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Combined Irradiation and Chemotherapy Better Prepares Children for Stem Cell Transplantation than Chemotherapy Alone

Treatment of childhood cancer is a success story, particularly for acute lymphoblastic leukemia (ALL). More than 90% of ALL patients below 18 years of age are rescued with contemporary chemotherapy. However, the remaining 10% have resistant or reoccurring leukemia and require alternative treatment regimens. One of the most powerful leukemia therapies is hematopoietic stem cell transplantation from a donor (allogeneic HSCT). Approximately 50-80% of pediatric ALL patients that receive allogeneic HSCT are cured, 20% experience leukemic reoccurrence (relapse), and 10% die from complications.

Allogeneic HSCT is a multistep procedure:

1. Identify a suitable donor, i.e., a compatible sibling or unrelated person.
2. Reduce the patient's leukemia to an undetectable level with chemotherapy, antibodies, or genetically modified cells from the patient ("CAR-T-cells").
3. Collect a donor graft by harvesting bone marrow, peripheral blood stem cells, or umbilical cord blood.
4. Prepare the patient for transplantation ("conditioning").
5. Perform the stem cell transplantation.

For high-risk leukemia, the gold standard conditioning procedure is a combination of total body irradiation (TBI) and high dose chemotherapy. This approach is very effective in controlling leukemia in the conditioning step, but patients may experience highly negative consequences of this procedure later in life: sterility, growth retardation, lung problems, and secondary cancer.

Therefore, a large consortium of pediatric transplant experts initiated a global study to investigate whether chemotherapy-based conditioning could substitute TBI. The study is called FORUM (For Omitting Radiation Under Majority Age) and had to be stopped because chemotherapy-based conditioning had significantly poorer outcomes (i.e., lower overall survival rates) than the combination of TBI and chemotherapy. The researchers will now perform prospective monitoring to better define the advantages and limitations of various conditioning approaches.

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Abstract: #S102 TBI OR CHEMOTHERAPY BASED CONDITIONING FOR CHILDREN AND



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