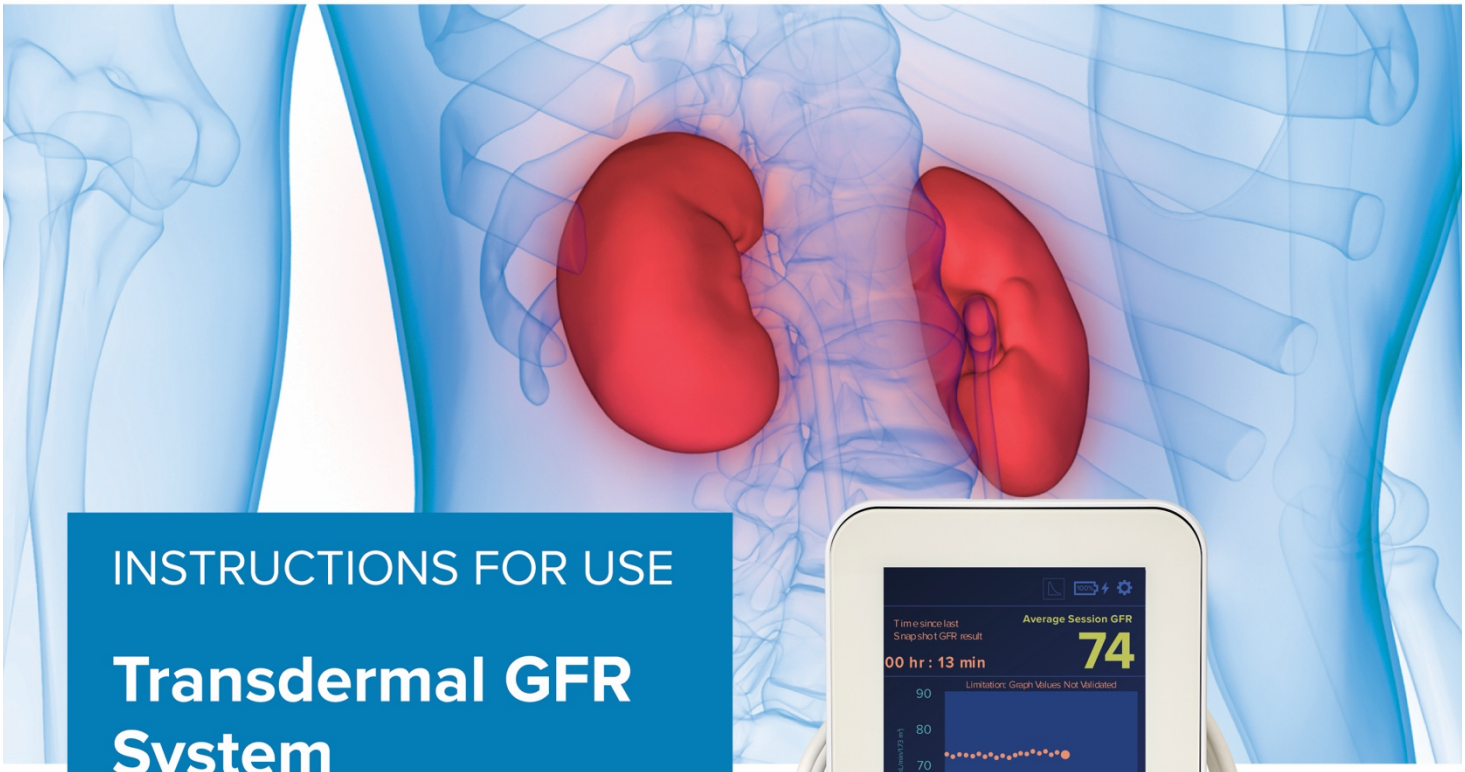
MediBeacon®
Transdermal GFR



INSTRUCTIONS FOR USE

Transdermal GFR System

℞ only

medibeacon.com

ML-0001-593-310

Table of Contents

Section I: About this Device

The MediBeacon® Transdermal GFR System (TGFR) determines glomerular filtration rate (GFR) by assessing the clearance of an intravenously administered tracer agent over time. GFR is determined using this proprietary fluorescent tracer agent which is only excreted renally and whose clearance rate is measured by transdermal fluorescence detection.

The MediBeacon TGFR is a medical device comprised of Lumitrace® (relmapirazin) 18.6 mg/mL injection for intravenous use, the MediBeacon® TGFR Monitor, and the MediBeacon® TGFR Sensor. All components are required to obtain a transdermal GFR assessment (tGFR).

Section II: System Description

The MediBeacon TGFR provides an assessment of GFR at the point of care. Noninvasive transdermal fluorescence detection of the agent clearance rate is converted by the system into GFR indexed by body surface area.

The MediBeacon TGFR is comprised of three distinct parts:

- Lumitrace® (relmapirazin) injection for intravenous use, is the novel and proprietary fluorescent tracer agent intravenously administered to a patient and then subsequently excreted from the body by the kidneys.
- The MediBeacon TGFR Sensor contains the light source and photo detector for noninvasively detecting Lumitrace fluorescence transdermally. This sensor is attached to the upper chest using a biocompatible adhesive. This sensor has a built-in cable that connects to the monitor.
- The MediBeacon TGFR Monitor provides power to the sensor, digitizes the data acquired from the sensor, contains the algorithms to convert sensor output to GFR (ml/min/1.73m^2), and reports GFRs to the clinician and/or caregiver.

The TGFR Sensor is applied externally to the upper chest, and background fluorescence is gathered by the TGFR Monitor for approximately twenty minutes. Lumitrace is then intravenously administered, and the monitor continues to acquire fluorescence data as a function of time. Data analysis algorithms convert the acquired signal into an indexed GFR value (tGFR) when a stable rate of fluorescence clearance is determined which will vary by subject. The tGFR is updated and reported on the monitor approximately every 15 minutes until the algorithm detects a fluorescence intensity too low for conversion into an accurate tGFR. For patients with normal renal function, this session time may be up to 8 hours; for Stage 4 CKD patients, this session time may be on the order of 12-24 hours.

The TGFR Sensor also has components to compensate for local time-varying tissue properties, such as changes in blood volume, by measuring diffusely-reflected light. This sensor is intended for a single use on a single patient and must be replaced between patients.

Key System Acronyms:

- **GFR -** Glomerular Filtration Rate
- **eGFR -** estimated GFR
- **nGFR -** plasma-derived indexed GFR
- **tGFR -** transdermally assessed GFR
- **TGFR -** Transdermal GFR System
- **Average Session GFR -** the validated GFR from a completed session; computed using a weighted average of the interim readings using a quality factor for each reading
- **Snapshot** - intermediate tGFR readings as the data are being acquired. These values have not been validated

Section III: Indications

The MediBeacon® Transdermal GFR System (TGFR) is intended to assess the Glomerular Filtration Rate (GFR) in adult patients with impaired or normal renal function by noninvasively monitoring fluorescent light emission from an exogenous tracer agent over time. This device has been validated in patients with stable renal function.

The MediBeacon® TGFR is not approved for use in patients with GFR <15 ml/min/1.73 m^2, GFR >120 ml/min/1.73m^2, patients on dialysis, or anuric patients. The use of this device in patients with dynamic and rapidly changing renal function has not been validated. This device is not intended to diagnose acute kidney injury (AKI).

The MediBeacon® TGFR Sensor and exogenous tracer agent, Lumitrace® injection, are single use and are only used with the MediBeacon® TGFR.

The MediBeacon® TGFR Sensor is a single use device intended to attach to the patient's skin and excite fluorescence in Lumitrace® injection, the tracer agent, and measure the returning light intensity. The data is sent to the MediBeacon® TGFR Monitor.

Lumitrace® is an injectable exogenous fluorescent tracer indicated for use with the MediBeacon® Transdermal GFR System (TGFR) for Glomerular Filtration Rate assessment.

Contraindications: There are no known contraindications.

Section IV: Accuracy

Average Session GFR results comparison with measured GFR results:

Ninety-four percent of the Average Session GFR values obtained using this device were within 30% of the measured GFR values (with a confidence interval of 89.4-96.9%). This was the outcome of the pivotal trial.

P30 Value	Upper 95% CI	Lower 95% CI
94.0%	96.9%	89.4%

Average Session GFR results comparison with estimated GFR (eGFR) results:

(using the creatinine-based 2009 CKD-EPI equation)

	Average Session GFR	eGFR*
P30	94.0%	92.9%
95% Confidence Interval	89.4-96.9%	88.1%-96.1%

*The eGFR results above were obtained via a post hoc analysis, (which was not the predetermined outcome measure from the study).

In the pivotal trial, 94.0% of the Average Session GFR values obtained using this device were within 30% of the measured GFR values and 92.9% of the eGFR values (creatinine based 2009 CKD- EPI equation) were within 30% of the measured GFR values. The confidence intervals overlap (see table above).

Subgroup population results:

Patients were grouped into Stratum 1 (eGFR ≥70 mL/min/1.73m^2) and Stratum 2 (eGFR < 70 mL/min/1.73m^2).

Patient Population	P30 Value	Upper 95% CI	Lower 95% CI
Stratum 1 (eGFR ≥70 mL/min/1.73m^2) N=90	95.6%	98.8%	89.0%
Stratum 2 (eGFR < 70 mL/min/1.73m^2) N=92	92.4%	96.9%	84.9%

Primary Endpoint Evaluation by Fitzpatrick Skin Scale (FSS)

Patient Population	P30 Value	Upper 95% CI	Lower 95% CI
FSS Type I-II N=77	96.1%	99.2%	89.0%
FSS Type III-IV N=69	92.8%	97.6%	83.9%
FSS Type V-VI N=36	91.7%	98.3%	77.5%

See Section XVII: Appendix for the clinical study summary.

Section V: Warnings, Cautions and Safety Information

Pay close attention to the following Warnings and Cautions statements. Some of these statements will appear elsewhere in the manual.

Warnings

1. Lumitrace® injection has light absorbance at 266 nm and 435 nm, and broad fluorescent emission at ~560 nm when excited at ~440 nm. There is potential interference for in vitro diagnostic assays that utilize wavelengths near these values. Any drug activated at these wavelengths should not be used in conjunction with Lumitrace.
2. Lumitrace injection may interfere with clinical laboratory tests. **DO NOT ADMINISTER** if the patient is expected to need clinical laboratory testing while Lumitrace is present in their system (up to 72 hours for renally impaired patients). The presence of Lumitrace decreased B-Type Natriuretic Peptide (BNP) results by around 20% in limited testing.
3. Follow the instructions for system set up and use. Not following system operational instructions may lead to patient injury or delayed session results.
4. To avoid risk of electric shock, this equipment must only be connected to a supply Mains with “protective earth". If integrity of the Protective Earthing (PE) conductor or the PE grounding system is questionable, do not use the TGFR Monitor.
5. The data port cover must be fully attached during all use of the system with the patient. Do not use the TGFR Monitor with the data port cover removed.
6. Do not use the system in the proximity of magnetic resonance imaging equipment.
7. Operating the system in the presence of equipment that radiates high energy electromagnetic and radio frequencies (e.g., cauterizing or electrosurgical equipment) can interfere with system performance.
8. Do not administer a second Lumitrace injection during an active session.
9. Avoid the use of fluorescein during a TGFR session as it may interfere with the assessment.
10. The TGFR Sensor is a single-use, disposable system component; do not reuse.
11. Do not adjust or manipulate the sensor after baseline is established.

Cautions

1. This system is not designed, sold, or intended for use except as indicated.
2. The system should only be used by trained personnel.
3. System equipment can only be modified by a qualified service provider. Appropriate inspection and testing must be conducted to ensure continued safe use of the equipment.
4. Be sure the pole clamp is fully tightened and secured to the IV pole. If clamp is not properly secured, the monitor may fall, causing injury to the patient or operator, or damage to the monitor.
5. System performance may be degraded if operated or stored outside the environmental conditions specified in this manual.

6. Be sure all safety labels are legible.
7. Do not open the TGFR Monitor, exposing internal components. Contact appropriate personnel for servicing.
8. To ensure proper ventilation, make sure the space at the back of the TGFR Monitor is clear of any obstructions that may block the system fan.
9. Do not use a damaged TGFR Sensor. If exposed wires or sharp edges from dropping or damage are observed, dispose of the damaged sensor following clinic or hospital procedures and guidelines.
10. Do not remove adhesive liner and place sensor until the site is properly prepared as outlined in the 'Site Preparation' section
11. Only place the sensor on intact healthy skin. Avoid cuts, abrasions, burns, or sites of irritation. Avoid areas of inconsistent skin tone, such as tattoos, moles, uneven pigmentation, etc.
12. Skin irritation from adhesive on the TGFR Sensor may occur at the point of patient contact.
13. Bolus infusions may impact the GFR assessment temporarily while the vasculature-tissue equilibrium is re-established.
14. Do not administer the Lumitrace injection until instructed by the TGFR Monitor's 'Administer Lumitrace' screen.
15. Clean and disinfect exterior surfaces of the TGFR Monitor according to instructions in section XIV.
16. Do not immerse the display TGFR Monitor or TGFR Sensor in water. The monitor and sensors are not waterproof.

Section VI: Symbols

Symbol	Definition
#	The model number of the product
REF	The manufacturer's catalog number so that the medical device can be identified.
LOT	The manufacturer's batch code so that the batch or lot can be identified.
SN	The manufacturer's serial number code so that the specific device can be identified.
	Medical device manufacturer.
	Medical device was manufactured YYYY-MM-DD.
Rx only	For prescription use only.
	Refer to the Instruction Manual
	Defibrillation-proof Type BF applied part (TGFR Sensor)

	Intended for connection to an external conductor for protection against electric shock in case of a fault, or the terminal of a protective earth (ground) electrode.
	Temperature limits to which the medical device can be safely exposed.
	Range of humidity to which the medical device can be safely exposed.
	Range of atmospheric pressure to which the medical device can be safely exposed.
	Discard must be sent to separate collection facilities for recovery and recycling. By separating this product from other household-type waste, the volume of waste sent to incinerators or landfills will be reduced and natural resources will thus be conserved.
	Projectile hazard: Keep out of MR scanner rooms
	Keep dry.
	Do not use if packaging is opened or damaged.
	Use by the date indicated on the sensor package labeling.
	Do not reuse.

Section VII: System Components

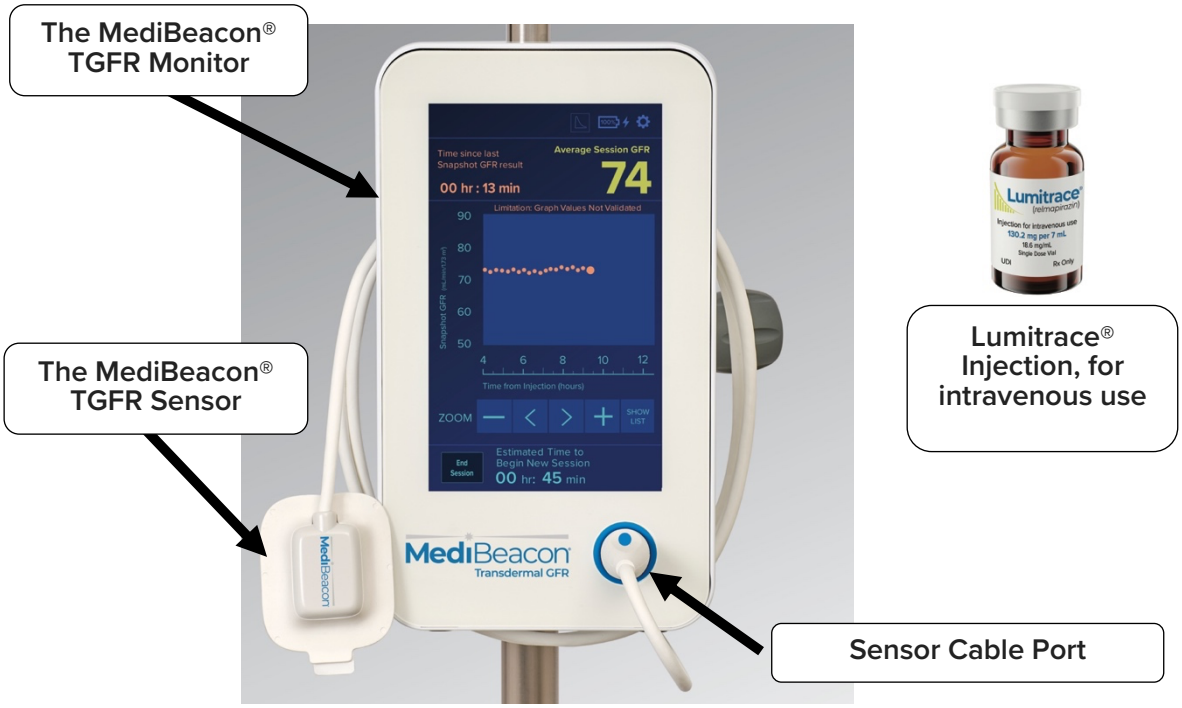


Figure 1. The MediBeacon Transdermal GFR System components

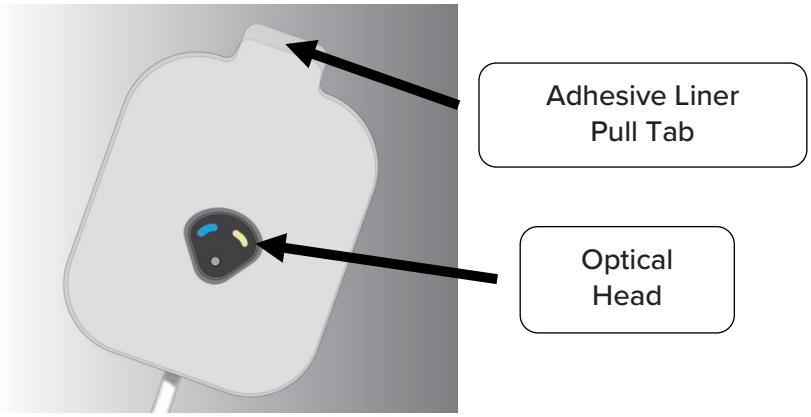


Figure 2. The MediBeacon TGFR Sensor optical head and adhesive surface

Component Information:

- The MediBeacon® TGFR Sensor is a single use device intended to attach to the patient's skin and excite fluorescence in Lumitrace injection, the tracer agent, and measure the returning light intensity. The data is sent to the TGFR Monitor.
- The MediBeacon® TGFR Monitor is intended to be connected to the TGFR Sensor and compute and display the transdermal GFR (tGFR).
- Lumitrace® is an injectable exogenous fluorescent tracer agent indicated for use with the MediBeacon Transdermal GFR System (TGFR) for Glomerular Filtration Rate assessment.

Getting Started

The following document outlines the instructions for use for the TGFR Device (TGFR Monitor and TGFR Sensor).

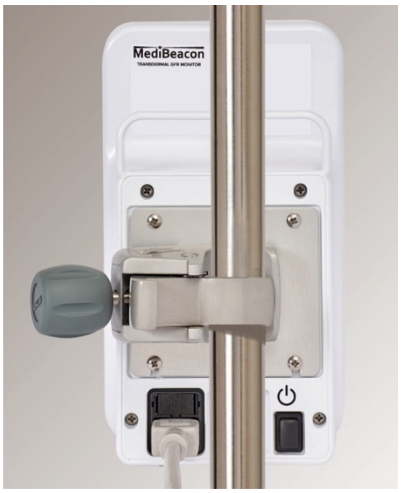
Follow the instructions for system set up and use. Not following system operational instructions may lead to patient injury or delayed session results. In addition to this IFU, there is a Quick Guide attached to the TGFR Monitor with a high-level summary of the instructions.

Caution: Do not administer the Lumitrace injection until instructed by the TGFR Monitor's 'Administer Lumitrace' screen.

System Setup

Remove the TGFR Monitor from the packaging.

1. The TGFR Monitor has a pre-attached pole clamp. Attach the monitor to a 5-wheel IV pole (1.9 in/ 4.825 cm wheel diameter with a 23 in / 58 cm minimum base diameter) at a maximum height of 3.3 ft/ 1 meter (clamp height) and securely tighten the pole clamp to the pole (Figure 3). Check to ensure the monitor and pole do not create a tipping risk.



Caution: Be sure the clamp is fully tightened and secured to the IV pole. If clamp is not properly secured, the monitor may fall, causing injury to the patient or operator, or damage to the monitor.

Figure 3. TGFR Monitor on pole

2. Connect the power cable to the port on the back of the monitor and to the wall outlet. Depressing the power button will power on the monitor (Figure 4, left). Maintain easy access to the power cord plugs at the monitor and wall outlet for disconnection from Mains power supply if required. Unplug the power cord to break Mains power supply.
3. Serial, USB and Ethernet ports are located on the left side of the monitor (Figure 4, right). These ports are not used during a regular session.

   Warning: The data port cover must be fully attached during all use of the system with the patient.

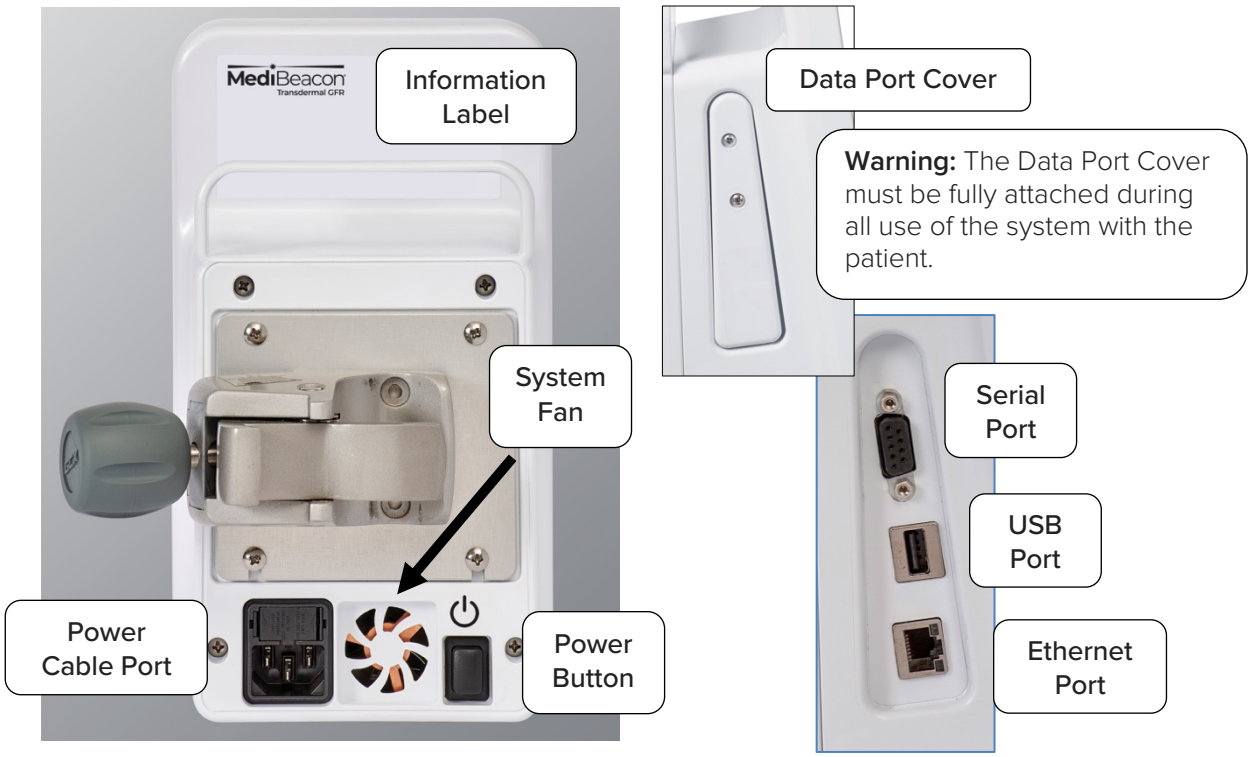


Figure 4. TGFR Monitor rear (left) and side (right) panels.

Data Ports

- **Serial Port:** For software updates and service. For MediBeacon Service use only.
- **USB Port:** Not user functional in current software release. For MediBeacon Service use only.
- **Ethernet Port:** Not functional in current software release.

During monitor power up, the Splash screen displays while the system software loads. Once the system software loads, the monitor will progress to the 'Connect Sensor' screen (Figure 5). The setup screens are divided into several sections as shown.

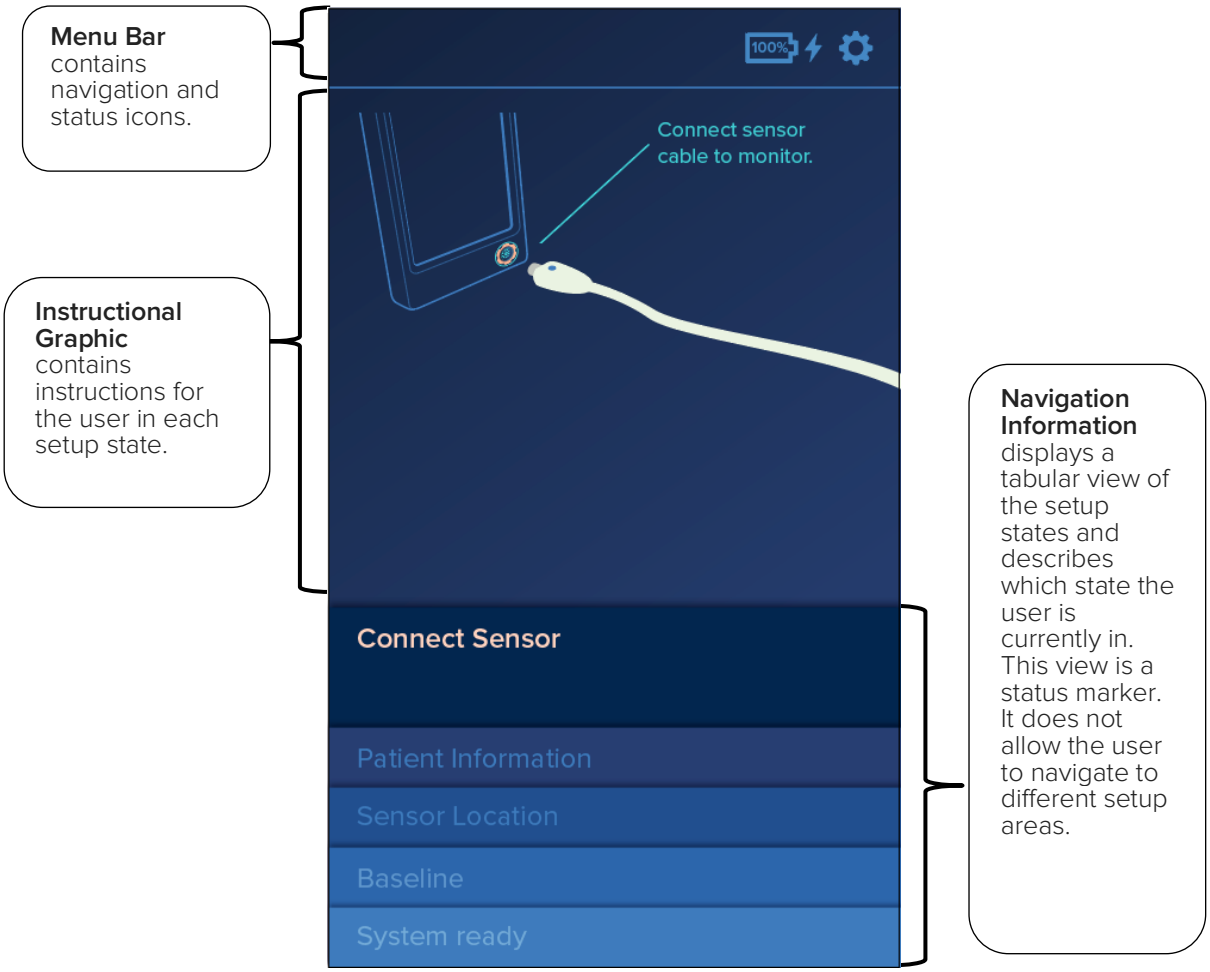


Figure 5. Connect Sensor screen

Menu Bar

The Menu Bar (Figure 6) appears at the top of the monitor touch screen. This bar displays a set of icons that can be used to navigate the monitor's menus. Icons available on this menu vary depending on the particular monitor screen.

Figure 6. MediBeacon TGFR Menu Bar with navigation icons.

Menu Bar icons (left to right):

1. **Back:** Available depending on system status. The back icon is available until the Ready to Administer stage. After this stage, the Back icon is unavailable except in the 'Settings' menu and submenus.
2. **Lumitrace Injection Clearance:** Available once the baseline sequence starts. Displays a graph of the Lumitrace clearance over time.
3. **Battery Level:** Indicates battery charge level (%) and charging status (thunderbolt). The charging status icon appears when the system is plugged in and battery is charging. The icon will display red when the battery is critically low.
4. **Settings:** Available on all monitoring screens. Selecting this icon will navigate to the 'Settings' menu.

Section VIII: Instructions for Use

REMINDERS

- **Follow instructions for attaching sensor to patient –** improperly attaching a sensor to a patient may lead to delay of treatment.
- **Follow Sensor placement instructions** – placing sensor on moles, scar tissue, or other skin blemishes may lead to delay of treatment.
- **Follow Sensor Site Cleaning procedures** – improper cleaning of the sensor site on a patient may lead to delay of treatment.
- **Keep Sensor Adhesive clean and free of debris before applying to patient** – improper handling of the sensor adhesive may lead to delay of treatment.
- **Patient movement during baseline readings could delay calculations.** – keep patient as still as possible during baseline.
- **The data port cover must be fully attached during all use of the system with the patient.**

Starting a NEW TGFR session

A "Session" is defined as the monitoring period of a single administration of the Lumitrace injection. The steps to start a session are listed below.

- Determine the Sensor and Cable Anchor Location
- Site Preparation
- Sensor Placement
- Patient Positioning / Posture
- Connecting a Sensor to the Monitor
- Patient Information Screen
- Sensor Location Screen
- Skin Tone Adjustment
- Establishing Baseline
- System Ready – Administer Lumitrace Injection, for intravenous use.

Caution: It is important to determine the sensor and cable location, prepare the site, place the sensor, and anchor the cable ***prior to*** plugging the sensor into the monitor.

Determine the Sensor and Cable Location

- The sensor can be placed on the patient's upper chest area. Priority should be given to the pectoralis major. **Caution: Do not remove adhesive liner and place sensor until the site is properly prepared as outlined in the 'Site Preparation' section.**
- Choose an area for the sensor that is free from tattoos, moles, surface blood vessels, scar tissue, irritation, discoloration, or other skin blemishes.
- For optimal contact of the sensor optical head to the skin, choose as flat a body area as possible. Surfaces with excessive curvature (especially concave) may result in loss of contact between the skin and optical head, disrupting sensor accuracy. Prior to removing the sensor adhesive liner, location can be tested by placing the sensor over the site of interest. To help minimize cable strain, align the long end of the sensor with the midline of the patient's body, especially if they are ambulatory.
- Additionally for optimal sensor attachment, the skin should be free of any lotions, creams, sweat, or any substance that would interfere with optical measurements or sensor attachment.
- Select the sensor site carefully as the sensor adhesive is limited to a single use. Once the sensor adhesive has been attached to the skin, the sensor placement cannot be changed without replacing the entire sensor. Additionally, removing the sensor typically causes temporary, mild skin redness. This area cannot be used for a session until the skin returns to its normal color.
- In addition to determining the sensor site, select an area to anchor the cable that is 2.5 to 3 inches towards the center of the chest, relative to the sensor. The cable does not have the same placement limitations, but should be placed on clean, healthy, intact skin. **Note:** If sensor is placed on the sternum, the cable can be taped on the pectoralis major.

Site Preparation

- Remove all hair from the selected body site over an area that is at least as large as the full area of the sensor. Body hair clippers are recommended. Avoid shaving or depilating creams as these can irritate the skin.
- Gently but thoroughly clean the area where the sensor will be placed with an IPA alcohol wipe. Allow the skin to dry (>30 seconds) before proceeding to the next step. Allow any redness to dissipate before placing sensor.

TGFR Sensor Placement

- Using the provided tab, pull the paper liner off of the sensor to expose the adhesive.
- Place the sensor on the selected body site, pressing down on the center of the sensor, and then pressing down on all areas of the flexible outer portion, until it is well-adhered over the full sensor area.
- Secure the sensor cable as shown in Figure 7. Anchoring the cable with tape in five places will inhibit cable movement and the potential for errors during a session.

