SENTINUS

SENTINEL LYMPH NODE IDENTIFICATION WITH CONTRAST ENHANCED ULTRASOUND IN BREAST CANCER

Trial Title: **SENTINUS: Technical feasibility and diagnostic accuracy of intradermal microbubbles and contrast enhanced ultrasound to identify sentinel lymph node metastases in breast cancer patients following training and mentorship of imaging specialists**

PHARMACY MANUAL

Date and Version No: 1.0 DEC-2021

Internal Reference Number: MTW_2020_KC01**/ Short title:** SENTINUS

IRAS Project ID: 274252

Ethics Ref: 20/LO/0833

CTIMP trial/ EudraCT 2020-000819-67

Author: Ian Pamphlett Nov 2021
Reviewer: Jo Patterson Nov 2021
Approver: Karina Cox Dec 2021

TABLE OF CONTENTS

1. Trial Contacts

Sponsor:
Maidstone and Tunbridge Wells NHS Trust
Research and Development Department
Above Breast Care Centre
Maidstone Hospital
Hermitage Lane
Maidstone
Kent ME16 9QQ
Tel: 01622 225627

Chief Investigator – Miss Karina Cox – karina.cox@nhs.net

Sponsor Pharmacy Department: mtw-tr.clinicaltrialspharmacy@nhs.net

2. Overview of protocol treatment

Phase II prospective multicentre pilot study incorporating training and mentorship of imaging specialists.

Imaging specialists will be recruited from 5 Breast Cancer Units within the UK. Two units will have prior experience of using intradermal microbubbles and CEUS to identify and biopsy sentinel lymph nodes in patients with early breast cancer and 3 units will be naïve to the technique. Each unit will put forward 2 imaging specialists to take part in the study, therefore 10 in total.

For those units without prior experience of intradermal microbubbles, if necessary, their existing ultrasound machines will be upgraded to allow contrast studies.

During the trial period, each unit will also prospectively audit their malignant lymph node detection rate with conventional B-mode axillary ultrasound and biopsy.

Following discussion at the breast cancer MDT, female patients aged over 18 years with early invasive carcinoma of the breast with a normal B-mode axillary ultrasound/ benign biopsy of indeterminate lymph nodes and planned primary surgical treatment will be approached to take part in this study. The 5 units will aim to recruit 50 patients over 24 months (250 in total) with each of the 10 participating imaging specialists performing 25 procedures. Participating patients will not receive any expenses.

3. Study Drug

SonoVue ultrasound contrast agent (BRACCO International, Amsterdam, The Netherlands)

Marketing authorization number: EU/1/01/177/002

RSI: SmPC
Molecular formula: F_6S

Sulphur Hexafluoride is a contrast agent composed of an inorganic fluorinated inert gas comprised of six fluoride atoms bound to one sulphur atom, with potential diagnostic activity upon imaging.

Physical description: Sulphur hexafluoride appears as a colourless odourless gas. Non-combustible. Shipped as a liquefied gas under own vapor pressure.

Decomposition: Sulfuryl and thionyl fluorides are the major decomposition products of sulphur hexafluoride.

Sulphur hexafluoride is an unreactive substance. Sulphur hexafluoride is not attacked by water, acids, or bases, at room temperature. It is resistant to the action of carbon, copper or magnesium at red heat, and will not react with sodium below its boiling point. It reacts with sulphur vapour or hydrogen at 400 °C.

ATC code: VO8DA05.

Pharmaceutical properties: Sulphur hexafluoride is an inert, innocuous gas, poorly soluble in aqueous solutions. There are literature reports of the use of the gas in the study of respiratory physiology and in pneumatic retinopexy. The addition of sodium chloride 9 mg/mL (0.9%) solution for injection to the lyophilised powder followed by vigorous shaking results in the production of the microbubbles of sulphur hexafluoride. The microbubbles have a mean diameter of about 2.5 µ m, with 90% having a diameter less than 6 µ m and 99% having a diameter less than 11 µ m. Each millilitre of SonoVue contains 8 µ L of the microbubbles. The intensity of the reflected signal is dependent on concentration of the microbubbles and frequency of the ultrasound beam. The interface between the sulphur hexafluoride bubble and the aqueous medium acts as a reflector of the ultrasound beam thus enhancing blood echogenicity and increasing contrast between the blood and the surrounding tissues.

SonoVue has been shown to be rapidly removed from the blood. The route of SF6 elimination was by means of the lungs in the expired air.

Formulation: SonoVue sulphur hexafluoride microbubbles 8 uL/mL. Powder and solvent for dispersion of injection. 1 vial containing 25 mg of powder to be reconstituted with 5mL sodium chloride 9 mg/mL (0.9%) solution for injection

4. Study Drug Supply

The commercially available SonoVue will be ordered directly from the manufacturer (Bracco) by the Pharmacy Department at each participating site.

Each site will be reimbursed for SonoVue used in the Sentinus Trial.

5. Storage and Temperature Monitoring

Store as per SmPC

This product does not require ring fencing for use in trial patients. It is the responsibility of each site to ensure there is enough SonoVue on site.

Follow local pharmacy temperature monitoring procedures.

6. Dispensing and Labelling

Pharmacy staff should receive and document training from the local Clinical Trials Pharmacy Team prior to screening / validating, dispensing and checking the trial prescription.

Once a patient has been registered to participate in the Sentinus Trial, the patient will be given a Participant Trial Number. This is allocated sequentially at each site.

Ensure when the Sentinus Trial Prescription is given to pharmacy a copy of the patient's trial registration form is attached to the prescription.

Dispense as per prescription.

Attach a local dispensing label and a trial sponsor provided supplementary label to the dispensed product.

Ensure when the prescription is collected it is signed for.

When the SonoVue has been administered the prescription must be returned to Pharmacy and stored in the Pharmacy Site File.

7. Drug Accountability

Complete the trial sponsor provided accountability log for each dispensing episode.

8. Administration

The SonoVue is to be reconstituted in the breast ultrasound department and will be administered Intradermally as per trial protocol. The administrator must sign and date the trial prescription.

9. Drug Destruction

SonoVue will be disposed of at site according to the sites institutional standard operating procedure.