DNA alkylation drug may improve outcomes for adolescents and young adults with central nervous system tumors

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In a phase II clinical trial, the drug 4-demethyl-4-cholesteryloxycarbonylpenclomedine (DM-CHOC-PEN) improved survival for some adolescent and young adult (AYA) patients with cancers involving the central nervous system, according to results presented at the AACR-NCI-EORTC Virtual International Conference on Molecular Targets and Cancer Therapeutics, held October 7-10, 2021.

"Adolescents and young adults with central nervous system cancers represent a new group of patients for which we didn't have a treatment option," said Lee Roy Morgan, MD, Ph.D., an adjunct clinical professor of medicine at Tulane University and CEO of DEKK-TEC Inc. "We are excited that we can use DM-CHOC-PEN to treat patients who fall between the cracks because they're too old to see a pediatrician and too young to see a general oncologist."

AYAs—defined as individuals aged 15 to 39—are diagnosed with around 200,000 cancer cases per year and face unique physical, social, and financial challenges compared with childhood or older cancer patients. With potentially decades of life remaining, long-term side effects, including toxicity to the kidneys, liver, and reproductive organs, are a significant issue for these patients, so the development of well-tolerated therapeutics is particularly crucial to this community, Morgan explained.

Additionally, about 10 percent of AYA cancers involve the central nervous system as either a primary tumor or a metastasis. The blood-brain barrier prevents many drugs from penetrating these tumors, limiting current therapeutic options to surgery, radiation, and select

chemotherapies.

Morgan and colleagues had previously developed DM-CHOC-PEN, which damages DNA by placing alkylating groups on guanine and cytosine bases. It readily crosses the blood-brain barrier and is selectively taken up by a transporter often overexpressed in cancer cells. The tumor-selective nature of DM-CHOC-PEN suggested it may have limited off-target toxicities, a finding that was confirmed in adult studies.

In this trial, the researchers enrolled 19 AYA patients with various types of tumors that either began in or metastasized to the central nervous system. They administered 98.7 mg/m^2 DM-CHOC-PEN to patients with normal liver function or 75 mg/m^2 to patients with impaired liver function once every 21 days. To date, the researchers have observed complete responses in two patients, partial responses in three patients, and stable disease in one patient. Three patients with responsive disease are still undergoing treatment at 12, 59, and over 72 months.

Morgan and colleagues also evaluated the toxicity of DM-CHOC-PEN in these patients. No severe (grade 3 or higher) toxicities were observed, and no cognitive, liver, hematological, cardiac, renal, or gastrointestinal dysfunction of any grade was noted. Morgan suggested that the lack of toxicities could bode well for its tolerability in combination with other treatments.

"Some of these patients had other tumors outside the nervous system, and their physicians combined DM-CHOC-PEN with another drug. So far, we've seen no toxicities, and we just finished a trial showing that it potentiates radiation as well, suggesting that DM-CHOC-PEN could be safely combined with other drugs," Morgan said.

Additionally, they found that DM-CHOC-PEN has a longer half-life in

the plasma of AYA patients than in the plasma of patients over 60; it was detectable for up to 50 days in AYAs but less than 21 days in older individuals, suggesting a prolonged effect in younger patients.

Limitations of this study include the small sample size, as well as the exclusion of patients with abnormal blood counts or debilitating comorbidities.

More information: Conference: www.aacr.org/meeting/aacr-nci- … cancer-therapeutics/

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