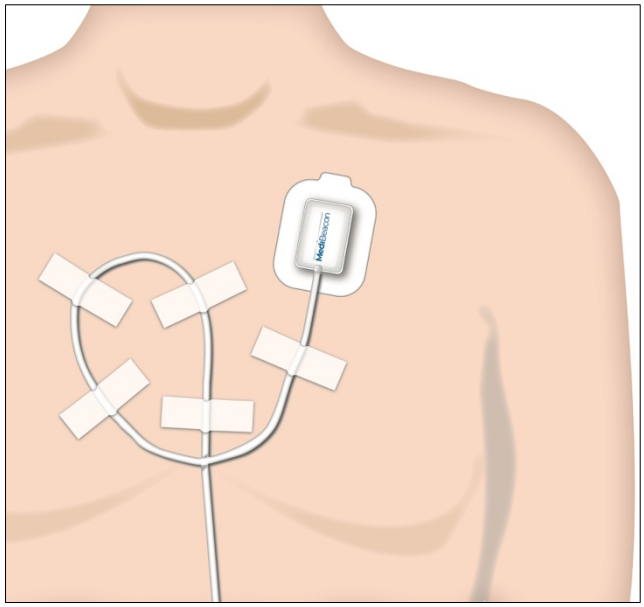


Figure 7. Typical TGFR Sensor placement and cable anchoring

Patient Positioning / Posture

- During a TGFR session, the patient should be as still as possible, especially during the "Establishing Baseline" stage. The system is designed to compensate for light activity such as reading or eating after the Baseline stage.
- The patient should lay or recline on their back for as much of the session as possible. Laying prone or on the side should be avoided as much as possible, as these postures can put excess pressure on the skin underlying the sensor.
- Avoid putting heavy or tight clothing over the sensor. These items can apply excess pressure to the skin underlying the sensor. Light, loose-fitting clothing such as scrubs or a loose-fitting t-shirt are ideal.
- Avoid crossing or folding arms over or near the sensor as this can apply excess pressure to the sensor area.
- Avoid direct sunlight or bright procedure lights at the sensor location.

Connecting a TGFR Sensor to the TGFR Monitor

Turn on the TGFR Monitor by pressing the power button. Once the 'Connect Sensor' screen (Figure 8) loads, connect the sensor cable to the port on the lower right corner of the monitor front panel. Be sure the blue dot on the cable connector points up to the 12 o'clock position as this will align the cable connector with the monitor's port (Figure 9). It can take up to 10 seconds after connection for the system to detect and verify the sensor is ready for use.

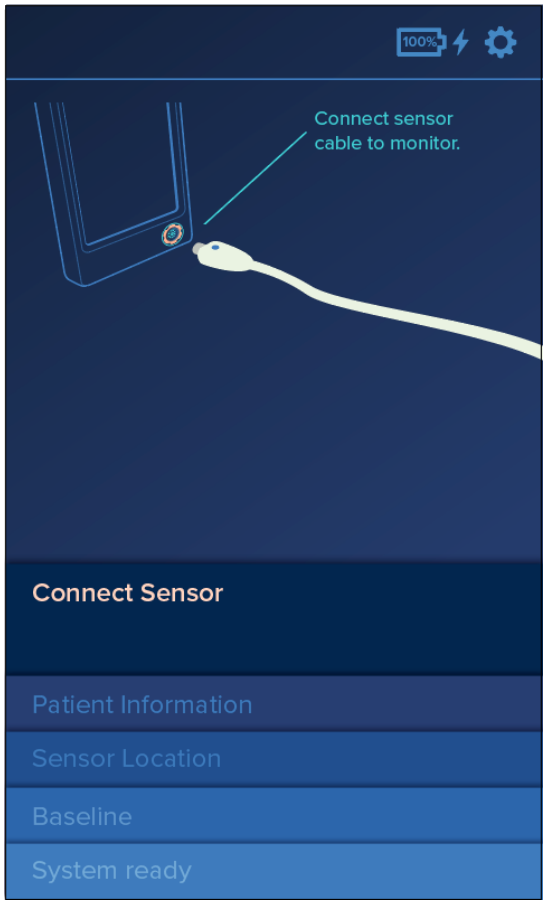


Figure 8. Connect Sensor screen

Figure 9. Sensor cable connection location on monitor

The ‘Connect Sensor’ screen displays when the system is ready to initiate a new session or restart/resume an existing session. The screen will automatically proceed to the ‘Patient Information’ screen (Figure 10) once a sensor is successfully connected.

Note: The sensor can be connected to the monitor prior to placing the sensor on the patient, but it is recommended that the sensor be placed on the patient first, as described in the section “TGFR Sensor Placement”. If restarting a current session, the user may reconnect the cable to the monitor, but the sensor in use must not be removed or re-applied to the patient.

Patient Information Screen

Once a sensor is connected, the monitor will automatically transition to the ‘Patient Information’ screen (Figure 10). Tap the Patient ID field located under the Menu Bar to bring up the touch screen keyboard. Enter the Patient ID using the touchscreen keyboard and tap ‘ENTER’. The monitor will advance to the ‘Sensor Location’ screen (Figure 11).

Note: A patient ID confirmation dialog will display if starting a new session with the same patient ID. Upon entering that Patient ID, a display will provide a countdown until the previous injection will be adequately cleared to start a new session (Figure 10a). If the sensor is detected as previously in use, see section Session Interruption: Sensor Disconnection from the Monitor and Restarting a Session.

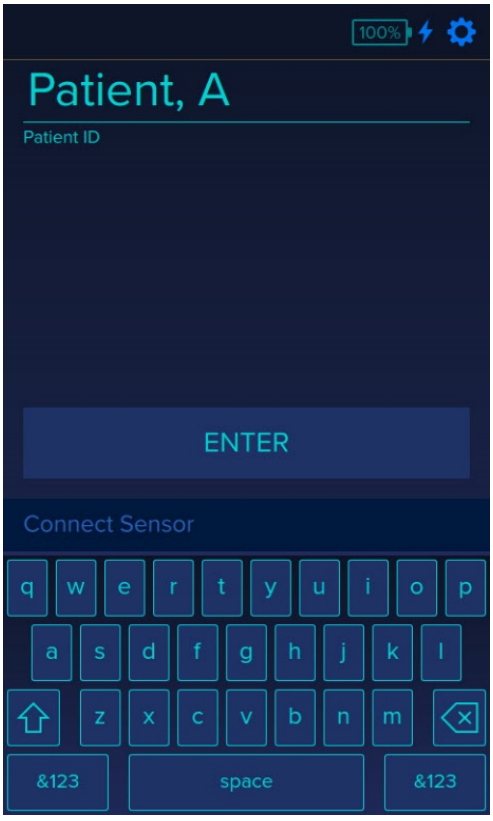


Figure 10. Patient Information screen

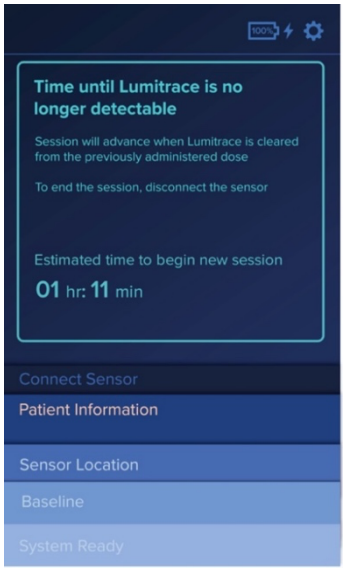


Figure 10a. If entering the same Patient ID, a timer may appear, indicating clearance time until the next session may be started with a new sensor.

TGFR Sensor Location Screen

After entering a patient's ID, the monitor will display the 'Sensor Location' screen (Figure 11). Two options for sensor location are available. Press the site location on the screen ONCE to confirm where the sensor was placed. The sensor icon will highlight when selected and the monitor will advance to the 'Skin Tone Adjustment' screen (Figure 12).

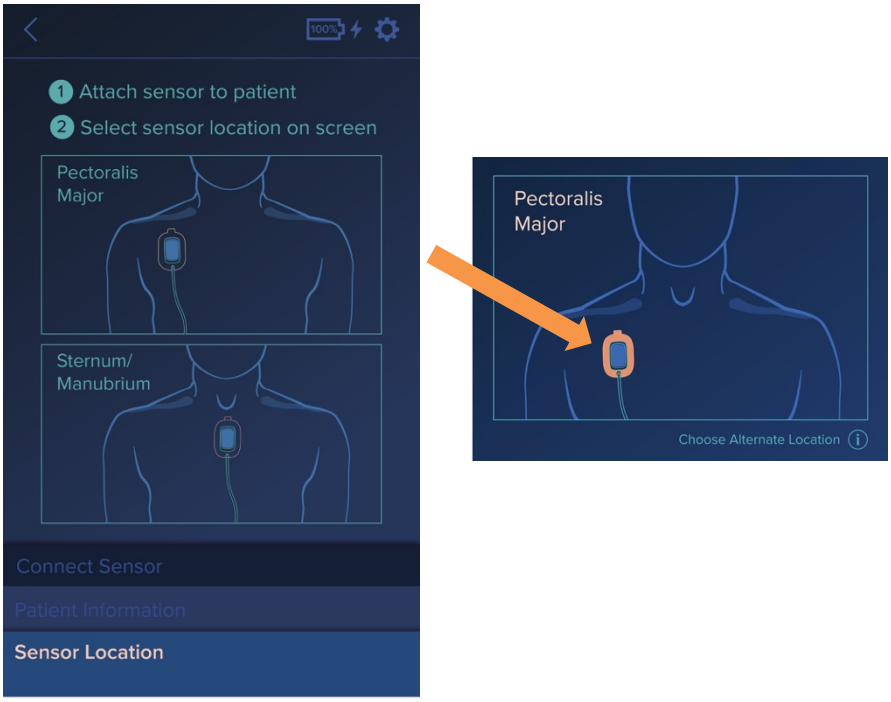


Figure 11. Selecting sensor location

Note: The sensor must be attached to the patient before selecting the sensor location on the monitor. If the sensor location graphic is selected on the screen prior to sensor attachment, the system will begin its skin tone adjustment process, and the user will receive a sensor error. If this occurs, disconnect the sensor from the monitor and proceed to the sensor placement section of the instructions. After the sensor has been correctly placed on the patient, the sensor can be plugged into the monitor to begin a new session. The patient ID must be confirmed when prompted, and a 'NEW' session must be selected when prompted. If 'Continue Session' is selected, the sensor error screen will appear.

Skin Tone Adjustment

Once a sensor site is confirmed, the system will automatically adjust the sensor to the patient's skin tone. The TGFR cycles the sensor LED power and selects the LED power level that provides an optimal signal (Figure 12). The sensor is now adjusted to the patient's skin and the 'Establishing Baseline' screen (Figure 13) will appear and begin counting down the time until baseline is complete. See Section IV for accuracy results related to skin tone.

During skin tone adjustment and establishing baseline, the patient should be as still as possible. Movement can affect skin tone adjustment or the baseline.

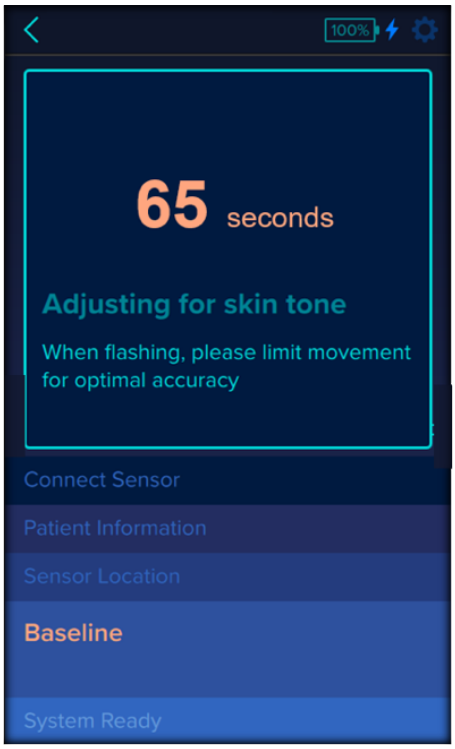


Figure 12. Skin Tone Adjustment screen

Establishing Baseline

The baseline is a reference value set prior to the Lumitrace injection, used to calculate GFR. During the baseline acquisition process the patient should be in a position consistent with posture they will generally maintain during the TGFR session. This process takes approximately 20 minutes. The patient should not apply external pressure to the sensor. Avoid laying on the sensor or placing arms or hands on the sensor. Disrupting the baseline reading process could delay the session. In addition to not perturbing the sensor, no other procedures should be performed on the patient while the baseline is being acquired. The 'Establishing Baseline' screen (Figure 13) will display the estimated time to baseline acquisition completion.

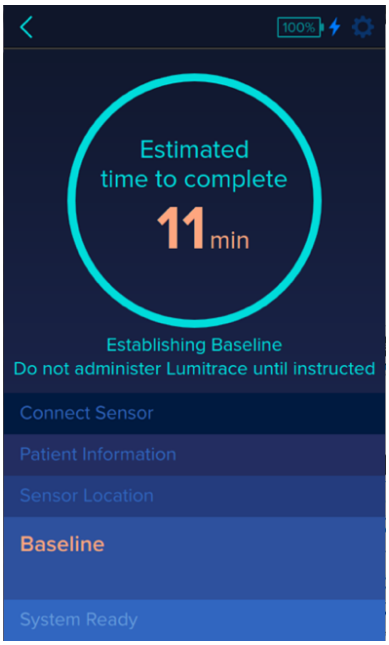


Figure 13. Establishing Baseline screen

Note: If the system cannot establish a baseline within approximately 21 minutes, a Baseline Timeout screen will display (Figure 14). Depending on the issue with establishing a baseline, the user may be prompted to replace the sensor or restart baseline acquisition (See Troubleshooting, Section X, 'Baseline').

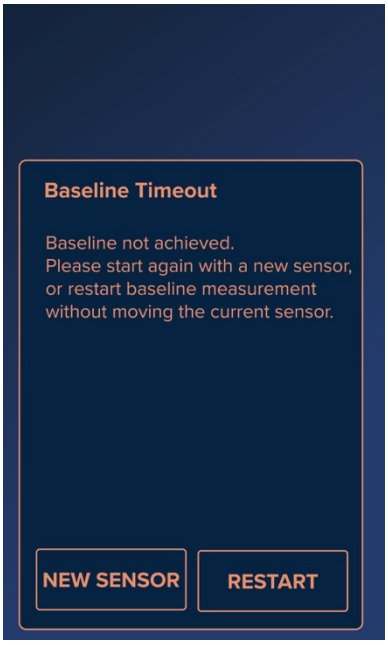


Figure 14. Baseline Timeout screen

Warning: Do not adjust or manipulate the sensor after baseline is established.

System Ready - Administer Lumitrace Injection

When a stable baseline is achieved, the 'Administer Lumitrace' screen will be displayed (Figure 15). The system is now ready for the Lumitrace injection to begin monitoring tGFR.

1. Administer the Lumitrace injection, for intravenous use, to the patient according to the instructions provided with the Lumitrace vial.
2. The 'Administer Lumitrace' screen will remain on the display until the Lumitrace injection is detected by the system.

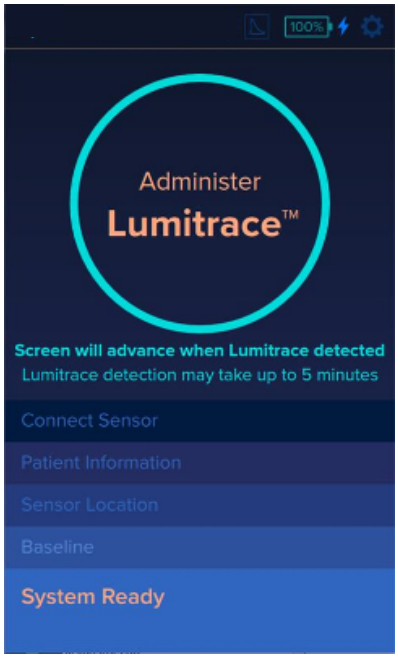


Figure 15. Administer Lumitrace screen

After Lumitrace has been administered to the patient, the system will automatically detect the injection. Detection usually occurs within 2 minutes. Once the Lumitrace injection is detected, the monitor will transition to the 'Approximate Time until GFR Result' screen (Figure 16). If the sensor does not detect the Lumitrace injection, the 'Lumitrace Administered?' or 'Lumitrace Not Detected' screens will appear (See Troubleshooting, Section XI, 'Lumitrace Not Detected').

