Imaging Manual

Study title:	**BIO89-100-002**
Imaging site:	**Valley Radiology**

The original signature page is archived in the Imaging Master File at Antaros

Approved by:

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Date (dd-MMM-yyyy)

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1 Objectives

This manual describes the process to be followed at the Imaging site when performing MRI in BIO89-100-002 study.

The workflow is described in the figure below:

2 Sites

Imaging site	Valley Radiology
Recruiting site	ProSciento 855 3rd Avenue, Suite 4430 Chula Vista, CA 91911

3 Objectives

3.1 Objectives with the BIO89-100-002 study

To characterize biomarkers, PD profile and biological activity of BIO89-100 administered at ascending doses and with both QW and Q2W dosing intervals

3.2 MRI Objectives

Secondary Objectives	Endpoint(s)
Pharmacodynamic assessment	Change from baseline in: • MRI-PDFF
Exploratory	
Pharmacodynamic assessment	Change from baseline in: • Abdominal visceral fat (VAT) • Abdominal subcutaneous fat (SAT) • Liver volume

4 Ethical/legal aspects

The study is approved by the Ethics Committee. All subjects that will be referred to the Imaging site have signed an informed consent at the recruiting site.

5 Incidental findings

Incidental finding: An image feature of potential pathological nature that is discovered unintentionally in addition to the study protocol required imaging endpoints. The incidental finding can additionally not directly be discarded as caused by an imaging artefact.

A radiologist at the Imaging site, e.g. hospital, where the imaging is acquired must do a medical reading of the MRI, i.e. will be handled in accordance with local procedures. The assessment will be reported to the Investigator at the referring site, who will review and file the assessment in the subject´s source documents and take the needed actions.

6 Procedure

6.1 Subject referral

The Recruiting Site:

- Will ask the subject if there is any contraindication for MR, i.e. pace-maker, intra-cranial clip according to normal routine at imaging site
- Ensure an informed consent for the MRI procedure is obtained

- Will refer the subjects to the Imaging site and will state when the MR should be performed. It is important that the timing of the MR procedure is in accordance with the protocol.
- Will remind the subjects of study recommendations i.e. not to eat four hours before the scan and that intake of water or liquid should be avoided or limited 2 hours before the scanning.

6.2 Initial procedures at imaging site

The Imaging site:

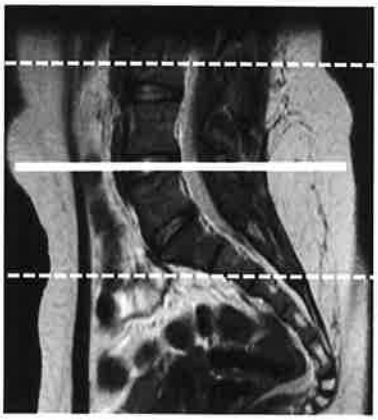
- Will schedule the MRI process
- Inform the referring Investigator immediately about any change to the MRI appointment date
- Identify the subject according to normal hospital procedure
- Perform routine check for all exclusion criterions for MR, e.g. pace-makers, intra-cranial clips
- Perform check of recommended study restrictions and record in Scan Log

6.3 MRI Visits and procedures

- **MR1 (Screening)** MRI-PDFF, Liver volume imaging and VAT/SAT
- **MR2 (Day 50)** MRI-PDFF, Liver volume imaging and VAT/SAT
- **MR3 (Day 92)** MRI-PDFF, Liver volume imaging and VAT/SAT
- **MR_ET** (in case of Early Termination) MRI-PDFF, Liver volume imaging and VAT/SAT

6.4 Imaging protocol

Subject positioning	• The subject is positioned in supine position with the head first and a cushion under the knees. Make sure that the coil is positioned so that the liver scan can be performed without repositioning.	
PLEASE NOTE:	• Do not change the FOV or angle of the scans except as specified below	
Survey of liver (breath hold, end exp).	• Perform a survey scan in breath hold including a coronal view of the liver.	
Liver Fat BH (PDFF): (breath hold – end exp)	• The patient should hold the breath at end expiration during all PDFF scans, as well as during scout scans and parallel imaging calibration scans • Position the axial scan to cover as much liver as possible as shown in the figure. • If the liver doesn't fit, cut equal amount of liver in both feet and head directions. • Do **NOT** angle the scan, use straight axial orientation **Check the image quality after the scan to make sure that the breath hold was successful. If not, repeat the investigation and make a note in the Scan Log.**	 **Typical Scan parameters:** 3D PDFF scan 30 slices 5 mm slice thickness FOV 380-400 mm IDEAL-IQ (GE) mDixonQuant (Philips) LiverLab: qDixon (Siemens) PDFF maps reconstructed

