

Newest Drugs of Lung Cancer That's Approved In 2020 (Article Review)

Zainab Sajid Mohammed¹, Wijdan Rajh Hamza Al-Kraity² and Hawraa Natiq Kabroot AL-Fatlawy³

¹ Faculty of Pharmacy, University of Kufa, Najaf, Iraq.

^{2,3} Faculty of Medicine, University of Kufa, Najaf, Iraq.

E-mail zainabs.hameedi@uokufa.edu.iq, wijdanr.alkraity@uokufa.edu.iq, hawraan.alfatlawy@uokufa.edu.iq

ABSTRACT

Background: The trend in incidence of malignancy in male patients has been decreasing in the past time since the middle of nineties in affluent countries but the same trend has been gradually rising in female patients. Thus, in the United States as well as in other industrialised nations, there have been sex convergences in the incidence rates of the lung carcinoma, particularly at lower ages. The differences in sex specific incidence may be explained by the histological subtype variations and changes in prevalence of smoking. Risk factors of pulmonary carcinoma include tobacco use, family history of cancer, the presence of antecedent pulmonary disease, and second-hand smoke, radon, asbestos, arsenic, air pollutants, or occupational carcinogenicity. There are some distinct subtypes of lung cancer that belong to different epidemiological and prognosis. Smoking has been identified to be one of the major etiological factors in regard to both small-cell lung carcinoma and squamous cell carcinoma. Among people of Western societies, more than eighty percent of the etiology of lung cancer can be associated with smoking. Interventions involving tobacco control such as higher excise on cigarettes, health warning labels, cessation counselling, and an all round advertising ban, have resulted in the reduction of the incidences of lung cancer. The comparatively common ones are adenocarcinoma and never-smokers that are prevalent in Asian women. A significant amount of information is available on epidermal growth factor receptor (EGFR) mutations prevalence in adenocarcinoma patients, with the prevalence rate being the highest (47%) in the Asia-Pacific region and the lowest (12%) in Oceania. Strong exposure response associations between second-hand smoke and cooking fumes have been implicated in the development of adenocarcinoma in Asian never-smokers with Chinese and Hong Kong studies providing evidence on this relationship. Surveillance of cancer prevention and treatment plans is crucial in assessing the disease burden on health systems in the present time and in measuring the effectiveness of interventions. In the framework of the Taiwan lung cancer epidemiology, the world surveillance data was limited, and reference material of the previous literature was outdated. The presented population-based study allowed revising the temporal patterns of prevalence, incidence, and overall survival of oncologic patients among the cohort used in the study.

Keywords: Lung Cancer Treatments , SCLC, And NSCLC

Article Information

Received: June 03, 2023; Revised: July 16, 2023; Online: August , 2023

INTRODUCTION

Lung cancer, also known as lung carcinoma is a malignant tumor in the pneumoniaic tissues whereby cells enhance their growth uncontrollably in the lungs [1,2]. In turn, it is the main cause of mortality in cancer-related conditions among men and the second most severe among women after breast cancer [3]. A typical etiologic agent is the chronic smoking of tobacco (85% of cases), and 10-15% of cases develop in never-smokers [4]. These sporadic cases are commonly predisposed by various environmental exposures such as work related contacts with random gases, asbestos, second hand smoke among other pollutants [5].

The two major histopathologic types are the small-cell lung carcinoma (SCLC) and non-small cell lung carcinoma (NSCLC) [6].

The commonest clinical features include haemoptysis, cachexia, dyspnea, and thoracic pain [7]. Confirmation can be done by diagnostic means that include chest radiography and computed tomography (CT) imaging with final confirmation that is carried out by bronchoscopy or CT-guided biopsy [8]. Regular treatment options are surgical debriefing, chemotherapy and radiation therapy. NSCLC refers to non-small-cell lung cancer. Stressors that can be avoided are tobacco consumption and air pollutants. Bronchioloalveolar carcinoma is a specific variant of adenocarcinoma with lepidic growth and little stromal and vasation. Suspicion of this carcinoma should be suspected by the presence of a solitary ground-glass opacity, the presence of a nodule or a mass-alveolar bronchogram, or refractory consolidative lesions in spite of antimicrobial treatment. In spite of its greater rate of false-negative results of fluorodeoxyglucose positive emission tomography (FDG-PET), bronchioloalveolar carcinoma also has a staging that is similar to the other subtypes of non-small lung cancer. According to the reports, pure non-small-cell lung cancer bronchioloalveolar accounts about 5% of all the cases [16].

