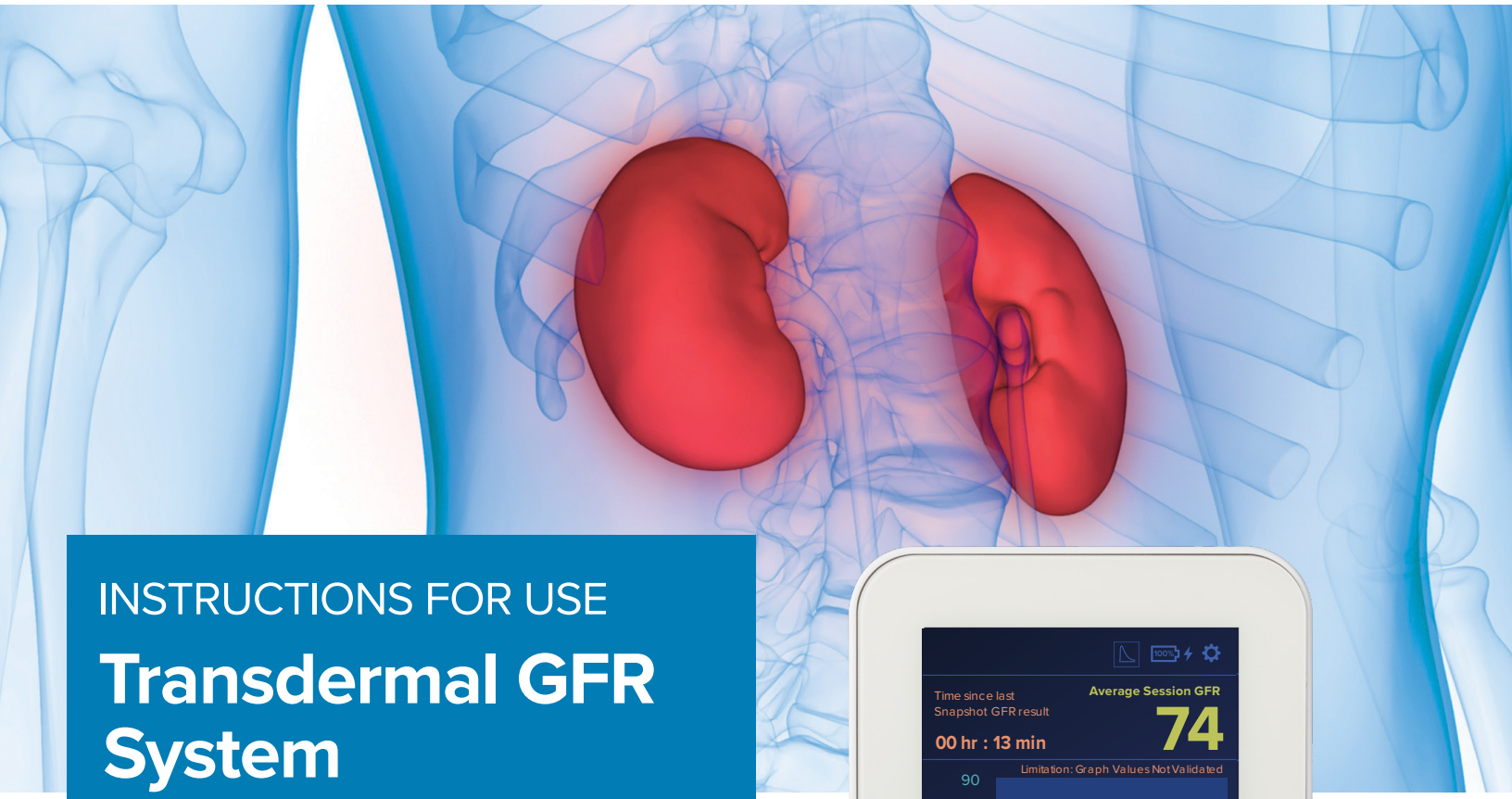
MediBeacon®
Transdermal GFR



INSTRUCTIONS FOR USE

Transdermal GFR System

℞ only

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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, the MediBeacon® TGFR Reusable Sensor, and the MediBeacon® TGFR Disposable Ring. All components are required to obtain a transdermal GFR (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 four 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.
- MediBeacon® TGFR Reusable Sensor is a multiuse sensor containing the light source and photo detector for the noninvasive detection of the transdermal fluorescence from Lumitrace injection and is attached to one of several positions on the body using a biocompatible adhesive on the TGFR Disposable Ring. This transdermal sensor has a built-in cable that connects to a display monitor.
- MediBeacon® TGFR Disposable Ring is a single use device that is assembled with the TGFR Reusable Sensor and attaches to the patient's skin during a TGFR session.
- MediBeacon® TGFR Monitor is the display monitor and provides power to the TGFR Reusable Sensor, provides the number of uses remaining on the TGFR Reusable Sensor, provides the user interface, digitizes the data acquired from the TGFR Reusable Sensor, contains the algorithms to run the sensor and convert the output to GFR (ml/min/1.73m^2), and displays the GFR to the clinician and/or caregiver.

The sensor assembly 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 Reusable Sensor also has components to compensate for local time-varying tissue properties, such as changes in blood volume, by measuring diffusely-reflected light. The TGFR Reusable Sensor is intended for multiple uses, after being cleaned and disinfected between each use. The TGFR Disposable Ring 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 Disposable Ring and the exogenous tracer agent, Lumitrace® injection, are single use and are only used with the MediBeacon® TGFR.

