Real-World Treatment Patterns of Lung Cancer in a Resource-Restricted Country: the Experience of Georgia

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ABSTRACT: Lung cancer (LC) is the most common malignancy responsible for 1.8 million of deaths worldwide. Lung and bronchus cancer represents 13% (n = 1217) of all new cancer cases in Georgia. In 2018, in Georgian males lung cancer age-standardized incidence rate was 35.7/per 100000, less compared to regional countries as Turkey (70.6), Russia (48.2), Ukraine (41.7), and Armenia (58.5), but higher than in neighbor Azerbaijan (25.5). Incidence is higher compared to central and eastern Europe (27.3) and near similar to North America (34.5). Georgia is an Eastern European, middleincome country with 3.7 million residents and one of the highest numbers of active smokers in the European Region. The Georgian health care system is divided into a public and a private sector, with coverage of nearly 100% of the population. There is a national healthcare system as well as private insurance and all patients, irrespective of insurance (private or governmental) can choose the hospital for treatment by themselves all over the country. The Basic Package of the Universal Health Care Program includes the treatment of oncologic patients, specifically surgery, chemotherapy, hormone therapy and radiotherapy and investigations and medications related to these procedures. The program covers all types of laboratory and instrumental investigations related to planned treatment. Georgia lacks an LC screening program for smokers and partially because of this, the majority of patients with lung cancer present at an advanced stage. The National Centre for the Disease Control (NCDC) showed that almost 90% of LC patients in the country present with advanced stages (III-IV) with 60% of patients having stage IV disease at diagnosis . Lung cancer is generally diagnosed at an advanced stage. For non-small cell lung cancer (NSCLC), the proportion with metastatic disease (TNM stage IV) ranged from 46.8% to 61.2% in developed countries. In recent years, there have been several publications addressing specifics of LC worldwide, but none concerning Georgia. In light of the rapidly changing landscape in the diagnosis, staging, and treatment of LC, we thought to define the state of practice in Georgia by convening specialists who treat LC across 13 institutions in our country with the goal to describe differences in access and approaches to LC.

KEYWORDS: Carcinoma, non-small-cell lung, small cell lung carcinoma, antineoplastic combined chemotherapy protocols, radiotherapy, thoracic surgery, molecular targeted therapy, Georgia (republic)

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Background

Lung cancer (LC) is the most common malignancy responsible for 1.8 million of deaths worldwide.1 Lung and bronchus cancer represents 13% (n=1217) of all new cancer cases in Georgia.² In 2018, in Georgian males lung cancer age-standardized incidence rate was 35.7/per 100000, less compared to regional countries as Turkey (70.6), Russia (48.2), Ukraine (41.7), and Armenia (58.5), but higher than in neighbor Azerbaijan (25.5). Incidence is higher compared to central and eastern Europe (27.3) and near similar to North America (34.5).³ Georgia is an Eastern European, middleincome country with 3.7 million residents and one of the highest numbers of active smokers in the European Region.⁴ The Georgian health care system is divided into a public and a private sector, with coverage of nearly 100% of the population. There is a national healthcare system as well as private insurance and all patients, irrespective of insurance (private or governmental) can choose the hospital for treatment by themselves all over the country. The Basic Package of the Universal Health Care Program includes the treatment of oncologic patients, specifically surgery, chemotherapy, hormone therapy, and radiotherapy and investigations and medications related to these procedures. The program

covers all types of laboratory and instrumental investigations related to planned treatment.⁵ Georgia lacks an LC screening program for smokers and partially because of this, the majority of patients with lung cancer present at an advanced stage. The National Centre for the Disease Control (NCDC) showed that almost 90% of LC patients in the country present with advanced stages (III-IV) with 60% of patients having stage IV disease at diagnosis.6 Lung cancer is generally diagnosed at an advanced stage. For non-small cell lung cancer (NSCLC), the proportion with metastatic disease (TNM stage IV) ranged from 46.8% to 61.2% in developed countries.7 In recent years, there have been several publications addressing specifics of LC worldwide, but none concerning Georgia. In light of the rapidly changing landscape in the diagnosis, staging, and treatment of LC, we thought to define the state of practice in Georgia by convening specialists who treat LC across 13 institutions in our country with the goal to describe differences in access and approaches to LC.