Malignant carcinoid tumor accounts to about 1 percent to 2 percent of the total number of excised pulmonary tumors and is very rare. Though the TNM staging system was not previously used in carcinoid lesions, the seventh edition currently values their incorporation as the three components are all Prognostically relevant. The staging of lung cancer measures the degree of spread of the disease out of its original location [12], which affects the prognosis and therapeutic choices [13,12]. The stage of NSCLC is determined by the TNM system: tumor, nodal, and metastases, which evaluate such factors as the size of the primary tumour, nodal, and distant metastases [14]. Patients can be classified into the stage of occult disease, stage II up to the stage IV, where the stage classifies the informing treatment of patients in the stage, as well as, the stage prognostication [15]. Tolerance Disease burden Traditionally, SCLC is either limited stage

(confined to one hemi-thorax within a single tolerable radiation field) or extensive stage (throughout the entire thoracic region and beyond a single tolerable field). Both grouping and TNM staging are useful in the estimation of prognosis [15].

The two modalities of assessment that assess both NSCLC and SCLC are clinical staging and surgical staging. Through clinical staging which follows before final surgery, it is based on imaging studies (CT and PET scan) and biopsy data. Assessment of surgical staging is performed before, during, and after the surgery, combining operative results with clinical data, with the inclusion of thoracic lymph node sampling [15]. Airways permeation with tumours may lead to airflow obstruction worsening dyspnea and can result in secretory obstruction near the damaging area, thus predisposing the patient to exacerbate pneumonia [1]. Systemic symptoms that the local disease could not explain might first occur, but these take clinical interest depending on the type of tumour. The possible paraneoplastic manifestations of lung cancer include hypercalcaemia, syndrome of inappropriate antidiuretic hormone secretion (SIADH, which is characterised with the concentrated urine and a low-toned plasma), as well as ectopic hormone production.

Numerous manifestations of lung cancer including anorexia, cachexia, fever, and fatigue are nonspecific [21]. When patients finally become aware of signs and symptoms and visit the doctor, the malignancy may have advanced too far and past its main area of concern [19]. Such signs as weight loss, osseous discomfort, and neurologic dysfunction indicate metastatic involvement, and its manifestations include cephalalgia, syncope, seizures, motor weakness [17]. Typical metastatic sites include the brain, skeleton, contralateral lung, hepatic parenchyma, pericardium and the renal systems [19]. About 10 percent of patients who have lung cancer are not observed exhibiting any symptoms in the first place, and the tumour is accidentally discovered

during the routine examination with the help of chest radiography [20].

Incidence and Epidemiology

More recent GLOBOCAN data indicate that 2,094,000 new lung cancer incidence was diagnosed globally in 2018, making it the most commonly occurring type of cancer. Lung cancer is second among men, after prostate cancer and the second most common among women with a rate of 1,369,000 cases. In the US, 229,000 new cases were estimated to occur in 2020 and this accounts to 12.7% of all the cancer cases. This rate has dropped to its highest point of 69.5 in 1992 to the present rate of 45.6 per 100,000, which can be credited to the smoking cessation programs. Although similar decrease has been observed in many countries in the West, developing countries like China and the former Soviet Union have not realized such decrease with, 65 percent of Chinese males beginning to smoke before age 50s- a phenomenon that augurs more growth in lung cancer cases over the decades [23, 24]. It is also increasing globally because of an increase in industrialization and increased availability of tobacco [25].

