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Preface

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Over the course of the last several months, following the invitation to guest edit this special issue, I have thought several times about what makes this the right time to investigate – in depth – our understanding of therapy-related myeloid neoplasms. I believe that we are currently poised at the nexus of several forces which are indelibly impacting patients diagnosed with these conditions: (1) an increasing number of individuals surviving their index condition, (2) an increasing number of non-cytotoxic options for cancers and (3) a rapidly accelerating understanding of pre-disposing conditions, conditions which play a much more important role in the pathophysiology of therapy-related myeloid neoplasm (t-MN) than any of us previously imagined. I am thrilled that with this issue, thanks to contributions from so many distinguished authors, we can present comprehensive reviews which contextualize these forces for readers and provide insights relevant to both clinical practice and translational research.

As those who practice in this field are well aware, traditional cytotoxic chemotherapy works because it selectively kills cells that duplicate quickly. Countless individuals around the world have lived longer, disease-free lives because of the prudent and appropriate use of agents like nitrogen mustard, cyclophosphamide or doxorubicin – cytotoxic agents which either were sufficient in and of themselves to induce remission and eventual cure or could achieve that end after being combined with radiation or surgery. Indeed, it's only because these agents are effective that one needs to consider the problem of t-MN. The success of adjuvant therapy for breast, testicular or non-Hodgkin Lymphoma means that more individuals live long enough to develop consequences like t-MN. A recent SEER study demonstrated just that – compared to the first part of this century (2001–2007) the incidence rate of therapy-related myeloid neoplasm from 2008 to 2014 increased 5-fold, from 0.04/100,000 to 0.20/100000 [1].

And yet, we are also seeing rapid changes in the paradigms of treatment. So-called targeted therapies, or agents that selectively damage cancer cells based on differences other than duplicative frequency, are flooding the clinic. Successful deployment of agents like immunotherapies, hormonal blockade, antibody-drug conjugates or small-molecule inhibitors are beginning to allow for de-escalation of cytotoxic therapy. One need only look at chronic lymphocytic leukemia, myeloma or even breast cancer to see that the future will mean a reduction in exposure to agents like alkylating agents or topoisomerase inhibitors. This trend should theoretically decrease the rates for t-MN in the future.

And then we have the third force at work – our growing understanding of baseline conditions like germline polymorphisms or clonal hematopoiesis. These conditions, present at birth or developing as we age, may have much more to do with the likelihood of developing therapy-related disease than the therapy itself. Discoveries like those described in the reviews here are the kind of revelations that permanently change the way we think of disease.

We have structured this issue such that while each submission can stand on its own, as a package they tell the story of these forces at work. We begin with an overview article. This clinicopathologic review will introduce readers to topics of key importance in a practical way. Following that, we are lucky enough to have leaders in the field of predisposing conditions explore the topics of clonal hematopoiesis, germline polymorphisms and the stem-cell niche. The issue then includes thorough reviews of the risks for therapy-related disease for individuals with a variety of index conditions: solid tumors, lymphoma, plasma-cell neoplasms, myeloproliferative disease and even auto-immune conditions. Each should provide the practicing clinician with a current assessment of the risks faced by the patients they are treating. We conclude with reviews on choosing induction therapy, how to manage p53-mutated disease and whether and when allogeneic stem-cell transplantation is useful.

I want to sincerely thank our authors. I learned so much from reviewing these contributions and I'm proud and pleased to be able to share their work with our readers. I am convinced that, years from now, this moment in time will be identified as a tipping point in our understanding of therapy-related myeloid disease. I imagine each of you is as grateful as I am to be witness to this kind of change.

Conflicts of interest

Laura C. Michaelis has received research funding from JAZZ pharmaceuticals and worked as a consultant to Incyte, Celgene, TG Therapeutics and Novartis.

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