The MediBeacon® TGFR Disposable Ring is intended to be assembled with the MediBeacon® TGFR Reusable Sensor and attaches to the patient's skin during a TGFR session.

The MediBeacon® TGFR Reusable Sensor is intended to 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

Transdermal GFR results comparison with measured GFR results:

In the clinical study with the TGFR Reusable Sensor, ninety-six percent of the tGFR values obtained were within 30% of the measured GFR values (with a confidence Interval of 87.9% - 99.3% for an alpha level of 3%).

Sensor	P30 Value	Upper CI	Lower CI
TGFR Reusable Sensor (N=75) 97% Confidence Interval (CI)	96.0%	99.3%	87.9%

Transdermal GFR (tGFR) results comparison with estimated GFR (eGFR) results: (using the creatinine-based 2009 CKD-EPI equation)

	tGFR TGFR Reusable Sensor 97% CI	eGFR* TGFR Reusable Sensor 97% CI	Paired Difference
P30	96.0%	90.7%	6.67%
Confidence Interval (CI)	87.9% - 99.3%	80.7% - 96.5%	-2.3% to 15.7%

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

In the clinical study with the TGFR Reusable Sensor trial, 96.0% of the tGFR values obtained using this device were within 30% of the measured GFR values and 90.7% 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). The pivotal study was conducted using a single use sensor and the details can be found in the appendix.

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 TGFR Reusable Sensor	97% Confidence Intervals TGFR Reusable Sensor
Stratum 1 (eGFR ≥70 mL/min/1.73m^2)	95.0% N = 40	81.7% - 99.5%
Stratum 2 (eGFR<70 mL/min/1.73m^2)	97.1% N = 35	83.6% - 100.0%

Primary Endpoint Evaluation by Fitzpatrick Skin Scale (FSS)

Patient Population	P30 Value TGFR Reusable Sensor	97% Confidence Intervals TGFR Reusable Sensor
FSS Type I-II	100.0% N = 25	84.5% - 100.0%
FSS Type III-IV	92.3% N = 26	72.9% - 99.3%
FSS Type V-VI	95.8% N = 24	76.9% - 99.9%

See Section XVIII: Appendix for the clinical study summaries.

