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Evaluation of genome sequencing as a diagnostic test in acute leukemia

Submission date
19/08/2021

Recruitment status
Recruiting

Registration date
01/09/2021

Overall study status
Ongoing

Last Edited
08/12/2025

Condition category
Cancer

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Acute leukemia includes the blood cancers acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL). About 350 adults and 100 children per year are diagnosed with acute leukemia in Sweden. Acute leukemias are characterized by recurrent genetic point mutations as well as large structural aberrations of the chromosomes. Increased knowledge of these genetic variants leads to a better understanding of why acute leukemias occur, and also has major importance for diagnosis, prognosis and choice of treatment, as well as evaluation of how the patient responds to treatment. Clinical diagnostics of acute leukemias currently include analysis of genetic variants using different molecular and microscopic methods. This study aims to perform comprehensive genetic analysis (whole-genome sequencing and whole-transcriptome sequencing) of acute leukemias in a clinical setting, to evaluate whether these methods can lead to improved clinical diagnostics and treatment.

Who can participate?
Patients with diagnosed or suspected acute leukemia, for whom a referral is written for genetic diagnostics, can participate. Both adults and children can participate, provided that the patient and/or guardian is able to provide informed consent.

What does the study involve?
Standard diagnostics of a suspected acute leukemia includes the collection of a bone marrow sample and one or several blood samples. In this study, leftover material from these samples will be used for a more comprehensive genetic analysis of the leukemia cells. To enable the comparison of the genetic variants observed in leukemia cells to those in healthy cells, a sample with normal cells is needed. This sample can be collected from a skin biopsy, buccal (mouth) swab, hair or nails. It can also be collected from normal blood cells that are isolated from the already collected blood or bone marrow sample or a blood sample collected when the patient is in remission.
The samples are sent to laboratories within healthcare that perform genetic diagnostics, where genetic material is extracted and analyzed. Information about identified genetic variants that are of relevance for the patient’s treatment or follow-up will be communicated to the treating physician.

What are the possible benefits and risks of participating?
Comprehensive genetic analysis can lead to the identification of genetic variants that enables improved risk stratification or additional treatment options. For most patients, participation in the study will not have any impact on treatment but may improve medical care in the future. Participation in the study can involve the collection of an additional sample for the extraction of healthy cells. A skin biopsy can, despite the use of local anesthetic, sometimes lead to a small discomfort.
Genetic analysis can lead to the identification of inherited genetic variants of two major types:
1. Inherited genetic variants in genes of importance for the development of blood cancer. Such variants can have significance for treatment and follow-up of the patient and will be communicated to the treating physician. Close relatives to the patient may carry the same variant and have an increased risk of developing blood cancer. Patients with this type of variant will be offered genetic counselling and recommendations from a specialist.
2. Inherited variants in genes of importance for inherited diseases other than blood cancer (e.g., inherited cancer, neurologic disease). Such variants will not actively be searched for but may be found incidentally. When consenting to the study, patients can opt to receive information about this type of variant. Should such a variant be found, the patient will be offered genetic counselling and recommendations from a specialist.

Where is the study run from?
Karolinska University Hospital (Sweden)

When is the study starting and how long is it expected to run for?
January 2020 to December 2026

Who is funding the study?
1. Karolinska University Hospital (Sweden)
2. Skånes University Hospital (Sweden)
3. Sahlgrenska University Hospital (Sweden)
4. University Hospital of Umeå (Sweden)
5. Linköping University Hospital (Sweden)
6. Uppsala University Hospital (Sweden)
7. University Hospital Örebro (Sweden)
8. University of Gothenburg (Sweden)
9. Linköping University (Sweden)
10. Lund University (Sweden)
11. Karolinska Institute (Sweden)
12. Umeå University (Sweden)
13. Uppsala University (Sweden)
14. Örebro University (Sweden)
15. Illumina (USA)
16. Investigator initiated and funded

Who is the main contact?
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Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Study information

Scientific Title
Implementation and validation of whole-genome and transcriptome sequencing as a comprehensive diagnostic test in acute leukemia

Acronym
GMS-AL-WGS

Study objectives
1. Whole-genome sequencing (WGS) and whole-transcriptome sequencing (WTS) can detect all mandatory genetic aberrations in acute leukemia
2. WGS and WTS data can be generated and interpreted in a time frame that is acceptable for a diagnostic test

3. WGS and WTS data can be generated and interpreted at a cost that is acceptable for a diagnostic test
4. WGS and WTS can improve classification or risk stratification of acute leukemias compared to current standard of care diagnostics
5. WGS and WTS can improve patient management or choice of therapy for patients with acute leukemia

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 17/03/2021, Swedish Ethical Review Authority (Etikprövningsmyndigheten, Box 2110, 750 02 Uppsala, Sweden; +46 (0)10 475 08 00; registrator@etikprovning.se), ref: 2020/06673
Children: approval pending

Study design
Multicentre observational longitudinal study

Primary study design
Observational

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Acute leukemia

Interventions
Tumor DNA and RNA are extracted from bone marrow and/or peripheral blood samples collected as part of standard diagnostics. An additional sample (skin biopsy, buccal swab or other tissue) may be collected for extraction of germline DNA.

In addition to standard molecular diagnostics, comprehensive genetic analysis, i.e. whole-genome sequencing and whole-transcriptome sequencing, will be performed.

