Lung Cancer in Thailand

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Introduction to Thailand
Thailand covers a total area of approximately 198,000 square miles with a population of 67.9 million people, making it the 12th largest country in Asia.1,2 The capital city is Bangkok. Thailand is divided into six regions by geography: north, northeast, central, south, east, and west, with respective differences in weather, culture, ethnicity, the local language, and lifestyle of each local population. The north and the west are the country’s highlands with many mountains, woodlands, rivers, waterfalls, and dams. The northeast features some of the highlands and gorgeous plateaus. The central region mainly consists of plains and a massive area for rice farming and agriculture. The south contains many beaches and islands located in the Gulf of Thailand and the Andaman sea. Eastern Thailand is a half mountain, half ocean region.2

The World Bank upgraded Thailand’s income categorization from a lower middle-income to an upper middle-income economy in 2011.3 The average household income was $900 U.S. dollars per month in 2017.4 Cancer is the leading cause of death in Thailand and mortality is steadily increasing. In 1997, the country’s cancer death rate was 43.8 deaths per 100,000 population, and the number rose to 120.5 deaths per 100,000 population in 2017.5 According to the latest report of the Global Cancer Incidence, Mortality and Prevalence published in 2018, lung cancer is noted to be the most common type of cancer in Thailand and accounted for 14.1% of all types of cancers (of which, 70% were diagnosed in the advanced disease stage).6 In addition, lung cancer has the second-highest mortality rate (18.7%) in Thailand next to liver cancer, which has the highest mortality rate (20.3%) as of 2018.6

Health Care System in Thailand
Health care in Thailand is overseen by the Ministry of Public Health, along with several other nonministerial government agencies. As of 2019, Thailand’s population of 68 million was served by 927 government hospitals and 363 private hospitals, complemented with 9768 government health centers and 25,615 private clinics. However, access to medical care in rural areas still lags far behind that in the cities. Thailand’s network of public hospitals provides universal health care to all Thai nationals through three government schemes: (1) the Civil Servant Medical Benefit Scheme (CSMBS) for civil servants and their families; (2) the Social Security Scheme (SSS) for private employees; and (3) the Universal Coverage Scheme (UC), introduced in 2002, which, theoretically, is available to all Thai nationals (Table 1).7,8 Some private hospitals participate in the programs but most of them are financed through patient self-payment and private insurance. According to the World Bank, 99.5% of the population has health care coverage under Thailand’s present health schemes.3

Smoking
In support of the WHO antitobacco statement in 1980, Thailand, under the leadership of Prof. Prawase Wasi, initiated an antitobacco campaign in 1985, which

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later developed into the Action on Smoking and Health Foundation Thailand in 1997.9

Tobacco Products Control act and Nonsmokers’ Health Protection Act were successfully launched in 1992 after a public referendum campaign. During that period, there was only an ordinance on the prohibition of smoking in theaters and public transport. The updated version of the Tobacco Products Control act in 2017 emphasized the protection of minors and nonsmokers’ health from tobacco products and enacts the prohibition of the sale of tobacco products to minors under 20 years of age. Advertisements, media broadcasts, and tobacco product giveaways were banned. Moreover, the sale of tobacco products in places without a tobacco sales license was prohibited. Tobacco manufacturers are also mandated to display campaigns for the reduction of the use of tobacco products. The 2017 Act further endorsed the protection of nonsmokers’ health by designating nonsmoking areas in public areas, workplaces, and municipal vehicles and imposing penalties for any violations.10

The success of the Action on Smoking and Health Foundation Thailand antitobacco campaign translated into a sustained decline in the country’s smoking rate. The smoking rate in the Thai population (from the age of 15 years and above) decreased from 32.0% in 1991 to 19.1% in 2017, which accounted for 10.7 million people in the total population of 55.9 million (Fig. 1).11 Electronic cigarettes are currently illegal in Thailand.

Lung Cancer Screening

The 2013 Thailand National Cancer Control Program documented exposures to tobacco products, asbestos, and air pollution as predisposing factors for lung cancer. Public policy on tobacco restriction, prevention of exposure to carcinogens (such as pesticides and asbestos), and air pollution control was implemented. However, there are currently no national lung cancer screening guidelines in Thailand.12

Diagnosis of Lung Cancer

Imaging of newly diagnosed lung cancer is routinely performed with computed tomography (CT) scan, but the quality of imaging is poor in rural areas. The use of positron emission tomography (PET) scan is gradually increasing, especially in university-based hospitals, and improves the accuracy of diagnosis and staging. However, there are only nine PET scan machines currently available in Thailand, with seven located in Bangkok, one in the northern region (Chiang Mai province), and the other in the northeastern area (Kho Kaen province). Tissue diagnosis follows the guidelines of the American College of Chest Physicians for the diagnosis of lung cancer.13 With limited resources, tissue diagnostic procedures vary in different hospitals in each region. Bronchoscopy and transbronchial biopsy are preferred for both central and peripheral lung lesions compared with transthoracic needle biopsy or aspiration (TTNB or TTNA); however, for lesions that are close to the pleura, TTNB or TTNA is preferred. TTNB or TTNA is usually performed by either an interventional radiologist or pulmonologist, depending on physician’s experience and the type of equipment in each institute. Typically, university-based hospitals or tertiary care hospitals have both interventional radiologists and pulmonologists who can implement their respective approaches.

