Advances in the Care of Adult Patients With Acute Lymphoblastic Leukemia: Optimism Tempered by Reality

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Outcomes for patients with acute lymphoblastic leukemia (ALL) have improved dramatically over the past 4 decades. Overall 5-year relative survival rates for patients with ALL have increased from 40.6% during the period between 1975 and 1977 to 70.7% for patients treated between 2006 and 2012. A series of advances in the treatment of childhood ALL—from single-agent chemotherapy in the 1950s to the use of risk-adapted therapeutic strategies—have helped to drive improvements in care and outcomes for patients of all ages (Figure 1).

The foundation for improvements in survival outcomes for patients with ALL is data generated from rigorous, iterative clinical trials. Pediatric clinical trials, in particular, have been extraordinarily successful in identifying treatment strategies associated with higher cure rates. Part of what has made pediatric clinical trials so central to advances in the care of patients with ALL is that this patient population is able to access care through a coordinated network of linked clinical and research sites; unlike adult patients with cancer, approximately 90% of children with cancer receive care at participating Children’s Oncology Group sites. It would be difficult to overstate the importance that this systematic approach to care delivery has had in advancing ALL treatment outcomes. Childhood ALL therefore provides an excellent paradigm for the rapid and successful evolution of the standard of care for a blood cancer.

Although the improvement in outcomes has been impressive, we are at the threshold of an even more dramatic period of change for patients with ALL. This exciting era has been facilitated by our increasing ability to harness genetic, molecular, genomic, and proteomic data to tailor therapeutic strategies for individual patients, exemplifying the extraordinary potential of “precision medicine.” The use of targeted therapeutic agents, such as tyrosine kinase inhibitors (TKI) for patients with Philadelphia chromosome (Ph)–positive ALL, and risk-adapted care strategies that leverage assessments of minimal residual disease (MRD) to enhance decision-making regarding

![Figure 1. Pediatric acute lymphoblastic leukemia: dramatic improvement in patient outcomes over time. Abbreviation: CNS, central nervous system.](image)
Despite the fact that a number of targets are under investigation for patients with Ph-like ALL, a subset of ALL that is ineffectively treated by existing therapeutic regimens. Patients with ALL are also likely to benefit in the coming years from the expanding array of immune-oncologic agents. The recent reports of efficacy of the monoclonal antibody rituximab, the immunoconjugate inotuzumab, the bispecific T-cell engaging (BiTE) antibody blinatumomab, and various chimeric antigen receptor (CAR) T-cell products foreshadow the potential for immune-oncologic agents to change the treatment paradigm for patients with ALL. As these and other trial results are published, our understanding of how best to treat patients with high-risk, persistent, and relapsed ALL is likely to change profoundly.

Inasmuch as there is cause for significant optimism regarding future treatments for patients with ALL, this optimism must be tempered by the reality that not all patients will be able to reap the benefit of these advances. A large part of what has made the care of pediatric patients with ALL a success story is the system of care that has allowed patients to benefit equitably from advances in treatment technology and access to the requisite clinical expertise. Unlike most pediatric patients, however, adult patients cannot avail themselves of a single, coordinated care and clinical trials network. Instead, adults diagnosed with ALL face significant challenges in navigating a care system that remains highly balkanized and difficult to navigate, making access to innovative diagnostic and therapeutic technologies elusive. Despite expansion of insurance coverage to many previously uninsured patients, gaps within the coverage system may actually prevent many patients from receiving the expert care they require. Narrow health care networks, in which patients are limited regarding which hospitals and physicians may provide their care, frequently exclude academic specialty centers or ALL centers of excellence. In a 2015 article reviewing the impact of narrow networks on access to expert cancer care, the author noted that, “Of 19 nationally recognized comprehensive cancer centers surveyed, only 4 said they were in all the insurance networks on their state exchange.” Despite the fact that a key factor for the successes of pediatric ALL outcomes has been based on access to a robust system of care, many adult patients are disenfranchised from benefiting from this essential resource.

Beyond health care infrastructural barriers, the high cost of targeted therapeutic agents and the growing patient financial burden associated with these costs imposes another set of barriers to patients accessing effective antileukemic care. As The Washington Post recently noted, “the $10,000-a-month cancer drug has become the new normal, to the dismay of physicians and patients who increasingly face the burden of financial toxicity.” As health care systems grapple with the questionable economic sustainability of administering prohibitively expensive pharmaceuticals, patients are burdened with egregious costs as they shoulder the life-changing copayment and co-

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insurance bills associated with these agents—bills that are the individual patient’s financial responsibility.\(^7,8\) The lack of reimbursement parity between oral and injectable pharmaceutical agents makes this burden even worse for patients receiving targeted oral agents.\(^9\)

As we advance toward a future of precision medicine solutions for patients with ALL, we need to ensure that this lofty vision is not undermined by the prosaic limitations of infrastructural and financial barriers imposed by our often-disorganized systems of care. The challenge that patients with ALL face is not one that can be remediated by science alone. It requires us as physicians, nurse practitioners, nurses, and health care professionals to become advocates not only for our patients, but also for systems-based change that can ensure that every patient diagnosed with ALL can benefit fully from the breadth of scientific knowledge and innovative therapeutic alternatives.

The IOM has characterized the 6 key characteristics of highly effective health care, and include care that is safe, effective, efficient, equitable, timely, and patient-centered.\(^10\) If we are ever to achieve care delivery for every patient with ALL who meets the IOM aims of care, then we will require the use of support tools, such as the NCCN Guidelines, to ensure that all patients can benefit equitably, sustainably, and transparently from the rapidly evolving wealth of ALL therapeutic innovation. Clinical practice guidelines not only may help practitioners master the rapidly evolving armamentarium of leukemia care innovations, but also may constitute an important set of tools for achieving more efficient, economically sustainable delivery of leukemia care in the process.\(^11\)

References