Methods

We gathered key opinion leaders within our institution to define consensus staging and work-up protocols for people



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with LC. At our center, all patients undergo CT scans followed by biopsy for diagnosis; a PET-CT is recommended, but its use is limited due to financial constraints. After this, patients are presented to the multidisciplinary team (MDT) for the final treatment decision-making. Our internal data were used to generate an interdisciplinary survey, consisting of both openended and single best choice answer questions (18 questions related to medical management, 38 questions related to radiation therapy, and 11 questions for surgical treatment), with separate sections for NSCLC and small cell (SCLC) cancers. Surveys were distributed to providers across 13 high-volume cancer institutions and cancer specialties throughout the country. The study was carried out in 6 months. Survey data was collected and descriptive statistics were used to present the results. The study was internally reviewed during a regularly scheduled scientific development review at our center in the

Results

The survey questionnaire was distributed across 13 high-volume cancer institutions in which more than 95% of patients with lung cancer are treated (by the National Cancer Registry). The survey went out to a total of 24 physicians representing medical oncology (n = 13), radiation (n = 7) and surgical thoracic oncologists (n = 4) and all responded. Thirteen were male and 11 were female; All physicians were with more than 5-year experience in treating lung cancer patients. All medical oncologists practiced general rather than thoracic-specific oncology.

absence of an Institutional Review Board.

NSCLC

Surgical approaches: The case volume varied between our surgeons ranging from less than 4 month to over 20 month. Although all patients in Georgia have access to surgery, it is not performed at diagnosis for the vast majority due to diagnosis at a later stage. Three of the four surgeons did not have access to or use an MDT conference.

Regarding the treatment of early-stage LC, only 2 performed video-assisted thoracoscopy (VATS). Three surgeons out of four performed systematic lymphadenectomy rather than lymph node (LN) sampling. When asked about the role of surgery in oligometastatic NSCLC, 2 did not offer surgery and 2 did so but only in selected patients, mostly in case of single brain or adrenal metastasis. In addition, 2 offered surgery for patients presenting with bulky T4 NSCLC, while the other 2 did not. All surgeons would consider neoadjuvant chemotherapy (CHT) or RT-CHT, followed by either pneumonectomy, or lobectomy/bilobectomy in medically fit patients.

Systemic therapy: All medical oncologists (n = 13) reported a limited ability to prescribe targeted treatments, mostly due to the costs; however, chemotherapy is widely available. While all had access to diagnostic biomarkers for lung cancer, testing for epidermal growth factor receptor (*EGFR*), anaplastic lymphoma

Rate of recommended molecular testing in clinical practice

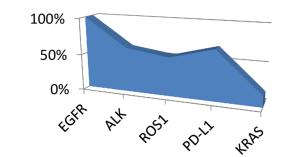


Figure 1. Rate of recommended molecular testing in clinical practice.

Rate of markers which are recommended in clinical practice

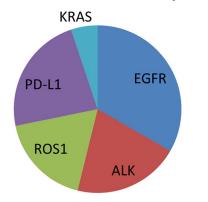


Figure 2. Rate of markers which are recommended in clinical practice.

kinase (*ALK*) and programmed death ligand-1(*PD-L1*) was not routinely used due to limitation in access to modern therapeutics. Notably, while molecular testing is available, it is performed on a send-out basis.

Despite these limitations, all medical oncologists (13 out of 13) would recommend EGFR testing, with ALK and ROS1 testing recommended by 8 and 7 clinicians, respectively. Nine felt testing for PD-L1 over expression was warranted; only 2 of them recommended testing for KRAS mutation. (Figure 1 and 2).

Patients with driver mutation can access to several TKIs within the public health system, albeit with only partial funding. We found that only approximately 16% (range, 0%-30%) of EGFR mutated patients received first-generation TKIs; with even less access to second or third generation agents.

In our survey, 5 out of 13 respondents had no access to clinical trials. Most clinical trials were evaluating immunotherapy (IMT). We identified that a high percentage (39.5%) of patients with lung cancer accessed these opportunities (range, 0%-95%). Only a very little number of patients receive IMT outside of clinical trials—average, 2 patients (range, 0-5) annually reflecting the lack of access to IMT drugs.

