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Assessing changes in an inflammation signal (interleukin 1) in vestibular schwannoma

Submission date
25/02/2026

Recruitment status
Not yet recruiting

Registration date
04/03/2026

Overall study status
Ongoing

Last Edited
04/03/2026

Condition category
Cancer

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

Plain English summary of protocol

Background and study aims
In vestibular schwannoma (VS), inflammation is associated with tumour growth, and studies have shown that one chemical mediator of inflammation called interleukin-1 (IL-1) is increased in patients with growing VS. Targeting IL-1 through drugs such as anakinra (Kineret ©) could reduce inflammation and growth in these tumours. This study aims to understand the best tests or biomarkers that can evaluate whether targeting IL-1 is having an effect within VS.

Who can participate?
Patients aged 18 years and over who are due to undergo surgery for a growing sporadic or NF2-related Schwannomatosis vestibular schwannoma (VS)

What does the study involve?
Participants will first undergo a research MRI scan for evaluation of tumour imaging biomarkers. Blood samples will also be collected so that levels of circulating pro-inflammatory chemicals (cytokines) can be evaluated. Following these tests, participants will receive a once-daily subcutaneous dose of an established safe IL-1 targeting drug called anakinra (Kineret©). This drug will be given for 14 days at home by a trained member of the research team, and at the end participants will then undergo the same MRI scan and blood tests described above so that changes can be measured. During planned surgery, excess tissue from the tumour (VS) will be taken, and specialised tests used to look for changes in the expression of inflammation-related genes and changes in the number of inflammatory cells. Data from anakinra-dosed tumours will be compared with a control cohort of participants with growing sporadic VS who are due to undergo surgery. This group of participants will not undergo anakinra administration but will undergo the same MRI imaging and blood sampling as detailed above, with imaging and blood sample collection at day zero and at day fourteen.

What are the possible benefits and risks of participating?
There are no direct benefits to you from taking part in the study, but participation in this study may help us develop new, important treatments for patients with VS in the future.
All doses of anakinra will be given by a trained member of the research team. Anakinra (Kineret®) is a licensed anti-inflammatory medication widely used in Europe and the United States for conditions such as rheumatoid arthritis. It has been tested in many clinical trials and

has a strong safety record. In this study, it will be given as an injection under the skin once a day for 14 days, and no safety issues are expected with this short course of treatment.
Some people may develop temporary redness, swelling, itching, or discomfort at the injection site. Rarely, allergic reactions can occur. Long-term use has been linked to infections and low white blood cell counts, but this is not expected with the short treatment period used in this study. Participants will be closely monitored, and treatment will be stopped if any significant side effects occur.

Where is the study run from?
This study is being run by the University of Manchester in collaboration with the Northern Care Alliance NHS Foundation Trust the Geoffrey Jefferson Brain Research Centre (UK)

When is the study starting and how long is it expected to run for?
April 2026 to April 2027

Who is funding the study?
The study is being funded by the Medical Research Council (UK) through the Translation Manchester Confidence for Translation (C4T) 2024 scheme

Who is the main contact?
Dr Daniel Lewis, daniel.lewis-3@manchester.ac.uk

Plain English summary under review with external organisation

Contact information

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Central Portfolio Management System (CPMS)
64798

Grant Code
MR/X502868/1

Integrated Research Application System (IRAS)
347607

Study information

Scientific Title
Interleukin-1 in Vestibular Schwannoma (IL-VS): a biomarker development study

Acronym
IL-VS

Study objectives
Primary objective:
To determine if IL-1 receptor antagonism, through once daily Anakinra (as an exemplar of the IL-1Ra compound class), is detectable within the VS tumour microenvironment as a reduction in the expression of proinflammatory cytokines/chemokines within resected growing VS tumour tissue, when compared to a control cohort of size and growth-matched VS.

