Vitamin A may reduce pancreatitis risk during ALL treatment

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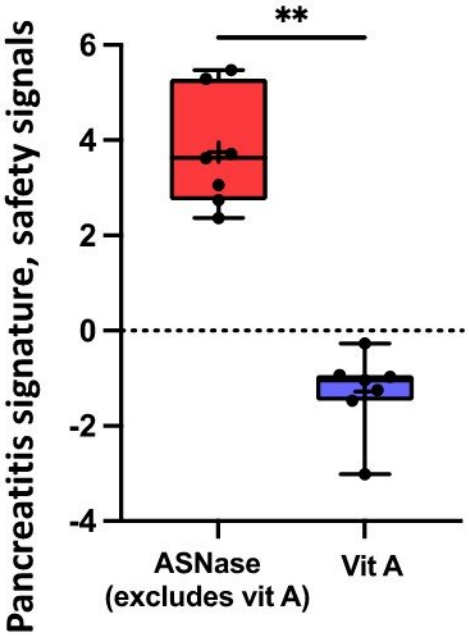

Fig 1: Pancreatitis safety signals are significantly lower in vitamin A than asparaginase in FAERS data analysis

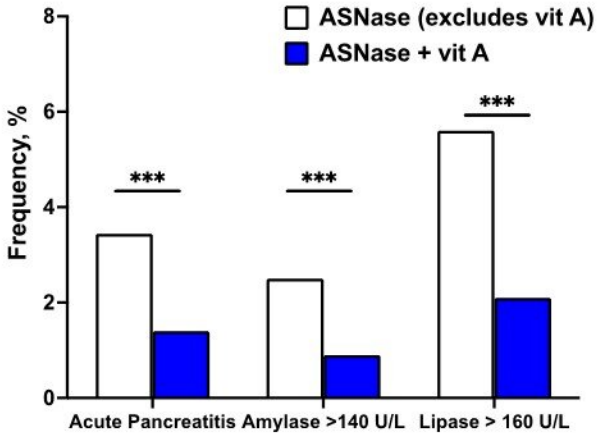

Fig 2: EHR data analysis showed a 60% reduction in pancreatitis among the asparaginase with vitamin A cohort

Study in *Science Translational Medicine* shows potential benefit of vitamin A treatment to reduce side effect risks during treatment for ALL. Credit: Cincinnati Children's

Consuming a diet rich in vitamin A or its analogs may help prevent children and young adults with acute lymphoblastic leukemia (ALL) reduce their risk of developing painful pancreas inflammation during chemotherapy treatment.

Details about this potential dietary solution to prevent a potentially life-threatening adverse event were published March 15, 2023, in *Science Translational Medicine*. The research team was led by Sohail Husain, MD, chief of Pediatric Gastroenterology, Hepatology, and Nutrition at Stanford University and Anil Goud Jegga, DVM, MRes, a computational biologist at Cincinnati Children's Hospital Medical Center.

For people with ALL, treatment with the enzyme asparaginase helps starve cancer cells by reducing the amount of asparagine circulating in the blood, which the cancer cells need but cannot make themselves. The medication, often used in combination with other chemotherapies, is given via injection into a vein, muscle, or under the skin.

However, an estimated 2% to 10% of asparaginase users develop inflammation of the pancreas in reaction to asparaginase treatment. For a third of these people, the symptoms can be severe.

Jegga and colleagues developed predictive analytics using over 100 million data points encompassing gene expression data, small-molecule data, and electronic health records to understand more of the mechanisms driving asparaginase-associated pancreatitis (AAP) and identify potential interventions to prevent or mitigate AAP.

First, they analyzed massive amounts of gene expression data to reveal that gene activity associated with asparaginase or pancreatitis might be reversed by retinoids (vitamin A and its analogs). The team found more supporting evidence by "mining" millions of of electronic health records from the TriNetX database and the U.S. Federal Drug Administration

Adverse Events Reporting System.

This number crunching and predictive analytics work included use of the AERS*Mine* software developed at Cincinnati Children's by Mayur Sarangdhar, Ph.D., MRes, and colleagues. The research team also studied data from mice experiments and compared plasma samples from people with ALL who developed pancreatitis and those who did not.

Ultimately, the team established two sets of human "real-world" experiences. They found that only 1.4% of patients treated with asparaginase developed pancreatitis when they were also taking vitamin A in contrast to 3.4% of patients who did not. Concomitant use of vitamin A correlated with a 60% reduction in the risk of AAP. Lower amounts of dietary vitamin A correlated with increased risk and severity of AAP.

"This study demonstrates the potential of mining 'real-world' data to identify therapy modifiers for improving patient outcomes. In cases where a primary drug induces toxicity but is critical to therapy, such as asparaginase, therapy modifiers, such as vitamin A and its analogs, may be of immediate relevance to patients on asparaginase and 'at-risk' for AAP," says Sarangdhar, a co-first author of the study.

Says Jegga, "Our study highlights the power of heterogeneous data integration and analysis in translational research. By leveraging existing 'omics and patient-centric data and a systems approach, we were able to identify new insights into the development of AAP and potential interventions to prevent or mitigate this side effect."

More information: Cheng-Yu Tsai et al, A systems approach points to a therapeutic role for retinoids in asparaginase-associated pancreatitis, *Science Translational Medicine* (2023). DOI: 10.1126/scitranslmed.abn2110.

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Provided by Cincinnati Children's Hospital Medical Center

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