Advanced NSCLC			SCLC		
EGFR mut	ALK/ROS1 trasnlocation	Non-squamous	Squamous	LD-SCLC	ED-SCLC
First line					
Erlotinib Osimertinib* (with high co- payment)	Crizotinib*	Paclitaxel/carboplatin OR Platinum/pemetrexed OR Pacli/carbo/Bevacizumab*	Cisplatin/gemcitabine OR Paclitaxel/carboplatin	Cisplatin/ etoposide with TRT followed by PCI	Cisplatin/ etoposide +/- TRT (in responders)
Second line					
Osimertinib* OR Platinum based chemotherapy	Chemotherapy	Mono chemotherapy with Pemetrexed, Docetaxel, or Vinorelbin	Mono chemotherapy with Docetaxel, Gemcitabine or Vinorelbin	Topotecan or Irinotecan	Topotecan or Irinotecan

EGFR -epidermal growth factor receptor, ALK- anaplastic lymphoma kinase, ROS1 - ROS Proto-Oncogene 1, Receptore Tyrosine kinase.

Limited access, with high co-payment *

Figure 3. Treatment algorithm for advance NSCLC and LD/ED-SCLC (Available Treatment Approaches).

The survey reported almost universal administration of platinum-based therapy for patients with wild type, advancedstage NSCLC in Georgia. Paclitaxel/carboplatin, cisplatin/ gemcitabine, cisplatin/pemetrexed, carboplatin/docetaxel, or carboplatin/pemetrexed were regimens in common use [Figure 3].

For metastatic squamous cell NSCLC most frequently used regimen in first line setting is cisplatin/gemcitabine (76%), followed by paclitaxel/carboplatin (38%). In non-squamous histology, most institutions use paclitaxel/carboplatin (54%), and then platinum compounds with pemetrexed (23%).

Radiation therapy: Seven out of 13 institutions offered RT. Six institutions house megavoltage linear accelerators (Linacs), while only 1 institution houses a single Cobalt machine capable of performing 3D RT. These external beam machines are coupled with brachytherapy and fully equipped medical physics equipment, in addition to available CT and MRI scans.

For people with early (Stage I-II) NSCLC, all institutions use 3D conventionally fractionated (CF) RT. Indications to use RT in this setting include technically operable but medical inoperable cases, those deemed elderly/frail as well as the occasional patient who refuses surgery. Total doses of RT range from hypofractionated 55 Gy in 20 daily fractions to CF 60 to 70 Gy in 30 to 35 daily fractions. Target volumes always include

visible tumors with or without lymph nodes and only in 1 case incorporate elective nodal irradiation. Three out of seven departments use stereotactic body RT (SBRT) in Stage I NSCLC with total doses given ranging from 27 Gy in 3 fractions to most commonly given 50 Gy in 5 fractions but also including 60 Gy in 8 fractions, all depending on the tumor location. Various means of tumor motion control are in use in these centers and are considered mandatory. Postoperative RT is instituted after surgery in early-stage NSCLC due to various reasons such as positive surgical margins (R+), pN2, extracapsular extension (ECE) in all institutions but at an extremely low rate. Total RT doses are 50 to 54 Gy given with a CF and only 2 departments use 60 Gy CF. In locally advanced (Stage III) NSCLC, 4 departments would not consider any surgical multimodality approach, while of the other 3, 2 specified patients with low tumor volume or single mediastinal LN station as potential candidates for induction CHT or RT-CHT followed by surgery as their treatment option. In a non-surgical scenario, 5 out of 7 departments would prefer concurrent RT-CHT, while 1 would also consider induction CHT followed by either RT or concurrent RT-CHT depending on the patient's PS. When, however, asked when they would consider induction CHT followed by either RT or concurrent RT-CHT, they mostly preferred induction CHT in bulky T and/or N due

to fear of concurrently giving CHT with "too" large RT fields leading to more toxicity as well as when extensive symptoms and poor PS are expected to resolve with CHT before RT. Contrary to these, the responders would consider concurrent RT-CHT in non-bulky tumors and young and fit patients with good performance status. Total doses and fractionation used in this setting included CF 60 to 70 Gy always given on all visible tumors only. In symptomatic Stage IV patients, responders would treat all existing symptoms. Thoracic RT would be used with total doses of 20 to 50 Gy given in 5 to 20 fractions and only a single department would consider 60 Gy in 30 fractions in this setting. Four out of 7 institutions recognized specifics of "oligometastatic" disease, but the number of metastasis deemed as appropriate for this designation varied between up to 3 and up to 5. Dose and fractionation of oligometastases greatly vary. Brain metastases were mostly treated with stereotactic radiosurgery (SRS) (15-24 Gy in a single fraction), while non-brain metastases located in various organs and tissues were treated with dose/fractionation regimens from 18 to 24 Gy in 1 to 3 fractions to 27 Gy in 3 fractions or to 30 Gy in 6 fractions or even to 50 Gy given in either 5 or 10 fractions, given sometimes on alternate days.

