

Access to Novel Drugs for Non-Small Cell Lung Cancer in Central and Southeastern Europe: A Central European Cooperative Oncology Group Analysis

TANJA CUFER,^a TUDOR E. CIULEANU,^b PETER BERZINEC,^c GABRIELA GALFFY,^d MARKO JAKOPOVIC,^e JACEK JASSEM,^f DRAGANA JOVANOVIC,^g ZHASMINA MIHAYLOVA,^h GYULA OSTOROS,ⁱ CHRISTIANE THALLINGER[ⓓ],^j MILADA ZEMANOVA,^k CHRISTOPH ZIELINSKI^l

^aMedical Faculty Ljubljana, University Clinic Golnik, Ljubljana, Slovenia; ^bDepartment of Medical Oncology, "Prof. Dr. Ion Chiricuta" Institute of Oncology, Cluj-Napoca, Romania; ^cDepartment of Oncology, Hospital of St Zoerardus Zobor, Nitra, Slovakia; ^dDepartment of Chest Surgery, Pest County Pulmonology Hospital, Törökbálint, Hungary; ^eDepartment for Respiratory Disease Jordanovic, University Hospital Centre Zagreb, Zagreb, Croatia; ^fDepartment of Oncology and Radiotherapy, Medical University of Gdansk, Gdansk, Poland; ^gDepartment of Palliative Medicine, University Hospital of Pulmonology, Clinical Center of Serbia, Belgrade, Serbia; ^hDepartment of Medical Oncology, Military Medical Academy, Sofia, Bulgaria; ⁱDepartment of Pulmonology, National Koranyi Institute of Pulmonology, Budapest, Hungary; ^jDepartment of Medicine I, Medical University of Vienna – General Hospital, Vienna, Austria and Central European Cooperative Oncology Group (CECOG); ^kDepartment of Oncology, University Hospital, Prague, Czech Republic; ^lVienna Cancer Center, Medical University of Vienna – General Hospital, Vienna, Austria and Central European Cooperative Oncology Group (CECOG)

Disclosures of potential conflicts of interest may be found at the end of this article.

ABSTRACT

Background. Treatment of non-small cell lung cancer (NSCLC) improved substantially in the last decades. Novel targeted and immune-oncologic drugs were introduced into routine treatment. Despite accelerated development and subsequent drug registrations by the European Medicinal Agency (EMA), novel drugs for NSCLC are poorly accessible in Central and Eastern European (CEE) countries.

Material and Methods. The Central European Cooperative Oncology Group conducted a survey among experts from 10 CEE countries to provide an overview on the availability of novel drugs for NSCLC and time from registration to reimbursement decision in their countries.

Results. Although first-generation epidermal growth factor receptor tyrosine kinase inhibitors were reimbursed and available in all countries, for other registered therapies—even for ALK inhibitors and checkpoint inhibitors in first-line—there were apparent gaps in availability and/or

reimbursement. There was a trend for better availability of drugs with longer time from EMA marketing authorization. Substantial differences in access to novel drugs among CEE countries were observed. In general, the availability of drugs is not in accordance with the Magnitude of Clinical Benefit Scale (MCBS), as defined by the European Society for Medical Oncology (ESMO). Time spans between drug registrations and national decisions on reimbursement vary greatly, from less than 3 months in one country to more than 1 year in the majority of countries.

Conclusion. The access to novel drugs for NSCLC in CEE countries is suboptimal. To enable access to the most effective compounds within the shortest possible time, reimbursement decisions should be faster and ESMO MCBS should be incorporated into decision making. *The Oncologist* 2020;25:e598–e601

INTRODUCTION

Lung cancer is the most frequent cause of cancer-related mortality worldwide, with high incidence and mortality rates in Central and Eastern Europe (CEE) [1]. Most patients are diagnosed with advanced disease, resulting in poor survival rates [2]. However, there is a trend toward better outcomes in developed countries mostly because of improved

systemic treatment strategies introduced in the beginning of this century [2–4].