Secondary objectives:
1. Establish whether changes in MRI-based surrogate imaging biomarkers of intratumoural inflammation (i.e., tumour Ktrans derived from DCE-MRI) are sensitive to IL-1 antagonism in VS, and whether these imaging-based biomarkers show differences in Anakinra-dosed tumours from controls.
2. Ascertain if alterations in the cellular immune microenvironment of resected growing VS as assessed by imaging mass cytometry are sensitive to IL-1 antagonism in Anakinra-dosed tumours when compared to controls.
3. Ascertain if changes in the circulating concentrations of pro-inflammatory cytokines and chemokines previously demonstrated to be elevated in patients with growing VS are sensitive to IL-1 antagonism in Anakinra-dosed tumours when compared to a cohort of control individuals.
4. Confirm that Anakinra crosses the blood-nerve barrier and is taken up within growing VS.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 10/02/2025, South East Scotland Research Ethics Committee 01 (2nd Floor, Waverley Gate, 2-4 Waterloo Place, Edinburgh, EH1 3EG, UK; Tel: Not available; Sandra.Wyllie@nhs.scot), ref: 25/SS/0001

Study design
Non-randomized; Interventional; Design type: Treatment, Imaging, Immunotherapy

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Vestibular schwannoma

Interventions
The focus of this study is to validate a panel of biomarkers of response to IL-1 antagonism in patients with VS. Ten patients who are listed for surgical resection of a growing sporadic or NF2-related schwannomatosis (NF2-SWN) will be recruited via the Greater Manchester Skull Base Unit based at Salford Royal Hospital. Recruited patients will initially undergo a comprehensive 3T MRI scan protocol at Salford Royal Hospital (scan duration ~ 40 minutes). During this protocol patients will be administered a GBCA chelate (gadoterate meglumine; Dotarem, Guerbet S.A.) up to a maximum dose of 0.2 mmol/kg. From this baseline imaging, imaging parameters relevant to VS growth, such as tumoural diffusion metrics and dynamic contrast enhanced (DCE) MRI-derived measures such as the transfer constant Ktrans (min-1), will be derived. At the time of IV cannula insertion, baseline blood samples (≤20 ml) will also be obtained and blood plasma analysed using previously described multiplex assays to quantify the circulating concentrations of 48 distinct chemokines, cytokines and growth factors.

Following these baseline tests, participants will receive 100 mg subcutaneous anakinra (Kineret©) once daily for 14 days, with the first dose being delivered at Salford Royal Hospital and subsequent doses delivered at the participant's home by a trained member of the research team. This dose will be administered as a subcutaneous injection into the lower abdomen, and the first dose administration will be followed by a period of observation for 1 hour for any adverse effects. These injections will continue for a maximum of 14 days (including the first injection) and will be timed so that the final dose is given the day before the participant's surgery. This duration and dose regimen is based upon prior pharmacokinetic model estimates of tumour penetration from our preclinical and clinical stroke trials. For each participant, 13 pre-filled 0.67 ml doses of anakinra will be delivered to the patient's home using cold delivery methods, and participants will be advised to keep these pre-filled syringes in the home refrigerator at 2-8°C at all times.

Following the completion of the 14-day anakinra course, participants will attend Salford Royal for repeat MRI and blood plasma sampling (≤20 ml). The participants will then undergo surgical resection as planned, and usually on the following day after completion of the anakinra dosing. On the morning of surgery we will take further blood samples (≤20 ml) to further evaluate plasma circulating biomarkers of inflammation, and where possible these blood samples will be taken at the same time as clinical blood collection (for example, blood group analysis) to reduce patient inconvenience. Participants will then undergo surgical resection as planned, and fresh

tumour tissue will be obtained during surgery and used for downstream imaging mass spectroscopy, imaging mass cytometry analysis and quantitative polymerase chain reaction (qPCR) analysis.

Imaging and tissue data obtained from anakinra-dosed tumours will be compared with a separate control cohort of patients with similarly growing sporadic VS who have undergone surgical resection. This cohort of patients, who are being prospectively recruited under a separate NHS ethics, will not have undergone anakinra administration but will have undergone the same MRI imaging and blood sampling protocol detailed above, with imaging and blood sample collection at day 0 and day 14 and blood sample collection just prior to surgery. This is so that the short-term repeatability in these metrics can be defined. Fresh and FFPE tumour tissue specimens from this patient control group will also be available and will have undergone the same imaging mass spectroscopy, imaging mass cytometry analysis and quantitative polymerase chain reaction (qPCR) analysis described above.

