

Latest Drug Reduces Fatal Transplant Side Effect By 50%



According to researchers at the University of Michigan Comprehensive Cancer Center a new class of drugs is capable to reduce patients' risk of contracting a serious and often deadly side effect of lifesaving bone marrow transplant treatments.

The innovative study, published in *The Lancet Oncology* and a first to test this treatment in humans, investigated the combination of the drug vorinostat with standard medications customarily given after transplant. The result was 22% of patients developing graft-vs.-host disease in comparison to 42% who typically develop this condition when treated with only standard medications.

Lead study author Sung Choi, M.D., assistant professor of pediatrics at the U-M Medical School explained that graft-vs.-host disease is the most serious complication from transplant, limiting its use. Prevention strategies currently used have remained mostly unchanged over the past two decades and as Choi stated, this study highlights a potentially fresh approach to preventing this condition.

Approved by the US Food and Drug Administration to treat certain types of cancer, vorinostat also has anti-inflammatory effects as found in U-M researchers' laboratory studies led by senior study author Pavan Reddy, M.D. The team hypothesized this to be potentially useful in preventing graft-vs.-host disease, or GVHD, a condition in which the new donor cells begin attacking other cells in the patient's body.

The study included 61 older adults from the University of Michigan and Washington University in St. Louis who were undergoing a reduced-intensity bone marrow transplant with cells donated from a relative. Patients received standard medication customarily prescribed after a transplant to prevent GVHD. They were also given vorinostat pills, to be taken orally. Fifty of the 61 participants completed the full 21-day course of vorinostat.

It was found that vorinostat's side effects were manageable and the drug safe and tolerable to give to this vulnerable population. Additionally, evaluating rates of patient death and cancer relapse among the study participants showed historical average similarity.

This approach had been studied in the laboratory using mice for eight years by Reddy, the Moshe Talpaz Professor of Oncology and professor of internal medicine at the U-M Medical School, and comparing the two researches showed that the findings mirrored each other.

According to Reddy this approach to preventing graft-vs.-host disease is entirely new, as specifically, vorinostat targets histone deacetylases, which are different from the usual molecules targeted by traditional treatments. Pointing out vorinostat's dual effect as an anti-cancer and an anti-inflammatory agent, Reddy, who is also co-director of the hematologic malignancies and bone marrow transplant program at the U-M Comprehensive Cancer Center, suspects this versatility to play a role in preventing the leukemia from returning.

Choi confirmed that the team was encouraged by their findings as vorinostat, when combined with standard graft-vs.-host disease prophylaxis after related-donor transplant, appeared to be safe and associated with lower than expected incidence of acute GVHD. She added that further studies were needed to assess the effect of vorinostat in broader transplant settings and concluded by saying that the researchers were currently in the process of investigating vorinostat plus standard therapies to prevent GVHD in transplants with an unrelated donor.

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