Nowadays, treatment strategy in advanced non-small cell lung cancer (NSCLC) mainly depends on molecular markers. The discovery of oncogene drivers such as epidermal growth factor receptor (*EGFR*) mutations and *ALK* and *ROS1*

Correspondence: Christiane Thallinger, M.D., Department of Internal Medicine, Division of Oncology, Medical University Vienna, Währingergrütel 18-20, 1090 Vienna, Austria. Telephone: 43-1-40400-44570; e-mail: christiane.thallinger@meduniwien.ac.at Received July 12, 2019; accepted for publication October 17, 2019; published Online First on November 29, 2019. <http://dx.doi.org/10.1634/theoncologist.2019-0523>

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Table 1. Availability of novel anticancer drugs for non-small cell lung cancer in 10 Central and Eastern European countries in relation to time from EMA MA and the ESMO MCBS

| Drug | Time from EMA MA to the survey (months) | Country | | | | | | | | | | ESMO-MCBS |
|----------------------------|---|---------|-------|-------|--------|--------|-------|-------|-------|--------|-------|-----------|
| | | AUT | BLG | CRO | CZR | HUN | POL | ROM | SRB | SLK | SLO | |
| First-line setting | | | | | | | | | | | | |
| Pembrolizumab | 14 | Green | Green | Green | Yellow | Green | Red | Red | Red | Green | Green | 5 |
| Afatinib | 54 | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | 4 |
| Erlotinib | 79 | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | 4 |
| Gefitinib | 105 | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | 4 |
| Crizotinib ^a | 28 | Green | Green | Green | Yellow | Green | Red | Red | Red | Green | Green | 4 |
| Crizotinib ^b | 19 | Green | Green | Red | Yellow | Green | Red | Red | Black | Green | Green | 3 |
| Bevacizumab | 127 | Green | Green | Red | Green | Green | Red | Green | Red | Green | Red | 2 |
| Necitumumab | 25 | Green | Red | Red | Red | Red | Red | Red | Black | Red | Red | 1 |
| Second-line setting | | | | | | | | | | | | |
| Nivolumab | 29 | Green | Red | Red | Red | Green | Red | Green | Red | Yellow | Green | 5 |
| Pembrolizumab | 20 | Green | Green | Red | Yellow | Green | Red | Red | Black | Yellow | Green | 5 |
| Osimertinib | 25 | Green | Green | Green | Yellow | Yellow | Green | Green | Red | Yellow | Green | 4 |
| Ceritinib | 34 | Green | Red | Green | Yellow | Green | Red | Red | Black | Yellow | Green | 4 |
| Alectinib | 13 | Green | Red | Green | Yellow | Green | Red | Red | Red | Red | Red | 4 |
| Nintedanib | 40 | Green | Red | Green | Green | Green | Red | Red | Black | Green | Green | 4 |
| Ramucirumab | 26 | Green | Green | Red | Red | Red | Red | Red | Black | Red | Red | 2 |
| Afatinib | 24 | Green | Green | Red | Green | Yellow | Red | Red | Red | Green | Red | 1 |
| Erlotinib | 150 | Green | Green | Green | Green | Green | Green | Green | Green | Green | Green | 1 |

^a Refers to use of crizotinib in ALK+ NSCLC.

^b Refers to crizotinib in ROS1+ NSCLC.

Abbreviations: AUT, Austria; BLG, Bulgaria; CRO, Croatia; CZR, Czech Republic; EMA MA, European Medicines Agency marketing approval; ESMO MCBS, European Society for Medical Oncology Magnitude of Clinical Benefit Scale; Hun, Hungary; POL, Poland; ROM, Romania; SLK, Slovakia; SLO, Slovenia; SRB, Serbia.

| Color Key | |
|-----------|--|
| | Registered and available for the majority of patients through governmental/private insurance |
| | Registered and available for only a minority of patients with special insurance/other ^c |
| | Registered, but not yet available/reimbursed |
| | Not yet registered at data cut-off |

^c Other includes patient access schemes and other forms of treatment access.

rearrangements paved the way to effective targeted therapies, whereas immunotherapy with checkpoint inhibitors (CPIs) became the standard treatment for the majority of patients with advanced NSCLC without oncogenic drivers [3, 4].

Access to novel therapies is one of the major factors contributing to disparities in cancer care [5]. Limited drug availability remains a prominent aspect of cancer care in CEE countries, still struggling with both financial and organizational shortages [6]. The Central European Cooperative Oncology Group (CECOG) created a network of activities to improve quality of cancer care in the region. The most

recent CECOG initiative consisted of two surveys on NSCLC. The first survey on molecular testing has recently been published [7]. The aim of the present survey was to investigate access to novel anticancer drugs for NSCLC and time from marketing authorization to national reimbursement.

MATERIALS AND METHODS

A panel of NSCLC experts from 10 CEE countries (Austria, Bulgaria, Croatia, Czech Republic, Hungary, Poland, Romania, Serbia, Slovenia, and Slovakia, each country represented by one expert, respectively) participated in the survey.

