Review Article

Novel Therapies in Cancer: Summit on Cancer Health Disparities, Keynote and Panel Discussion

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Molecularly-targeted therapeutics play a pivotal role in the therapeutic arena in cancer medicine, in many cases prolonging overall survival. However, despite decades since their foray into the cancer therapy armamentarium, many targeted therapies are beyond the reach of cancer patients due to high, sometimes exorbitant cost. Moreover, in some cases failure of uptake of targeted therapies is due to the lack of use of sophisticated molecular diagnostic tests (many of which are also extremely expensive), and therefore patients are deprived of potentially life-saving treatment options. In this article, we will discuss the main points of Dr. Jerry Radich's lecture at the Binaytara Foundation 2023 summit on cancer health disparities held in Seattle, WA from April 28 to April 30. Dr. Radich's keynote address was followed by a panel discussion led by experts including Dr. Parameswaran Hari, Dr. Lidia Schapira, Dr. Manali Patel, Sydney Osborne, and Dr. Linda Armstrong. Dr. Mark Pegram moderated the session, which focused not only on the disparities in cancer treatment in low- and middle-income countries (LMIC), but also highlighted great disparities here in the U.S. The session explored collaborative efforts at uprooting these disparities across various branches of cancer care.

Take Home Message

- Together we rise- If we envision a mission on humanitarian grounds, nothing is implausible if it comes from a prudent determination to improve cancer care worldwide.
- Novel therapies will continue to remain novel unless we collectively voice and navigate the obstacles in their perpetuation globally.
- Just like the phrase, "each and every drop counts", similarly each and every voice matters, be it physicians, support groups, patients and their caregivers, pharmaceutical companies, policymakers and many more in the pathway of healthcare equity. After all, no one should suffer from, or succumb to cancer by being bereft of life-prolonging resources.

The session began with our keynote lecturer Dr. Jerry Radich who shared his real-life logistical and diagnostic obstacles over the delivery of tyrosine kinase inhibitors (TKIs) to LMIC for CML. Chronic Myeloid Leukemia (CML) is a myeloproliferative disorder characterized by dysregulated proliferation of hematopoietic progenitor cells in the granulocyte lineage. It accounts for 20% of all leukemias affecting adults, with a slight male predominance.[1]

CML has made a historical landmark since it became the first known disease with an identifiable chromosomal anomaly. It arises from a reciprocal translocation between chromosome 9 and chromosome 22; t(9;22), resulting in the fusion of two genes: BCR::ABL1, termed the Philadelphia (Ph) chromosome. Its origin dates to 1960 when Drs. Nowell and Hungerford examined cancer cells from two CML patients and noticed one of the 46 chromosomes was abnormally short. This drove them to look for more CML cells from other cancer patients. This abnormal short chromosome later became known as "the Philadelphia chromosome", named after the city where it was discovered. It encodes for a chimeric protein with aberrant, constitutively active, potent tyrosine kinase activity.[2]

Dr. Radich racontoured the optimistic therapeutic transition with the evolution of TKIs and the hardships endured in making these accessible to the far-reached population in LMIC. As history unfolds, CML therapy was initially restricted to busulphan and hydroxyurea before the 1980s. During the period of 1980s-1990s, allogeneic stem cell transplantation and interferon alfa were the treatments of choice.[3] A revolutionizing life-prolonging turnaround occurred after the year 2000 with the introduction of imatinib

mesylate, the first TKI that specifically targeted the BCR-ABL1 oncoprotein.[4] TKIs have significantly increased the survival rate and quality of life of patients of all ages, making it comparable to that of the general population. The second-generation (2G) TKIs, namely nilotinib, dasatinib and bosutinib are approved as a treatment for CML and are able to overcome the resistance mechanisms to imatinib.[5,6]

After the discovery of TKIs, a question arose regarding their global accessibility, particularly for people in areas without adequate diagnostic technology. Even though imatinib became generic in February 2016, the expense burden of TKIs remains an obstacle. The annual costs in the United States range from $4,400 to $82,000, and outside of the United States, they range from $2,000 to $8,000.[7] Escalating TKI price and high out-of-pocket expenditure place financial pressure on patients, which may manifest as an increased risk of CML-specific death in low-income patients. This finding supports the need for policy interventions that mitigate the financial burden of cancer.

Pat Garcia-Gonzalez, the CEO and co-founder of the Max Foundation, made a noteworthy philanthropic contribution by launching the Gleevec International Patient Assistance Program (GIPAP) with her unwavering determination. GIPAP successfully supplied over 63,000 CML patients from about 93 countries with daily doses of Imatinib between 2001 and 2014. After years of challenges and difficulties, this story became a momentous success. Having lost her stepson Max to CML within three years of diagnosis, Ms. Garcia-Gonzalez was undeterred in ensuring no CML patient faced barriers in procuring the life-saving drug. She contacted Novartis (the manufacturer of Gleevec (imatinib), who agreed to provide a lifetime supply of Gleevec to patients who could not receive the drug after being diagnosed with CML. However, the next impediment that stood in her path was that people from developing countries could not easily be tested for CML as they did not have access to a diagnostic molecular laboratory.

Pat Garcia-Gonzalez connected with Dr. Radich through one of his former patients, which led to a collaboration to bring cutting-edge therapies to the world of CML globally. The first-ever fresh blood sample was sent to Dr. Radich's Fred Hutch's Molecular Oncology Laboratory in Seattle from El Salvador to be tested for CML. This marked their successful international cooperative efforts. Nevertheless, not all patients could afford the one-time cost of sample shipment to Seattle, costing about $500-600. This opened a gateway for partnership with Cepheid, Inc. (Sunnyvale, CA) to establish reduced-cost molecular diagnostic machines that conduct real-time PCR assays for BCR::ABL fusion genes. However, what if it's still challenging to afford Cepheid-based diagnostic tests in certain countries? Dr. Radich's team always thought a step ahead. Their goal was to test as many CML patients as possible, improving CML diagnostics in even the most remote parts of the world. "The mind, once stretched by a new idea, never returns to its original dimensions," - Ralph Waldo Emerson, truly justified their states of mind. Dr. Radich in collaboration with his laboratory researchers including Mr. Jordan Smith, developed a cost-efficient paper-based test that could be sent via surface mail across borders with dried blood samples of patients to be tested for CML. These samples were first sent from designated CML patients in Adelaide, Australia via an ordinary postal system that cost a mere 68 cents and was sufficient to accurately confirm the presence of the Ph chromosome. Such was the power of innovative minds at work.

As the saying goes, Rome was not constructed in a single day. The story features the joint efforts of a woman with a strong vision for change, a physician and his team of researchers, patients, and their relentless support groups, a pharmaceutical company, and diagnostic laboratories. Together, they all worked towards a joint mission on humanitarian grounds. Ms. Garcia-Gonzalez firmly believed that every test played a crucial role in saving lives through her compassionate actions. She continues to be the voice of thousands of people with CML worldwide. Because she firmly abides by the fact that everyone deserves access to treatment and support regardless of their location. Today, we have entered an era where the efforts put into perpetuating treatments for CML have paid off. As a result, CML patients now have as high a chance of survival as the general population.

In the second session on Novel Therapies in Cancer, a vibrant interactive panel discussion was convened by an expert panel of speakers, namely Dr. Parameswaran Hari, Dr. Lidia Schapira, Dr. Manali Patel, Sydney Osborne and Linda Armstrong, addressing disparities in seeking healthcare. The session was moderated by Dr. Mark Pegram, who is Professor and Medical Director of the Clinical and Translational Research Unit, and Associate Dean for Clinical Research Quality at Stanford University in Palo Alto, CA. In addition, Dr. Pegram's cancer research is focused on studying the cancer-associated gene that encodes HER2 and developing novel agents to treat patients with HER2-positive cancers, particularly breast cancer.

The first to comment in the panel discussion, Dr. Schapira, led the conversation as a prominent figure in the Stanford University School of Medicine's cancer survivorship program. Her goal is to improve the quality of life for patients and their caregivers living with and beyond cancer. Growing up in Argentina, she understands firsthand how one's living environment influences healthcare, which can have a significant impact. She believes in the importance of collaboration and involvement from all members of society to ensure that everyone benefits from scientific research and its implications. In doing so, she underlined the potential of motivated, creative minds to use the resources available to them and create something extraordinary. She believes that effective communication can be achieved through mass engagement by presenting a narrative with a clear mission, plan of action, solutions to challenges, and ultimately reaching the desired outcome of equity in healthcare.