SCLC

Surgical approaches: There are extremely few cases of early stage SCLC in the country and 2 of the 4 surgeons reported seeing less than 3 surgical cases/annually. Both do not offer surgery for SCLC.

Systemic therapy: Platinum plus etoposide chemotherapy is the cornerstone regimen in the treatment of patients with SCLC. Cisplatin with etoposide is mostly used combination in both LD—and ED-SCLC, 77% and 54% respectively. In most institutions platinum/etoposide CHT combined with thoracic RT is the choice for patients with limited disease (LD SCLC), while CHT alone is used in patients with extensive disease (ED SCLC) followed by thoracic RT (TRT) in responders. Other regimens used in ED-SCLC in first-line setting are a combination of carboplatin/etoposide and cisplatin with either topotecan or irinotecan.

Radiation therapy: In LD SCLC domain, 5 departments would consider starting concurrent part of the combined RT-CHT approach during either the first or the second cycle of CHT, 1 department preferring the third cycle of CHT while only 1 department opted for sequential CHT-RT approach with RT starting after the fourth CHT cycle. In cases when RT starts with the \geq 2 cycle of CHT, only 1 department would use pre-CHT volumes to be treated. Dose and fractionation included either 45 Gy in 30 fractions in 15 treatment days (1.5 Gy bid) (n=3) or 60 to 70 Gy in 30 to 35 daily fractions (n=2) while 2 departments were using both regimens without clearly specifying preferences for the use of either of these two. All 7 departments use prophylactic cranial irradiation (PCI) after

the end of complete RT-CHT, allowing 1 month after it for the evaluation of response. Dose of 25 Gy in 10 daily fractions was used in 6 departments of which only 1 allowed 20 Gy in 5 daily fractions, while the sole RT department practices 30 Gy in 10 daily fractions. All 7 departments use thoracic RT in ED SCLC and do that after 3 cycles of CHT (n=3) or after 4 to 6 cycles of CHT (n=4). Four out of six would use thoracic RT given concurrently with CHT, 2 departments would practice sequential CHT and RT approach, and one department would use both. Thoracic RT doses and fractionation used in this setting included 45 Gy in 15 daily fractions (n = 2), 46 to 54 Gy in 23 to 24 daily fractions (n=1), 30 Gyin 10 fractions (n=2), 60 Gy in 30 fractions (n = 1), 30 to 40 to 45 Gy in 10 to 15 fractions (n=1) and 50 to 60 Gy in 2 Gy daily fractions (n=1). Target volumes included visible tumor in 6 and pre-CHT volumes in 1 case. Three institutions do not use PCI after RT-CHT and 4 use it after RT-CHT was finished (allowing a gap of 1 month); PCI is given in cases of CR at both intrathoracic and distant sites. When used, PCI was given in 25 Gy in 10 daily fractions while only 1 department also allowed 20 Gy in 5 daily fractions.

Discussion

In this work, the very first 1 studying the patterns of practice in LC in Georgia, we have assembled as many institutions as possible. Six of them offer only CHT treatments, and the remaining 7 are capable of administering both RT and CHT. Due to non-existing accredited training programs in thoracic surgery, and the limited number of surgeons treating LC, we have surveyed only those surgeons known to us as having substantial experience in LC surgery. While this may be a disadvantage of our survey, these surgeons are attending MDT meetings in LC and are actively contributing to the whole decision-making process; hence, our data reflect our own ("real world") situation. The changes in the country's health care system in the past 10 to 15 years had dramatically improved many aspects of LC treatment. Contrary to previous periods, there is now an abundance of well-equipped hospitals around the country. Many young oncologists have regularly participated in training and fellowship programs abroad, while various international oncology conferences were organized in Georgia, all helping improve knowledge and skills in LC.

In the largely underutilized surgical treatment domain, differences were observed among surgeons on the optimal timing and the extent of surgery, as well as the role of surgery in specific clinical situations such as bulky T4 NSCLC disease and LD-SCLC. While prevalent advanced stages detected worldwide limit its use to some 20% to 25% of all LC cases worldwide, the situation in Georgia is much worse where almost 90% of all patients are inoperable. Hopefully, with the future establishment of screening programs and widespread, better diagnostics the number of surgical candidates would rise. Not to be forgotten, the expected rise of the patient numbers would also request for timely preparation of the thoracic surgery community as to be able to implement modern surgical aspects such as VATS.