Treatments

Nevertheless, surgery, radiotherapy, and chemotherapy through their own combinations or combinations are the most used therapeutic modalities used on lung cancer within the last 50 years. Operation, especially preceding the operations, is highly sophisticated, and it enhances the chances of recovery. Improvement of radiotherapy has facilitated high dose schedules, better field planning and accurate target enclosure. The use of chemotherapy has also improved: the majority of medications utilized in the fifties of the previous century were replaced with new medications, and the modern regimens have better-adjusted scheduling and duration and manage more of the side effects, with the focus on the quality of life. However, 1-, and 5-year survival rates have not varied substantially over the past three decades (Figure). A future therapeutic approach occurs where a specific tumor antagonist is used. The modern management of patients is more associated with multidisciplinary teams including thoracic surgeons, radiation and medical oncologists, radiologists, pathologists, palliative specialists, and specialized nurses. This strategy is outlined in the mentioned business case [26].

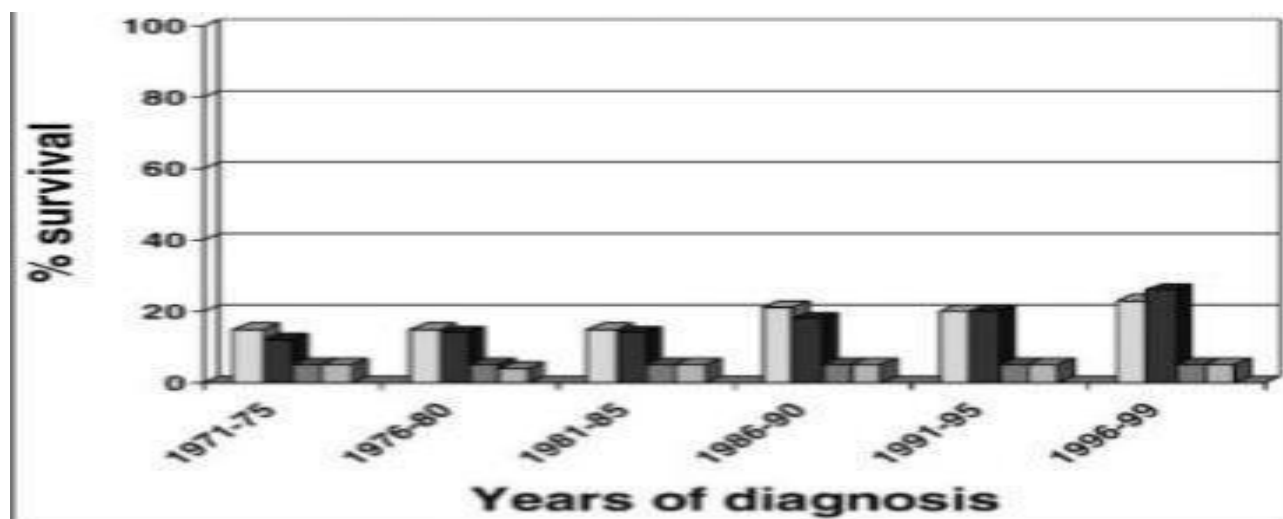


Figure 1: Shows the 1- and 5-year survival rates for all lung cancer cases in the UK during the previous 30 years. 1 year for light bars, 1 year for dark bars, 5 years for medium dark bars, 5 years for medium light bars, 5 years for medium light bars, 5 years for medium light bars, 5 years for medium light bars, 5 years for medium light bars, 5 years for medium light bars, 5 years for medium light bars.

Lung cancer has surpassed heart disease as China's third biggest cause of mortality

The third cause of death in China has been surpassed by heart diseases by lung cancer. In

June 2019, the Lancet published the burden-of-disease data of China on the web with close to 30-year scope [27]. Cerebrovascular disease and ischemic heart disease now rank second and third

behind lung cancer in the list of most common deaths in China as per data provided by professor Xiaofeng Liang of Chinese Center of Disease Control and Prevention. Between 1990 and 2017, age-standardised mortality and years of life lost (YLLs) due to lung cancer rose, which changed its position to 13th in ranking to the 3rd. This tendency and modern conditions imply that the process of prevention and control of lung-cancer must be approached in a similar way that the most common illnesses like diabetes or obesity are treated.

