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The effect of the addition of carbogen inhalation and nicotinamide to conventional chemotherapy for hypoxia parameters in non-Hodgkin lymphoma patients

Submission date
06/06/2021

Recruitment status
No longer recruiting

Registration date
14/06/2021

Overall study status
Completed

Last Edited
09/07/2025

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Diffuse large B-cell lymphoma (DLBCL) is one of the most common blood cancers in the world. Chemotherapy with R-CHOP (rituximab, cyclophosphamide, vincristine, doxorubicin, prednisone) has been standard treatment for almost 40 years with a remission rate of about 60-70%. Tumor hypoxia (the situation where tumor cells have been deprived of oxygen) plays an important role in cancer growth, survival, and spread. The aim of this study is to test the effect of modulating tumor hypoxia with nicotinamide/vitamin B3 and carbogen inhalation (95% oxygen and 5% carbon dioxide) in DLBCL patients who experience tissue hypoxia.

Who can participate?
Patients aged 18-65 with DLBCL and proven tumor hypoxia

What does the study involve?
Participants are randomly allocated to be treated with nicotinamide/vitamin B3 and carbogen inhalation or no additional treatment. Tumor size reduction and blood parameters are measured before and after 1 cycle of chemotherapy.

What are the possible benefits and risks of participating?
Patients in the study group might have a better reduction in tumor size after chemotherapy but might have adverse events such as hot flushing, headache, and itching.

Where is the study run from?
Kariadi General Hospital (Indonesia)

When is the study starting and how long is it expected to run for?
January 2021 to May 2022

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
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Contact information

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Scientific

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Additional identifiers

Protocol serial number
EAP-HYP-1

Study information

Scientific Title
The effect of the addition of carbogen inhalation and nicotinamide to conventional chemotherapy against hypoxia, angiogenesis, apoptotic pathway, glycolytic metabolism, and inflammatory pathway parameters in diffuse large B-cell lymphoma patients

Study objectives
There is an effect of giving inhaled carbogen-nicotinamide addition on the hypoxia, angiogenesis, apoptotic pathway, glycolytic metabolism, and inflammatory pathway parameters in diffuse large B-cell lymphoma (DLBCL) patients who experience tissue hypoxia and receive R-CHOP (rituximab, cyclophosphamide, vincristin, doxorubicin, prednisone) chemotherapy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 08/02/2021, Health Research Ethics Committee RSUP Dr. Kariadi Semarang (Sutomo St. no. 18, Semarang, Indonesia; +62 (0)24 8413476; kepk.rskariadi@gmail.com), ref: 736/EC /KEPK-RSDK/2021

Primary study design
Interventional

Study design
Single-center open-label randomized controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Diffuse large B-cell lymphoma

Interventions
Participants are randomised by simple random sampling.

Patients in the study arm will take nicotinamide 2 g 1 hour before chemotherapy and inhale 10 liters/min carbogen for 10 minutes on and off, starting 10 minutes before R-CHOP chemotherapy until the finish.

The control group will not receive any intervention.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Nicotinamide, carbogen (oxygen 95% & CO_2 5%)

Primary outcome(s)

Tumor size measured with blood oxygenation level dependent (BOLD) MRI before chemotherapy and 1 week after 1st cycle of R-CHOP chemotherapy

Key secondary outcome(s)
1. Hypoxia parameters (HIF-1 alpha & miRNA-210 serum) measured using ELISA and qRT PCR, respectively
2. Angiogenesis parameters (VEGF serum) measured using ELISA
3. Glycolytic parameters (lactate and blood gas analysis) measured using enzymatic and colorimetric methods and ion-selective electrode, respectively
4. Apoptotic parameters (p53, BCL-2 serum) measured using ELISA
5. Inflammatory parameters (TNF-alpha, sIL-2R serum) measured using ELISA
6. Safety and adverse events of the intervention categorized by Common Terminology Criteria for Adverse Events (CTCAE) v6.0 and monitored during carbogen intervention and 1 day after

Timepoints:
Study group: measured before chemotherapy, 10 minutes after carbogen and nicotinamide, and 1 week after 1st cycle of R-CHOP
Control group: measured before chemotherapy and 1 week after 1st cycle of R-CHOP

Completion date
31/05/2022

Eligibility

Key inclusion criteria
1. DLBCL patients with increased expression of HIF-1α (>10%) via tissue immunohistochemistry
2. Do not have anemia (hemoglobin ≥11 g/dl)
3. Age 18-65 years
4. Do not have obstructive pulmonary disease (normal x-ray thorax and spirometry)
5. No heart problems (normal electrocardiogram (ECG) and/or normal left ventricular ejection fraction (LVEF) echocardiography)
6. Have no cerebrovascular disease
7. Do not experience severe liver function problems
8. No severe renal function impairment
9. Do not suffer from diabetes mellitus (fasting blood glucose 126 mg/dl or random blood glucose <200 mg/dl)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit

65 Years

Sex
All

Total final enrolment
40

Key exclusion criteria
1. Eastern Cooperative Oncology Group (ECOG) ≥2
2. Pregnancy before or while undergoing chemotherapy
3. History of chemotherapy for non-Hodgkin lymphoma (NHL) cases before
4. Allergic reaction to chemotherapy treatment

Date of first enrolment
02/07/2021

Date of final enrolment
30/05/2022

Locations

Countries of recruitment
Indonesia

Study participating centre
RSUP Dr. Kariadi, Semarang
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Sponsor information

Organisation
Dr. Kariadi Hospital

ROR
https://ror.org/040f86t49

Funder(s)

Funder type

Other

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 are/will be available upon request from Daniel Rizky (danielrizky@hotmail.co.id). Raw datasets will be available for 5 years. Informed consent will be obtained directly from the patients, and the patient's identity will be hidden using initials. There are no ethical or legal restrictions.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/04/2024	09/07/2025	Yes	No
Basic results			12/07/2023	No	No