The majority of medical oncologists in Georgia usually refer to the international guidelines and recommendations. Using it in daily practice makes treatment more modern and standardized in the whole country. Some hospitals begin implementation of MDT meetings, which is a relatively new practice and more and more patients receive their treatment based on team decisions.⁸ Unfortunately, even though most oncologists work according to high-quality clinical guidelines, in everyday practice they have limited access to novel agents, which is an obvious challenge that brings to patient care.

Targeted therapies and ICBs provide effective and tailored options for patients with NSCLC. Molecular testing generally is employed at the discretion of the treating oncologist in the country and recent years more oncologists perform routine driver mutational analyses and PD-L1 expression testing and results are already exist on molecular profiling of NSCLC.⁹ As in many Eastern European countries, there is somewhat limited access to all molecular profiling platforms of the tumor at a large scale.¹⁰ Although it is more available in some countries and tertiary centers of excellence, many patients will not realize the full benefits of precision oncology.

For the first line, of the Food and Drug Administration Agency (FDA)-approved agents used for patients with advanced or metastatic NSCLC with mutations in EGFR (EGFR-TKIs), only erlotinib is available in the country with patient co-payment. Management challenges are related to the difficulty in accessing the most recent targeted and IMT agents due to the high cost and lack of reimbursement from insurance companies. There are limitations for the use of the newer (second/third) generations of TKIs. However, some programs of Tbilisi City Hall and the Ministry of Health (MoH) help partially cover third generation TKI drug osimertinib which significantly improves PFS when compared with gefitinib or erlotinib.¹¹

Regarding CHT aspects, the combination of paclitaxel and carboplatin is the most common regimen for non-squamous NSCLC, followed by a combination of platinum compounds with pemetrexed, likely because the latter is found to have a statistically significant improvement in OS compared to cisplatin plus gemcitabine.¹² Some institutions use pemetrexed maintenance therapy based on the PARAMOUNT study, which found a significant reduction in the risk of disease progression, improved OS and increased PFS.¹³ The most frequently used regimen for metastatic squamous cell NSCLC in first line setting is cisplatin/gemcitabine.

In the treatment of SCLC, the standard first-line systemic treatment remains a combination of cisplatin/etoposide, similarly to the rest of the world, but with only limited national access to atezolizumab.¹⁴ IMT drugs are not reimbursed in Georgia, neither in first—nor in subsequent lines, although the

drugs are registered and available at the patient's expense. Despite this fact, some patients receive ICBs by enrollment in clinical trials. For 2 decades clinical research has been growing steadily in the country and participating in trials are the only way for patients to get novel treatment drugs.

Our survey shows that many hospitals don't have even 1 clinical trial. Generally, the number of ongoing clinical trials with novel targeted therapies and IMT in Georgia is quite low, leading to delayed access to new drugs. Enrollment in clinical trials that further enhances the development of tailored therapies is widely recognized as advantageous and is highly recommended at all stages of treatment.¹⁴

Regarding RT aspects, there is a total of 15 external beam machines of which 13 are functional. This would likely indicate the scenario of under equipment as international estimates for limited resource setting¹⁵ would indicate the need for additional 4 to 6 functioning external beam machines. In addition, of 7 existing centers offering RT services, 5 are located in its capital, Tbilisi, with the obvious need for facilities in distant regions of the country.

In cases of NSCLC, RT is employed in early (Stage I-II) cases either as 3D or 4D conventionally fractionated RT or SBRT. Indications for its use and dose/fractionation regimens changed a little in the past 20 years.¹⁶ Similarly, SBRT regimens employed in 3 out of 7 departments used several widely practiced fractionated regimens depending on the tumor location.¹⁷ Recent data on the use of modern postoperative TRT¹⁸ seem to overcome the negative impact of historic data,¹⁹ since it enabled effectively concentrating on patients harboring high-risk features. In Stage IIIA NSCLC, less than a half of the institutions would still consider surgical multimodality approach likely due to a number of group/society guidelines and recommendations²⁰ even though serious criticism and several flaws and fallacies have been highlighted in recent years.^{21,22} In, inoperable cases, the vast majority of departments would prefer concurrent RT-CHT, following the highest level of evidence existing for more than a decade.^{23,24} Only big and bulky tumors led 2 departments to consider induction CHT followed by either RT or RT-CHT, due to expected significant acute side effects of exclusive concurrent RT-CHT. All institutions treat only visible tumors. Although the majority of institutions nowadays use 60 Gy, some suggested 70 Gy, in contradiction to recent results of the Radiation Therapy Oncology Group (RTOG) 0617.25 In cases of Pancoast tumors, only 1 institution opted for preoperative RT-CHT followed by surgery. This seems to reflect both few experienced and practicing thoracic surgeons in the country, lack of accredited training programs as well as lack of experience the vast majority of existing surgeons seems to suffer seemingly due to low volume LC surgeries nationwide. In symptomatic stage IV patients, RT would be used to treat all existing symptoms with only 1 institution offering 60 Gy in 30 daily fractions in this setting. Following general and worldwide trends,^{26,27} the majority of institutions

