPTS IN LUNG CANCER MANAGEMENT: UNRAVELLING CONTROVERSIES, NEW BIOMARKERS AND TREATMENT OPTIONS

5.1 Current controversies in management of stage I NSCLC

Stage I NSCLC diagnosis is anticipated to increase over the next few years after a wider implementation of lung cancer screening (1, 2). Although its management appears to be uncomplicated, current guidelines are controversial in some aspects of treatment (60-65) and this has been discussed at this year’s congress. According to the 8th TNM classification of NSCLC (66), stage I NSCLC is defined as any lesion ranging from minimal invasion (Tmi) up to 4cm (T2a) without any accompanying lymph node invasion (N0) or metastatic spread (M0). Despite the golden standard being anatomical resection (preferred over wedge resection) with a preference for VATS (video assisted thoracic surgery), there are controversies in the management of T2aN0M0 disease. ESMO guidelines suggest adjuvant chemotherapy for surgically resected stage I tumors in the upper limit of T2a (i.e. measuring 4cm) with R0 resection (i.e. clear surgical margins) while NICE guidelines suggest no adjuvant chemotherapy for these and NCCN suggests adjuvant for those R0 resected that are deemed high risk (i.e. poor differentiation, visceral pleura etc) (60, 64, 65). The above allude to the fact that patients receive different care depending on where they are diagnosed and treated. Discrepancies appear also in the management of surgically resected stage I tumours with R1 resection, where ESMO recommends post operative radiotherapy and adjuvant chemotherapy, whereas NCCN recommends re-resection or radiotherapy for T1a-c and for T2a re-resection with or without chemotherapy or radiotherapy (60, 65).

5.2 New concepts in the management of resectable lung cancer and oligometastatic disease

In the perioperative stage of lung cancer treatment, research in the last couple of years has changed the treatment approach that had been relatively unchanged for a long period of time. In general, advancements made in stage IV lung cancer and in precision medicine for metastatic lung cancer have trickled down to the earlier stages, more precisely in the perioperative stage of lung cancer treatment. A number of studies have been conducted with regards to neo-adjuvant and adjuvant immunotherapy (supplementary to the more standard chemotherapy), and have found an improvement in progression free survival and a survival benefit (table 2). Similar to targeted therapies for EGFR mutated lung cancer in the perioperative phase (table 2), the expectation is that new guidelines will evolve in the future to incorporate a combination of chemo and immunotherapy in the treatment of resectable lung cancer. Questions remain with regards to which patients will benefit the most, especially since PD-L1 status and pathological
response seem to be related to outcome. Furthermore, compelling evidence have demonstrated the role of circulating tumour DNA as a potential biomarker to predict neoadjuvant immunotherapy efficacy and to predict recurrence free-survival in resectable disease (67-69). Another ongoing challenge is the precise identification of NSCLC patients that could benefit from adjuvant chemotherapy. RNA-based expression of 12 genes from 139 surgically resected patients was retrospectively evaluated. Overall and event-free survival were assessed, and patients were stratified as low-risk (adjuvant chemotherapy non-benefit) and high-risk (adjuvant chemotherapy -benefit). The 12-gene expression panel successfully stratified low- and high-risk patients regardless of adjuvant chemotherapy, with a 0.8% failure rate, and may be a promising tool for clinical management of early stages NSCLC patients (70). Moreover, a validation study was also performed to unravel the value of a 5-gene signature to predict prognosis in early-stage NSCLC patients. RNA-based expression of DUSP6, ERBB3, LCK, MMD, and STAT1 genes were assessed from surgically resected patients. Subgroup stratification as low-risk and high-risk of recurrence was performed. High expression of DUSP6 and ERBB3 genes were associated with better overall survival (HR=0.64; p=0.001 and HR=0.68; p=0.003), being a promising tool to predict prognosis in early stages of NSCLC (71).

Regarding the treatment of oligometastatic lung cancer, new ASTRO/ESTRO guidelines were published this year (78) and were presented and discussed at this year’s congress. Oligometastatic lung cancer is defined as metastatic disease limited in number and location for whom a radical treatment is technically feasible with acceptable toxicity. This recent guideline suggests that multimodal treatment should be considered in oligometastatic lung cancer patients with less than five distant metastasis and that the decision lies with the Multidisciplinary Team (MDT). Radiotherapy is favored if feasible to avoid pauses in systemic treatment and, with regards to timing, systemic treatment should be given first for a duration of three months. In case of oligo-progression after curative local treatment, the decision to re-treat lies again with the MDT but should be considered if toxicity of treatment is acceptable.

PLEURAL MESOTHELIOMA AND MALIGNANT PLEURAL EFFUSION: ARE WE STILL THERE?

Biomarkers for diagnosis and predicting treatment response in mesothelioma

12% of individuals diagnosed with non-specific pleuritis (NSP) develop pleural mesothelioma (PM) within two years, but predicting development of PM remains a significant challenge (79). Meso-Origins is a study that will address this by following up patients with asbestos-associated pleural inflammation (80). Pleural fluid mesothelin may help; high levels (>20nmol/L) were associated with eventual PM diagnosis in 185 patients with NSP (OR 31.2 (95%CI 8.5-114.7)) (81). Biomarkers with diagnostic utility in PM remain to be identified (82). A novel proteomic technique identified PM-specific tissue leakage proteins and shows promise for improving diagnosis, but requires external validation (83).