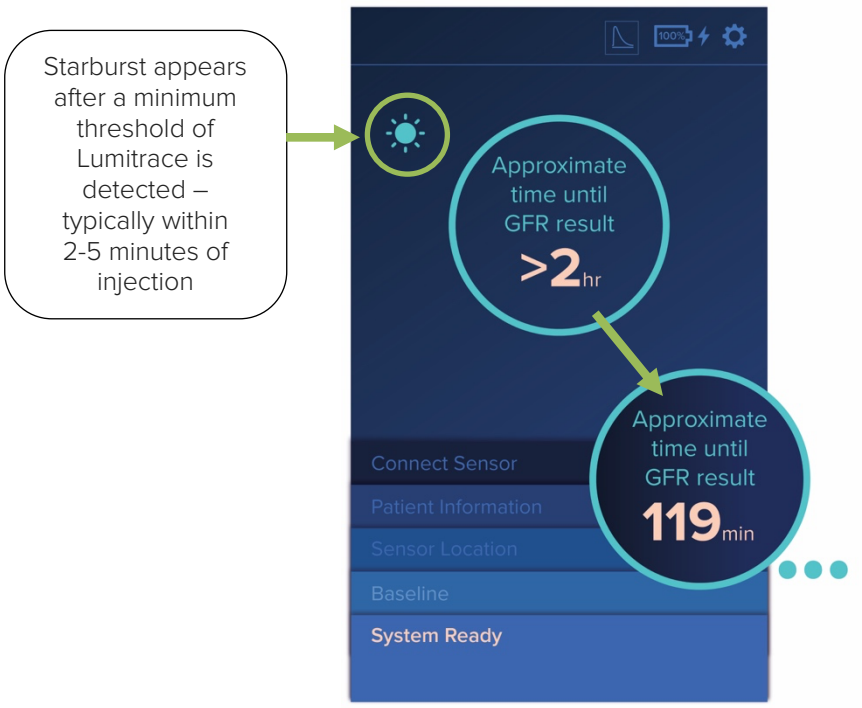


Figure 16. Approximate Time until GFR Result screen

System Ready - Approximate Time until GFR Result Screen

During the 'System Ready' process, the 'Approximate Time until GFR Result' screen (Figure 16) will be displayed, notifying the user that the system is gathering data to report tGFR assessments. The time until an initial tGFR assessment is estimated and reported on the TGFR Monitor. These snapshot assessments of GFR (unvalidated) are utilized in calculating the validated Average Session GFR. Only the final Average Session GFR should be used for clinical decisions.

During the 'System Ready' process, the TGFR Monitor must detect a minimum threshold from the Lumitrace injection in order to continue to report GFRs. Once the system detects this threshold, a "starburst" icon appears in the left corner of the display (Figure 16). This informs the user that the tGFRs will be reported. The approximate time to the first GFR assessment is shown on the screen.

The 'System Ready' process is complete when the first graph value is available. The system will then proceed to the 'Monitoring' screen.

Note: If the 'System Ready' process times out, the user will see the following notification screen, 'Equilibration Not Reached'. This screen informs the user that the session must be restarted after an appropriate wait time to allow the Lumitrace injection to clear out of the patient's body (Figure 17).

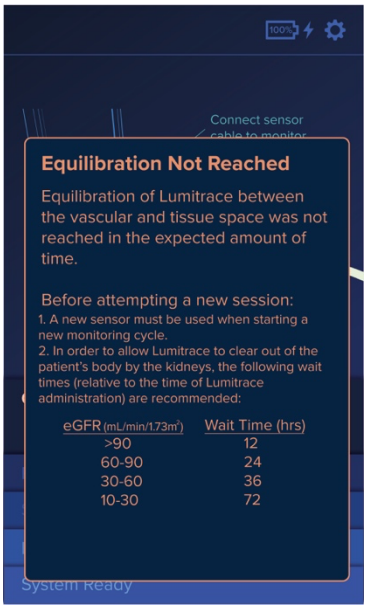


Figure 17. Equilibration Not Reached screen

Monitoring Screen

The image below shows the 'Monitoring' screen (Figure 18) of a typical monitoring session that has been running for approximately 7 hours.

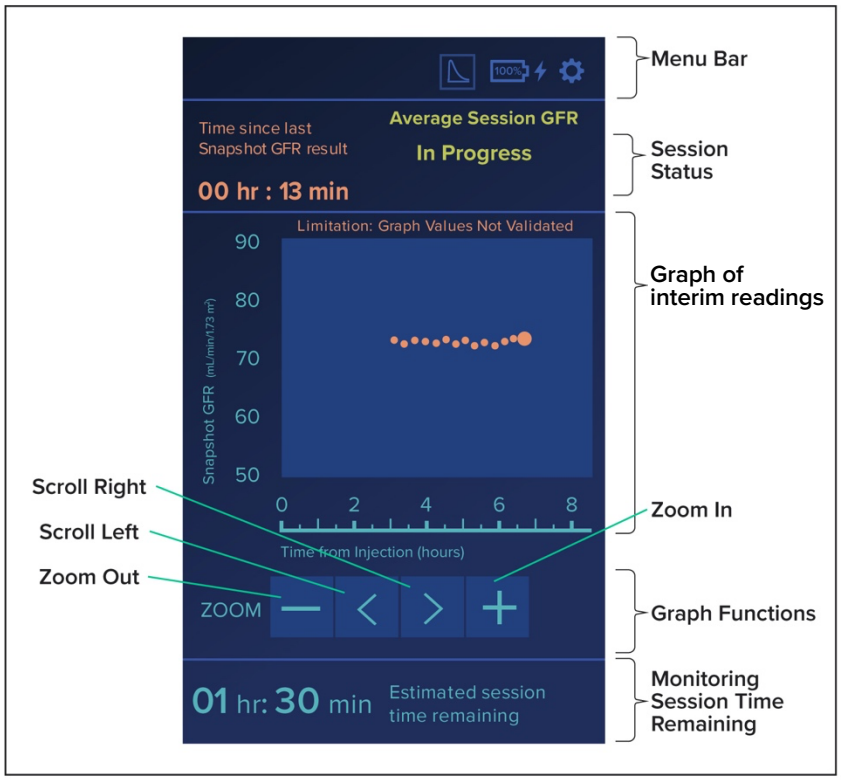


Figure 18. Monitoring screen – graph view

As readings are obtained during the monitoring process, they are displayed on the 'Monitoring' screen on the graph. As new readings are obtained, previous readings remain available on the graph.

Limitation: Graph values are for reference only and are not validated.

The estimated session time remaining until the session is complete is shown at the bottom of the 'Monitoring' screen.

Monitoring Screen Layout and Icons:

Time since last Snapshot GFR result – time (hr:min) since the last value was reported by the monitor.

Last Value – this value is emphasized in the GFR graph with a larger point on the plot.

Graph Values – plot of reported reading values vs time (hours since Lumitrace detected). Readings are calculated every 15 minutes until the monitoring session ends. The Graph Function icons, located below the plot, can be used to browse the plot of reported values. Only the Average Session GFR is validated.

Graph Functions icons

1. **Scroll right** – scrolls the graph field of view to the right
2. **Scroll left** – scrolls the graph field of view to the left
3. **Zoom In** – magnifies the graph in 4 hour or 2-hour increments
4. **Zoom Out** – reduces the graph in 2 hour or 4-hour increments

Low or High Results on Graph

The system provides specific tGFR values between 10 and 120. Any values outside that range will be displayed as arrows at the bottom or top of the graph area. (Figure 19).

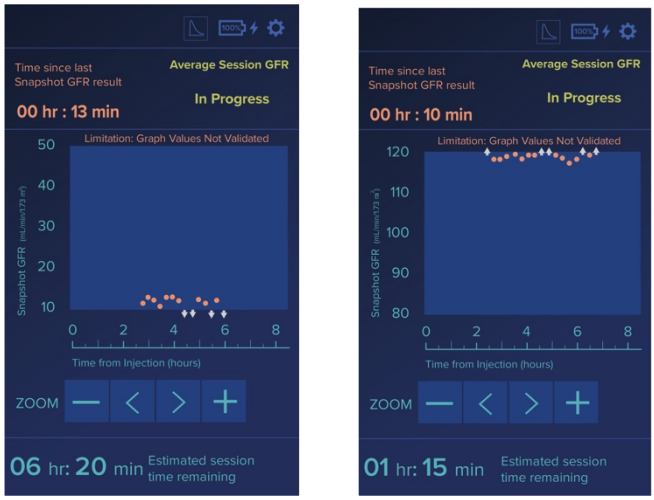


Figure 19. Low and High tGFR points on graph

Lumitrace Clearance Graphs

Pressing the menu bar graph button displays the Lumitrace Clearance Graph. This graph shows the in-progress clearance of the Lumitrace injection from the patient's body. This graph is available in the 'Approximate Time until GFR Result' screen and the 'Monitoring' screen graph. The graph x-axis automatically updates based on whether the Lumitrace injection has been detected or is awaiting detection. The initial graph displays as a linear y-axis scale. The logarithmic y-axis can be accessed by tapping the menu bar graph button again (Figure 20). Press the menu bar graph button again to return to the Monitoring screen graph view.

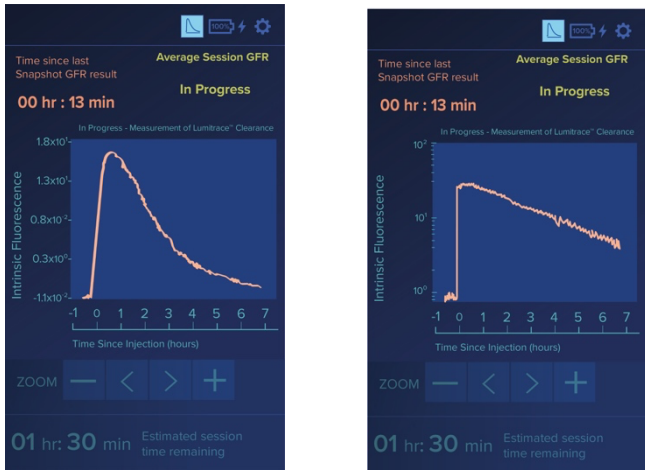


Figure 20. Lumitrace clearance linear (left) and semi-log scale (right).

Completing a TGFR Session

The session continues until the level of the Lumitrace is cleared below accurate detection levels. At that time, the screen will display a "Measurement Session Ended" pop-up to confirm that the fluorescence measurements are complete. The monitor will calculate an Average Session GFR and display it in green in the upper right of the screen (Figure 21).

Note: If the session was stopped prior to reaching the Lumitrace clearance condition, the monitor will display the 'Session Interrupted' Screen (Figure 22).

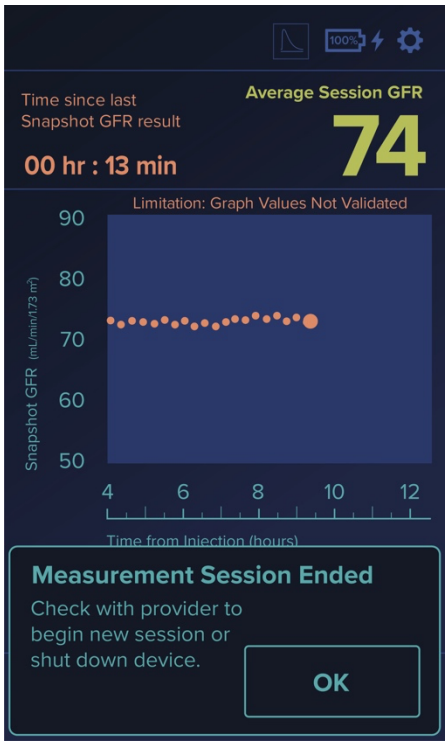


Figure 21. An Average Session GFR value appears in green on the display at the end of a full session.

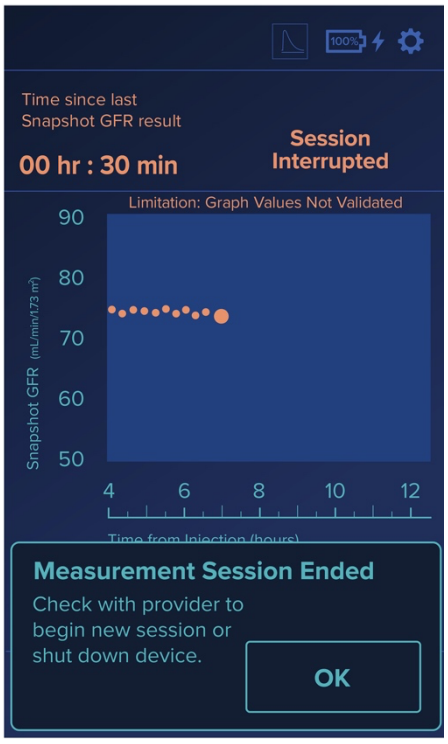


Figure 22. A Session Interrupted message will appear if the session was stopped before Lumitrace clearance was completed.

Follow the steps below to record session results and prepare the system for the next use.

1. **COLLECT DATA:** Transcribe the Average Session GFR.
2. Press "OK" to advance to the 'End Session' screen.

Reminder: Be sure to transcribe the Average Session GFR prior to selecting "End Session".

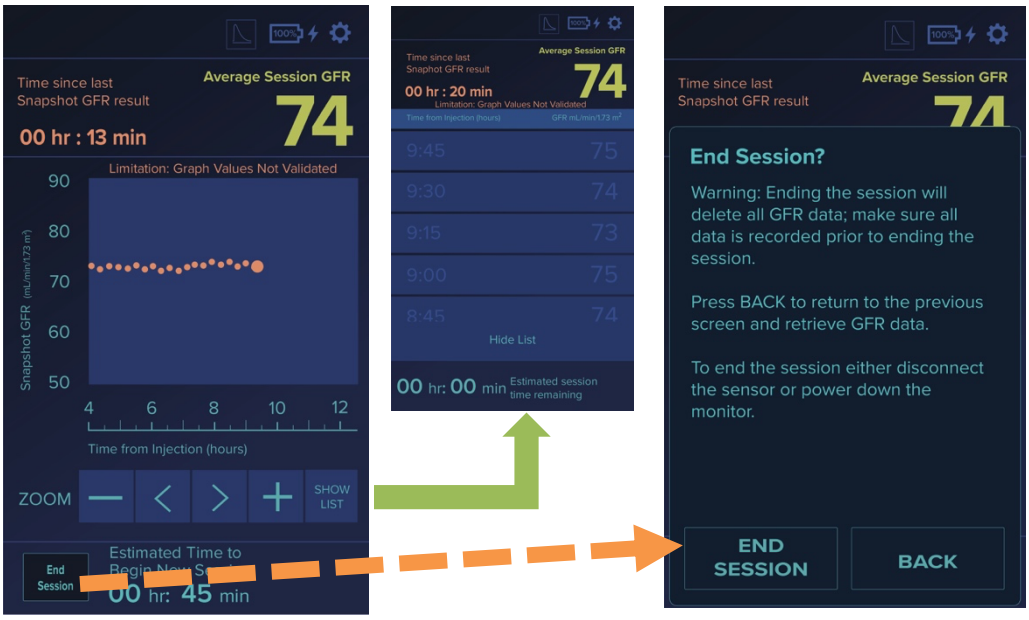


Figure 23. Workflow screens for ending a monitoring session. Press the "SHOW LIST" button to display and manually collect session data (Green Arrow), then return to the 'End Session' screen. Press "End Session" button (Orange Dashed Arrow) which will show a confirmation screen. When the Average Session GFR is recorded, press the "END SESSION" button on the confirmation screen.

Note: The intermediate tGFR values were not validated during the development of this device. The Average Session GFR is a weighted average of these interim values. The interim values should not be relied upon.

