# Considering a Bone Marrow Transplant

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**Andrew Schorr:**
Great.

So there [are] some interesting, and quite possibly, powerful therapies being explored in clinical trials, including ABT-199, CAR T-cell therapy and novel combination drug therapies. What are the pros and cons of continuing with therapy versus a bone marrow transplant?

**Dr. Thompson:**
This is one of the commonest dilemmas that we face in the clinical, actually, in that we have patients with CLL that maybe have high-risk features that are doing well on these new therapies, and we have to decided should we or should we not refer a patient for a bone marrow transplant? Bone marrow transplant is the only treatment that's ever been proven to cure high-risk CLL. By high risk, I mean patients who have high-risk cytogenetic features like a deletion on chromosome 17p or a deletion on chromosome 11q. It can achieve what we call a long-term remission, or a cure, in up to half of patients with CLL.

But it comes with a cost, and that cost is substantial. The likelihood of dying as a result of complications from a transplant is anywhere between 20 and 30 percent depending on a number of factors. In addition, many of the patients who survive the procedure and may be cured of their CLL run into long-term complications related to the fact that a transplanted immune system can cause damage to a patient's normal organs, and this is called graft versus host disease, and it can be devastating for survivors of a bone marrow transplant.

For that reason, we and patients have been trying to find better and less toxic treatments. In CLL, we're blessed, all of a sudden, with an amazing array of new therapies that can be given as tablets or can be given as an IV infusion. And are much more precisely targeted to the disease, and they cause far less—I call it—collateral damage.

These have been well publicized over the last few years. You have kinase inhibitors like ibrutinib (Imbruvica), which is now FDA approved. You have a new generation of Bruton tyrosine kinase inhibitors, such as ACP-196 or acalabrutinib, which is coming down the pipeline, and you also have ABT-199 or venetoclax (Venclexta).

What we're going to see over the next few years is a number of studies, which are looking at combinations of these new agents, which I think will achieve significantly superior results to these new agents as single therapies. The problem we have is for patients who are already taking a drug like ibrutinib and are doing well, but we know that they have features of their CLL that suggest that they might be at higher than average risk of relapse.

Most of the time these patients feel really well, and they don't want to take the risk of a bone marrow transplant like I've described. The problem is that when the disease comes back in these patients, it can often be very hard to achieve a remission again, and the best time to do a transplant is actually when there's very small amount of disease and when the patient is well and in good shape.

That's the highest likelihood of it being successful. Of course, human nature being what it is, this is the time when we are least wanting to take a risk. It is a hard decision, and we're trying to work on refining ways of predicting who's going to relapse and who's not. But we're also looking at clinical trials where we add certain medications to drugs like ibrutinib in patients who are already taking them in order to improve their response.

For example, at MD Anderson, we're interested in trying to harness the power of the immune system to kill cancer cells. There's been lots of work done on this in solid tumors, but hematologic blood malignancies have lagged behind a little bit. We have a trial using a molecule called a checkpoint inhibitor. Immune checkpoints are part of your body's normal response to prevent your immune system from being overactive, and cancer actually subverts this mechanism to prevent the cells from being killed by the immune system, and we have, now, antibodies that break some of these interactions and can allow the immune system to kill the cancer cells. We're testing one of these antibodies in combination with ibrutinib to see whether we can improve responses and reduce the likelihood that patients will relapse while taking ibrutinib.

The advantage of this is it's much less risky that undergoing a bone marrow transplant.