Changes in tumour DCE-MRI-derived microvascular parameters and circulating plasma biomarkers in anakinra-exposed treated vs control patients will be compared. Within resected tissue the expression levels of several pro-inflammatory proteins, including TNF-α, IL-1β, IL-6, IL-18, NLRP3, CD163 and Iba1, within treated tumours will be compared to the untreated control cohort and a previously acquired historical control cohort of 15 growing sporadic VS and 4 growing NF2-SWN-associated VS tumour specimens. Imaging mass cytometry-acquired images will be analysed using established pipelines, and the infiltration of immune cells, principally TAMs, within anakinra-dosed tumours will be compared to these prospective control samples. To confirm that administered anakinra has crossed the blood-CSF and the blood-nerve barrier and accumulates in sufficient amounts within VS, snap-frozen tumour tissue and tissue from the cohort of size-matched untreated VS will also be subjected to MALDI-TOF mass spectroscopy.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Anakinra

Primary outcome(s)
Relative abundance of key inflammatory genes in anakinra-dosed VS (TNF-α, IL-1β, IL-6, IL-18, NLRP3) compared to a control cohort of size and growth-matched VS, measured using quantitative PCR analyses on tumour tissue specimens obtained at time of surgical resection and after 14 days of anakinra dosing.

Key secondary outcome(s))
1. Delivery of anakinra across the blood-nerve barrier to VS measured using MALDI-TOF mass spectrometry on tumour tissue specimens obtained at time of surgical resection and after 14 days of anakinra dosing
2. Circulating biomarkers of inflammation (IL1-α, IL1-β, IL-6, IL-18, IL-33) measured using multiplex cytokine assays from baseline (day 0) to day 12-14
3. VS tumour microenvironment measured using tumour DCE-MRI-derived microvascular parameters (Ktrans, ve, vp, absolute tumour blood flow) from baseline (day 0) to days 12-14
4. VS tumour microenvironment cellular composition measured using absolute and relative

inflammatory cell (macrophage, T cell) abundance, measured on tumour tissue specimens obtained at time of surgical resection and after 14 days of anakinra dosing

Completion date
30/04/2027

Eligibility

Key inclusion criteria
1. Adult patient (>=18 years old) diagnosed with a growing VS, for whom surgical resection is planned

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
100 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Uncertain diagnosis of VS
2. Known active tuberculosis or active hepatitis.
3. Known active malignancy.
4. Known Still's Disease
5. Neutropenia (ANC <1.5 x 109 /L)
6. Abnormal renal function (creatinine clearance or estimated Glomerular Filtration Rate (eGFR) <30 ml/minute) documented in the last 3 months
7. Live vaccinations within the last 10 days (please see Appendix 1)
8. Previous or concurrent treatment with IL-1Ra known at the time of study entry or previous participation in this study
9. Current treatment with TNF antagonists (please see below for the prohibited medication)
10. Known to have participated in a clinical trial of an investigational agent or device in the 30 days prior to study enrolment
11. Known to have participated in a clinical trial of an investigational agent or device within five half-lives (of the previous agent or device)
12. Known to be pregnant or breastfeeding or inability to reliably confirm that the patient is not pregnant (please see further guidance on pregnancy prevention below)
13. Clinically significant serious concurrent medical condition, pre-morbid illnesses, or concurrent serious infection (including confirmed or suspected COVID-19 infection), at the PI's

(or designee's) discretion, which could affect the safety or tolerability of the intervention. Please see the precaution of use section for further guidance.
14. Known allergy to IL-1Ra or any of the excipients listed in the drug SmPC (please see section below)
15. Known allergy to other products that are produced by DNA technology using the microorganism E. coli (i.e., E. coli-derived protein)
16. Current treatment with IL-6 or IL-1 inhibitors or drugs affecting the IL-1 axis. Please see below for the prohibited medication
17. Current treatment with CYP450 substrates with a narrow therapeutic index (e.g., warfarin and phenytoin)
18. Previous active treatment for VS, including previous surgical resection; previous stereotactic radiosurgery or fractionated radiotherapy; or the administration of bevacizumab within 3 months of study enrolment.
19. Inability to provide informed consent to participate in the study

Date of first enrolment
06/04/2026

Date of final enrolment
28/02/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Northern Care Alliance NHS Foundation Trust
Salford Royal
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Sponsor information

Organisation
University of Manchester

ROR
https://ror.org/027m9bs27

Funder(s)

Funder type
Government

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available