The next discussant to share her eye-opening thoughts was Dr. Manali Patel. She grew up in Shelby, North Carolina. She has served as a Chair of the Equity Committee under the American Society of Clinical Oncology (ASCO). She is a thoracic oncologist at the Veterans Affairs Clinic in

Palo Alto, CA. Based on her own experience, she noted that there is a significant difference in estimated life expectancy just a few miles away in East Palo Alto. Residents of East Palo Alto lack access to quality healthcare due to limited resources. As a physician, she firmly believes that taking responsibility for advocating for your patient's care is essential. This includes negotiating prices and meeting with stakeholders like policymakers, community health workers, and payers. Dr. Patel remarked that one should speak up for policy changes that benefit patient welfare. At the end of her comment, she concluded that the people at the table and those with access to it or even a seat at it are crucial factors. An example of some success in controlling patient care costs is the Pharmaceutical Pricing Agreement in the Veteran's Administration, which is able to negotiate more affordable drug costs for the VA constituency.

The next successive narrator, Dr. Parameswaran Hari, was raised in Kerala, a state on the Malabar Coast of southwest India. As a myeloma specialist and current Chief Development Officer at Obsidian Therapeutics, he has experience as both a physician and a dedicated scientist. Kerala has one of the highest levels of background radiation from its thorium-containing Monazite sand, so Dr. Hari observed many cancer cases in all age groups. He discussed how improved technology can significantly reduce the cost of treatment. He shared his personal experience with the approval of ruxolitinib for myeloproliferative disorders. He observed that patients who received ruxolitinib also were at risk to develop tuberculosis, which led him to speculate that it may be related to perturbation of T cells. He noted the potential benefits of collaborating with other countries to gain valuable insights and knowledge from clinical research. Such research can yield valuable pearls of wisdom that are beneficial to all parties involved.

For the panel discussion, Dr. Pegram made a special request for frontline representation from pharmaceutical companies. To do so, special arrangements were made to accommodate industry participation in a Continuing Medical Education (CME) conference, including the Binaytara Foundations' foregoing of some industry sponsorship of the conference. As a result of these efforts, Sydney Osborne from Seagen and Dr. Linda Armstrong from Novartis were invited to speak and share their perspectives. Ms. Sydney is head of Healthcare and Payment Policy and Provider Advocacy at the Seagen. At Seagen, she is a vital member of the patient support group programs. These programs provide patients with emotional, financial, and psychosocial support during complex journeys through cancer diagnosis and treatment. In addition, she is dedicated to helping patients navigate these challenges seamlessly. Additionally, she expressed appreciation for the Inflation Reduction Act, which aims to revitalize Medicare's Part D program that has been in place for over a decade. One of the most significant outliers addressed is the $2,000 limit on annual Part D out-of-pocket prescription costs beginning in 2025.

Dr. Armstrong, a former pulmonologist, is currently the Novartis Foundation President and leads the US Corporate Responsibility team. She provides an example from Sub-Saharan Africa, where the stigma surrounding sickle cell disease could be overcome through collaborative efforts among pharmaceutical and diagnostic laboratories to raise awareness in remote, isolated areas. She led our direction toward how now all phase III trials would be required to have a diversity plan to be representative of the overall population characteristics and traits. Finally, she discussed a solution that involves a 10-year commitment from pharmaceutical companies and non-governmental organizations to support medical schools of the nation's Historically Black Colleges and Universities (HBCUs) and Predominantly Black Institutions (PBIs) in the USA. This commitment will ensure education, scholarships, mentorships, maintenance of clinical trial centers, promotion of research, creation of unbiased clinical algorithms, and sustainable development of future physicians. At the end of her remarks, she cites former White House Chief of Staff (under the Obama administration), Rahm Emanuel's statement, "You should never let a serious crisis go to waste." As an example, COVID-19 was a severe health crisis that globally unveiled major healthcare disparities. Thus, we need to work together as one team while eyeing our goal of equitable solutions.

CONFLICT OF INTEREST

Dr. Mehndi Dandwani: none.
Dr. Mark Pegram: none.
Dr. Jerry Radich: none.
Dr. Lidia Schapira: has served as advisor to Blue Note Therapeutics and as consultant to Novartis.
Dr. Manali Patel: none.
Dr. Parameswaran Hari: none.
Sydney Osborne: none.
Dr. Linda Armstrong: is an employee of Novartis Pharmaceutical Company.

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ETHICAL STATEMENTS

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AUTHOR CONTRIBUTIONS

i. All authors: conception and design
ii. All authors: data collection and assembly
iii. All authors: data analysis, manuscript writing
All authors have approved the manuscript

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