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, such as fluorescein.
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, which may be for up to 72 hours.
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. Do not use the system in the proximity of magnetic resonance imaging equipment.
6. 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.
7. Do not administer a second Lumitrace injection during an active session.
8. The TGFR Reusable Sensor is a multiple use component that can be used 20 times with proper cleaning and disinfection procedures. However, the TGFR Disposable Ring is a disposable system component; do not reuse. Attempted reuse of the ring can result in detachment, which will prematurely end a session.
9. 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. A linear regression analysis found that mean of the difference tGFR - nGFR tended to decrease by -0.37 mL/min/1.73m² per year increase in age after adjustment for nGFR, Sex, Race and Fitzpatrick skin scale, which all had insignificant effects. For example, a 10-year increase in age will tend to decrease the difference by 3.7 mL/min/1.73m².
3. In the study tGFR tended to underestimate nGFR (mean difference -5.3, 95% CI -7.8, -2.9). For example, if the nGFR value is 30 ml/min/1.73m², then the TGFR reports a GFR value was on average about 25ml/min/1.73m².
4. The system should only be used by trained personnel.
5. 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.
6. 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.
7. System performance may be degraded if operated or stored outside the environmental conditions specified in this manual.
8. Be sure all safety labels are legible.
9. Do not open the TGFR Monitor. Exposing internal components could compromise system function or pose cyber-security risk. Contact appropriate personnel for servicing.
10. 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.
11. Do not use a damaged TGFR Reusable 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.
12. Do not remove the adhesive liner and place the sensor on the patient until the site is properly prepared as outlined in the 'Site Preparation' section.
13. 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.
14. Skin irritation from adhesive on the TGFR Disposable Ring may occur at the point of patient contact.
15. Bolus infusions may temporarily impact the GFR assessments while the vasculature-tissue equilibrium is re-established.
16. Do not administer the Lumitrace injection until instructed by the TGFR Monitor's 'Administer Lumitrace' screen.
17. Clean and disinfect exterior surfaces of the TGFR Monitor and TGFR Reusable Sensor according to instructions in section XIV.
18. Do not immerse the TGFR Monitor or TGFR Reusable Sensor in water. The monitor and sensors are not waterproof.

Section VI: Symbols

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

	Refer to the Instruction Manual.
	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.
	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 re-use. The TGFR Disposable Ring is single-use.
	TGFR Reusable Sensor can perform 20 sessions.
	Indicates the item is a medical device.
IPX0	Ingress rating of Monitor
IP53	Ingress rating of Sensor
	European Conformity to safety, health, and environmental requirements
	European Authorized Representative
	Underwriters Laboratories (UL) certification - safety, quality, and compliance standards have been tested and achieved.

Section VII: System Components

Figure 1. The MediBeacon Transdermal GFR System components

Component Information:

- The MediBeacon® TGFR Reusable Sensor is a reusable device intended to excite fluorescence in Lumitrace injection, the tracer agent, and measures the emitted fluorescence intensity. The data is sent to the TGFR Monitor. The sensor is held in place with the MediBeacon® Disposable Ring which attaches to the patient's skin.
- The MediBeacon® Disposable Ring is a single use device intended to be assembled with the MediBeacon® TGFR Reusable Sensor and attaches to the patient's skin during a TGFR Session.
- The MediBeacon® TGFR Monitor is intended to be connected to the TGFR sensor assembly 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.

TGFR Reusable Sensor and TGFR Disposable Ring Components

TGFR Reusable Sensor (Figure 2):
A two-piece sensor configuration, affixes to the skin with a single-use Disposable Adhesive Ring

1. The TGFR Reusable Sensor with cable functions for 20 monitoring sessions and should be retained, cleaned, disinfected, and reused until its useful life is expired. The monitor detects the number of uses, will notify when it reaches 20 uses, and will prevent use in excess of 20 sessions.
2. The TGFR Disposable Ring holds the sensor securely to the patient's skin for a single session. It is replaced for each new session – even when starting a new session on the same patient.

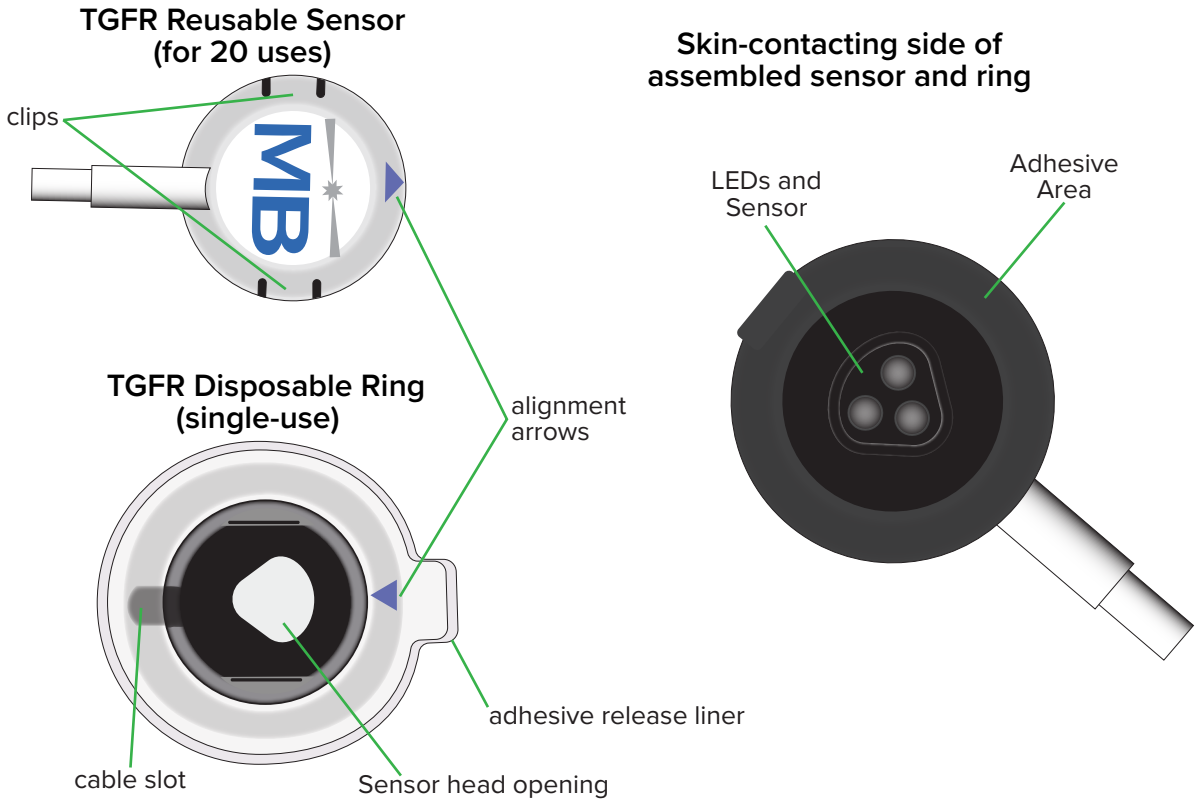


Figure 2. MediBeacon TGFR Reusable Sensor and TGFR Disposable Ring

Getting Started

The following information outlines the instructions for use for the TGFR.

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).

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.

Figure 4. The back of the TGFR Monitor

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 to start a session are divided into several steps as described in the following sections.

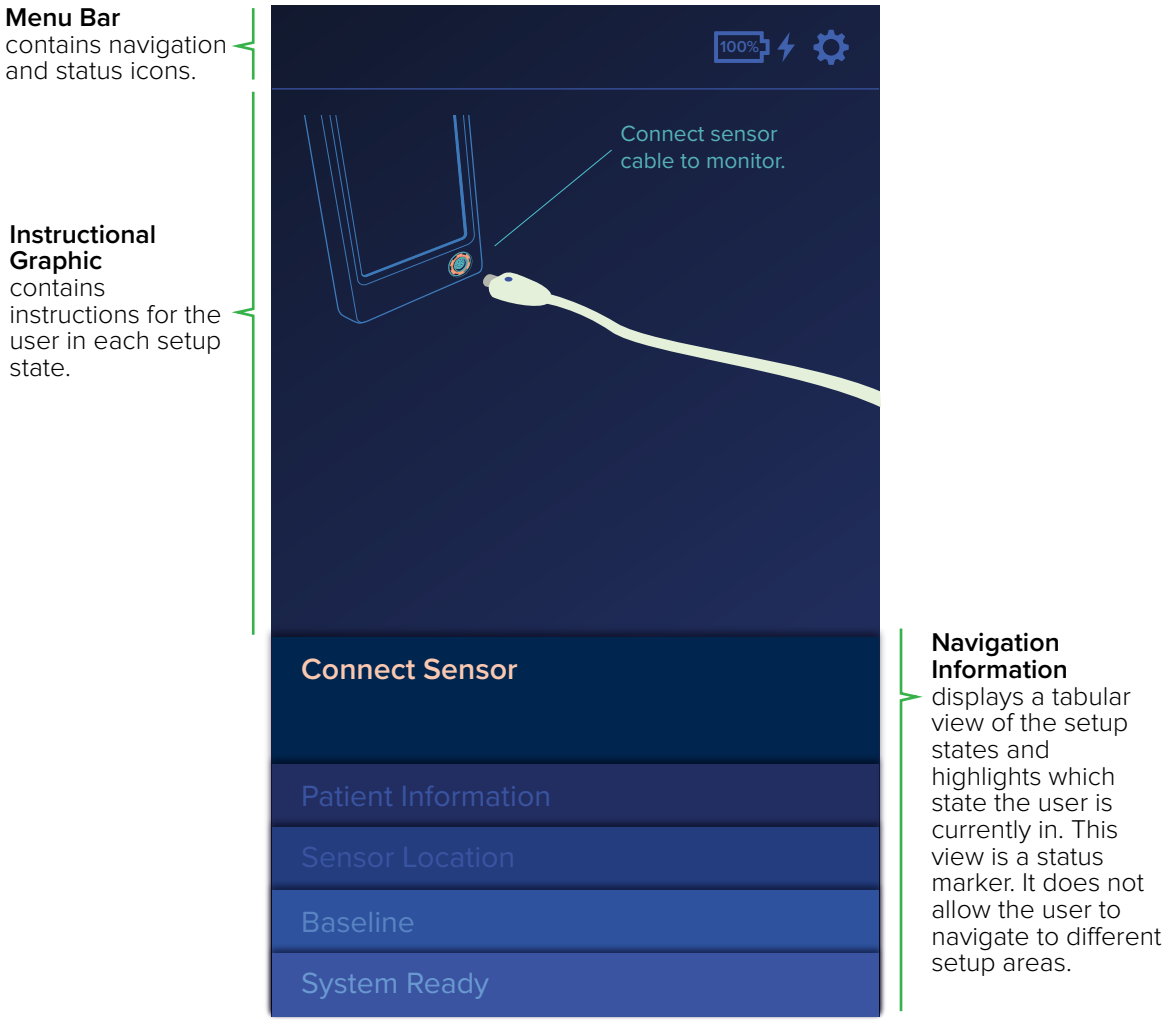


Figure 5. Connect Sensor screen

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:** Press to revert back a step during setup. 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. Press to show the linear and semi-log clearance graphs.
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 ring adhesive may lead to delay of treatment.
- **Patient movement during baseline readings could delay calculations.** – keep patient as still as possible during skin tone adjustment and baseline.

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.

Note: 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 sensor as shown in Figure 7, 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.

Sensor Assembly and Placement

- Attach a TGFR Disposable Ring to a clean and disinfected TGFR Reusable Sensor head by aligning the arrows and pressing together (Figure 7).
- Using the provided tab, pull the paper liner from the disposable adhesive ring to expose the adhesive.
- Place the sensor on the selected and prepared body site, pressing down on the center of the sensor, and then pressing down on all areas of the ring, until it is well-adhered over the full sensor area.
- Secure the sensor cable as shown. Anchor the cable with tape in five places as shown in Figure 7. This will inhibit cable movement and the potential for errors during a session.

Note: Avoid putting any tape over 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 shirt are ideal.

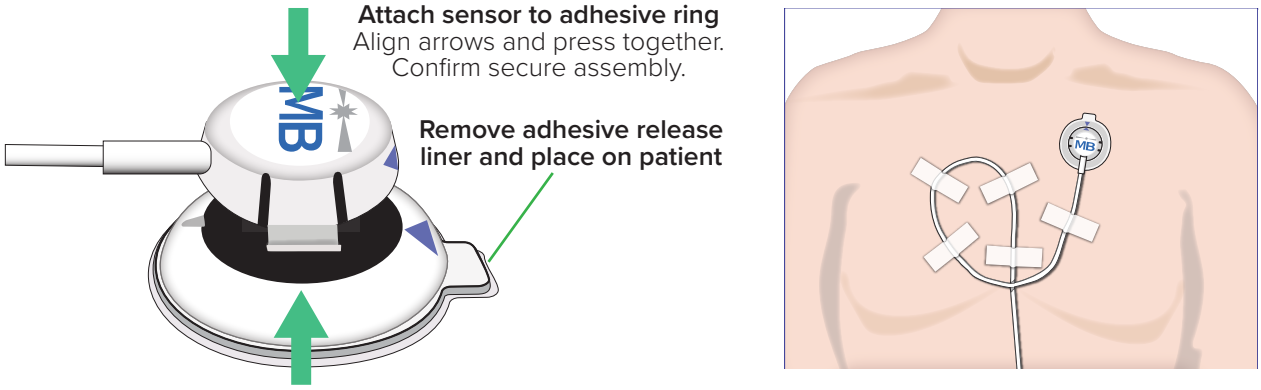


Figure 7. TGFR Reusable Sensor assembly and cable securement

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 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 Reusable Sensor to the TGFR Monitor

Note: Ensure the sensor is attached to the patient before connecting the sensor to the monitor.