Serum mesothelin (SM) may be beneficial for disease monitoring (84, 85). In the largest such study to date of 209 patients, serial SM changes predicted survival (adjusted HR 2.28 (95% CI 1.31-3.93)), progression (adjusted OR 1.51 (1.01-1.95)) and disease response (adjusted OR 1.40 (1.03-1.92)) regardless of age, treatment, histology and initial SM value (86). Similarly, a study of 15 patients identified 6 VOC in exhaled breath which differentiated between stable and progressive disease (87). Replication and validation in larger populations is needed.

Surgery for early resectable mesothelioma
In some centres, PM is deemed technically resectable at stage T1-3, N0-1, M0, although criteria for this vary. However, surgical treatment remains contentious at this stage, as achieving an R0 resection is widely acknowledged to be impossible (88, 89). The MARS trial reported extra-pleural pneumonectomy (EPP) was associated with higher morbidity, showing it may not offer any benefit (89). MARS2 recently reported that adding extended pleurectomy decortication to chemotherapy increased the risk of death and serious adverse events (90). Other surgical options such as VATS pleurectomy confer no improvement in survival, prolong hospital stay and show reduced quality of life at 12 months compared to talc pleurodesis (91). However, ‘early’ PM may be defined as disease localised to the pleura (T1NOM0). Stage I is a reasonable surrogate of this but also includes T2 and T3 tumours. If staged accurately, the prevalence of Stage I PM is reported as high as 54% (92). There is little robust data on appropriate treatment in this group, including the use of surgery, as almost all studies have predominantly included participants with later stage disease.

Diagnosis of ‘early’ PM requires careful differentiation from ‘mesothelioma in situ’ (MIS), a pre-invasive lesion that may evolve into invasive PM in some patients (93). Diagnosis of MIS requires a combination of pathological, radiological and clinical input. It is usually diagnosed in patients with non-resolving pleural effusion, with a single layer of non-invasive bland mesothelial cells growing along the pleural surface, without thoracoscopic or radiological evidence of tumour and with either BAP1 loss and/or CDKN2A/p16 homozygous deletion. A small case series suggests median progression to PM after 60 months (range 12 – 92) (94) but evidence is limited.

**Malignant pleural effusion (MPE)**

Pleural effusion affects 15% of all cancer patients and 90% of PM (95). Indwelling pleural catheters (IPC) are beneficial for ambulatory management. Time to IPC insertion varies, with median duration 70 days in one study (96). 70% of patients interviewed would consider IPC insertion over pleural aspiration as a first procedure, emphasising the importance of patient choice in managing malignant pleural effusions (96, 97). Individuals with IPCs may develop drainage-related pain (98), which may be related to non-expandable lung. A novel system delivering lower fluid drainage pressure was trialled in 15 patients and demonstrated possible reduced pain, but conclusions were limited by study size (99).

If pleurodesis is prioritised, talc pleurodesis via intercostal chest drain (ICD) is more effective than talc instillation via IPC (97, 100), although protocols vary. One study of 108 patients suggested waiting for drainage less than 150ml/24hours was unnecessary, with early ICD removal (12 hours following talc) having similar pleurodesis rates (101). While talc is recommended for pleurodesis (102), a pilot study of patients undergoing video-assisted thorascopic surgery (VATS) found high pressure intra-pleural chemotherapy had similar pleurodesis rates to talc poudrage and may be explored for oncological benefit (103).

Moreover, MDT working is of the utmost importance (104). Following implementation of the Scottish Mesothelioma Network in 2019, there was an improvement in survival for non-epithelioid PM, not fully explainable by immunotherapy introduction (105). With rapidly changing definitions, treatments and new clinical trials (106, 107), MDT input for optimising mesothelioma care is more important than ever.

**CONCLUDING REMARKS**

New challenges in LCS were highlighted in this year ERS Congress. Revolutionary approach of early stages NSCLC was also discussed. The discovery of new biomarkers will provide better decisions and move closer to an even more personalized medicine. Pleural disease remains a constant challenge, however new clinical trials give us hope for better survival and quality of life.
in these patients. ERS Congress will continue to contribute to the dissemination of high-quality research and to the best clinical practices.

Footnotes

The authors do not have any conflict of interest to declare.

References

5. Blum TG. The pioneering Strengthening the screening of Lung Cancer in Europe (SOLACE) project has now been launched [Available from: https://www.ersnet.org/news-and-features/news/solace-project-launch/].


Figure 1. Representation of the T-descrptor and the possible diagnoses of GGOs according to tumour and invasive part sizes. **IAD:** Invasive adenocarcinoma with a lepidic component; **LPA:** Lepidic predominant adenocarcinoma; **MIA:** Minimal invasive adenocarcinoma; **AIS:** Adenocarcinoma in situ; **AAH:** Adenomatous hyperplasia.
<table>
<thead>
<tr>
<th>Lung Nodules</th>
<th>COVID-19</th>
<th>Lung Cancer</th>
<th>P value</th>
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<td>89%</td>
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<td>Peripheral 74%</td>
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<td>Median 1</td>
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<td>Number of segments</td>
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<tr>
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<td>66%</td>
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<td>Pure &amp; Mixed GGO</td>
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**Table 1.** Comparison between the characteristics of GGOs in COVID-19 and early-stage lung cancer (59).
<table>
<thead>
<tr>
<th>Name of study</th>
<th>Year of publication</th>
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<td>Adjuvant</td>
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<td>Adjuvant</td>
<td>Osimertinib</td>
<td>DFS improvement</td>
</tr>
<tr>
<td>ALINA(^{(77)})</td>
<td>NA (pending)</td>
<td>IB-IIIa</td>
<td>Adjuvant</td>
<td>Alectinib</td>
<td>NA (results pending)</td>
</tr>
</tbody>
</table>

Table 2. \(^a\): Added to standard treatment; DFS: disease free survival; EFS: event free survival; PCR: pathological complete response.