In October 2019, Xiao-ou Shu and the team at Vanderbilt University published a meta-analysis of 10 prospective cohort studies that had 1.44 million participants, and a mean follow-up of 8.6 years in total in JAMA Oncology [28]. The consumption of dietary fibre and yoghurt was reported to be linked with the risk of lung cancer reduction. Residents who were in the top quintile of fibre and yoghurt intake had relative risk wards of 17.9 per cent and 19.9 per cent, respectively, as compared to those who were in the bottom quintile. Further, the risk of lung cancer reduced by 33 per cent when participants who did not take yoghurt and had the least fibre intake were compared with their counterparts who took yoghurt and had maximum fibre intake. The authors came to the conclusion that the protective effect can be specifically strong during the youthful adults. Liquid biopsy (LBx) is a potential detection modality of lung cancer in its early stages. The findings of a Circulating Cell-free Genome Atlas (CCGA) Study, which were unveiled at the ASCO and ESMO conferences [30,31], suggest that an integrated test related to whole-genome bisulfite sequencing (WGBS), whole-genome sequencing (WGS), and a 507-gene targeted assay can identify signals of a dozen malignancies at an early stage. The overall sensitivity of the combined method was 55,000 per cent. in all cancer stages and histologies and tissue-of-origin localisation was also 100,000,000 per cent. Sensitivity to early disease (stages I-III) was as 32, 76 and 85 per cent. at stages one, two and three respectively. The results are in line with the findings of the CCGA lung-cancer sub-trial which was reported last year at the ASCO annual

meeting heralding the much needed breakthrough in terms of diagnosis.

NADIM was the initial multicenter trial that used to combine conventional chemotherapy and immuno-oncologic agent in the neoadjuvant in stage IIIA non-small-cell lung cancer. The combination of neoadjuvant regimen consisted of three cycles of nivolumab and paclitaxel carboplatin and a period of 1 year adjuvant nivolumab taken after the surgery. R0 resection was carried out on all forty one recruited patients; chemotherapy and immunotherapy were well tolerated. Post adjuvant treatment downstaging was achieved in 90% of cases with major pathological response (MPR) and pathologic complete response (pCR) 83 and 71 per cent respectively. Radiologic response rate (RECIST) was 71 per cent partial and 7 per cent complete. None of the patients stopped the treatment before surgery because of the development of the disease or safety reasons. The information above provides a strong indication that neoadjuvant immunotherapy (especially with chemotherapy) has an impressive pathological reaction and can potentially dramatically alter the treatment regimen of early-stage lung cancer.

There is still debate on the possibility of combining immunotherapy with simultaneous concurrent chemoradiotherapy. A study, published at the 2019 ASCO annual meeting, found that addition of atezolizumab to concurrent chemoradiotherapy was linked to favourable safety profile in patients with locally advanced non-small-cell lung cancer, indicating that concurrent administration does not add any toxicity to chemoradiotherapy before adjuvant immunotherapy. The PACIFIC-2 trial currently underway is aimed at assessing the ability of concomitant immunotherapy and chemoradiotherapy to improve the level of effectiveness.

Does prophylactic cranial irradiation or not work in patients with locally advanced non-small lung cancer? The most recent update posted in the JAMA Oncology [41] review was investigating the RTOG 0214 trial, a multicentre phase-III randomised study. Though the incidence of brain metastases and significant improvement in disease-free survival (DFS) with prophylactic

cranial irradiation was achieved in patients who did not develop disease following local radiotherapy, there was no incremental effect in disease-free survival (DFS) of patients in this subgroup as compared with those under observation.

