The impacts of biomarkers on precision medicine at AstraZeneca

An interview with Omar Perez

Q1. How has precision medicine impacted oncology at AZ – e.g., not only NGS but also pan-omic modalities for biomarker and drug development?

A. At AstraZeneca, our ambition is to dramatically accelerate biomarker testing across all tumor types and cancer stages by 2025. Regardless of care setting, tumor type, or disease stage, every person should have access to timely, accurate information about the unique qualities, or genetic mutations, causing their specific cancer. We focus where it matters most by aiming to treat disease earlier and working to unleash new treatments for precise targets to make sure patients get the right medicine at the right time.

Our commitment to precision medicine is evident in our clinical pipeline, our successful development of new drugs, and our investment in diagnostic partnership initiatives. Today, approximately 90% of our pipeline takes a precision medicine approach.[1] With precision medicine applied to a large share of our clinical pipeline, we have the portfolio and the pipeline to make a difference.

Q2. How have biomarkers affected the development and validation of diagnostics used in clinical trials? Likewise, how have biomarkers affected the drug development and selection process?

A. Since 2005, the number of FDA-approved targeted therapies has increased dramatically.[2] In the first six months of 2020, the FDA approved 21 targeted oncology medicines, exceeding its total number of targeted therapies for the full year in 2019.[3] And the progress hasn't stopped with 42% of all agents in clinical development being targeted medicines.[4,5] Oncology is leading the field with targeted agents comprising 73% of the oncology agents in clinical development.[4,5]

Q3. What barriers have AstraZeneca overcome to achieve biomarker testing in oncology? What barriers remain and how is AstraZeneca addressing these barriers?

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A. We've identified a number of barriers that occur along the oncology care continuum and are setting out to help deliver tangible change and progress across three main areas: evidence generation, education, and access and policy.

First is ***evidence generation***; solutions to address inadequate testing must be based on real-world data and generating evidence that demonstrates the value of precision medicine. As an organization, we are collecting and analyzing data to generate evidence that will help guide decision-making around tangible solutions to address barriers to biomarker testing. An example of this is the work we're doing as part of the MYLUNG consortium to evaluate biomarker testing rates in patients with non-small cell lung cancer within community centers, as well as implement specific intervention protocols to improve access to biomarker testing and utilize quality measures to monitor this effectively within community practices.[6]

The second area is ***education***, because we know that a lack of knowledge and poor communication among stakeholders are key barriers to optimal testing.[7-10] To address this education barrier, we are supporting efforts that raise awareness, educate, and inform patients, policymakers, and healthcare providers about precision medicine and biomarker testing.

We are leading and participating in several educational efforts, including *No One Missed*, *Complete Your Diagnosis, YOUR Cancer*, and many others. One of my personal favorites is the *No One Missed* campaign, which we helped launch earlier this year to empower patients and caregivers to request comprehensive biomarker testing from their healthcare team at the time of diagnosis, recurrence, or progression. This campaign also includes a first-of-its-kind lung cancer patient's bill of rights for understanding critical biomarker test results to help inform treatment options.

Our third and final area of focus is ***access and policy***. Coverage for biomarker testing in the US is failing to keep up with innovation, potentially leaving large coverage and access gaps.[11] We are working with policy and decision-makers to solidify access and integrate biomarker testing into policies, practices, and care delivery models.

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Q4. How can pharma companies collaborate with other stakeholders to improve biomarker access for patients?

A. Achieving our ambition of redefining cancer care by accelerating biomarker testing across tumor types is just one piece of the puzzle. To drive meaningful change for those affected by and living with cancer, multidisciplinary collaborative approaches to solving complex issues like biomarker testing can only be accomplished through the collective expertise of the whole oncology community. We are finding opportunities to partner and collaborate to address some of these challenges together.

Our focus centers around three areas: identifying and supporting specific policy solutions to remove barriers; expanding access to precision medicines; and improving patient outcomes. Our guiding principle in these areas is collaboration. With progress underway, we are optimistic and strongly committed to continuing to collaborate with patient advocacy groups, legislators, the oncology medical community, and others to help drive policy change to advance precision medicine and help enable its full potential to positively impact the lives of patients living with cancer.