Endobronchial ultrasound system (EBUS)–transbronchial needle aspiration combined with fluoroscopy is the main technique for tissue diagnosis in some of the university-based hospitals. However, most institutes and

| Table 1. Characteristics of Public Health Care Scheme in Thailand |
|------------------------|------------------------|------------------------|
| **Legislation**        | **CSMBS**              | **SSS**                | **UC**                |
| **Purchaser**          | 4.9 Million            | 14.4 Million           | 48.8 Million          |
| **Source of finance**  | Tax-based              | Tripartite contribution by employer, employee, and government | Tax-based             |
| **Budgeting**          | Open-ended budget      | Closed-ended budget    | Closed-ended budget   |
| **Expenditure in 2018, Thai Baht** | 63 billion | 48.5 billion | 126.5 billion |
| **Payment method**     | Fee-for-service        | Capitation             | Capitation (including prevention and health promotion) |
| **Out-patient**        | Diagnostic-related groups with multiple cost bands | Diagnostic-related groups within the global budget | Diagnostic-related groups with the global budget, fee schedule for the specific high-cost procedure |
| **Inpatient**          | Capitation             | Capitation             | Capitation (including prevention and health promotion) |

CSMBS, Civil Servant Medical Benefit Scheme; SSS, Social Security Scheme; UC, Universal Coverage Scheme.
hospitals in Thailand do not have this system; thus, most diagnostic tissue acquisitions are performed under fluoroscopic guidance. Staging of lung cancer is essential for lung cancer treatment, especially mediastinal lymph node staging. EBUS is currently used rather than blind transtracheal/transbronchial aspiration or biopsy. Most institutes follow the guidelines of the American College of Chest Physicians for mediastinal staging. In some cases, PET scan is also used in some institutes together with EBUS; however, the lack of process for uniform reimbursement in performing PET scans serves as a barrier for the staging of lung cancer (Table 2). The cost of equipment and procedure are issues hindering the utilization of EBUS-transbronchial needle aspiration (Table 2). In addition, the limited experience of pulmonologists practicing outside of the university hospital setting is also one of the main problems.

Several university-based hospitals in Bangkok have started to use navigational bronchoscopy for some lesions in difficult locations. However, the critical problem limiting its use is the cost of equipment and the complexity of the procedure. Many patients are referred to university-based hospitals for tissue diagnosis, and this presents as one of the health care burdens in the country because many patients are unable to travel outside of their hometowns owing to socioeconomic factors.

Recently, the Thoracic Society of Thailand under Royal Patronage endorsed an interventional pulmonology training program to improve the quality of diagnosis and to increase the experience of general pulmonologists who practice in nonuniversity-based hospitals in Thailand. This society will likewise develop clinical practice guidelines for lung cancer diagnosis.

**Thoracic Surgery**

Surgical resection of NSCLC is generally considered in patients with stage I and stage II cancer. The surgical procedure of choice is lobectomy if the patients are medically fit and have a good cardiopulmonary reserve. However, sublobar resection (wedge resection or segmentectomy) carries a lower rate of complications. For older patients with impaired cardiopulmonary reserve or small peripheral tumor, sublobar resection may achieve similar survival rates when compared with lobectomy. Given below are the surgical approaches followed in Thailand for the various TNM stages.

- For stage I and II, the surgical technique is almost always video-assisted thoracoscopic approach.

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**Figure 1.** Smoking prevalence in Thailand by year, according to sex. Adapted with permission from Tipayarungsrit and Punkrajang.11
For the T3 category, the role of surgical procedure depends on the following: (1) the extent of chest wall invasion, (2) the proximity to the carina, and (3) the expertise of the surgeon. To achieve complete resection, the surgical technique of choice is open thoracotomy.

For the T4 category, because of the invasion of important structures, a combined multimodality approach including chemotherapy, radiotherapy, or both is considered and should be discussed with the multidisciplinary team (MDT). If the patient is responsive to the treatment and complete resection is possible, then surgical resection is considered.

For the N0/N1 category, the indication for surgical resection and the type of surgical technique depend on the T category.