would follow currently accepted RT approach in "oligometastatic" disease, although their consideration seems to reflect current uncertainties. Dose and fractionation depended on the number of metastases, metastatic site, primary tumor histology, following major evidence worldwide.^{28,29}

In cases of LD SCLC, the majority of departments confirmed policy to start RT concurrently as early as possible.³⁰ Choice of RT fields also follows general trends in being based on post-CHT volumes, except when RT starts concurrently with the first cycles of CHT. While the majority of institutions use either hypo-or hyper fractionated RT, some institutions still use CF RT with doses as high as 70 Gy, contradicting accumulated evidence.^{31,32} When PCI is considered, institutions seem to have firmly adopted 20-year old results of metaanalysis.33 Doses and fractionation of PCI are also in concordance with existing recommendations.³⁴ Institutions request response evaluation after 1 month after the end of CHT, after which MRI is usually used for choosing patients suitable for PCI (all CR and good PR). In cases of ED SCLC, the pivotal study of Jeremic et al³⁵ and the following study of EORTC³⁶ was seemingly the strongest advocates for the use of thoracic RT since all departments use it. The vast majority of institutions would give RT concurrently with CHT and only occasionally sequentially as per EORTC.37 A variety of dose/fractionation regimens were used, likely reflecting a lack of consensus on the optimal dose/fractionation aspects in this setting. Similar to LD SCLC, the vast majority of institutions would use visible (post-CHT) RT volumes. The use of PCI in ED SCLC left institutions almost split between using it or not, likely reflecting the impact of recent Japanese data³⁸ that challenged EORTC study results.³⁹ When given, PCI was administered after brain imaging done 1 month post-CHT showed CR on both intrathoracic and distant sites.

Conclusion

Georgian health care system improved over the past years and followed the trends observed in the rest of the European Region. Availability of anticancer drugs and the existence of modern RT technology with increasing thoracic oncologists' knowledge and skill are coupled with the slow appearance of country-adapted diagnostic and therapeutic guidelines and protocols as well as enforcing MDT meetings. However, Georgian patients with LC still suffer from shortcomings when considering several aspects of their LC care. Our study leads to some practical recommendations: the great need to introduce screening programs in high-risk groups with additional measures focusing on smoking cessation, enforcing MDT meetings, improve access to modern treatment modalities and standardize national diagnostic and treatment protocols are urgently needed, more clinical researches/trials are of paramount importance for better LC care. Also, psychological support and high-quality palliative care, currently hardly

-existing, are deemed especially important for the country. There is still much work to be done, with all these steps considered mandatory to improve the effectiveness and quality of care of LC patients.

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Author Contributions

All authors have substantially contributed to the conception of the present work. Ivane Kiladze—conceptualization, methodology, writing—original draft preparation, data collection; Elene Mariamidze—data curation, visualization, writing original draft preparation; Branislav Jeremic—supervision, writing-reviewing and editing. All authors have approved the final version of the manuscript, and are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated.

Ethics and Consent

Institutional ethics committee waived its consideration/ approval as no patient data was included in this multi institutional practices survey. Written informed consent was obtained from all participants. No consent was sought since there are no patient data included in this study (survey of practices not the patients' data).

Paper Context

We provided first ever patterns of practice in the treatment domain of lung cancer in our country with indicating the future strategies for improved cancer care. Information about practices was collected throughout the country. Majority of patients present with advanced stages at diagnosis. There is limited access to expensive novel agents and psychological support.

