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LEGACY01: STUDY DESIGN

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ABSTRACT

This protocol details the study design in an experimental medicine study of seasonal influenza vaccination responses in Lymph nodE single-cell Genomics in AnCestrY (LEGACY01).

ATTACHMENTS

602-1266.docx

GUIDELINES

STUDY DESIGN

Interventional experimental medicine study using a model vaccine, seasonal influenza vaccine, as a probe to stimulate the immune system in vivo with sampling to collect serum, plasma, PBMC and LNC at specified time points pre and post immunisation. The study is single arm, non-randomised and open label.

Duration: Three years

Number and type of subjects: Thirty healthy adult volunteers of African or Asian ancestry will be enrolled. Participants may enrol into either cohort 1 (influenza season 2022-2023) or cohort 2 (influenza season 2023-2024).

Study intervention: A single dose of a licensed seasonal influenza vaccine will be administered intramuscularly into the deltoid muscle. See Appendix 1 for current (2021-2022) recommendations for seasonal influenza vaccines in the UK.

INFLUENZA VACCINE

The influenza vaccine of choice for this study is adjuvanted quadrivalent influenza vaccine (aQIV), also marketed as Fluad Tetra (Seqirus UK Ltd). One 0.5 mL dose of aQIV contains 15 µg of haemagglutinin from two A and two B strains of influenza propagated in hens' eggs. It is adjuvanted with MF59C.1 which contains per 0.5 mL dose, squalene (9.75 mg), polysorbate 80 (1.175 mg), sorbitan trioleate (1.175 mg), sodium citrate (0.66 mg) and citric acid (0.04 mg).

Clinical studies have been conducted in individuals aged 65 years and over and in children aged 6 months to 6 years. In studies V118_20 and V118_18, n=4269 subjects aged 65 years and older were vaccinated. AEs were injection site pain (16.3% and 31.9%), fatigue (10.5% and 16.0%) and headache (10.8% and 12.0%) and resolved within three days. In the first study, during the 2017-2018 Northern Hemisphere influenza season Fluad Tetra met non-inferiority for influenza A/H1N1, A/H3N2, B/Yamagata and B/Victoria and superiority for the B strains not included in the Fluad aTIV comparators, aTIV-1 and aTIV-2.[19,20]

Study V118_05 assessed Fluad Tetra in children aged 6 months to 6 years and elicited a higher immune response than the non-adjuvanted vaccine that persisted to 12 months. A higher incidence of local and systemic reactions was reported. Although acceptable immunogenicity was reported, the vaccine did not meet its primary efficacy endpoint in this paediatric study.

Safety and immunogenicity data of Fluad, the trivalent formulation, is relevant for aQIV because they have similar compositions and are manufactured in the same way. Post marketing surveillance data are not available yet for aQIV but are available for Fluad and are detailed in Appendix 3. [21]

The aQIV is licensed for clinical use in patients aged 65 years and over due to its immunogenicity profile in this age group. Coupled with the paediatric data, it is expected that this vaccine will deliver high titres of influenza-specific antibody at least equivalent to the unadjuvanted vaccine which includes 15 µg of haemagluttinin per strain and which is currently widely used in younger adults. aQIV contains haemagglutinin from four strains of influenza virus. As a result, participants choosing to enter this study during the Northern hemisphere influenza season and who receive the study vaccine are not expected to be disadvantaged compared with individuals who receive an influenza vaccine through the NHS.

An adjuvanted vaccine is chosen for this experimental medicine study in order to investigate lymph node responses to immunisation where the adjuvant will stimulate a local innate response. It is expected that swelling of the cortex will be visible using greyscale (or conventional) US. The published safety and tolerability profile of aQIV is in line with expected responses for an influenza vaccine. A similar safety and tolerability profile is expected in adults aged 18 – 55 years.

Participants will undergo a fine needle aspiration of a suitable axillary lymph node on two occasions at sites ipsilateral and contralateral to the site of injection.

REFERENCES

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21. Fluad, Suspension for injection in pre-filled syringe - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)