

Numerous treatment options have emerged for lymphomas, but there are still considerable challenges to be tackled to increase the chances of long-term survival.

BY MICHAEL EISENSTEIN

LYMPHOMA

4 BIG QUESTIONS

QUESTION	WHY IT MATTERS	WHAT WE KNOW	NEXT STEPS
<p>1 <i>Will immunotherapy rewrite the prognosis for recurrent lymphoma?</i></p>	<p>For many patients, first-line treatment buys little or no relief, and relapsed or refractory disease entails more-intensive treatment and a worse outlook. Therapies that reprogram immune cells to attack cancer could deliver longer-lasting recovery.</p>	<p>Two chimeric antigen receptor T-cell therapies (CAR-T therapies) are available for certain non-Hodgkin's lymphomas. Last year, a trial reported that more than half of the participants achieved complete remission, with at least one still cancer-free two years on.</p>	<p>Dozens of trials of CAR-T therapy for B-cell lymphomas are underway. Some are exploring alternative targeting approaches to adapt the treatment to different forms of the disease. Others aspire to mitigate toxic side effects.</p>
<p>2 <i>Can real-time monitoring help oncologists stay a step ahead in lymphoma treatment?</i></p>	<p>Clinicians need to understand the nature and extent of a patient's cancer to manage treatment, but existing tools have limitations. Biopsies are invasive and offer a limited view of the tumour, whereas imaging can generate false positives and requires repeated radiation exposure.</p>	<p>At least three studies indicate that monitoring circulating tumour DNA (ctDNA) in blood might be a powerful complement to imaging in terms of assessing treatment efficacy for diffuse large B-cell lymphoma. And ctDNA levels could give an early indication of disease recurrence.</p>	<p>Researchers have obtained promising preliminary results for ctDNA-based methods in Hodgkin's lymphoma and other diseases. But the accuracy of such assays needs to be carefully validated before they can reach the clinic.</p>
<p>3 <i>How can treatment of early-stage Hodgkin's lymphoma be tweaked to improve long-term outcomes?</i></p>	<p>The standard therapy, in which patients receive multiple rounds of chemo- and radiotherapy, delivers excellent cure rates for Hodgkin's lymphoma. But survivors face a heightened risk of complications such as heart disease and further malignancies in the decades that follow.</p>	<p>Radiotherapy is a major source of toxicity. Some studies indicate that forgoing it might not meaningfully reduce overall survival in early-stage disease, possibly because of a reduced chance of death from treatment-related causes — but some such studies used outdated regimens.</p>	<p>It might be possible to identify which patients will benefit the most from chemotherapy alone. Trials are also exploring whether some second-line treatments might make safer first-line treatments.</p>
<p>4 <i>Can allogeneic stem-cell transplantation be made safer?</i></p>	<p>Stem-cell transplantation is a last resort for recurrent lymphoma. Patients who are ineligible for transplantation with their own stem cells must receive cells from a donor — but there is a high risk that they could develop graft-versus-host disease (GvHD).</p>	<p>Chronic GvHD is a major cause of mortality. But the 2017 approval of ibrutinib, which blocks production of GvHD-exacerbating B cells, has shown that it's possible to make transplantation safer. Other therapies in development might make transplantation more attractive.</p>	<p>Studies suggest that the infusion of regulatory T cells derived from umbilical cord blood can limit rejection in transplant recipients. Scientists are exploring whether such infusions can prevent GvHD.</p>

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