Antaros Medical

Imaging Manual

Study title:	**HM-GCG-102**
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)

This manual supersedes N/A, first version

Confidential

Table of Contents

1 Objectives

This manual describes the process to be followed at the Imaging site when performing MRI in the HM-GCG-102 study.

The workflow is described in the figure below:

2 Sites

Imaging site	Valley Radiology
Recruiting site	ProSciento, Inc. 855 3rd Avenue, Suite 4400 Chula Vista, CA 91911 PI: Dr. Julie Willard julie.willard@prosciento.com

3 Objectives

3.1 Objectives with the HM-GCG-102 study

To evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of multiple doses of HM15136 in obese or overweight subjects with co-morbidities (a Phase 1 study).

3.2 MRI Objectives

Exploratory Objectives	Endpoint(s)
Pharmacodynamic assessment	Change from baseline in: • MRI-PDFF* • Abdominal visceral fat (VAT) *$PDFF^{Day\ 85}$ only if $PDFF^{Day\ -1} \geq 10\%$

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, e.g. via email, 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 MRI, 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 MRI 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:

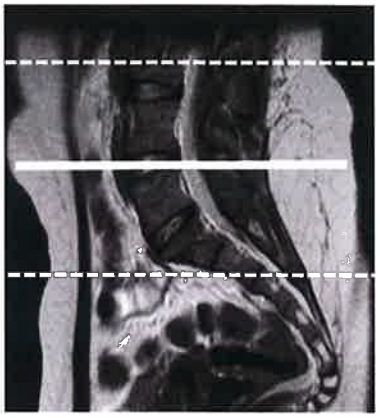
- Will schedule the MRI process
- Inform the referring Investigator immediately about any change to the MRI appointment date
- Identify the subject according to normal hospital procedure
- Perform routine check for all exclusion criterions for MRI, e.g. pace-makers, intra-cranial clips
- Perform check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

6.3 MRI Visits and procedures

- MR1 (Day -1) MRI-PDFF and VAT
- MR2 (Day 85) if MRI-PDFF^{MR1} ≥10% → MRI-PDFF and VAT
  if MRI-PDFF^{MR1} <10% → VAT
- MR_ET (unscheduled, e.g. early termination)

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 • If a parameter is changed, document this change in the ScanLog • For all follow-up scans, review the previous ScanLogs so all scanning for a subject is performed with the same parameter settings	
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

Adipose tissue imaging BH (VAT): (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 and make a note in the Scan Log.** **Make sure that no foldover appears that includes subcutaneous adipose tissue**	 **Typical Scan parameters:** 3D axial Water Fat Dixon scan 40 axial slices 5 mm slice thickness 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

Image data must be coded before transfer to Antaros; subject identifiers must be removed from images and headers, e.g. name, date of birth etc.

- ☐ 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.

9 Image File transfer to Antaros Core Lab

9.1 Timelines

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

9.2 Transfer the image files to a CD or USB memory

This step (9.2) is only performed if USB or CD are needed to transport the image files to the computer to be used for file transfer to Antaros.

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 (if CD or USB was used)
- ☐ 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, e.g MR1 or MR2
  - **YYYYMMDD** is scan date, e.g. 20190815

- ☐ Use a Web Browser to open the Antaros Medical SharePoint webpage. For address and site specific login details, see Appendix A, 'Login Details', in the site binder.
  - Username: *site specific, see Appendix A*
  - Password: *site specific, see Appendix A*
  - Select folder
  - Click: **Upload**
  - Select the zipped file to be uploaded and select **Open**
- ☐ Notify CoreLab that data is uploaded, see 9.4 below.

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 to inform that the zipped scan file is uploaded.

Recipient: corelab@antarosmedical.com
Mail subject: HM-GCG-102 data transfer notification
Attachments: please attach scanned copy of the ScanLog for the uploaded data

The message text should include:

- Study Name
- Subject ID
- Visit code
- Scan date

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.

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.