Advancements in Non-Small Cell Lung Cancer

Solving access to lung cancer care across Europe

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Ensuring access to emerging therapies remains a priority in cancer care. Today more than ever novel therapeutics are arriving at an ever-escalating rate. As new promising treatments emerge, however, not all geographic locations and people within have similar access. Political, social, regulatory, socioeconomic, distribution-chain, and cost elements serve as some reasons for perceived or actual barriers to patients with the same cancer not having the same access. As clinician-researchers, we hope new and important medicines are as reachable to patients battling disease world-wide.

In Two papers published in *The Lancet Regional Health: Europe*, for the Series on "Advancements in Non-Small Cell Lung Cancer", the authors provide a thoughtful and data-derived summary of therapeutic breakthroughs for early-stage non-small cell lung cancer (NSCLC) over the past few years,[1] and the challenges that this paradigm shift brings with it.[2]

Yet, the authors dive deeper and explain, with evidence-supported theories, why access to such newly-proven treatments may not be even across the European Union (EU) or even between the United States of America (US) and the EU. By analyzing differences in regulatory approval steps, payor influences, member state budgetary and cost factors, non-standardization endpoints for drug effectiveness acceptance, and study design heterogeneity which make streamlined approval more challenging, the authors provide rationale why adoption is less uniform. Thus, a commendable job is done in these articles outlining the contemporary advances in therapies for NSCLC, including targeted therapy for resectable disease and recent trials demonstrating advances with neoadjuvant or adjuvant immunotherapy for early-stage cancer, as well as in exploring the challenges with access.

By outlining the intricate differences between the EU and US, and the member state dynamics within the EU, the readership appreciates where the root causes of access disparities exist and potential solutions rest. The authors' accompanying viewpoint offers suggestions on how to overcome some of these barriers. These recommendations include, without limitation, (i) how inter-member and EU–US focus on database registry symmetry could help drug access equity in post-marketing with consistent data point tracking, (ii) how adoption of consistent, standardized trial end-points could result in more uniform drug acceptance, (iii) how consensus building and agreement for drug approval could harmonize uniform early adoption of promising therapies, (iv) how global agreement on guideline recommendations along with integrating novel therapies could substantiate standard of care acceptance earlier, (v) how novel strategies for coverage reimbursement negotiations at a central level could alleviate some cost barriers to early adoption. It's the hope of the authors, and of the commenters here, such changes could help to resolve some access issues to lung cancer advances.

As new strategies to improve access are contemplated, it's important to recognize that the EU is a relatively new union comprised of numerous states with varied histories. These histories are each equally or if not more different to each other than US' states. However, unlike the US with its highly centralized Food and Drug Administration (FDA) and broader jurisdiction over therapeutic modalities, the EU has a more laborious and dis-articulated framework for approvals. Unlike the FDA, which serves dual streamlined functions of both review and approval after confirming safety and efficacy, the EU uses the European Medicine Agency (EMA) involving all 27-member states for approval which only then offers recommendations to the European Commission (EC) for a final verdict.

Further, while FDA approval is technically non-binding on insurance payors, per se,[3] the majority of FDA-approved medications and devices are covered by the US' national and commercial payors, highlighting the close alignment between approval, coverage, and adoption even if not statutorily mandated.[4] Alternatively, when the EC approves a medication for sale, the decision to adopt, cover, and pay for it by individual member states varies widely and is often up to each state's discretion. Therefore, the lack of a streamlined review/approval process in the EU is a material reason it takes up to twice as long to approve novel NSCLC breakthroughs as the US. It's also a reason that, even

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after approval, the access to such treatments vary in timing and absolute access across the 27 members.

The solution to help bring symmetry to access within the EU and between the EU and the US has been an area of progress. However, it is important to mention the EU and US recognize such disparities between and within both unions could be better tackled together. They have partnered in various ways to learn lessons and synchronize processes for approval analysis, offering optimism for symmetry which the authors argue will be important for solutions in the years to come. Specifically, collaboration and communication has become more common between the two and has accelerated over the past two decades. Since 2003,[5] sharing confidential information regarding scientific evidence, clinical practices, and more product and device details helps harmonize recommendations for novel approvals. Both bodies engage in cluster activities to further discuss topics requiring further collaboration when it comes to drug approval in the form of regular and constant virtual communication and meetings.

As a result of the COVID-19 pandemic,[6] the EMA, EC, and FDA are more closely partnered through the International Coalition of Medicines Regulatory Agencies and committed to other intermediary bodies and programs to strengthen ties and thought-leadership. While still having a far way to go, the work to narrow the divide in access across hemispheres—and consequently within hemispheres and the EU as the authors argue—continues to strengthen with an FDA Europe Office acting as a node to drive stronger relations and parallel activates between the two.[7] With time, it's hoped both will begin to close the gap among access between and within their regions.

As far as disparities within the EU, an important step forward has been the development and promulgation of Europe's Beating Cancer Plan in 2020.[8] While not entirely prescriptive, and with equal access to treatment as only one of the four prongs, it highlights the grave need for the EU in harmonizing access across its geopolitically and socioeconomically diverse landscape. The ultimate action taken by such initiatives will determine whether there's success, but the commitment offers enthusiasm that access to novel NSCLC therapeutics in the future may be greater, especially if these campaigns become duplicated or furthered by political and agency bodies in the future.

Contributors

Eric Brooks contributed with conceptualization, investigation, methodology, resources, visualization, project administration, writing the original draft, reviewing and editing. Alexandra De Leo contributed with investigation, validation, writing the original draft, reviewing and editing.

Declaration of interests

All authors declare no conflicts of interests.

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