3. Select "END SESSION" button (Figure 23). A confirmation screen will appear. Select "END SESSION" or disconnect the sensor from the monitor. Either action will advance to the next step. These actions will clear the session data from the screen, and it will no longer be displayed. **Be sure the Average Session GFR data is captured before clicking "END SESSION".**
4. **Remove the used sensor from the patient's skin:** Slowly peel the sensor's adhesive from the patient, being careful to ensure separation from the skin without harm. Start by loosening the adhesive from the skin at the pull tab located at the top of the sensor. Stabilize the skin near the sensor holding the skin down while slowly peeling the sensor away.
5. Discard the used sensor following the institution policy for disposable skin-contacting leads and device components.
6. If the sensor is already disconnected from the monitor, the screen will display the 'Connect Sensor' screen (Figure 24, left). If the sensor is still connected, the monitor will prompt you to disconnect and use a new sensor with the 'Replace Sensor' screen (Figure 24, right).
7. The system is ready to start a new session when the 'Connect Sensor' screen appears.
    a. If you are starting a session, place a new sensor on the patient, connect the sensor to the monitor (after it is placed on the new patient) and proceed to the steps in Starting a New TGFR Session.

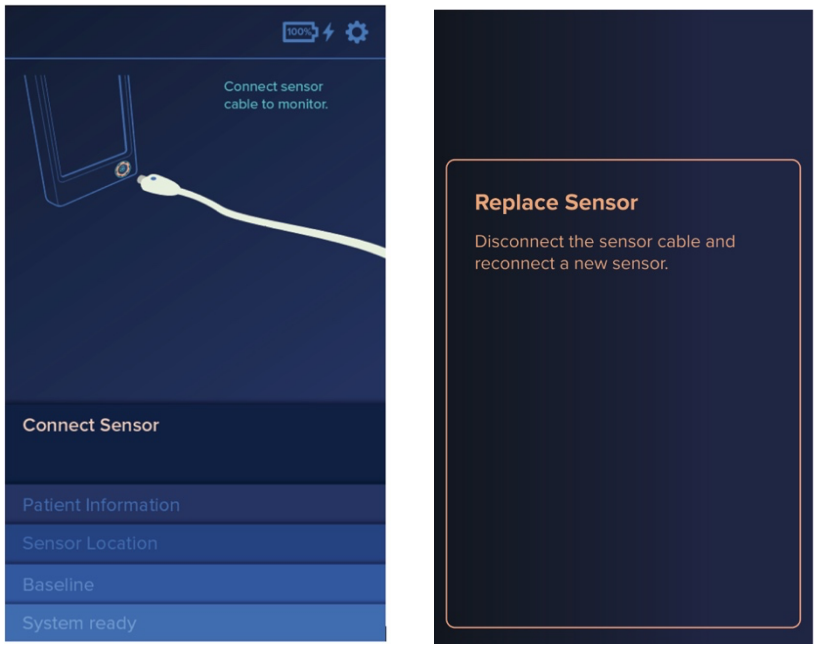


Figure 24. Workflow after session end. The monitor will either go to the 'Connect Sensor' screen (left) if the sensor is already unplugged from the monitor, or the 'Replace Sensor' screen (right) if the sensor is still connected to the monitor.

Workflow Following a Completed Session

Session For a New Patient

Connect new sensor and enter the Patient ID on the 'Patient Information' screen (Figure 25). The monitor will return to the initial startup sequence for a new patient.

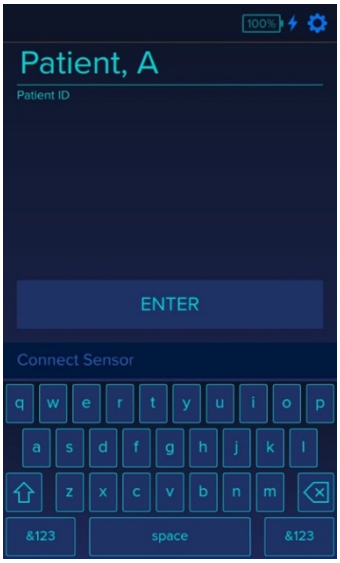


Figure 25. Session for a new patient. Enter Patient ID to start workflow.

Session For the Same Patient

The sensor is single use and must be replaced for each monitoring session. Once a new sensor has been placed on the patient, connect new sensor to the monitor and enter the Patient ID in the 'Patient Information' screen (Figure 25). If there is uncleared Lumitrace remaining from the previous session, the monitor will enter a countdown to clear any detectable Lumitrace from the patient before a new session can be started (Figure 26, left). The 'Sensor Location' screen will appear once this countdown is completed (Figure 26, right). If Lumitrace has already cleared, the monitor will automatically transition to the 'Sensor Location' screen.

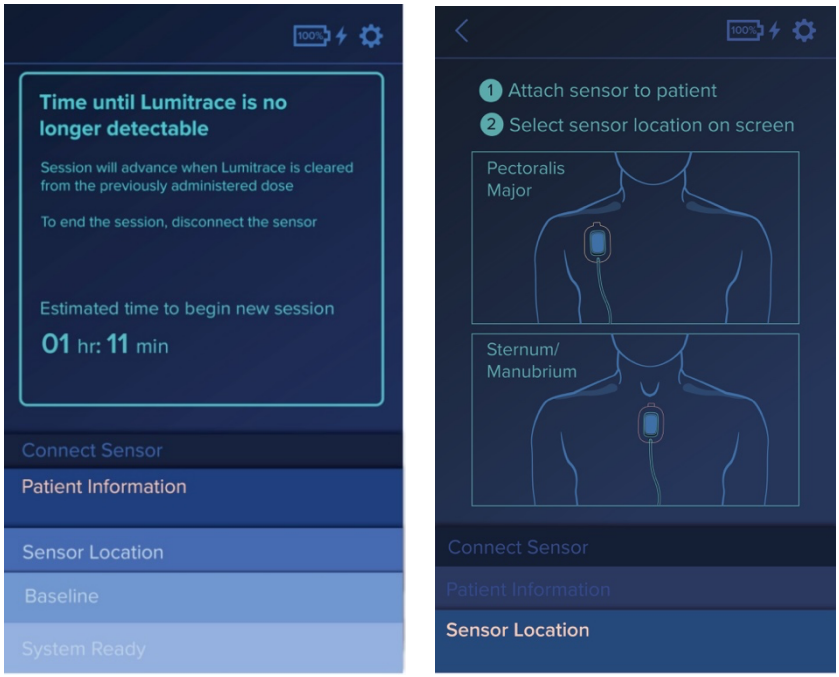


Figure 26. Session for the same patient. The TGFR Monitor will initiate a countdown before the next injection if the previous Lumitrace injection has not been cleared (left). Wait until the countdown is complete and workflow will automatically transition to the 'Sensor Location' screen (right).

TGFR Sensor Detachment from the Patient

The sensor adhesive is single-use and cannot be reapplied. If the sensor is removed or dislodged from the patient's skin for any reason, a new sensor must be used and a new session started. If a Lumitrace injection has been administered to the patient prior to sensor detachment from the skin, **a waiting period is required before attempting a new session** (See Section X: Troubleshooting, or estimated clearance times in Table 1 below).

When the system detects that a sensor has become detached from a patient, one of three screens will appear.

Detachment Prior to Lumitrace Injection

If the sensor becomes detached **prior to the Lumitrace injection**, the 'Sensor Detached' screen will appear as shown in Figure 27.

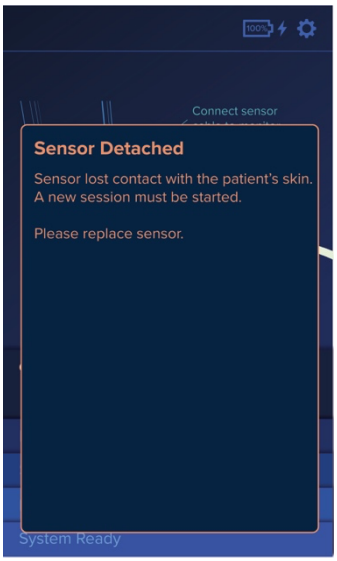


Figure 27. Detached sensor PRIOR to injection

1. Remove the sensor completely from the patient and disconnect from the monitor. Discard this sensor.
2. Once the sensor is disconnected from the monitor, the alert screen will advance to the 'Connect Sensor' screen. Follow the screen prompts to initiate a new session from the beginning.

Detachment After Lumitrace Injection – before detected

NOTE: If the Lumitrace injection was administered just prior to the detachment from the patient, a new session should not be restarted until adequate Lumitrace clearance time has elapsed. Use the patient's estimated GFR (eGFR) from their medical chart to find the recommended estimated clearance times (Table 1). After appropriate clearance time, follow the instructions for a new session.

Table 1: Estimated Lumitrace Clearance Time

eGFR Range	Estimated Clearance Time
> 90 GFR	12 hours
60-90 GFR	24 hours
30-60 GFR	36 hours
10-30 GFR	72 hours

Detachment After Lumitrace Injection – before readings are plotted

If the sensor becomes detached from the patient after Lumitrace has been detected and **the 'Approximate Time until GFR Result' screen is displayed,** the 'Sensor Detached' alert screen will be displayed as shown in Figure 28. Any data collected during the session will be lost: NO tGFR data can be assessed for this session.

1. Remove the sensor completely from the patient and disconnect from the monitor. Discard the sensor.
2. Because detachment occurred after administration/detection of Lumitrace, a new session cannot be started until the recommended clearance time has elapsed (Figure 28 or Table 1).

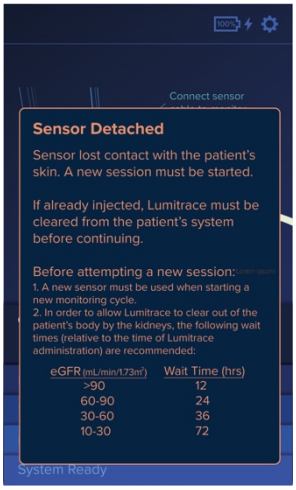


Figure 28. Detached sensor AFTER injection, PRIOR to first result

Detachment After readings are plotted

If the sensor becomes detached from the patient **after readings have been plotted**, the end session message will be displayed as shown in Figure 29. Select OK. A message stating "Session Interrupted' will be displayed on the screen.

Note: If the session is interrupted, the graph is not available after confirming the end of session.

1. After confirming the end of the session, remove the sensor completely from the patient and disconnect from the monitor. Discard the sensor.
2. Because detachment occurred after administration/detection of Lumitrace, a new session cannot be started until the recommended clearance time has elapsed (Figure 28, above).

Figure 29. Detached sensor AFTER first reading.

Section IX: Settings Options

Only the Screen Brightness from the 'Settings' screen can be changed without using a password. Change the brightness parameters via the 'Settings' screen which is accessed by tapping the Settings icon  (Figure 30).

Figure 30. Settings screen

Section X: System Alerts

Audio Alerts

Single tones cue many data and screen functions on the monitor when tapping buttons, including some alerts on required data or incorrect entry. In addition, the following situations generate audible alerts requiring user attention.

An alert plays a series of beeps until cleared:

- Battery Low
- System Error (Generic System Error)
- Equilibration Timeout
- Agent Not Detected
- Agent Detected Too Early
- Sensor Detached Post-Injection
- “Test Audio” button from the service screen
- Battery Charge Critically Low
- Battery Fault

Alert Screens

The system displays informational prompt screens to inform the user of various system issues or conditions. Depending upon what system alert screen is shown, some screens require user input, and some disappear on their own after 3 seconds (e.g., Sensor Disconnected). Alerts requiring prompt attention sound an audible tone alert which repeats until the condition is resolved. Follow the instructions on each prompt. System Alert screens are shown in Figures 31 – 51.