Implantation of national screening program, countryadapted guidelines, enforcing MDT meetings, continuous professional development should lead to improved LC care effectiveness

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REFERENCES

- Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBO-CAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2018;68:394-424.
- The Global Cancer Observatory. IARC. Accessed May 2019. https://gco.iarc.fr/ today/data/factsheets/populations/268-georgia-fact-sheets.pdf.
- Jemal A, Torre L, Soerjomataram I, Bray F, eds. The Cancer Atlas. 3rd ed. American Cancer Society; 2019.
- European School Survey Project on Alcohol and Other Drugs: Georgia Country Report. 2016. Tbilisi: National Centre for Disease Control and Public Health of the Ministry of Labour, Health and Social Affairs of Georgia.
- Cancer Profile. Georgia. Accessed April 2018. https://www.moh.gov.ge/ uploads/files/2018/Failebi/16.04.2018.pdf
- NCDC. Cancer statistics. Accessed 2019. https://www.ncdc.ge/Pages/User/ News.aspx?ID=bec659c0-56a2-4190-9c0c-e47a63bcca4f.
- Walters S, Maringe C, Coleman MP, et al. Lung cancer survival and stage at diagnosis in Australia, Canada, Denmark, Norway, Sweden and the UK: a population-based study, 2004–2007. *Thorax.* 2013;68:551-564.
- Kiladze I, Mariamidze E, Jeremic B. Lung cancer in Georgia. J Thorac Oncol. 2020;15:1113-1118.
- Kiladze I, Mariamidze E, Baramidze A, Lomidze M, Meladze K, Jeremic B. Molecular profiling and characteristics of non-small-cell lung cancer patients in Georgia. *Future Oncol.* 2021;17:3585-3594.
- Ryska A, Buiga R, Fakirova A, et al. Non-Small cell lung cancer in countries of Central and southeastern Europe: diagnostic procedures and treatment reimbursement surveyed by the Central European Cooperative Oncology Group. Oncologist. 2018;23:e152-e158.
- Soria JC, Ohe Y, Vansteenkiste J, et al. Osimertinib in untreated EGFR-mutated advanced non-small-cell lung cancer. *New Eng J Med.* 2018;378:113-125.
- Scagliotti GV, Parikh P, von Pawel J, et al. Phase III study comparing cisplatin plus gemcitabine with cisplatin plus pemetrexed in chemotherapy-naive patients with advanced-stage non-small-cell lung cancer. J Clin Oncol. 2008;26:3543-3551.
- 13. Paz-Ares L, de Marinis F, Dediu M, et al. Maintenance therapy with pemetrexed plus best supportive care versus placebo plus best supportive care after induction therapy with pemetrexed plus cisplatin for advanced non-squamous non-small-cell lung cancer (PARAMOUNT): a double-blind, phase 3, randomised controlled trial. *Lancet Oncol.* 2012;13:247-255.
- Leora H, Mansfield A, Szczęsna A, et al. First-Line Atezolizumab plus chemotherapy in extensive-stage small-cell lung cancer. *New Eng J Med.* 2018;379:2220-2229.
- Abdel Karim N, Kelly K. Role of targeted therapy and immune checkpoint blockers in advanced non-small cell lung cancer: a review. *Oncologist*. 2019;24:1270-1284.
- Zubizarreta EH, Fidarova E, Healy B, Rosenblatt E. Need for radiotherapy in low and middle income countries – the silent crisis continues. *Clin Oncol.* 2015;27:107-114.
- Jeremic B, Classen J, Bamberg M. Radiotherapy alone in technically operable, medically inoperable, early-stage (I/II) non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys.* 2002;54:119-130.
- Timmerman RD, Herman J, Cho LC. Emergence of stereotactic body radiation therapy and its impact on current and future clinical practice. J Clin Oncol. 2014;32:2847-2854.
- Patel SH, Ma Y, Wernicke AG, Nori D, Chao KS, Parashar B. Evidence supporting contemporary post-operative radiation therapy (PORT) using linear accelerators in N2 lung cancer. *Lung Cancer*. 2014;84:156-160.
- Burdett S, Rydzewska L, Tierney J, et al. Postoperative radiotherapy for nonsmall cell lung cancer. *Cochrane Database Syst Rev.* 2016;10:CD002142.
- Bezjak A, Temin S, Franklin G, et al. Definitive and adjuvant radiotherapy in locally advanced non-small-cell lung cancer: American Society of clinical Oncology clinical practice guideline endorsement of the American Society for Radiation Oncology evidence-based clinical practice guideline. J Clin Oncol. 2015;33:2100-2105.

