Is stem cell transplantation the treatment of choice in pediatric chronic myeloid leukemia?

I read with interest the article written by Belgaumi *et al.*[1] about their experience in managing 12 children with chronic myeloid leukemia (CML). In the conclusion the authors recommended that those children with a suitably matched family donor should undergo stem cell transplantation (SCT). However, such a conclusion or recommendation is not fully supported by their data. In 6 of their 12 patients who received imatinib without SCT, only one patient relapsed and this patient could be salvaged with dasatinib. In the other 6 patients who received SCT, 2 patients relapsed, with one being rescued successfully with dasatinib and one remitted after a second SCT. It thus appears that the outcomes are similar for those with or without SCT. While imatinib probably needs to be continued indefinitely to maintain disease control, complete molecular remission after SCT might not be durable or equate to "cure", as exemplified by patient #12 in the author's cohort.

It is well known that stem cell transplantation, even with a matched sibling donor, is associated with risks of mortality and morbidity. However, these risks have not been mentioned by the authors and I am afraid that readers might be misled to firmly believe in the superiority of SCT compared to tyrosine kinase inhibitors as first-line treatment for chronic myeloid leukemia in children. Patients who undergo SCT can die prematurely from treatment-related toxicities, which include serious infections, acute graft-*versus*-host disease among other complications, although the risks are lowest when a matched family donor (MFD) is used. The conditioning chemotherapy is also well known to be associated with long-term morbidity, such as secondary malignancies (from etoposide and alkylating agents), infertility (from cyclophosphamide) and organ dysfunction (*e.g.*, lung fibrosis from busulfan). On the other hand, imatinib has not been reported to be associated with these adverse effects and mortality directly attributable to imatinib is extremely rare when it is used with care. That's exactly why imatinib is now widely adopted in many adult guidelines as the first-line management option in favor of matched family donor SCT for chronic myeloid leukemia in chronic phase. Although high quality evidence is limited in pediatric patients to arrive at a firm recommendation as the authors rightly pointed out, it is entirely reasonable to regard imatinib as at least as good as matched family donor SCT in pediatric patients based on extension of a vast amount of adult data. Because of all these considerations and uncertainties, our center has adopted a non-directive approach in counseling pediatric patients with chronic myeloid leukemia in chronic phase to the two treatment options. These are: indefinite use of imatinib or matched family donor SCT, discussing the advantages (potentially curative without long-term medication) and disadvantages (definite albeit small risk of early mortality, potential long-term complications) of SCT *versus* the advantages (safe treatment with very low risk of mortality, reversible and usually manageable toxicity, good results reported in adult patients) and disadvantages (indefinite treatment with higher cumulative cost, unknown small risk of long-term adverse effects for children) of tyrosine kinase inhibitor. We provide them with our best estimates of the probabilities of these risks and let them choose their preferred option based on their own values and considerations.

We definitely need well-designed clinical trials and longer follow up of more pediatric chronic myeloid leukemia patients before we can definitely conclude which should be the preferred treatment option for these patients. Research into the quality of life in patients who follow one of these two different treatment pathways, as well as cost-benefit analyses, are invaluable to provide further insights to guide clinicians and patients. Before good evidence is available, a non-directive approach instead of matched family donor SCT for all, might be the most appropriate management strategy for pediatric chronic myeloid leukemia patients.

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