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Testing vitamin A to prevent pancreas inflammation in children with leukemia during treatment

Submission date 09/10/2024	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 19/10/2024	**Overall study status** Ongoing	
Last Edited 18/10/2024	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims
Asparaginase (ASNase) is one of the preferred drugs for the current treatment of acute lymphoblastic leukemia (ALL). Since the drug introduced into the treatment of pediatric ALL in the 1960s, the survival rate for pediatric ALL has gradually increased from 50% to nearly 90%. However, during the course of treatment with ASNase, approximately 2%-10% of patients develop asparaginase-associated pancreatitis (AAP). Once AAP occurs, due to the high risk of re-use, the drug is typically discontinued in clinical practice, leading to poor outcomes in children with ALL. Due to the unclear pathogenesis, current clinical methods for preventing AAP are limited. Although low-fat, low-oil dietary strategies have been implemented in clinical practice for children undergoing ASNase treatment, they have not proven to be effective in preventing AAP. Recently, the researchers suggest that ASNase reduces retinoid levels in patients, and intake of vitamin A may reduce the risk of pancreatitis in leukemia patients treated with ASNase. These findings provide an important reference for the clinical prevention of AAP, but since the data are based on retrospective studies in European and American children and adult ALL populations, the strength of the evidence needs to be further reinforced. Therefore, this study aims to design a prospective study to evaluate the correlation between vitamin A levels and AAP incidence, thereby providing data and theoretical support for the clinical prevention of AAP.

Who can participate?
Children with age between one month and 18 years old and diagnosed with ALL.

What does the study involve?
Participants are asked to join this study while they are staying in the hospital. Participants who meet the inclusion and exclusion criteria will receive vitamin A. After enrollment, the patients were observed for 60 days. The study will lasts two years in total.

What are the possible benefits and risks of participating?
There will be immediate direct benefit to those taking part, or not. But there should be benefit to the patients in the future because the results of the study are likely to reduce the incidence of AAP. The main risk of giving vitamin A is that bone and joint pain, swelling, itchy skin, chapped

lips, fever, headache, vomiting, constipation, diarrhea and nausea, which can be resumed when the drug is stopped.

Where is the study run from?
The PREVAIL study is being run by the Children's Hospital of Soochow University in China.

When is the study starting and how long is it expected to run for?
September 2024 to October 2026

Who is funding the study?
Children's Hospital of Soochow University (China)

Who is the main contact?
1. Prof. Shaoyan Hu, hsy139@126.com
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Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
The Supplementation of Vitamin A for the Prevention of Asparaginase-Associated Pancreatitis in Children With Acute Lymphoblastic Leukemia: A Prospective Single-arm Clinical Trial

Acronym
PREVAIL

Study objectives
Vitamin A can reduce the incidence of asparaginase-associated pancreatitis in children with acute lymphoblastic leukemia

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 24/09/2024, Children's Hospital of Soochow University (No.92 zhongnan street, SIP, Suzhou, 215000, China; +86 512-80693506; sdfetyyec@163.com), ref: 2024016

Study design
Single center interventional single-arm clinical trial

Primary study design
Interventional

Study type(s)
Prevention, Efficacy

Health condition(s) or problem(s) studied
Prevention of asparaginase-associated pancreatitis in children with acute lymphoblastic leukemia

Interventions
After completing screening measurements and acquiring written informed consent, children participating in this study will receive 3600 unit vitamin A orally per day for 30 days. The dosage will be adjusted based on the blood level of vitamin A but will not exceed 8000U/L. A historical retrospective cohort will be used as the control group.

Intervention Type
Supplement

Primary outcome(s)
The incidence of asparaginase-associated pancreatitis within 60 days after enrollment measured using patient records

Key secondary outcome(s))
1. Incidence of elevated blood amylase within 30 days of enrollment: blood amylase levels are routinely monitored twice weekly for 30 days after the use of asparaginase. Any value above the normal range at any monitoring point is defined as elevated.
2. Length of Hospital Stay: the duration from enrollment to discharge measured using patient records.
3. 28-Day Mortality after enrollment measured using patient records
4. The vitamin A levels monitoring: the plasma vitamin A levels is monitored at enrollment, and 1, 2, 3, 4 and 6 weeks after enrollment.
5. Duration of Enteral Nutrition Interruption within 60 days of enrollment measured using patient records.
6. Prothrombin time, International Normalized Ratio, Activated partial thromboplastin time, fibrinogen, AT-III, albumin levels within 30 days after enrollment.
7. Cumulative use of plasma within 30 days after enrollment.

Completion date
31/10/2026

Eligibility

Key inclusion criteria
1. One month< age ≤18 years
2. Diagnosis with acute lymphoblastic leukemia, which was confirmed by cell morphology, immunology, cytogenetics and molecular biology

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
1 months

Upper age limit
18 years

Sex
All

Key exclusion criteria
1. Previous history of pancreatitis or other conditions that may lead to pancreatitis (such as hyperlipidemia, hypercholesterolemia, and cholelithiasis)

2. Treatment course delays of more than two weeks due to financial issues
3. Exclusion of cases where acute pancreatitis occurs without the use of PEG-asparaginase (PEG-ASP)
4. The patient switching from PEG-ASP to L-ASP or Erwinia-ASP treatment due to adverse reactions other than AAP
5. Expected hospital stay of less than 2 days
6. Use of vitamin A supplements prior to enrollment within 1 month

Date of first enrolment
01/11/2024

Date of final enrolment
31/10/2026

Locations

Countries of recruitment
China

Study participating centre
Children's Hospital of Soochow University
No.92 Zhongnan street, SIP
Suzhou
China
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Sponsor information

Organisation
Children's Hospital of Soochow University

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study will be published as a supplement to the results publication.

IPD sharing plan summary

Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file			18/10/2024	No	No