- Jeremic B, Casas F, Dubinsky P, Cihoric N, Gomez-Caamano A. The trimodality treatment approach in stage III/pN2 non-small cell lung cancer: "Usually Appropriate" may well be a very inappropriate treatment option. *Am J Clin Oncol.* 2015;38:645.
- Jeremić B. Induction therapies plus surgery versus exclusive radiochemotherapy in stage IIIA/N2 non-small cell lung cancer (NSCLC). Am J Clin Oncol. 2018;41:267-273.
- Aupérin A, Le Péchoux C, Rolland E, et al. Meta-analysis of concomitant versus sequential radiochemotherapy in locally advanced non-small-cell lung cancer. J Clin Oncol. 2010;28:2181-2190.
- O'Rourke N, Roqué I Figuls M, Farré Bernadó N, Macbeth F. Concurrent chemoradiotherapy in non-small cell lung cancer. *Cochrane Database Syst Rev.* Published online June 16, 2010. doi:10.1002/14651858.CD002140.pub3.
- 26. Bradley JD, Paulus R, Komaki R, et al. Standard-dose versus high-dose conformal radiotherapy with concurrent and consolidation carboplatin plus paclitaxel with or without cetuximab for patients with stage IIIA or IIIB non-small-cell lung cancer (RTOG 0617): a randomised, two-by-two factorial phase 3 study. *Lancet Oncol.* 2015;16:187-199.
- Palma DA, Olson R, Harrow S, et al. Stereotactic ablative radiotherapy versus standard of care palliative treatment in patients with oligometastatic cancers (SABR-COMET): a randomised, phase 2, open-label trial. *Lancet.* 2019;393: 2051-2058.
- Gomez DR, Tang C, Zhang J, et al. Local consolidative therapy vs. Maintenance therapy or observation for patients with oligometastatic non-small-cell lung cancer: long-term results of a multi-institutional, phase II, randomized study. *J Clin Oncol.* 2019;37:1558-1565.
- Guckenberger M, Lievens Y, Bouma AB, et al. Characterisation and classification of oligometastatic disease: a European Society for Radiotherapy and Oncology and European Organisation for Research and Treatment of Cancer consensus recommendation. *Lancet Oncol.* 2020;21:e18-e28.
- Dingemans AC, Hendriks LEL, Berghmans T, et al. Definition of synchronous oligometastatic non-small cell lung Cancer-A consensus report. J Thorac Oncol. 2019;14:2109-2119.
- Jeremic B. Timing of concurrent radiotherapy and chemotherapy in limited-disease small-cell lung cancer: "meta-analysis of meta-analyses." *Int J Radiat Oncol Biol Phys.* 2006;64:981-982.
- Jeremic B, Shibamoto Y, Acimovic L, Milisavljevic S. Initial versus delayed accelerated hyperfractionated radiation therapy and concurrent chemotherapy in limited small-cell lung cancer: a randomized study. J Clin Oncol. 1997;15:893-900.
- Faivre-Finn C, Snee M, Ashcroft L, et al. Concurrent once-daily versus twicedaily chemoradiotherapy in patients with limited-stage small-cell lung cancer (CONVERT): an open-label, phase 3, randomised, superiority trial. *Lancet* Oncol. 2017;18:1116-1125.
- Aupérin A, Arriagada R, Pignon JP, et al. Prophylactic cranial irradiation for patients with small-cell lung cancer in complete remission. Prophylactic cranial irradiation overview collaborative group. *New Eng J Med.* 1999;341:476-484.
- Le Péchoux C, Dunant A, Senan S, et al. Standard-dose versus higher-dose prophylactic cranial irradiation (PCI) in patients with limited-stage small-cell lung cancer in complete remission after chemotherapy and thoracic radiotherapy (PCI 99-01, EORTC 22003-08004, RTOG 0212, and IFCT 99-01): a randomised clinical trial. *Lancet Oncol.* 2009;10:467-474.
- Jeremic B, Shibamoto Y, Nikolic N, et al. Role of radiation therapy in the combined-modality treatment of patients with extensive disease small-cell lung cancer: a randomized study. *J Clin Oncol.* 1999;17:2092-2099.
- Slotman BJ, van Tinteren H, Praag JO, et al. Use of thoracic radiotherapy for extensive stage small-cell lung cancer: a phase 3 randomised controlled trial. *Lancet.* 2015;385:36-42.
- Takahashi T, Yamanaka T, Seto T, et al. Prophylactic cranial irradiation versus observation in patients with extensive-disease small-cell lung cancer: a multicentre, randomised, open-label, phase 3 trial. *Lancet Oncol.* 2017;18:663-671.
- Slotman B, Faivre-Finn C, Kramer G, et al. Prophylactic cranial irradiation in extensive small-cell lung cancer. *New Eng J Med*. 2007;357:664-672.