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COMMENTARY

Bridging the Knowledge Gaps in Cancer Medicine: A Call for Precision, Equity and Real-World Evidence

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Dear Colleagues,

Cancer medicine has achieved remarkable advancements in recent years, driven by innovations such as immunotherapy and artificial intelligence (AI)-based technologies, paving the way for personalized treatments. Yet, significant gaps remain that limit our ability to ensure that all patients benefit equally. These gaps span tumor biology, translating clinical trials into real-world solutions, addressing health equity and supporting long-term survivorship care. Bridging these challenges requires a collaborative, focused approach to enable sustainable and meaningful transformation in cancer care.

The biology gap: Understanding tumor heterogeneity

Tumor heterogeneity remains one of the most significant barriers to advancing precision medicine.[1] Variability within and between tumors complicates predictions about treatment efficacy and contributes to resistance.[2] Tools such as liquid biopsies and single-cell sequencing are advancing our ability to detect minimal residual disease (MRD) and resistant cell populations.[3] These tools are critical for identifying problematic subclones and overcoming treatment resistance. B-cell malignancies highlight this challenge, particularly with covalent Bruton's tyrosine kinase (BTK) inhibitors such as ibrutinib, which can lose effectiveness due to mutations like *C481S*.[4] Third-generation inhibitors such as pirtobrutinib are tackling this problem by targeting both wild-type and mutant BTK proteins. Clinical trials have shown pirtobrutinib's promise in heavily treated cases of mantle cell lymphoma (MCL) and chronic lymphocytic leukemia (CLL).[5] Such innovations underscore the power of precision medicine in addressing resistance pathways and improving outcomes, offering hope for tackling similar challenges in other cancers.[5]

The real-world evidence (RWE) gap: From trials to practice

Real-world evidence (RWE) plays a pivotal role in closing the gap between clinical research and practical application. While clinical trials remain the gold standard, their narrow inclusion criteria often exclude frail or comorbid patients, leading to an incomplete understanding of treatment effects across diverse populations.[6] The ECHO trial successfully used RWE to study a

regimen of acalabrutinib, bendamustine and rituximab in older MCL patients, demonstrating improved progression-free survival with manageable side effects.[7] Similarly, studies on immune checkpoint inhibitors (ICIs) have highlighted how RWE can provide valuable insights into the safety and efficacy of treatments for underrepresented groups, such as older patients.[8] By integrating RWE with clinical insights, we can ensure that advances in cancer care are inclusive and effective for vulnerable populations.[6]

The health equity gap: Who gets access to innovation?

Health equity remains one of the most pressing challenges in oncology. Disparities in access to advanced treatments disproportionately affect marginalized populations, particularly in low- and middle-income countries (LMICs) and underserved communities within wealthier nations.[9] Chimeric antigen receptor (CAR) T-cell therapies exemplify this inequity, with high costs creating significant barriers to access.[10] Marginalized groups are often excluded from such innovations.[10] Promising efforts like allogeneic CAR T-cell therapies may lower costs, but systemic hurdles persist.[11] Achieving equity in cancer care requires systemic changes, including inclusive clinical research and policies, to ensure treatments reach all patients regardless of socioeconomic or geographic barriers.[12]

The survivorship gap: Addressing long-term toxicities

Cancer survivors often face lasting challenges, from cardiovascular issues and neurocognitive impairments to emotional distress and fatigue. These long-term toxicities highlight gaps in survivorship care, which leave many to manage chronic complications without adequate support. Immunotherapy, such as ICIs, has revolutionized outcomes for cancers like melanoma.[8] However, immune-related adverse events can persist for years, undermining the benefits of these therapies if not addressed. An integrated approach to survivorship care, combining oncologists, cardiologists, mental health professionals and tools such as digital platforms and personalized lifestyle programs, is essential for improving survivors' quality of life and ensuring holistic, long-term support.[13,14]

Moving forward: A call for action

To transform cancer care, we must address barriers directly. Inclusive research is crucial to represent diverse populations and meet the needs of underserved communities.[9] Collaboration across academia, industry and healthcare systems is key to turning breakthrough innovations into life-saving treatments. Accelerating investments in AI and digital health can refine real-world data and solve emerging challenges.[15] Policy-driven solutions are vital to ensure that advanced therapies are accessible to all, not just the privileged

few. At this pivotal moment, closing the gaps in equity, collaboration and research is essential. Together, we can unlock the future of cancer care, transforming lives with equitable medicine.

Sincerely,

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Conflict of interest

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