Comprehensive genetic analysis can lead to findings of inherited genetic variants of two major types:
1. Inherited genetic variants that are of importance for the development of blood cancer. All participants will receive information about this type of variants if they are carriers, and offered genetic counselling and recommendations from a specialist.
2. Inherited genetic variants that are of importance for the development of other diseases than blood cancer. This type of variants will not be searched for actively but may be found incidentally. When consenting to the study, participants can opt to receive information about this type of variants. If such variants are found, participants will be offered genetic counselling and recommendations from a specialist.

Follow-up of participants will be according to standard healthcare protocols.

Intervention Type
Genetic

Primary outcome(s)
1. Percentage of acute leukemia patients for whom all mandatory genetic aberrations found by SoC are also detected by WGTS is measured by comparison of variants retrieved from WGTS and SoC, respectively, after completion of patient inclusion
2. Percentage of acute leukemia patients for whom genetic variants relevant for classification or risk stratification are identified by WGTS but not by SoC is measured by comparison of variants retrieved from WGTS and SoC, respectively, after completion of patient inclusion

Key secondary outcome(s))
1. Percentage of patients for whom WGTS analysis and interpretation is successful in a given timeframe is measured by comparison of the number of days needed for WGTS analysis of each patient to the required turnaround-time, after completion of patient inclusion
2. Percentage of acute leukemia patients for whom patient management and/or therapy decision is changed based on variants only detected by WGTS is measured by analysis of patient journals/health records, after completion of patient inclusion
3. Micro-costing of WGTS compared to SoC is measured by comparison of costs associated with WGTS and SoC, respectively, after initiation of the study

Completion date
31/12/2026

Eligibility

Key inclusion criteria
1. Patients with diagnosed or suspected acute leukemia, for whom a referral is written for genetic diagnostics
2. Patients of any age can be included

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
All

Sex
All

Total final enrolment
0

Key exclusion criteria
Patients or guardians that are unable to provide written informed consent

Date of first enrolment
01/06/2021

Date of final enrolment

30/06/2026

Locations

Countries of recruitment
Sweden

Study participating centre
Karolinska University Hospital
Clinical Genetics
Stockholm
Sweden
17 176

Study participating centre
University Hospital of Umeå
Clinical Genetics
Umeå
Sweden
90737

Study participating centre
Uppsala University Hospital
Clinical Genetics
Uppsala
Sweden
75185

Study participating centre
Sahlgrenska University Hospital
Clinical Genetics
Gothenburg
Sweden
41345

Study participating centre
Skåne University Hospital
Clinical Genetics
Lund
Sweden
22242

Study participating centre
Linköping University Hospital
Clinical Genetics
Linköping
Sweden
58185

Study participating centre
Örebro University Hospital
Clinical Pathology and Genetics
Örebro
Sweden
70185

Sponsor information

Organisation
Karolinska University Hospital

ROR
https://ror.org/00m8d6786

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Karolinska University Hospital

Funder Name
Skånes universitetssjukhus

Alternative Name(s)
Skåne University Hospital, SUS

Funding Body Type

Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
Sweden

Funder Name
Sahlgrenska Universitetssjukhuset

Alternative Name(s)
Sahlgrenska University Hospital, SU

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
Sweden

Funder Name
University Hospital of Umeå

Funder Name
Linköping University Hospital

Funder Name
Uppsala University Hospital

Funder Name
Universitetssjukhuset Örebro

Alternative Name(s)
Örebro University Hospital, USÖ

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
Sweden

Funder Name
Göteborgs Universitet

Alternative Name(s)
University of Gothenburg

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
Sweden

Funder Name
Linköpings Universitet

Alternative Name(s)
Linköping University, Linköping University, LiU

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
Sweden

Funder Name
Lunds Universitet

Alternative Name(s)
Lund University, Universitas Lundensis, Universitas Gothorum Carolina, Royal Caroline Academy, Regia Academia Carolina, Lund University | Lund, Sweden | LU, Lunds universitet, LU

Funding Body Type

Government organisation

Funding Body Subtype
Universities (academic only)

Location
Sweden

Funder Name
Karolinska Institutet

Alternative Name(s)
Karolinska Institute, KI

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
Sweden

Funder Name
Umeå Universitet

Alternative Name(s)
Umeå University, Ubmeje universitiähta, Universitas Umensis

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
Sweden

Funder Name
Uppsala Universitet

Alternative Name(s)
Uppsala University, UU_University, Uppsala Universitet, Sweden, UU

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
Sweden

Funder Name
Örebro Universitet

Alternative Name(s)
Örebro University

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
Sweden

Funder Name
Illumina

Alternative Name(s)
Illumina, Inc.

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Funder Name
Investigator initiated and funded

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository. Data will be processed and stored according to the regulations within the General Data Protection Regulation (GDPR). Initially, data will be stored at each participating centre, with so-called restricted access. To enable population-based studies, data will be transferred to the National Genomic Platform within Genomic Medicine Sweden. If required upon publication, data will be stored in the European Genome-phenome Archive (EGA). Data will not be accessible to the public but will require permission from a Data Access Committee (DAC) which will be formed within the GMS working group for hematology. In addition to individuals with clinical hematologic and genetic expertise, the DAC will include individuals with juridical/ethical expertise. Consent from participants has been obtained to share genetic data for research and development purposes.

IPD sharing plan summary

Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		24/03/2022	25/03/2022	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes