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Determining functional B cell response in lung cancer

Submission date 19/03/2019	**Recruitment status** Suspended	[X] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 02/07/2019	**Overall study status** Completed	
Last Edited 16/10/2020	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims
The aim of this study is to determine the functional B cell response in patients with non small cell lung cancer (NSCLC) through vaccination against pneumococcus. Essentially what this means is that the researchers intend to assess the quality and strength of the antibody-producing component of the immune response in lung cancer patients, and one of the best ways to do this is by measuring these responses after stimulation with vaccination. A significant proportion of cancer patients may die from non-cancer related causes such as infection. Data has showed that for lung cancer patients admitted to hospital over the last 2 years, 34% were for respiratory infection and 65% of all in-hospital deaths were due to respiratory infection. Infection appears to be an enormous unmet need, infection prevention is key and vaccination remains a useful tool. The strength of the B cell and antibody response to vaccination will be compared to outcome in NSCLC to see if there is a reduced incidence of morbidity and mortality due to pulmonary infection. The hospital burden of respiratory infection in lung cancer patients is high, but it is also preventable, which remains key to reducing morbidity, mortality and overall costs.

Who can participate?
Patients with NSCLC undergoing surgery or chemo/immunotherapy, patients aged 65 or over, and patients aged between 18 to 65 who have a long-term health condition such as COPD, diabetes, chronic kidney disease or liver disease, who therefore require PPSV23 vaccination

What does the study involve?
Participants receive the PPSV23 vaccine in their non-dominant arm by injection into the muscle. Their functional B cell response is measured by collecting blood samples 4 weeks and 12 months later to determine if it can be used to indicate outcome or prognosis, and if there is a reduced incidence of morbidity and mortality due to pulmonary infection.

What are the possible benefits and risks of participating?
Most people can safely receive the majority of vaccines. As per exclusion criteria, vaccinations will not be offered if the participant is suffering from an acute infectious illness requiring antibiotics or any acute form of treatment. This will be determined by the clinician in the pre-treatment setting (Visit 2). Hypersensitivity reactions/anaphylaxis are described but very rare occurrences (1-2 per million vaccine doses); vaccination is routinely given in the community in GP

practices and pharmacies. Participants will be informed as to what to expect and to attend their local GP or A&E department should this happen. There is a risk is that patients that have pre-existing immunity to vaccine components will have a strong immune response (arthus reaction) to the vaccine. The rates of arthus reactions in other studies of immune response to vaccination are published and as for clinical experience with these vaccinations in the routine recommended vaccination schedules are <1%. Participants will be informed as to what to expect and to attend their local GP or A&E department should this happen. The most common side effects reported in clinical trials were injection site reactions, such as: redness, swelling, pain at the injection site, limitation of arm movement. Less common systemic side effects include: fatigue, headache, muscle pain, joint pain, decreased appetite, chills, or rash. Participants will be informed as to what to expect and to attend their local GP or A&E department should this happen.

Where is the study run from?
1. Queen Elizabeth Hospital (UK)
2. Heartlands Hospital (UK)

When is the study starting and how long is it expected to run for?
January 2019 to October 2022 (updated 16/10/2020, previously: October 2021)

Who is funding the study?
University of Birmingham (UK)

Who is the main contact?
Dr Alex Richter
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
RG_18-218

Study information

Scientific Title
Determining the functional B cell response in patients with non-small cell lung cancer (NSCLC) through vaccination

Acronym
FUNCtIoN

Study objectives
The literature suggests that functional antibody assessment to vaccination in NSCLC patients has not yet been done. The paradigm of immune incompetence as a function of the lung cancer suggests that response to vaccine may also be impaired and assessing immune competence in these patients could be used to stratify or indicate prognosis/outcome.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 31/07/2019, Email: hra.approval@nhs.net, HCRW.approvals@wales.nhs.uk, REC ref: 19/WM/0182, Protocol number: RG_18-218, IRAS project ID: 262536

Study design
Experimental single-centre, mixed methods, basic science feasibility study

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Non-Small Cell Lung Cancer

Interventions
VISIT 1: Initial patient assessment clinic (surgical/oncology)*
Inform patient about study, hand out patient information sheet (PIS), and check if patient has had PPSV23 vaccination in the last five years. If patients do not know about their vaccine history, they will be asked to follow-up with their GP. Ample time given to consider participation in study

VISIT 2: Pre-operative or Pre-treatment clinic*
1. Review of Eligibility Criteria
2. Consent participant
3. Clinical assessment: collect basic demographic, comorbidity data, current medications, full vaccination history (if known), past pneumococcal illnesses
4. Cellular and immunochemical biomarkers of inflammation, innate and specific immunity (baseline bloods)

5. PPSV23 vaccination
6. Samples: Blood clotted 6 ml (red top), Blood EDTA 6 ml (purple top), Blood Vacutainer CPT 3*8 ml (24 ml)

VISIT 3: First clinical follow-up appointment – 4 weeks (+/-7 days) post-surgery/treatment*
1. Cellular and immunochemical biomarkers of inflammation, innate and specific immunity
2. Collect information about morbidity from respiratory infection in order to explore trends with functional antibody responses
3. Collect disease-specific information; progression-free and overall survival
4. Samples: Blood clotted 6 ml (red top), Blood EDTA 6 ml (purple top), Blood Vacutainer CPT 3*8 ml (24 ml)

VISIT 4: 52 week (+/- 7 days) follow-up appointment post-surgery/treatment*
1. Cellular and immunochemical biomarkers of inflammation, innate and specific immunity
2. Collect information about morbidity from respiratory infection in order to explore trends with functional antibody responses
3. Collect disease-specific information; progression-free and overall survival
4. Samples: Blood clotted 6 ml (red top), Blood EDTA 6 ml (purple top), Blood Vacutainer CPT 3*8 ml (24 ml)

The PPSV23 vaccination is an NHS standard of care treatment available to all adults aged 65 and over, as well as anyone from the ages of 2 to 65 years with a long-term health condition such as COPD, diabetes, chronic kidney or liver failure or immunosuppression.

People over 65 only need a single vaccination at any time which will protect for life; those with a long-term health condition may just need a single one-off vaccination or five-yearly vaccination depending on their underlying health problem (https://www.nhs.uk/conditions/vaccinations/pneumococcal-vaccination/). As the vaccination can be offered at any time on the NHS in accordance with the above criteria; participants will receive PPSV23 vaccine in their non-dominant arm by intra-muscular injection in the deltoid muscle bulk. This will take place during visit 2.

1. Study setting:
The data will be collected across two sites within the same NHS Trust. The sites are as follows:
1.1. Heartland's Hospital, the regional thoracic surgical unit where all lung cancer resections take place within the region. Surgical cohort will be recruited here through their routine clinical avenues. There are no further site-specific requirements to run the study here.
1.2. Queen Elizabeth Hospital Birmingham, the cancer centre treats lung cancer patients with advanced disease through first-line immunotherapy +/- chemotherapy. The second cohort of patients will be recruited here though their routine clinical avenues. There are no further site-specific requirements to run the study here.

The research setting is within the Clinical Immunology Service (CIS) at the University of Birmingham (UoB). This facility offers all laboratory and experimental capabilities required in order to handle, process, store and perform all experimental analyses on the samples collected throughout the study.

Intervention Type
Biological/Vaccine

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Pneumovax (PPSV-23) vaccination

Primary outcome(s)
1. Functional in vivo B cell response measured using serum immunoglobulin levels by class and by antibodies specific for bacterial and viral target antigens using standard laboratory ELISA and multiplex immunoassays including functional antibody tests (clotted blood). Tests include Luminex, opsonophagocytic killing assays (OPKA) and total IgG, A and M. Measured at 4 weeks (+/- 7 days) and 52 weeks (+/- 7 days) post vaccination
2. Lymphocyte subset numbers, measured using mass cytometry at baseline, 4 weeks and 52 weeks
3. Antigen-specific B cell phenotyping measured by ELISpot and CyTOF (cytometry by time of flight method)] at 4 weeks (+/- 7 days) and 52 weeks (+/- 7 days) post vaccination
4. The feasibility of carrying out this study using the proposed research methods in the NSCLC cohorts described. Feasibility is defined in terms of study uptake rates (% of those approached who are recruited), recruitment rates (n/month) and retention rates (% of those who provide samples and data at follow-up appointments)

Key secondary outcome(s))
1. Outcome or prognosis in this cohort of patients, measured by collecting data on overall survival and progression free survival in days and correlating with imaging data and clinical entries from routine follow-up visits with surgical or oncology teams, at 3, 6 and 12 months
2. Functional immune response assessed with serial blood samples and laboratory testing of biomarkers of specific adaptive immunity (as those listed above) at baseline, 4 weeks and 52 weeks

Completion date
20/10/2022

Eligibility

Key inclusion criteria
1. Patient is able to give informed consent and undertake the patient assessment as detailed in the protocol
2. Patient has resectable NSCLC and be scheduled for surgical resection of the NSCLC from the time of baseline blood withdrawal OR has advanced disease NSCLC that is eligible for chemo /immunotherapy
3. Patient is aged 65 or over OR patient is aged between 18 to 65 years AND have a long-term health condition such as COPD, diabetes, chronic kidney disease or liver disease, and therefore meeting standard of care requirements for PPSV23 vaccination

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Previously vaccinated with the PPSV23 vaccine in the last 5 years
2. Oral steroids or other form of immunosuppression that will affect vaccine response
3. Suppressed immune system caused by a health condition such as HIV
4. Allergic to components of the study vaccines
5. Suffering from an acute infective illness (as determined by the clinician at visit 2)

Date of first enrolment
01/09/2019

Date of final enrolment
01/01/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Queen Elizabeth Hospital, UHB NHS Trust
Edgbaston
Birmingham
United Kingdom
B15 2TH

Study participating centre
Heartlands Hospital, UHB NHS Trust
Bordesley Green
Birmingham
United Kingdom
B9 5SS

Sponsor information

Organisation

University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
University/education

Funder Name
University of Birmingham

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			26/07/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes