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## Lung cancer in 2022 and beyond!

**Kamalram Thippu Jayaprakash<sup>1,2</sup>, Gerard G Hanna<sup>3,4</sup>, Matthew Hatton<sup>5</sup>**

<sup>1</sup>Oncology Centre, Addenbrooke's Hospital, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom;

<sup>2</sup>Department of Oncology, The Queen Elizabeth Hospital King's Lynn NHS Foundation Trust, King's Lynn, United Kingdom; <sup>3</sup>Cancer Centre, Belfast City Hospital, Belfast, United Kingdom; <sup>4</sup>Queen's University Belfast, United Kingdom; <sup>5</sup>Weston Park Hospital, Sheffield, United Kingdom.

Correspondence: [k.thippujayaprakash@nhs.net](mailto:k.thippujayaprakash@nhs.net)

Lung cancer is one of the common cancers and is the leading cause of cancer mortality in the UK (1). Major advances in molecular biology, drug development, improvement in surgical and radiotherapy (RT) techniques, immunotherapy revolution and patient education are improving outcomes, but survival remains poor in comparison to many other cancers. The incidence of lung cancer worldwide continues to increase with profound consequences for patients, carers, and wider society. This places a huge responsibility on us to optimise our treatment and in this *Clinical Oncology* Lung Cancer Special Issue, we cover many aspects of lung cancer and mesothelioma, which celebrates our success but also challenges lie ahead for our shared mission to improve outcome for patients with lung cancer.

We are delighted that the Journal has published a second editorial to accompany this Lung Cancer Special Issue that shares patient experience. We are very grateful to *Janette Rawlinson* for sharing her story which sheds light on the challenges facing the never smoking lung cancer population (*CLINONC-2022-449*). This group is an increasing part of our patient population, and her article highlights the need for increasing understanding of their different survivorship issues, to raise the profile of this issue and to remove the stigma associated with smoking and lung cancer.

Survival in lung cancer has historically been poor due to various factors. The UK Lung Cancer Audit programme has been pivotal in benchmarking performance as well as highlighting areas for improvement. In this Special Issue, *Conibear et al* summarise this important work and the impact of Covid-19 on lung cancer services in the UK (*CLINONC-2022-394*), and the concern about declining lung cancer patient outcomes, in spite of a prior decade of progress. To our knowledge this is the first we have seen declining cancer outcomes in the UK, and this alone should act a clarion call for urgent investment into cancer diagnostic and treatment services, and above all the implement of lung cancer screening. As *Balata et al* indicate (*CLINONC-2022-408*) that lung cancer screening is recognised in the National Health Service 'Long Term Plan' (<https://longtermplan.nhs.uk>) which sets a target of diagnosing 75% of all cancer at stage I-II by 2028.

Stereotactic ablative body radiotherapy (SABR), has now become the standard of care in medically inoperable patients in early stage non-small cell lung cancer (NSCLC), with single fraction regimens, akin to surgical approach increasingly adopted into routine clinical practice (2). *Gulstene et al* explores the many questions regarding the role of SABR still to be answered, including safety in ultra-central location, role in operable tumours, use in multiple tumours and in patients with interstitial lung disease (*CLINONC-2022-313*). Despite its effectiveness, local, regional and distal relapse pose a problem; one way to minimise this risk is to combine SABR with immunotherapy and several studies are underway examining this approach (3).

The PACIFIC study has transformed the treatment landscape of inoperable stage III NSCLC (4). In parallel to the investigation of immunotherapy in combination with RT, the CONCORDE trial (5) explores the possibility of combining radical thoracic radiation with DNA damage repair inhibitors. Similarly, immunotherapy had become a new standard of care in the management of small cell lung cancer (SCLC). *Meriea et al* in this issue provide an overview of evidence supporting the use of RT in

SCLC, how this may be integrated in the treatment pathway in the immunotherapy era (*CLINONC-2022-304*). Standardising lung RT would be help in reducing variations in the quality of lung RT. *Tumelty et al* describes the progress and challenges in implementing the recently published Royal College of Radiologists lung cancer consensus statements (*CLINONC-2022-310*).

Defining ‘oligometastases’ in metastatic cancer (6) has revolutionised our approach and management of metastatic cancers. In parallel to the continued efforts to improve our understanding, classification of oligometastatic disease (7), treatment options, such as SABR, have evolved over the years with some studies demonstrating overall survival benefit in both synchronous and metachronous oligometastatic NSCLC (8-10). However, SABR for oligometastatic disease continues to divide opinion (11, 12), some advocating whilst others having a more cautious view, waiting for more evidence to emerge. The outcomes from the UK’s SARON and HALT trials are eagerly awaited (13)(14) and *Ratnakumaran et al* describe this in detail in this issue (*CLINONC-2022-421*).

The evidence that palliative RT in lung cancer is an effective therapeutic modality to alleviate symptoms (15) is long standing and it is recognised that high dose palliative radiotherapy can provide durable local control and improve survival (16). However, this evidence was acquired prior to the exponential growth in first line systemic anti-cancer treatment (SACT) and SACT treatment options. The sequencing and role of radiotherapy with palliative SACT is less well understood and its role alongside our newer biological agents and immune checkpoint inhibitors is becoming increasingly questioned. *King et al* provide an overview of the current status of palliative RT in lung cancer and introduces the soon-to-be opened TOURIST Trial Platform (17) that aims to close the current evidence gap regarding palliative RT in metastatic lung cancer in the era of novel therapeutics (*CLINONC-2022-355*).

Heterogeneity in NSCLC genotype is well known, which has led to the development of several molecularly targeted biological agents that improved survival in oncogene-driven cancers, so it is vital we aspire testing these tumours for actionable genetic aberrations. Whole genome sequencing may provide clues for resistance mechanisms as shown by *Suryavanshi et al* in this issue (*CLINONC-2022-599R2*) and newer targets is becoming an integral component in clinical management of lung cancer. *Cox et al* in this issue summarises status of genomic testing for lung cancer in Wales (*CLINONC-2022-348*).

Lung cancer often a disease in people with multiple comorbidities that poses a challenge when assessing patients’ suitability for their oncological treatments. Prehabilitation and rehabilitation programmes, tailored to individual needs could help in some patients to be considered for radical treatments which otherwise would not have been possible. In this issue *Burnett et al* provide their view on this important often overlooked area in lung cancer management (*CLINONC-2022-347*).

Our understanding of molecular biology has been limited to histological subtypes in pleural mesothelioma and treatment options to cytotoxic chemotherapy for long time. *Jose Luis Leal et al* outlines the promising role of immunotherapy in mesothelioma and emerging molecular targets that may play an important role in mesothelioma precision oncology (*CLINONC-2022-343*).

We hope that this Special Issue on Lung Cancer provides a timely update across the field of lung cancer and mesothelioma management and lays out future challenges faced. As many of the articles highlight, there is a myriad of areas of unmet need in lung cancer detection, treatment and survivorship. Whilst acknowledging the concerns that the prior improvement in outcomes might be stalling, as flagged by *Conibear et al* (*CLINONC-2022-394*), the progress we have made over the last

decade, gives great hope that that we will continue to make such advances for the benefit of patients with lung cancer.

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