Q5. How has the COVID-19 pandemic impacted precision medicine and cancer care for better and/or worse? For example, could processes such as emergency use approval more readily accelerate treatments for cancer to the clinic? Has avoidance of scheduling appointments made more patients delay detection and early intervention?

A. The COVID-19 pandemic has had a

significant effect on cancer care due to fear, facility shut-downs, and other factors, making patients unable or reluctant to visit physicians for routine wellness and preventive screenings.[12] This is impacting the prospect of early diagnosis and, consequently, improved patient outcomes.[13] Throughout the pandemic, many patients with diagnosed cancer also discontinued treatment, due to a myriad of reasons, such as appointments being delayed, screening being deprioritized in an overburdened healthcare system, and to reduce the risk of spreading COVID-19.[14,15] These issues lead to disruptions in treatment initiation and continuation, as well as in biomarker testing, a critical step in determining an individual's biomarker status to inform treatment decisions.[16]

There is, however, a silver lining – and that is the pandemic has forced the medical community to think and act differently, to deliver new innovations in the face of complicated challenges brought on by the pandemic. It is our belief that these innovations and changes, brought about by the pandemic, could result in better overall cancer care.[17]

Positive changes have been identified in such areas as: value in cancer care, digital communication, convenience, inclusivity and cooperation, decentralization of cancer care, acceleration of policy change, human interactions, hygiene practices, health awareness and promotion and systems improvement.[17]

In Brazil, for example, we worked with our clinical trial collaborators to introduce at-home testing to check patients for cancers with EGFR mutations, which has now been replicated in other countries.[18]

Q6. How do you see the future direction of precision medicine in the following areas:

Applications to other therapeutic areas – e.g., inflammatory, respiratory and other diseases?

A. Understanding immune responses as a function of disease is an area of active research. Immune-related signatures to better identify the appropriate treatment for patients or evaluate mechanisms of resistance are a major focus of translational efforts.

Discovery/development of new drug modalities – e.g., cell-based therapies? Others?

A. Precision medicine has been incorporated into over 90% of our portfolio.1 New modalities, such as antibody drug conjugates and cell-based therapies, require a better way to help identify patient populations that may be likely to respond. AstraZeneca has active developments utilizing liquid biopsy technologies for patient identification, minimal residual disease monitoring, and early cancer detection.

Novel biomarkers and diagnostics, particularly for companion diagnostics?

A. There are advancements for AI-driven multi-analyte assessments and AI-driven digital pathology efforts to improve the diagnosis of patients with cancer and improve cancer screening for earlier detection. These efforts are making their way through the regulatory process, and we anticipate future approvals in this space. JPM

Dr Omar Perez

Omar has over 17 years of experience in designing, deploying, and leading high-visibility oncology initiatives supporting global companion diagnostic developments, strategic partnerships and commercialization opportunities. Before joining AstraZeneca, he oversaw the global CDx developments for the GSK oncology portfolio. During his time at Pfizer, he led global CDx activities supporting various drug approvals. Notably, he led the first FDA-approved NGS product for multiple targeted agents and helped establish the Center for Precision Medicine in LATAM to support Pfizer oncology products. Dr. Perez's background includes roles in biotech and diagnostic companies, including co-founding Nodality, a diagnostic company focused on hematological malignancies. He is an inventor of the multiparametric phospho-proteomic flow technologies and an author of 37 publications and 35 patents.

About AstraZeneca:

AstraZeneca is leading a revolution in oncology with the ambition to provide cures for cancer in every form, by following the science to understand cancer and all its complexities to discover, develop and deliver life-changing medicines to patients. The Company's focus is on some of the most challenging cancers. It is through persistent innovation that AstraZeneca has built one of the most diverse portfolios and pipelines in the industry, with the potential to catalyze changes in the practice of medicine and transform the patient experience. AstraZeneca has the vision to redefine cancer care and, one day, eliminate cancer as a cause of death. At AstraZeneca, our precision medicine ambition is to dramatically accelerate biomarker testing across all tumor types and cancer stages by 2025. It is our firm belief that – regardless of care setting, tumor type, or disease stage – every person should have access to timely, accurate information about the unique qualities, or genetic mutations, causing their specific cancer. This vision can become a reality with the acceleration of biomarker testing in the US.

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