For the N2 category, if CT reveals a bulky node (>2 cm on the short axis) or multistation nodes (>1 cm on the short axis), tissue confirmation should be considered through EBUS or endoscopic ultrasound. If the EBUS or endoscopic ultrasound result is negative for malignancy, then mediastinal node dissection by mediastinoscopy or video-assisted thoracoscopic approach should be performed. Surgical resection is considered after N2 negative is confirmed. If CT reveals a single station node (>1 cm in the short axis) and the T category is T1 or T2, surgical resection is performed; but if the T category is T3, chemotherapy, radiotherapy, or both are considered and should be discussed with the MDT.

For the M1 category, the presence of a contralateral lung nodule should be confirmed and discussed with the MDT, emphasizing that it is a metastasis or a synchronous primary, especially if the mediastinal node is negative. If tissue diagnosis reveals it to be a synchronous primary, a two-stage lobectomy is performed or sublobar resection for patients who are elderly or have a limited cardiopulmonary reserve is carried out. Cases with malignant pleural effusion are considered to be unresectable.

For the M1b category, if an isolated distant metastasis is curable and there is no mediastinal node metastasis, surgical resection is considered and should be discussed with the MDT.

### Table 2. Reimbursement of Procedures and Treatments for NSCLC in Thailand on the Basis of the Health Care Scheme

<table>
<thead>
<tr>
<th>Procedure and treatment</th>
<th>CSMBS</th>
<th>SSS</th>
<th>UC</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT and MRI scan</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>PET scan (for curable disease only)</td>
<td>✓</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Conventional bronchoscope</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>EBUS</td>
<td>✓</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Mediastinoscopy</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Transthoracic biopsy</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>VATS</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>SBRT</td>
<td>✓</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Double-platinum based chemotherapy</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Except: pemetrexed (for first-line Rx)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mediastinoscopy</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Maintenance therapy with pemetrexed</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Single-agent chemotherapy</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Except: pemetrexed (for first-line Rx)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EGFR TKI (only Gefitinib)</td>
<td>✓</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>ALK inhibitors (only Ceritinib)</td>
<td>✓</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>ROS inhibitors</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>BRAF inhibitors</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Immunotherapy</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>(for second/third-line treatment in nontargetable NSCLC only)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*CSMBS, Civil Servant Medical Benefit Scheme; CT, computed tomography; EBUS, endobronchial ultrasound system; MRI, magnetic resonance imaging; PET, positron emission tomography; Rx, treatment; SBRT, stereotactic body radiation therapy; SSS, Social Security Scheme; TKI, tyrosine kinase inhibitor; UC, Universal Coverage Scheme; VATS, Video-assisted thoracoscopic surgery.

NTRK inhibitor, Lorlatinib, and Dacomitinib are not available in Thailand now.
Robotic-assisted thoracic surgical approach is rarely performed because of the high cost and lack of reimbursement. Surgeons also have limited experience with this approach. In Thailand, only three institutes in Bangkok have robotic-assisted surgical systems and are mostly used for urologic surgeries.

Thailand only has under 200 active thoracic surgeons who are under the Society of Thoracic Surgeons of Thailand. Although thoracic surgeons are present in all regions, most are situated in Bangkok. The waiting time for patients undergoing lung cancer surgery is an issue of utmost concern.

Radiation Therapy

Radiation therapy (RT) plays an integral part of multimodality treatment in the definitive, adjuvant, and palliative management of lung cancer, both in NSCLC and SCLC. RT in Thailand first started on a two-dimensional technique. Afterward, advanced RT was developed including three-dimensional conformal RT (3D-CRT) and the more advanced techniques, such as stereotactic body RT (SBRT), intensity-modulated RT (IMRT), and image-guided RT.

RT Facilities in Thailand

Currently, a total of 35 RT facilities operate throughout the country: 16 in Bangkok, 13 in northern, two in central, two in southern, one in eastern, and one in the western part of Thailand (Fig. 2).

Three-Dimensional Conformal RT

3D-CRT is currently the minimum technological standard and most frequently used RT method for the treatment of lung cancer in Thailand because it can achieve maximum tumor control with minimal treatment complications. Every RT center in our country has a CT simulator and linear accelerator with a multileaf collimator combined with a computer planning system that enables us to implement the 3D-CRT. For definitive and adjuvant treatment of lung cancer, the conventional fractionated RT doses of 60 to 70 Gy and 45 to 54 Gy are usually applied.

Figure 2. Distribution of radiation facilities in Thailand.
Intensity-Modulated RT

IMRT and volumetric modulated arc therapy are novel advanced RTs, which can achieve higher conformal dose distributions with better target coverage while sparing healthy tissue, as compared with the conventional 3D-CRT. The recent prospective data from the RT Oncology Group 0617 revealed that treatment of NSCLC with IMRT had a lower rate of severe pneumonitis and lower cardiac dose than 3D-CRT despite its higher proportion of stage IIIB lesions and larger treatment volumes. At the same time, they both yielded similar survival and tumor control outcomes. The use of these advanced technologies in the treatment of lung cancer (particularly in stage III NSCLC) has been increasing rapidly since its adoption in the last decade.