Liver Volume BH (breath hold)	• Position the scan in the axial position. Make sure that the total scan volume covers the entire liver. • If not, increase the slice thickness so that the liver is covered. **If the slice thickness was increased, make a note of this in the Scan log and make sure the same slice thickness is used for the follow up scans.** Run the scan in a single breath-hold at end expiration. Check the image quality after the scan to make sure that the breath hold was successful. If not, repeat the investigation and make a note in the Scan log.	 **Scan parameters:** 3D axial Water Fat Dixon scan LAVA-FLEX (GE) VIBE eDixon (Siemens) mDixon (Philips) No angulation. 5 mm slice thickness 56 slices. FOV 420-450 mm **Water and fat images reconstructed**
Adipose tissue imaging BH: (breath hold – end exp)	•Run a sagittal survey of the Lumbar spine •Center the scan on the L4-L5 interface (disc) as shown in the image. Do **NOT** angle the scan, use straight axial orientation •Run the scan in a single breath-hold at end expiration **Make a note of any change to the slice thickness in the Scan Log and make sure the same slice-thickness is used for the follow-up scans.** **Check the image quality after the scan to make sure that the breath hold was successful. If not, repeat the investigation**	 **Typical Scan parameters:** 3D axial Water Fat Dixon scan 40 axial slices 5 mm slice thickness

	and make a note in the Scan Log. **Make sure that no foldover appears that includes subcutaneous adipose tissue**	FOV 450 mm LAVA-FLEX (GE) mDixon (Philips) eDixon (Siemens) **Water and Fat images reconstructed**

7 Archiving

Image data should be archived at the Imaging site according to normal hospital/site procedure.

8 Coding the examination

- ☐ Select current subject under "Administration"

- ☐ Select **Tools** and **Anonymise Patient**
- ☐ In anonymised exam open **Edit Patient**
- ☐ Substitute the **subject's name** with **subject ID**,
  - ☐ Substitute the subject's **Patient ID** with the **Visit code** (MR1, MR2 or MR3)
  - ☐ Remove the **accession number**
  - ☐ Remove the **referring physician**
  - ☐ Replace the month and day in the subject's date of birth with 01-Jan. Example, a subject with date of birth 29/10/1956 becomes 01/01/1956.
  - ☐ **Save**

9 Image File transfer to Antaros Core Lab

9.1 Timelines

Image file should be transferred to Antaros within 2 working days of acquisition.

9.2 Transfer the image file to a CD or USB memory

9.3 Transfer file to fileserver

If you have questions regarding this procedure, contact Corelab on the following e-mail corelab@antarosmedical.com.

- ☐ Insert the CD or USB-drive on the computer used for file transfer
- ☐ Pack all images to a zip-file (Windows computers: right-click folder, select Send to, and then select Compressed (zipped) folder)
- ☐ Name the zip-file: **ID_VC_YYYYMMDD.zip** where
  - **ID** is **Subject Identifier** e.g. 101001,
  - **VC** is **Visit Code (MR1, MR2 or MR3)**, and
  - **YYYYMMDD** is **scan date**

- ☐ Use a Web Browser to open the Antaros Medical SharePoint webpage. **The user login details are in Appendix A, 'Login Details'.**
  - Username: site specific
  - Password: site specific
  - Select folder
  - Click: **Upload**
  - Select the zipped file and select **Open**

MRI Site's staff shall use Antaros' cloud server Microsoft SharePoint ("Server") for uploading files in accordance with the directions and trainings provided by Antaros.

The access to the Server shall be permitted only to the MRI Site's staff that have been previously trained and approved by Antaros. MRI Site shall not allow access to the Server to other external parties.

MRI Site's staff is not permitted to undertaking actions or upload files on the Server that are contrary to the directions and trainings provided by Antaros.
In case the electronic upload of images is not possible, then transfer file to CD and Courier to Antaros

9.4 Inform Antaros Medical

Send an e-mail to corelab@antarosmedical.com and inform that the zipped scan file is uploaded.
The mail should include:

- Study Name
- Subject ID
- Visit code
- Scan date
- Also include a copy of the completed Scan Log

9.5 Transfer Scan Log to the referring investigator

Send an email with the Scan Log to the referring investigator.

9.6 Antaros Corelab QC and feedback

All incoming images will go through Antaros Corelab QC process. Process is described in detail in the Corelab manual.

Corelab will perform three major QC steps:

- Administrative QC (Scan log, documentation, files, signing, dates)
- Data QC (Verifying coding, check parameters, reconstruction)
- Visual QC (Check export, image position, image quality)

If a QC-issue is detected in the QC process Corelab will mail QC feedback to site preferably within two working days. This is to prevent that issue will not be repeated in new scans and to inform site if a rescan will be needed.