REFERENCES

- [1]. Lung Carcinoma: Tumors of the Lungs. Merck Manual Professional Edition. online edition. Retrieved 15th August 2007.
- [2]. Non-small cell lung cancer Treatment-Patient.NCL.May 12, 2015.
- [3]. World Cancer Report 2014.World Health Organization. 2014. Chapter 1.1.ISBN 9283204298.
- [4]. Thun MJ, Hannan LM, Adams-Campbell LL, et al.Lung cancer occurrence in never smokers:an analysis of 13 cohorts and 22 cancer registry studies. PLoSMed. 2008;5(9):1185.
- [5]. O'Reilly KM, McLaughlinAM, BeckettWS, et al. Asbestos-related lung disease. American Family Physician. 2007;75(5):683-688.
- [6]. Doll R. Evolution of knowledge of the smoking epidemic. Tob Sci Policy Public Heal 2010. doi:10.1093/acprof:oso/97801995
- [7]. Hom L, Lovly CM, Johnson DH (2015).Chapter 107.Neoplasm of the Lung. In Kasper DL; Hauser, SL, Jameson, JL, Fauci AS, Longo DL, LoscalzoJ. Harrison's Principles of Internal Medicine(19th ed.), McGraw-Hill.ISBN 978-0-07-180216-1.
- [8]. Lu C, OnnA, VaporciyanAA, et al.(2010).78:Cancer of the Lung.Holland-Frei CancerMedicine(8th ed.).People's Medical Publishing House.ISBN 978-1-60795-014-1.
- [9]. Chapman S, Robinson G, Streadling J, et al(2009).Chapter 31.Oxford Handbook of Respiratory Medicine(2nd ed.)Oxford University Press.ISBN 978-0-19-954516-2.
- [10]. Lung Cancer Prevention-Patient Version(PDQ R)NCI.November 4, 2015.
- [11]. Travis WD, Giroux DJ, Chansky K, et al. The IASLC Lung Cancer Staging Project: proposals for the inclusion of broncho-pulmonary carcinoid tumors in the forthcoming (seventh) edition of the TNM classification for Lung Cancer. J Thorac Oncol 2008;3(11):1213–1223.
- [12]. Connolly JL, Goldsmith JD, Wang HH, et al. (2010). "37: Principles of Cancer Pathology". Holland-Frei Cancer Medicine (8th ed.). People's Medical Publishing House. ISBN 978-1-60795-014-1.
- [13]. Horn L, Lovly CM (2018). "Chapter 74: Neoplasms of the lung". In Jameson JL, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J (eds.). Harrison's Principles of Internal Medicine (20th ed.). McGraw-Hill. ISBN 978-1259644030.
- [14].Rami-Porta R, Crowley JJ, Goldstraw P (2009). "The revised TNM staging system for lung cancer". Annals of Thoracic and Cardiovascular Surgery. 15 (1): 4–9.
- [15]. Lu C, Onn A, Vaporciyan AA, et al. (2010). "Chapter 78: Cancer of the Lung". Holland-Frei Cancer Medicine (8th ed.). People's Medical Publishing House. ISBN 978-1-60795-014-1.
- [16]. Arenberg D; American College of Chest Physicians. Bronchioloalveolar lung cancer: ACCP evidence-based clinical practice guidelines. 2nd ed. Chest 2007;132(3 suppl):306S–313S.
- [17]. Horn L, Lovly CM (2018). "Chapter 74: Neoplasms of the lung". In Jameson JL, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J (eds.). Harrison's Principles of Internal Medicine(20th ed.). McGraw-Hill. ISBN 978-1259644030.
- [18]. Honnorat J, Antoine JC (May 2007). "Paraneoplastic neurological syndromes". Orphanet Journal of Rare Diseases. 2 (1): 22. doi:10.1186/1750-1172-2-22.
- [19]. Frederick L. G. (2002). AJCC Cancer Staging Manual. Berlin: Springer-Verlag. ISBN 978-0-387-95271-0.