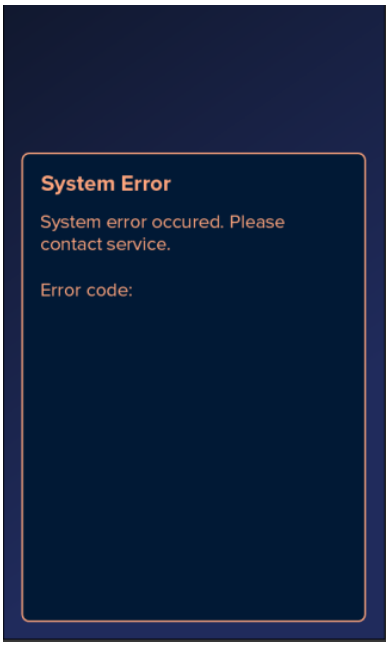


Figure 31. System Error

Figure 32. Sensor Incompatible

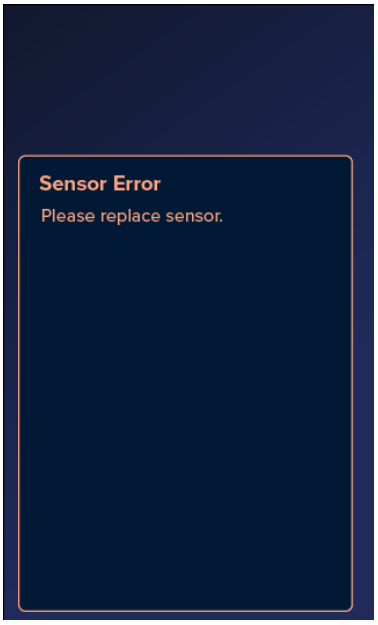


Figure 33. Sensor Error

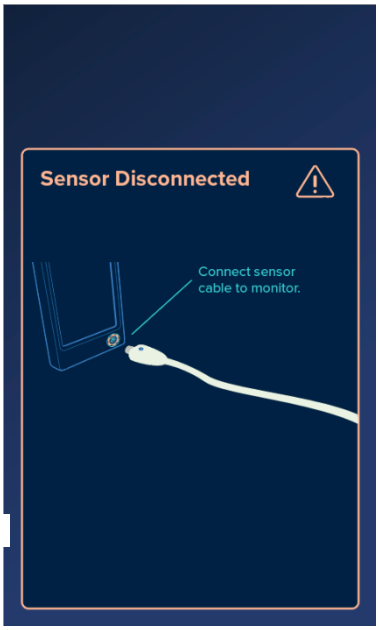


Figure 34. Sensor Disconnected

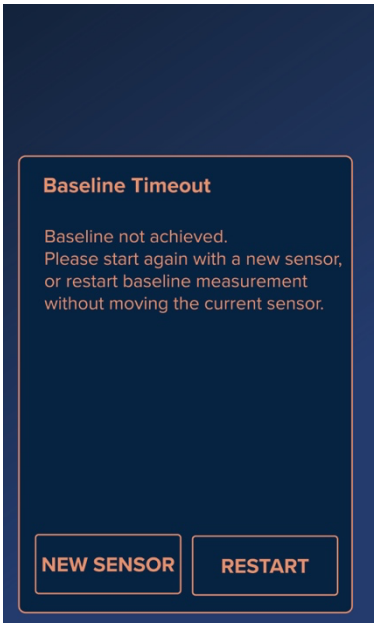


Figure 35. Baseline Timeout

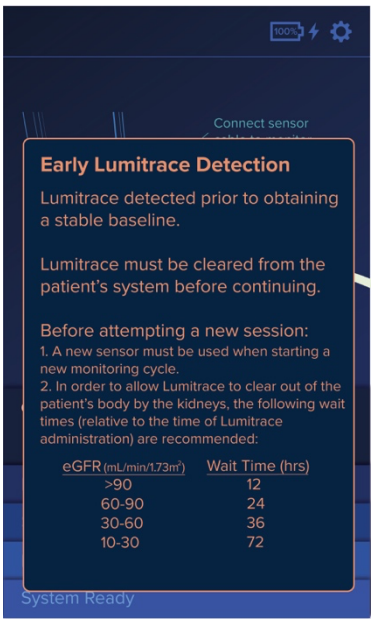


Figure 36. Early Lumitrace Detection

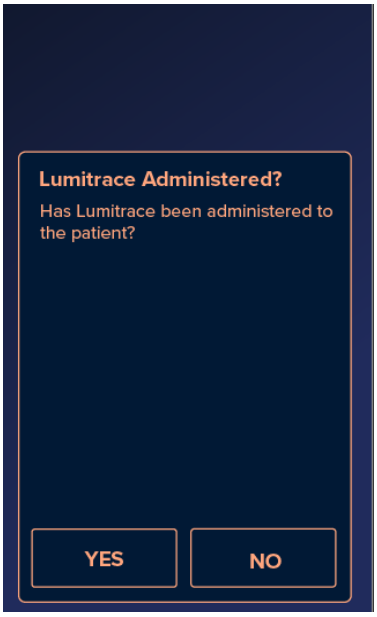


Figure 37. Lumitrace Administered? Prompt

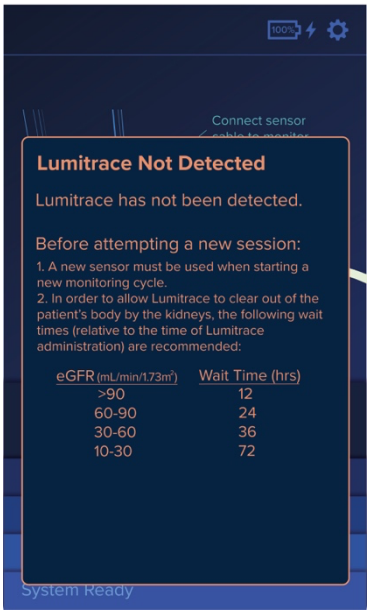


Figure 38. Lumitrace Not Detected

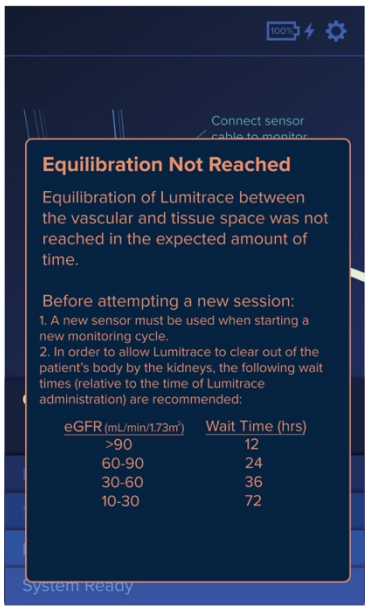


Figure 39. Equilibration Not Reached

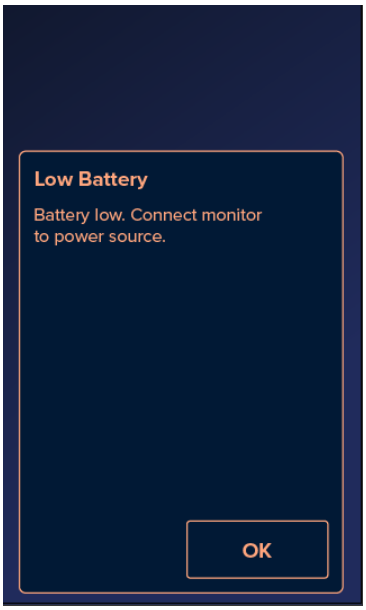


Figure 40. Low Battery

Figure 41. Critically Low Battery

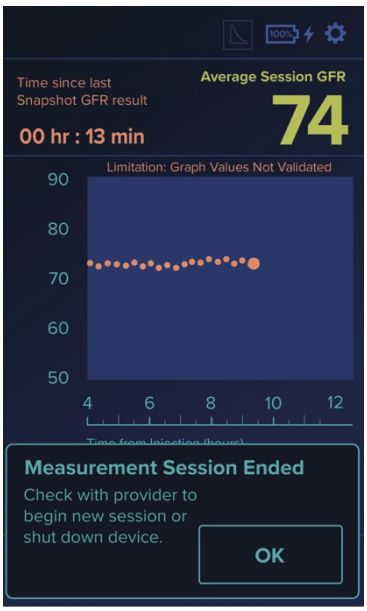


Figure 42. Measurement Session Ended

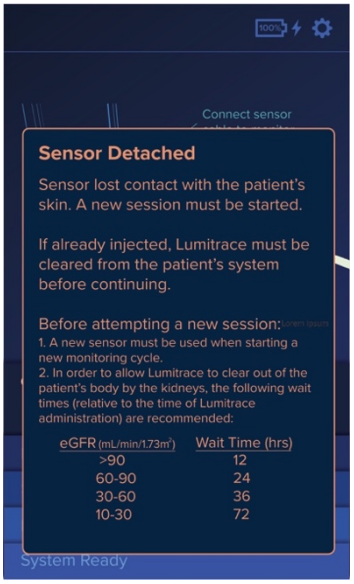


Figure 43. Sensor Detached – post-detection

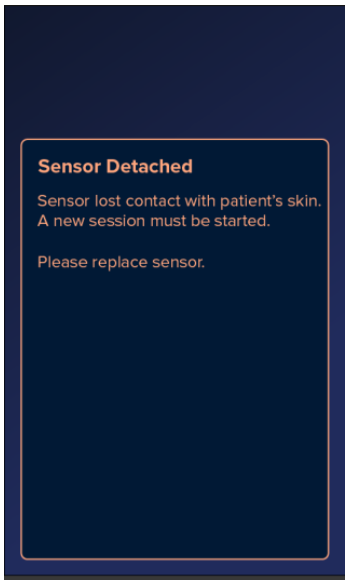


Figure 44. Sensor Detached - pre-detection

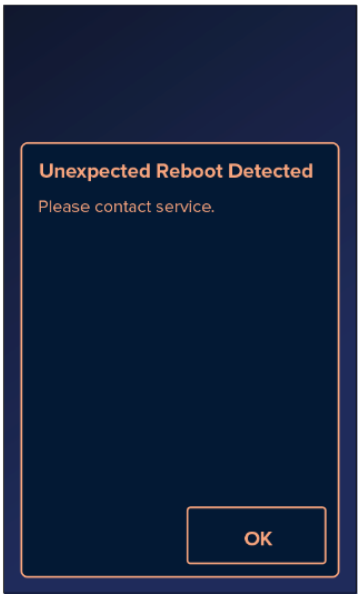


Figure 45. Unexpected Reboot Detected

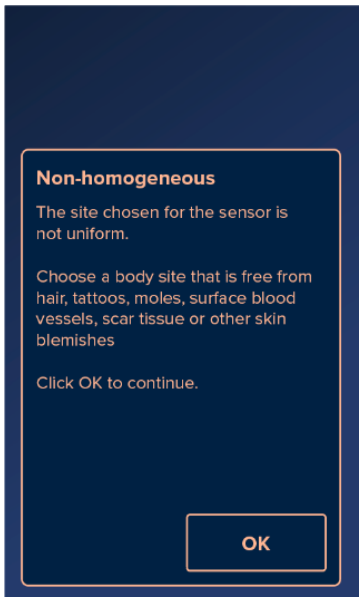


Figure 46. Sensor Site Non-homogeneous

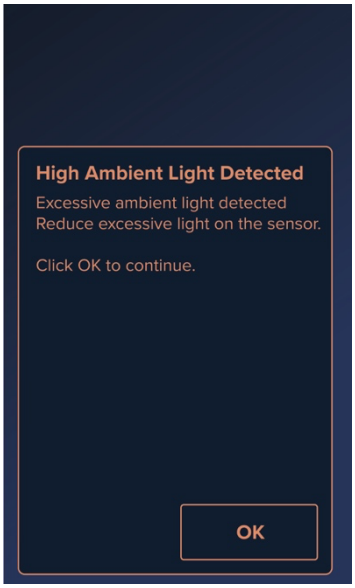


Figure 47. High Ambient Light

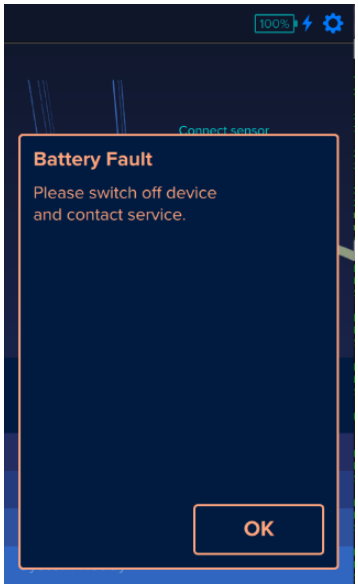


Figure 48. Battery Fault

Figure 49. Baseline Expired

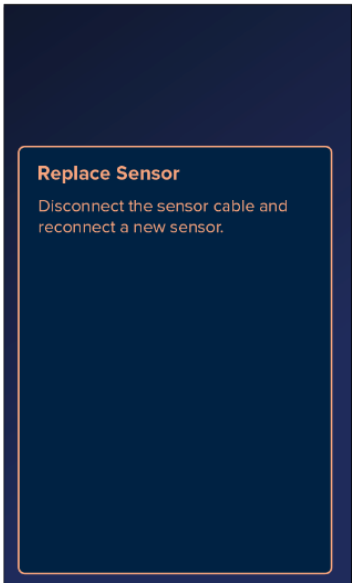


Figure 50. Replace Sensor

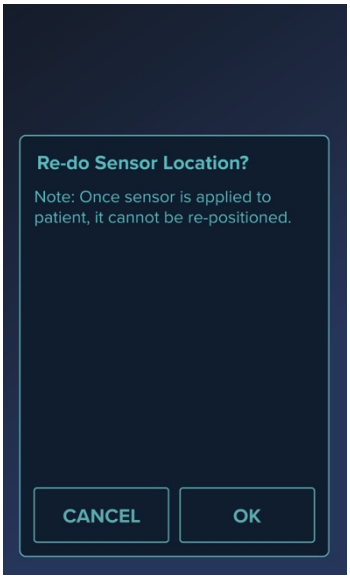


Figure 51. Re-confirm Sensor Location

Section XI: Troubleshooting

This section describes nonstandard usage scenarios and how to address them.

Patient ID

NOTE: If the sensor is detected as previously in use, a patient ID confirmation dialog will display (see Figure 27) asking the user to confirm that the ID from the sensor matches with the ID of the patient. If this ID does not match with the patient, the user must replace the sensor. If it does match the same patient, refer to the section on Returning to an Existing Session.

- If no previous session exists for the patient, then the Sensor Location screen is displayed.
- If a previous session was interrupted prior to the Lumitrace injection, the user will be directed to continue the previous session or start a new session.
- If a previous session was interrupted after the Lumitrace injection, the user will only be allowed to continue the previous session. If a new session is needed, the sensor must be replaced.
- In any case, the user is not allowed to resume a session if the sensor is removed from the patient's skin.

Skin Tone Adjustment

The TGFR Monitor may prompt a sensor error at the end of the skin tone adjustment sequence if there was excessive movement during the count down, or if there was insufficient contact with the skin. Skin tone adjustment can be attempted two more times if this error occurs. Follow the steps below to reattempt Skin Tone Adjustment:

- Disconnect the sensor from the TGFR Monitor. The display will momentarily shift to the Sensor Disconnected screen, then advance to the Connect Sensor screen. This screen will remain visible until the sensor is reconnected to the monitor.
- Once the sensor is reconnected to the monitor, the screen will advance to confirm the patient identity. (See Figure 27) Press "YES" to advance to the 'Existing Session Found' screen.
- The screen will display "NEW" and "CONTINUE" options. (see Figure 29) Ensure the patient can remain still for the skin tone adjustment sequence. You must select "NEW" to attempt a new skin tone adjustment. Select the sensor location and continue following prompts.
- If you have attempted Skin Tone Adjustment three times with a single sensor, the sensor will have to be removed and a new sensor used for the session.
- If a sensor error prompt follows the second skin tone adjustment attempt, sufficient contact with the skin was likely not established. The sensor will have to be removed and a new sensor placed.

Note: When a sensor is removed, inspect the sensor site for blemishes, discoloration, or other features that may disrupt readout. It is recommended that a new sensor site be selected. If another site is not available, allow the patient's skin to return to its normal tone as sensor removal may cause temporary redness.

Baseline Timeout

The TGFR Monitor may prompt a 'Baseline Timeout' (Figure 14) at the end of baseline sequence if there was excessive movement during the count down. Remind the patient to stay as still as possible during the skin tone adjustment and the baseline equilibration steps. Excessive movement, laying on or pushing on the TGFR Sensor, or tight clothing, can all cause interference and inhibit the baseline equilibration.

The first time the system prompts a Baseline Timeout message, choose "RESTART". If it happens again, press the Back button. The "Re-do Sensor Location" (Figure 52) message will appear. Press OK, choose the correct Sensor Location, and follow instruction on the prompts.

Warning! Do not adjust or manipulate the sensor after baseline is established.

Baseline Expired

The TGFR Monitor may prompt a 'Baseline Expired' notification (Figure 49) if baseline no longer has the quality to assess tGFR. The sensor will need to be replaced. The site may be used again if there is no evidence of blemishes, discoloration, or other features that may disrupt readout, and the patient's skin has returned to its normal tone. If Lumitrace was administered, the patient must wait the recommended clearance time before starting a new session. (See Table 1).

Lumitrace Not Detected

If Lumitrace is not detected within 2.5 hours, the user will receive a prompt asking if the injection has been administered (Figure 52a). If the user taps "NO", the 2.5-hour timer will restart. If the user taps "YES", the system will wait an additional 30 minutes to detect Lumitrace. If Lumitrace is not detected within 30 minutes, the system will display a "Lumitrace Not Detected" prompt (Figure 52b) informing the user that a new session must be started.

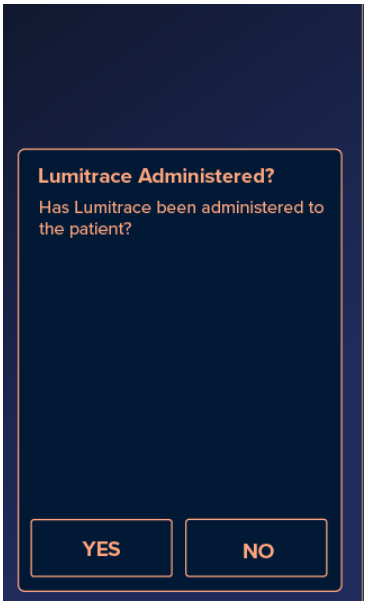


Figure 52a. Lumitrace Administered?

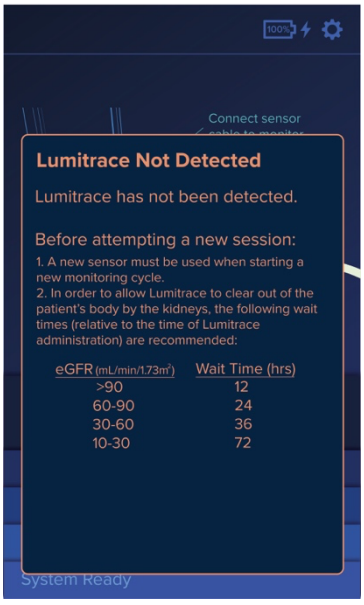


Figure 52b. Lumitrace Not Detected

Device Use Interference Caution:

The potential for electromagnetic interference in all environments cannot be eliminated. Use caution if the TGFR is used near electronic equipment such as devices utilizing Radio Frequency Identification (RFID), Wireless Power Transfer (WPT) devices, anti-theft equipment, metal detectors, high-frequency surgical devices, or medical equipment such as diathermy and electrocautery equipment. Please keep the TGFR away from such equipment, otherwise degradation of the performance of this equipment could result.

Non-homogeneous

The TGFR Monitor may prompt a Non-homogenous Sensor error (Figure 46) if the skin tone becomes too irregular to collect useful data. The sensor will have to be removed and a new sensor placed on a new site. When the sensor is removed, inspect the sensor site for blemishes, discoloration, or other features that may have disrupted readout. The new site can be in or near the original site as long as the sensor's optical head is on skin that is as clean and uniform as possible. If a non-homogeneous sensor error occurs after Lumitrace injection administration refer to Table 1 for required wait times before attempting a new session.

System Error

If a system error screen is encountered contact customer support and include the error code presented on the prompt. Avoid using the error-reporting monitor until advisement has been given by MediBeacon customer support. If the error occurred during a tGFR session after Lumitrace injection has been administered, wait until the advised Lumitrace injection clearance time has passed before starting a new session.

TGFR Sensor Detached

A sensor detachment occurs if the optical head loses contact with the patient's skin. The adhesive may or may not show evidence of detachment as well. If a sensor detached screen is encountered disconnect the sensor. Remove the sensor, replace with a new sensor, and choose a new sensor site or wait until any discoloration has cleared from the sensor site. If the error occurred after Lumitrace injection administration, wait until the advised clearance time has passed before re-administering the Lumitrace injection (Table 1).

TGFR Sensor Error

If a sensor error screen is encountered disconnect the sensor and replace the sensor. If the sensor was attached to a patient, remove the sensor, replace with a new sensor and choose a new sensor site or wait until any discoloration has cleared from the sensor site. If the error occurred after Lumitrace administration, wait until the advised clearance time has passed before starting a new session and re-administering the Lumitrace injection (Table 1).

Unexpected Reboot

If an 'Unexpected Reboot' screen (Figure 45) is encountered select 'OK'. The monitor should recover the current session and resume monitoring.

Section XII: Frequently Asked Questions

1. **When is a TGFR session complete?**

   A TGFR session is completed when an Average Session GFR is displayed in green text in the upper right corner of the monitoring screen. The Average Session GFR is also accompanied by a 'Measurement Session Ended' message in the lower portion of the monitoring screen.

2. **Aside from the pectoralis major or sternum, can the sensor be mounted anywhere else?**

   No other sensor sites are validated.

3. **Can additional securement methods be used for the sensor**

   Once a sensor site is properly prepared no additional securement is needed for the TGFR Sensor. Do not place tape, Tegaderm™ or other securement devices over the TGFR Sensor as this may push the sensor too far into the skin. Securing the TGFR Sensor cable to the body as shown in Figure 7 is encouraged to prevent cable movement from interfering with sensor readout.

4. **Can the subject be active during the TGFR session?**

   Subjects should remain as inactive as possible for the TGFR reading. It is important that the subject remain completely still during skin tone adjustment and baseline, as these readings calibrate the sensor to the subject. Once the Lumitrace injection is administered the subject may engage in light activity such as reading, or watching television, eating/drinking, or restroom breaks. Ideally the subject should remain in a comfortable, reclined position during the TGFR reading, and limit ambulatory movement to restroom breaks, or to relieve discomfort from inactivity.

5. **Why is the patient's urine discolored/bright orange?**

   The Lumitrace injection has a bright orange color and is cleared from the bloodstream via the urine. Lumitrace is inert, and is not metabolized or modified by the body, and will remain intact when excreted, causing chromaturia or coloration of the urine.

6. **Can the sensor be taken off during a read?**

   The TGFR Sensor should not be removed from the skin until the session is complete. Removing the sensor from the skin will disrupt readout and end the TGFR session.

7. **Does the entire sensor site have to be uniform and free of abrasions, discolorations, tattoos, etc.?**
   The entire sensor site does not have to be uniform, but the area that the optical head engages needs to be as consistent as possible.

8. **How long does the TGFR session provide a TGFR reading?**

   TGFR reading duration varies with kidney function. The higher a patient's GFR, the faster the TGFR session will complete. The duration range is typically around 8 hours for a patient with higher GFR and up to 24 hours for a patient with low GFR.

9. **Can I use intermediate graph readings for clinical decisions?**

   No, the intermediate graph readings are not validated. They are utilized to calculate the Average Session GFR using a weighted average based on the quality factor of the individual readings.

10. **How long before another TGFR session can begin?**

    The time between TGFR reads varies depending on the GFR of a patient. The higher the GFR, the sooner the patient can undergo another TGFR reading. When a tGFR assessment is completed, the monitor will prompt a recommended time to allow residual tracer agent to clear. Also, refer to Table 1 for tracer agent clearance times if a TGFR session was not completed.

11. **Can I review patient results after ending a session?**

    The patient data is not readily accessible to the clinician after the end of session is confirmed. Make sure all patient data is transcribed before Ending the Session.

Section XIII: System Maintenance and Service

Follow local governing ordinance and recycling instructions regarding the disposal or recycling of the monitor, sensors, and accessories.

Caution: The monitor can only be serviced by qualified personnel. There are no user-serviceable parts inside.

The monitor and sensors require no calibration. The expected battery life is two to three years.

If service is necessary, for battery replacement or additional serviceable errors, contact qualified service personnel or your local MediBeacon representative.

Section XIV: System Cleaning

Cleaning

TGFR Monitor
A mild, common dish washing liquid detergent should be used to thoroughly clean the monitor body and power cord. The detergent should be used with a 20:1 ratio of water to detergent mixture. The water and detergent mixture should not exceed 55°C (130°F).

Caution: The use of other cleaners and disinfectants may cause significant damage to the TGFR Monitor and may void warranty. Never use an abrasive pad on any surface of the TGFR Monitor.

Cleaning Frequency
It is recommended that the TGFR Monitor and power cord be cleaned after each use.

Directions for Cleaning
Thoroughly clean the surfaces of the TGFR Monitor and power cord with a damp cloth using a mild detergent as previously described, removing all visible soil. Ensure all excess fluid is squeezed from the cloth before cleaning. If the cloth is excessively wet, the detergent and water solution may penetrate the monitor and affect functionality. Inspect all components and repeat cleaning steps until there is no visible contamination. After cleaning the monitor and power cord, wipe the monitor with a clean lint free damp cloth to remove the mild detergent mixture. Dry the monitor with a clean lint free cloth. Never use an abrasive pad or abrasive cleaner on the monitor.

TGFR Sensor
The TGFR Sensor is a single-use device and generally should not require cleaning. Should the sensor become soiled while in use, the cleaning method listed above should be followed. Extra care should be given to ensure cleaning fluids do not come in contact with the adhesive portion of the sensor.

Disinfection

TGFR Monitor
The TGFR Monitor and power cable can be disinfected by dampening their surfaces with a Sani-Cloth® Bleach Wipe.

Disinfection Frequency
It is necessary to disinfect the TGFR Monitor and power cord after each use.

Directions for Disinfecting the TGFR Monitor and Cord
Dampen the surfaces of the TGFR Monitor and power cord using a Sani-Cloth® Bleach Wipe, or an equivalent lint free wipe wetted with a bleach: water mixture at 1:10 ratio. Wipe the monitor as necessary to maintain visual wetness for a minimum duration of 1 minute. After disinfecting the monitor and cable, allow each to air dry completely.

Caution: The TGFR Monitor is not designed to be immersed, soaked, rinsed, or sprayed with water. Do not immerse, soak, rinse, or spray the TGFR Monitor in water or other cleaning solutions. Failure to follow the cleaning procedures described herein could result in hazards to users, patients, and clinicians. As with any medical electrical equipment, care must be taken to prevent liquid from entering the monitor to avoid electrical shock hazard, fire hazard, or damage to the electrical components.

TGFR Sensor
The TGFR Sensor is a single-use device and generally should not require disinfection. Should the sensor need to be disinfected, the disinfection method listed above should be followed. Extra care should be given to ensure disinfection fluids do not come in contact with the adhesive portion of the sensor.

Section XV: Specifications

Compliance

Compliance	Standard
Product Safety	IEC60601-1 edition 3.1 2012-08
Flammability	VR2
EMC	IEC 60601-1-2 :2014 4th edition
Enclosure Protection	IPx0
Drop Test Compliance	Portable Equipment

Physical Specifications

Height, Overall	12 in / 30.5 cm
Width, Overall	10.75 in / 27.3 cm
Depth, Overall	10 in / 25.4cm
Weight, Overall	Approx 7 lbs
Power Cord, Length	6.5 ft / 2 m
Tip Test (Pole Mounted)	At 3.3 ft / 1 m height 5 wheel 1.9 in / 58 cm diameter IV Pole
Shipping Durability	ASTM-D4169 level 1
TGFR Monitor Expected Service Life	5 years from Date of Manufacture
TGFR Sensor Shelf Life	2 years from Date of Manufacture

Electrical Specifications

Supply Power Input	100-230VAC, 50/60Hz, 0.5A
Type of Current	AC
Fuses	5x20mm Ceramic, Time-lag, 1A, 250VAC
Ingress Protection Rating	Monitor: IPxO Sensor: IP53

Environmental Specifications

Operation Ambient Temperature	15-35C
Operation Relative Humidity	10-85%
Operation Altitude	-450 to 2400 meters
Transportation & Storage Temperature	-18C to 60C,
Transportation & Storage Pressure	70 to 107 kPa
Transportation & Storage Relative Humidity	10-85%

Section XVI: EMC Guidance and Manufacturer's Declarations

Guidance and Manufacturer's Declaration – Electromagnetic Emissions	
Emissions Test	
RF emissions	CISPR 11 RF emissions CISPR 11
Harmonic emissions	IEC 61000-3-2
Voltage fluctuations/flicker emissions	IEC 61000-3-3
Note: Compliance using 100-240V 50/60Hz with AC power cord length of **2 m.**	

Guidance and Manufacturer's Declaration – Electromagnetic Immunity	
Immunity Test	
Electrostatic discharge (ESD)	IEC 61000-4-2
Electrical fast transient/burst	IEC 61000-4-4
Surge	IEC 61000-4-5
Voltage dips, short interruptions and voltage variations on power supply input lines	IEC 61000-4-11
Power frequency (60 Hz) magnetic field	IEC 61000-4-8

Guidance and Manufacturer's Declaration – Radiofrequency Electromagnetic Immunity	
Conducted RF	IEC 61000-4-6
Radiated RF	IEC 61000-4-3

Emissions Test	Compliance	Electromagnetic Environment Guidance
RF radiated emissions CISPR 11	**Class B**	The MediBeacon TGFR uses RF energy only for its internal function. Therefore, its RF emissions are very low and are not likely to cause any interference in nearby electronic equipment.
RF conducted emissions CISPR 11	**Class B**	The MediBeacon TGFR is suitable for use in all hospital and clinical environments excluding Operating Room environments.
Harmonic emissions IEC 61000-3-2	**Class B**	
Voltage fluctuations/ flicker emissions IEC 61000-3-3	**Pass**	

Immunity Test	IEC 60601 Test Level	Compliance Level	Electromagnetic Environment Guidance
Electrostatic discharge (ESD) IEC 60601-1-2 : 2014 levels	±2, 4, 8 kV contact ±2, 4, 8, 15 kV air	±2, 4, 8 kV contact ±2, 4, 8, 15 kV air	Floors should be concrete, or ceramic tile. Synthetic materials and low humidity may cause higher levels of ESD .
Electrical fast transient/burst IEC 61000-4-4	±2 kV for power supply lines ±1 kV for input/output lines	±2 kV for power supply lines ±2 kV for input/output lines	Line power quality should be that of a typical commercial or hospital environment.

Immunity Test	IEC 60601 Test Level	Compliance Level	Electromagnetic Environment Guidance
Surge IEC 61000-4-5	±1 kV differential mode ±2 kV common mode	±1 kV differential mode ±2 kV common mode	Line power quality should be that of a typical commercial or hospital environment.
Voltage dips, short interruptions, and voltage variations on power supply input lines IEC 61000-4-11	<5% UT (>95% dip in UT) for 0.5 cycle 70% UT (30% dip in UT) for 25 cycles <5% UT (>95% dip in UT for 5 sec)	<5% UT (>95% dip in UT) for 0.5 cycle 70% UT(30% dip in UT) for 25 cycles <5% UT (>95% dip in UT for 5 sec)	Line power quality should be that of a typical commercial or hospital environment. If the user of the MediBeacon TGFR requires continued operation during power line interruptions, it is recommended that the MediBeacon TGFR be powered from the battery. Note: UT is the A.C. line voltage before application of the test level.
Power frequency (50/60 Hz) magnetic field IEC 61000-4-8	30 A/m	30 A/m	Power frequency magnetic fields should be at levels characteristic of a typical commercial or hospital environment.
Conduced RF IEC 61000-4-6	3 Vrms 150 kHz to 80 MHz 6 Vrms 150 kHz to 80 MHz in ISM bands	3 Vrms 150 KHz to 80 MHz 6 Vrms 150 kHz to 80 MHz in ISM bands	Recommended separation distance: d = 1.17 P
Radiated RF IEC 61000-4-3	3 V/m 80 MHz to 2.7 GHz	3 V/m 80 MHz to 2.7 GHz	Recommended separation distance: d = 0.35. 80 MHz to P 800MHz Recommended separation distance: d = 0.70. 800MHz to P 2.5 GHz where P is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer and d is the recommended separation distance in meters (m). Field strengths from fixed RF transmitters, as determined by an electromagnetic site survey, should be less than the compliance level in each frequency range.

Electromagnetic Environmental Recommendations			
Recommended separation between portable and mobile RF communications equipment and the MediBeacon TGFR Monitor			
The monitor is intended for use in an electromagnetic environment in which radiated RF disturbances are controlled. The user can help prevent electromagnetic interference by maintaining a minimum distance between portable and mobile RF communications equipment (transmitter) and the monitor as recommended below, according to the maximum output power of the communications equipment.			
Separation distance according to frequency of transmitter (meters)			
Max Output Power Watts (W)	150 kHz to 80 MHz d=2√P	80 MHz to 800MHz d=2√P	800 MHz to 2700 MHz d=2√P
0.01	0.2	0.2	0.2
0.1	0.632	0.632	0.632
1	2.0	2.0	2.0
10	6.32	6.32	6.32
100	20.0	20.0	20.0
	For transmitters rated at a maximum output power not listed above, the recommended separation distance (d) in meters (m) can be estimated using the equation applicable to the frequency of the transmitter, when power (P) is the maximum power of the transmitter in watts (W). **Note 1:** at 80MHz and 6800 MHz, the separation distance for the higher frequency range applies. **Note 2:** The guidelines might not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.		

CAUTION: The potential for electromagnetic interference in all environments cannot be eliminated. Use caution if the TGFR is used near electronic equipment such as devices utilizing Radio Frequency Identification (RFID), Wireless Power Transfer (WPT) devices, anti-theft equipment, metal detectors, high-frequency surgical devices, or medical equipment such as diathermy and electrocautery equipment. Please keep the TGFR away from such equipment, otherwise degradation of the performance of this equipment could result.

Section XVII: Appendix 1: Summary of Primary Clinical Study

MediBeacon TGFR Pivotal Study

The objectives of the MediBeacon TGFR pivotal study included the following:

Establish that Lumitrace® transdermal measured GFR using the MediBeacon TGFR is comparable to the measured Lumitrace plasma GFR.

- Evaluate the safety and tolerability of a single dose of Lumitrace injection in subjects
- Evaluate the safety and effectiveness of the MediBeacon TGFR for the non-invasive transdermal fluorescence detection of Lumitrace® in subjects.

A. Study Design

This is a multi-center, open-label, pivotal study comparing transdermal glomerular filtration rate (tGFR) to plasma-derived indexed GFR (nGFR) with Lumitrace® (relmapirazin) injection as the fluorophore. Participants will span the GFR range of values from normal to stage 4 chronic kidney disease (CKD) and span the entire range of human skin colors as defined by the Fitzpatrick Skin Scale (FSS). The safety and pharmacokinetics of Lumitrace and the safety of the MediBeacon TGFR will also be evaluated.

A total of 249 subjects were enrolled.

1. CLINICAL INCLUSION AND EXCUSION CRITERIA

Enrollment in the MediBeacon TGFR pivotal study was limited to subjects who met the eligibility criteria.

The full list of selection criteria is provided here:

Inclusion Criteria:

- Eligible female non-pregnant participants who are either not of child-bearing potential or willing to use adequate contraception during the trial
- Males must be willing to practice abstinence or utilize adequate contraception from dosing day to at least 7 days post-dose
- For women of child-bearing potential, the participant should have a negative serum pregnancy test at screening, and agrees to one of the following acceptable contraceptive methods used consistently and correctly i.e. abstinence, oral contraceptive either combined or progesterone alone; injectable progesterone, implants of levonorgestrel, estrogenic vaginal ring, percutaneous contraceptive patches, IUD device or system or male partner sterilization
- Men will not donate sperm during the study and for 1 month following the last dose of study drug
- Participants who are capable of directly providing informed consent and who can comply with the requirements and restrictions required by the protocol
- Adequate venous access sufficient to allow blood sampling per protocol requirements

Exclusion Criteria:

- Participants positive via PCR testing for COVID-19 (Vaccinated participants without symptoms of COVID-19 are not required to undergo PCR testing but may be tested at the discretion of the study site)
- Recent donation or loss of blood or plasma: 100 mL to 499 mL within 30 days prior to the initial dose of the study medication; or more than 499 mL within 56 days prior to the initial dose of study medication
- Non-steroidal anti-inflammatory (NSAID) use within 3 days of Lumitrace injection dosing

- Participant has participated in a clinical trial and has received an investigational product within the following time ranges: prior to the first dosing day in the current study: either 30 days or 5 half-lives of the investigational product (whichever duration is longer).
- History of skin sensitivity to adhesives (e.g. Band-Aids, surgical tape)
- History of severe allergic hypersensitivity reactions (unacceptable adverse events) or anaphylactoid reaction to any allergen including drugs, Lumitrace injection or other related products (intolerance to a drug is not considered a drug allergy).
- Any characteristics which, in the opinion of the investigator, makes the participant a poor candidate for participation in the clinical trial
- Significant scarring, tattoos or alterations in pigmentation on the sternum or other sensor location testing areas that would alter sensor readings versus other areas of the skin
- Any serious or uncontrolled medical disorder, active infection, physical exam finding, laboratory finding, or psychiatric condition that in the opinion of the investigator would limit the participant's ability to complete study requirements or may put the participant at increased risk or compromise the interpretability of study results.
- Currently receiving dialysis
- Currently anuric
- Positive serum pregnancy test
- Participants with an eGFR > 120 mL/min/1.73m^2

2. Follow-Up Schedule

Follow-up was conducted within 7 +/- 3 days of dosing. Clinical assessments during follow-up included:

- Physical Assessment (at a minimum: Assessment of head, ears, eyes, nose, throat, (HEENT) respiratory, cardiovascular, abdominal systems)
- Vital signs including blood pressure, respiration rate, heart rate and temperature
- Concomitant medications administered through follow-up
- Adverse events

3. Clinical Endpoints

Primary Efficacy Endpoint: The primary endpoint is the performance measure of P30 for transdermal-derived GFR with respect to the plasma-derived indexed GFR, with a 95% confidence interval. Success for the study will be that the P30 lower limit of the 95% CI is greater than 85% (the performance goal is 85%).

Primary Safety Endpoint: Safety of the Lumitrace injection was evaluated through treatment emergent adverse events (TEAEs), where treatment emergence is defined with respect to the dosing of Lumitrace injection. Safety of the MediBeacon TGFR will be evaluated through treatment-emergent adverse events, where treatment emergence is defined with respect to the start time of Transdermal GFR Measurement System use (placement of the sensor on the skin)

Additional safety variables include physical examinations, clinical laboratory assessments, ECGs, and concomitant medication use. All safety analyses will be done for subjects receiving a single dose of Lumitrace injection.

B. Accountability of PMA Cohort

A total of 505 subjects were screened and enrolled globally, of whom 249 (49.3%) subjects were dosed and 243 (48.1%) subjects completed the study. Reasons for not completing the study included screen failure (30.7%), cohort full (20.4%), and lost to follow-up (0.8%).

A total of 249 subjects were enrolled at 8 investigational sites. Subject disposition and visit compliance through the follow-up can be found in Table 2 and Figure 53.

Table 2: Visit Compliance for TGFR Pivotal Study

Study Visit	US	China	All
Dosing Day	195	54	249
Follow-up (7+/-3 days)	191(97.9%)	54(100%)	245(98.4%)

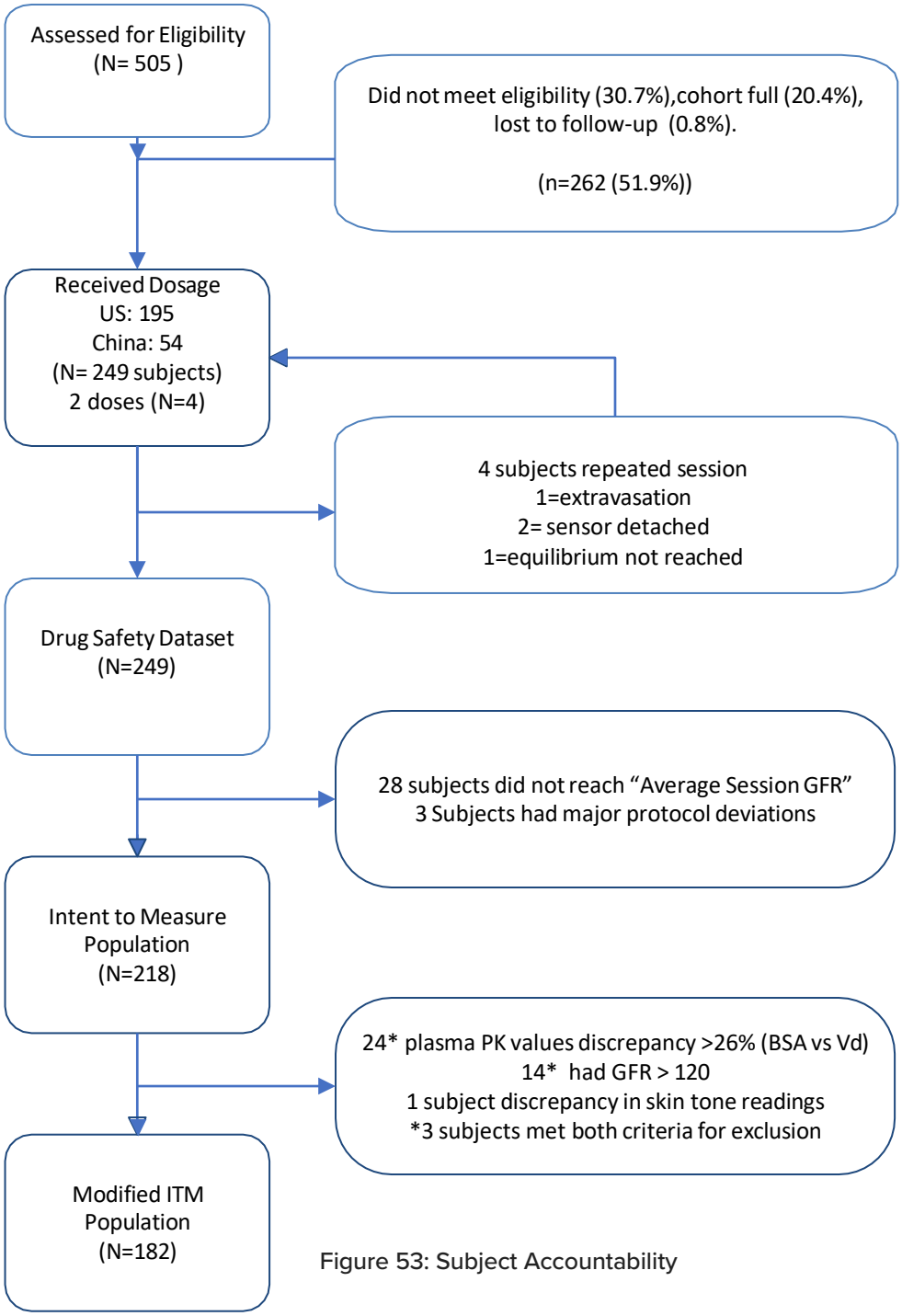


Figure 53: Subject Accountability

C. Study Population Demographics and Baseline Parameters

Subject demographics and baseline characteristics are provided in Table 3. As targeted, the modified intent to treat population of subjects with impaired and normal renal function equally in the study; 49% with an eGFR ≥ 70 mL/min/1.73m^2 and 50% with an eGFR < 70 mL/min/1.73m^2. Likewise, in the US, the modified intent to measure population was studied across the spectrum of the Fitzpatrick Skin Scale (FSS) with 55% of subjects with a FSS of I-III and 45% of subjects with a FSS of IV-VI. Note that in the total study population 27% of subjects in the mITM population were from China.

Of 249 subjects included in the Safety Population, 201 (80.7%) subjects had at least one current medical history record. The most common (≥20% of subjects) medical histories were cardiovascular (57.8%), genitourinary (51.0%), endocrine metabolic (41.4%), gastrointestinal (27.7%), musculoskeletal (23.7%), neurologic (22.9%), head, eyes, ears, nose, and throat (HEENT) (22.1%), and other (20.1%) conditions.

Table 3: Baseline Demographics

Characteristic Statistic	Stratum 1 (N=130) n (%)	Stratum 2 (N=119) n (%)	Total (N=249) n (%)
Age at Screening (years)			
n	130	119	249
Mean (SD)	46.9 (14.19)	61.5 (13.45)	53.9 (15.63)
Median	46.5	64.0	57.0
Min, Max	19, 79	21, 87	19, 87
Sex, n (%)			
Male	68 (52.3)	74 (62.2)	142 (57.0)
Female	62 (47.7)	45 (37.8)	107 (43.0)
Race, n (%)			
White	58 (44.6)	49 (41.2)	107 (43.0)
Black or African American	33 (25.4)	43 (36.1)	76 (30.5)
Asian	37 (28.5)	27 (22.7)	64 (25.7)
American Indian or Alaska Native	2 (1.5)	0	2 (0.8)
Ethnicity, n (%)			
Hispanic or Latino	36 (27.7)	14 (11.8)	50 (20.1)
Not Hispanic or Latino	94 (72.3)	103 (86.6)	197 (79.1)
Unknown or Not Reported	0	2 (1.7)	2 (0.8)
Height (cm)			
n	129	119	248

Characteristic Statistic	Stratum 1 (N=130) n (%)	Stratum 2 (N=119) n (%)	Total (N=249) n (%)
Mean (SD)	168.151 (9.5878)	168.239 (9.2247)	168.194 (9.3964)
Median	167.600	168.900	167.640
Min, Max	144.00, 198.00	144.80, 185.50	144.00, 198.00
eGFR Result Group			
≥ 90	80 (61.5)	0	80 (32.1)
60 - 89	38 (29.2)	30 (25.2)	68 (27.3)
45 - 59	0	39 (32.8)	39 (15.7)
30 - 44	0	24 (20.2)	24 (9.6)
15 - 29	0	18 (15.1)	18 (7.2)
Weight at Dosing (kg)			
n	129	119	248
Mean (SD)	80.806 (17.6937)	85.528 (21.2543)	83.071 (19.5867)
Median	78.300	83.688	80.593
Min, Max	43.64, 147.60	48.60, 135.90	43.64, 147.60
Body Mass Index at Dosing (kg/m^2) [a]			
n	129	119	248
Mean (SD)	28.420 (5.1634)	30.071 (6.4389)	29.213 (5.8571)
Median	28.192	29.237	28.638
Min, Max	18.18, 46.65	17.46, 45.71	17.46, 46.65
Mexameter-Based Skin Color Type			
Type I	16 (12.3)	27 (22.7)	43 (17.3)
Type II	25 (19.2)	21 (17.6)	46 (18.5)
Type III	34 (26.2)	22 (18.5)	56 (22.5)
Type IV	29 (22.3)	16 (13.4)	45 (18.1)
Type V	9 (6.9)	17 (14.3)	26 (10.4)
Type VI	17 (13.1)	15 (12.6)	32 (12.9)
Missing	0	1 (0.8)	1 (0.4)
Mexameter-Based Skin Color Group			
Type I-III	75 (57.7)	70 (58.8)	145 (58.2)
Type IV-VI	55 (42.3)	48 (40.3)	103 (41.4)
Missing	0	1 (0.8)	1 (0.4)

D. Safety and Effectiveness Results

A total of 249 patients were dosed and 182 patients completed the session obtaining an average tGFR reading and are considered evaluable in the modified Intent to Measure population. The key safety outcomes for this study are presented below. Adverse effects for the tracer agent are reported in Table 4. There were no device related adverse events.

1. Safety Results

A total of 26 subjects had at least one adverse event reported 26/249 (10.4%), and of these adverse events, 0 (0.0%) were considered serious adverse events. The most common adverse event was injection site extravasation. If extravasation occurred it was known at the time of the injection due to yellow staining and potential pain at the injection site.

There was one subject who experienced a moderate adverse event. Subject 401-030 experienced moderate nausea at 15:05 resolving by 18:48 on 12 July 2022 that required treatment with ondansetron and was considered possibility related to Lumitrace by the investigator. The subject was dosed at 09:00 on 12 July 2022. This subject also experienced an unrelated moderate headache (start time 11:30 and ending at 22:30) and nasal congestion (mild, unrelated also starting at 16:00 and resolving at 18:48).

As subjects in Pilot 2, Group 3 were also dosed with Lumitrace and no other drug product, the following table provides safety results for those subjects in Pilot 2, Group 3 and in the Pivotal to represent the overall safety profile of Lumitrace and what will be used to support the tracer agent package insert labeling.

Table 4: Lumitrace Injection Adverse Events by Type

Adverse Event Type	Events (N) Pilot 2 114 Subjects	Events (N) Pivotal Study 249 Subjects	Subjects n (%) 363 Subjects
Injection site extravasation	6	3	9 (2%)
Headache	1	4	5(1%)
Ecchymosis	0	3	3 (1%)
Cardiac Murmur	0	2	2 (1%)
Hypertension	0	2	2 (1%)
Oropharyngeal pain	1	0	1 (<1%)
Rash	1	0	1 (<1%)
Hot Flush	1	0	1 (<1%)
Fatigue	0	1	1 (<1%)
Oedema	0	1	1 (<1%)
Diarrhoea	0	1	1 (<1%)
Dyspepsia	0	1	1(<1%)
Nausea	0	1	1 (<1%)
Blood Glucose Increased	0	1	1 (<1%)
Weight Decreased	0	1	1 (<1%)
Pruritus	0	1	1 (<1%)
Haematoma	0	1	1 (<1%)
Hyperglycemia	0	1	1 (<1%)
Hypoglycemia	0	1	1 (<1%)
Cough	0	1	1 (<1%)
Nasal congestion	0	1	1 (<1%)
Urinary tract infection	0	1	1 (<1%)
Contusion	0	1	1 (<1%)
Glycosuria	0	1	1 (<1%)

There were no device related adverse events.

2. Effectiveness Results

The primary endpoint of this study was a P30 value with a lower 95% confidence interval that was greater than 85%. The clinical study yielded a P30 value of 94.0%, with a lower 95% confidence interval of 89.4% and an upper 95% confidence interval of 96.9%. The primary endpoint was achieved.

Accuracy

Average Session GFR results comparison with measured GFR results:

Ninety-four percent of the Average Session GFR values obtained using this device were within 30% of the measured GFR values (with a confidence interval of 89.4-96.9%). This was the outcome of the pivotal trial.

P30 Value	Upper 95% CI	Lower 95% CI
94.0%	96.9%	89.4%

Average Session GFR results comparison with estimated GFR (eGFR) results:

(using the creatinine-based 2009 CKD-EPI equation)

	Average Session GFR	eGFR*
P30	94.0%	92.9%
95% Confidence Interval	89.4-96.9%	88.1%-96.1%

*The eGFR results above were obtained via a post hoc analysis, (which was not the predetermined outcome measure from the study).

In the pivotal trial, 94.0% of the Average Session GFR values obtained using this device were within 30% of the measured GFR values and 92.9% of the eGFR values (creatinine based 2009 CKD- EPI equation) were within 30% of the measured GFR values. The confidence intervals overlap (see table above).

Subgroup population results:

Patients were grouped into Stratum 1 (eGFR ≥70 mL/min/1.73m^2) and Stratum 2 (eGFR < 70 mL/min/1.73m^2).

Patient Population	P30 Value	Upper 95% CI	Lower 95% CI
Stratum 1 (eGFR ≥70 mL/min/1.73m^2) N=90	95.6%	98.8%	89.0%
Stratum 2 (eGFR < 70 mL/min/1.73m^2) N=92	92.4%	96.9%	84.9%

Primary Endpoint Evaluation by Fitzpatrick Skin Scale (FSS)

Patient Population	P30 Value	Upper 95% CI	Lower 95% CI
FSS Type I-II N=77	96.1%	99.2%	89.0%
FSS Type III-IV N=69	92.8%	97.6%	83.9%
FSS Type V-VI N=36	91.7%	98.3%	77.5%

Subgroup Analyses

Results are shown in the table below which also has the strata subgroups globally and for each region. Note the P30 value for all the subgroups is greater than 90% yielding consistency of the performance measure.

Table 5: Primary Endpoint Evaluation by Stratum (mITM)

Variable Statistic	Stratum 1	Stratum 2	Total
Global: P30	**N=90**	**N=92**	**N=182**
Point Estimate	0.956	0.924	0.940
Lower 95% CI	0.890	0.849	0.894
Upper 95% CI	0.988	0.969	0.969
USA: P30	**N=65**	**N=68**	**N=133**
Point Estimate	0.938	0.912	0.925
Lower 95% CI	0.850	0.818	0.866
Upper 95% CI	0.983	0.967	0.963
China: P30	**N=25**	**N=24**	**N=49**
Point Estimate	1.000	0.958	0.980
Lower 95% CI	0.863	0.789	0.891
Upper 95% CI	1.000	0.999	0.999

Abbreviations: CI, confidence interval; eGFR, estimated glomerular filtration rate; mITM, Modified Intent-to-Measure; USA, United States of America. Stratum 1: eGFR ≥70 mL/min/1.73 m^2; Stratum 2: eGFR <70 mL/min/1.73 m^2.

3. Pediatric Extrapolation

In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 13 investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

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