Stereotactic Body RT

SBRT or Stereotactic Ablative RT is usually recommended for patients with early-stage NSCLC who are inoperable, or for those who refused to have surgery after having been evaluated by a thoracic surgeon. At present, its most frequently prescribed doses are 45 to 60 Gy in three fractions for peripheral tumors and 50 to 55 Gy in five fractions for central tumors, which can achieve excellent local control and survival rate comparable with lobectomy and higher than 3D-CRT. In Thailand, SBRT is currently performed mostly in academic and university hospitals. Nonacademic radiation centers outside Bangkok are still unavailable owing to the lack of necessary resources and infrastructure; however, some are planning to adopt SBRT for their practice soon.

Systemic Treatment

Cancer has been the most common cause of death in Thailand for the past 20 years. Many areas, especially the western and southern regions, face a scarcity of medical oncologists. Currently, there are only 261 medical oncologists in Thailand under the Thailand Society of Medical Oncology. Most of the medical oncologists are located in Bangkok and the central region (Fig. 3). Even though there are medical oncology training programs in university-based hospitals, the capacity for training is only between 20 to 25 medical oncologists.
per year. Thus, medical oncologists have heavy workloads and patients in rural areas have limited access to their services.

The standard first-line NSCLC treatments in Thailand are illustrated in Figure 4. With a three-payer health care system in Thailand as mentioned above, the delivery of expensive cancer therapy needs to achieve a balance between access and affordability, taking into consideration the economic status of our country (Table 2). Most (72%) of our population is covered under the UC scheme. National price negotiation is performed through the National Health Security Office, which is the legal entity organization to ensure equal pricing for all health care systems. Furthermore, Thailand has initiated the Oncology Prior Authorization Program (OCPA), which is responsible, under the Comptroller General’s Department that comes under the Ministry of Finance, to deal with the high-cost cancer drugs for patients with CSMBS. Currently, 15 high-cost cancer drugs need electronic submission by oncologists through OCPA for preauthorization approval, of which four drugs are for lung cancer (gefitinib for EGFR-positive NSCLC, osimertinib for T790M-positive NSCLC, ceritinib for ALK-positive NSCLC, and atezolizumab for second or third-line treatment of EGFR/ALK-negative NSCLC). In addition to making the decision for OCPA drugs for CSMBS, the Thailand Society of Medical Oncology and National Health Security Office have developed national guidelines for cancer treatment in adults to guide the reimbursement process under the universal health coverage scheme in 2018. For those under the SSS, the Social Security Office also complies with the national guidelines for cancer treatment.

Drug accessibility is another important problem in Thailand. Although all cancer drugs for NSCLC treatment approved by the U.S. Food and Drug Administration (FDA) are also approved and available in Thailand, the approval process for Thailand FDA usually takes about 2 to 3 years after the U.S. FDA approval. Most patients also have limited access to the drug owing to the differences in health care coverage, as illustrated in Table 2. For instance, gefitinib has just only been approved for reimbursement under CSMBS as first-line treatment in 2018; earlier it was reimbursed only as third-line treatment. In contrast, none of the patients with UC and SSS can get reimbursed for EGFR tyrosine kinase inhibitors; they have to pay out-of-pocket.

Molecular testing is also one of the main obstacles for lung cancer treatment. We also have a scarcity of molecular pathologists in Thailand and most of them are in the university-based hospital. Patients with UC and SSS cannot not get reimbursed for EGFR tyrosine kinase inhibitors; they have to pay out-of-pocket.

Figure 4. First-line treatment for advanced NSCLC in Thailand. CSMBS, Civil Servant Medical Benefit Scheme; PD-L1, programmed death-ligand 1; SSS, Social Security Scheme; UC, Universal Coverage Scheme.
mutation testing by either reverse transcriptase-polymerase chain reaction or sequencing and 1 week for ALK and programmed death-ligand 1 testing by immunohistochemistry staining. Molecular testing in Thailand is not routine; oncologists have to order the test after reviewing the pathologic report. Next-generation sequencing in Thailand is mainly performed in private hospitals and only in the research setting.

Conclusion
Technologies for investigation, diagnosis, and treatment of lung cancer have advanced to improve patient survival. These have developed rapidly in the past decade. Drug accessibility and lack of personnel, such as medical oncologists, radiation oncologists, thoracic surgeons, molecular pathologists, oncology nurses, and oncology pharmacists are the critical problems and obstacles in Thailand. The multidisciplinary approach to lung cancer management is beneficial for patients and medical personnel.

References