- [20]. Collins LG, Haines C, Perkel R, Enck RE (2007). "Lung cancer: diagnosis and management". American Family Physician. 75 (1): 56–63.
- [21]. Lu C, Onn A, Vaporciyan AA, et al. (2010). "Chapter 78: Cancer of the Lung". Holland-Frei Cancer Medicine (8th ed.). People's Medical Publishing House. ISBN 978-1-60795-014-1.
- [22]. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018; 68: 394-424.
- [23]. Global Cancer Observatory: Cancer Today. International Agency for Research on Cancer. Lyon, France. Available at: <https://gco.iarc.fr/today> (Accessed: 15.09.2020).
- [24]. Howlander N, Noone AM, Krapcho M, et al. SEER cancer statistics review 1975–2016. National Cancer Institute, 2019.
- [25]. Barta JA, Powell CA, Wisnivesky JP. Global epidemiology of lung cancer. Ann Glob Health 2019; 85: 8.
- [26]. Alberts MW, Bepler G, Hazelton T, Ruckdeschel JC, Williams JH. Practice organization. Chest 2003;123:332s–337s.
- [27]. Zhou M, Wang H, Zeng X, et al. Mortality, morbidity, and risk factors in China and its provinces, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2019;394:1145-58.
- [28]. Yang JJ, Yu D, Xiang YB, et al. Association of Dietary Fiber and Yogurt Consumption With Lung Cancer Risk: A Pooled Analysis. JAMA Oncol 2019. [Epub ahead of print].
- [29]. Dai J, Lv J, Zhu M, et al. Identification of risk loci and a polygenic risk score for lung cancer: a large-scale prospective cohort study in Chinese populations. Lancet Respir Med 2019;7:881-91.
- [30]. Cohn AL, Seiden M, Kurtzman KN, et al. The Circulating Cell-free Genome Atlas (CCGA) Study: Follow-up (F/U) on non-cancer participants with cancer-like cell-free DNA signals. J Clin Oncol 2019;37.
- [31]. Oxnard GR, Klein EA, Seiden MV, et al. Simultaneous multi-cancer detection and tissue of origin (TOO) localization using targeted bisulfite sequencing of plasma cell-free DNA (cfDNA). Ann Oncol 2019;30:912.
- [32]. Liang W, Zhao Y, Huang W, et al. Non-invasive diagnosis of early-stage lung cancer using high-throughput targeted DNA methylation sequencing of circulating tumor DNA (ctDNA). Theranostics 2019;9:2056-70.
- [33]. Kwiatkowski DJ, Rusch VW, Chaft JE, et al. Neoadjuvant atezolizumab in resectable non-small cell lung cancer (NSCLC): Interim analysis and biomarker data from a multicenter study (LCMC3). J Clin Oncol 2019;37.
- [34]. Cascone T, William WN, Weissferdt A, et al. Neoadjuvant nivolumab (N) or nivolumab plus ipilimumab (NI) for resectable non-small cell lung cancer (NSCLC): Clinical and correlative results from the NEOSTAR study. J Clin Oncol 2019;37.
- [35]. Provencio M, Nadal E, Insa A, et al. Neoadjuvant chemo-immunotherapy for the treatment of stage IIIA resectable non-small-cell lung cancer (NSCLC): A phase II multicenter exploratory study—Final data of patients who underwent surgical assessment. J Clin Oncol 2019;37.
- [36]. Ball D, Mai GT, Vinod S, et al. Stereotactic ablative radiotherapy versus standard radiotherapy in stage 1 non-small-cell lung cancer (TROG 09.02 CHISEL): a phase 3, open-label, randomised controlled trial. Lancet Oncol 2019;20:494-503.

- [37].Zeng Y, Mayne N, Yang CJ, et al. A Nomogram for Predicting Cancer-Specific Survival of TNM 8th Edition Stage I Non-small-cell Lung Cancer. *Ann Surg Oncol* 2019;26:2053-62.
- [38].Zhao Y, Wang W, Liang H, et al. The Optimal Treatment for Stage IIIA-N2 Non-Small Cell Lung Cancer: A Network Meta-Analysis. *Ann Thorac Surg* 2019;107:1866-75.
- [39].Gray JE, Villegas AE, Daniel DB, et al. Three-year overall survival update from the PACIFIC trial. *J Clin Oncol* 2019;37.
- [40]Hui R, Özgüroğlu M, Villegas A, et al. Patient-reported outcomes with durvalumab after chemoradiotherapy in stage III, unresectable non-small-cell lung cancer (PACIFIC): a randomised, controlled, phase 3 study. *Lancet Oncol* 2019;20:1670-80.
- [41].Sun A, Hu C, Wong SJ, et al. Prophylactic Cranial Irradiation vs Observation in Patients With Locally Advanced Non-Small Cell Lung Cancer: A Long-term Update of the NRG Oncology/RTOG 0214 Phase 3 Randomized Clinical Trial. *JAMA Oncol* 2019;5:847-55.