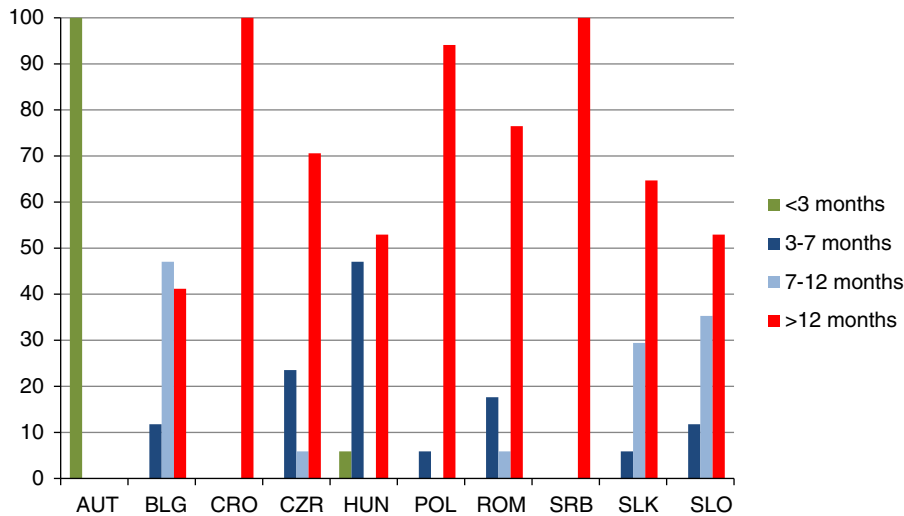


Figure 1. Time from marketing authorization to reimbursement of novel drugs for non-small cell lung cancer in 10 Central and Eastern European countries. Data are expressed as percentage of drugs available in particular timeframe. Abbreviations: AUT, Austria; BLG, Bulgaria; CRO, Croatia; CZR, Czech Republic; HUN, Hungary; POL, Poland; ROM, Romania; SLK, Slovakia; SLO, Slovenia; SRB, Serbia.

Novel drugs with European Medicines Agency (EMA) marketing approval (MA) for particular indication and recommended by European Society for Medical Oncology (ESMO) guidelines [3] were included. In a majority of countries (9 out of 10, i.e., European Union [EU] members), the time from marketing approval was the same, as a result of EMA licensing. Only in Serbia, a national approval procedure was still in place, with 5 out of 17 drugs without national MA at the time of survey.

The obtained answers were further verified on the official websites of National Drug Agencies, National Insurance Houses, and Ministries of Health. The data lock was March 31, 2018.

Each drug was identified by one of three categories: (a) the drug is registered and available for the majority of patients through established governmental or private insurance; (b) the drug is registered and available only to a minority of patients with special insurance or other access programs; or (c) the drug is registered by EMA, but neither reimbursed nor available in the country.

ESMO Magnitude of Clinical Benefit Scale (MCBS) scores available at the moment of survey [3, 8] were included.

RESULTS

Major gaps and differences in the availability of novel anticancer drugs for NSCLC in the CEE region were recorded (Table 1), with the most profound lack of access observed in countries with lower levels of economic development, such as Serbia and Romania [7]. Although first-generation EGFR tyrosine kinase inhibitors (TKIs) were reimbursed and available in all countries, there were apparent gaps in access to ALK TKIs and CPIs in first-line. There was a trend for better availability of compounds with longer intervals from EMA MA to the survey. It is quite obvious that availability of drugs was not in accordance with the ESMO MCBS. Drugs with high scores, like crizotinib for ALK-positive disease or nivolumab (MCBS 4 and 5, respectively)

were not available in a number of countries even after a long interval of 2 years from MA.

Time from MA to reimbursement differed between <3 months in a striking minority of countries to >12 months needed for most novel drugs to get reimbursement in a vast majority of countries (Fig. 1). In Croatia and Serbia, the lag time between registration and reimbursement was more than 1 year for all drugs. Almost no reimbursement decision for any novel drug has been made in any country except Austria within a period of <3 months, thus precluding rapid access to effective compounds with high ESMO MCBS.

DISCUSSION

Based on our survey, the access to novel anticancer drugs for NSCLC in the CEE region is far from satisfactory. Notably, a vast majority of drugs being approved by EMA for 2 years or more and recommended by current ESMO treatment guidelines [3] were not available to CEE patients with NSCLC at the time of our survey. The major reason for poor availability seems to be a long lag interval between EMA or national MA and national reimbursement decisions, which is particularly worrisome for drugs with high ESMO MCBS scores [8]. Despite some recent optimistic reports of decreasing time intervals between EMA registrations and national reimbursement decisions of anticancer drugs in Western and Northern European countries [9], our results are not in line with those encouraging data.

The first comprehensive analysis on the availability of anticancer drugs for major cancers in Europe was performed by ESMO in 2014 [5]. With novel and effective drugs entering the market, the proportion of non-reimbursed and thus unavailable novel drugs for NSCLC has even increased in some CEE countries, based on our observation. This is particularly worrisome for NSCLC, which constitutes a paradigmatic driver of cancer-related morbidity and mortality in the CEE region.

It has been shown that economic disparities, differences in health care systems, and reimbursement decisions are the main reasons for inequalities in access to novel anticancer drugs across Europe [5, 6, 10]. The existing gaps are certainly due to disparities in gross domestic product (GDP), with CEE countries spending about 2.5 times less on anticancer drugs than Western European countries despite using a higher share of their GDP [10]. However, more funds do not seem to be the ultimate answer; to retain a sustainability of system and to close the gap in access to novel anticancer drugs, more rational, value-oriented uptake of novel drugs should be implemented.

CONCLUSION

With lung cancer representing a major burden in the CEE region, the data of the current survey indicate not only that time intervals between drug registrations on the EU level and reimbursement decisions on the national level should be shortened but also that value scores, like ESMO MCBS, should be taken into account in order to enable patient access to the most effective compounds in the shortest possible time.

ACKNOWLEDGEMENTS

We thank MedInteractiv Plus for summarizing survey outcomes and for writing assistance in parts of the manuscript. Support for data collection conducted by CECOG and for writing services were obtained from financial support by

AstraZeneca. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

DISCLOSURES

Tanja Cufer: AstraZeneca, Boehringer Ingelheim, Roche, Pfizer, Bristol-Myers Squibb, Takeda, Merck Sharp & Dohme (H); **Tudor E. Ciuleanu:** A&D Pharma, Amgen, Astellas, AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, Janssen, Merck, Sanofi (C/A, H); **Peter Berzinec:** AstraZeneca, Boehringer Ingelheim, Merck Sharp & Dohme, Pfizer, Roche (H), Boehringer Ingelheim, Merck Sharp & Dohme (C/A); **Gabriela Galfy:** Roche, Bristol-Myers Squibb, Merck Sharp & Dohme, Boehringer Ingelheim, AstraZeneca, Berlin Chemie, Novartis (C/A), Roche, Bristol-Myers Squibb, Merck Sharp & Dohme, Boehringer Ingelheim, AstraZeneca, Berlin Chemie, Novartis, Mylen, Ipsen, Pfizer (ET); **Marko Jakopovic:** AstraZeneca, Roche, Boehringer Ingelheim, Novartis, Novartis Oncology, Merck Sharp & Dohme, Berlin Chemie, Pfizer, Sandoz, Abbot, Eli Lilly (C/A), Roche, Novartis Oncology, Boehringer Ingelheim, AstraZeneca, Eli Lilly (ET); **Jacek Jassem:** Roche (travel support), G1 Therapeutics (C/A); **Dragana Jovanovic:** AstraZeneca, Boehringer Ingelheim, Roche, Pfizer (C/A, H); **Zhasmina Mihaylova:** AstraZeneca, Roche, Eli Lilly, Boehringer Ingelheim, Pfizer (C/A), Bristol-Myers Squibb, Merck Sharp & Dohme (C/A, ET); **Gyula Ostoros:** Bristol-Myers Squibb, Merck Sharp & Dohme, Pfizer, Roche, AstraZeneca (C/A); **Milada Zemanova:** Novartis, GlaxoSmithKline (C/A, H, ET), Bayer, Novartis (travel grants); **Christoph Zielinski:** Roche, Novartis, Bristol-Myers Squibb, Merck Sharp & Dohme, Imugene, Ariad, Pfizer, Merrimack, Merck KGaA, Fibrogen, AstraZeneca, Tesaro, Gilead, Servier, Shire, Eli Lilly, Athenex (H). The other author indicated no financial relationships.

(C/A) Consulting/advisory relationship; (RF) Research funding; (E) Employment; (ET) Expert testimony; (H) Honoraria received; (OI) Ownership interests; (IP) Intellectual property rights/inventor/patent holder; (SAB) Scientific advisory board

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