If the monitor is not yet powered on, press the power button on the back of the monitor. Once the 'Connect Sensor' screen (Figure 8, left) 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 8, right). It can take up to 10 seconds after connection for the system to detect the sensor and verify the system is ready for use.

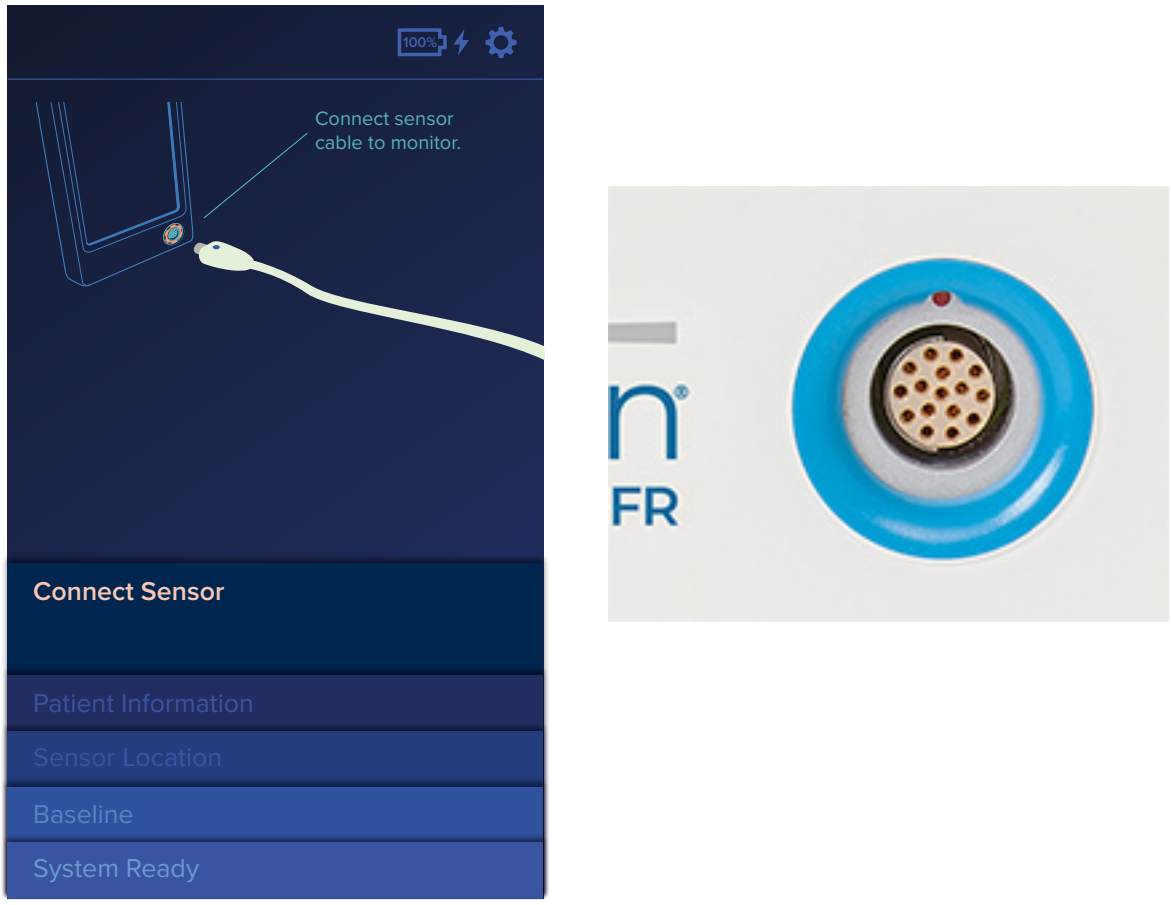
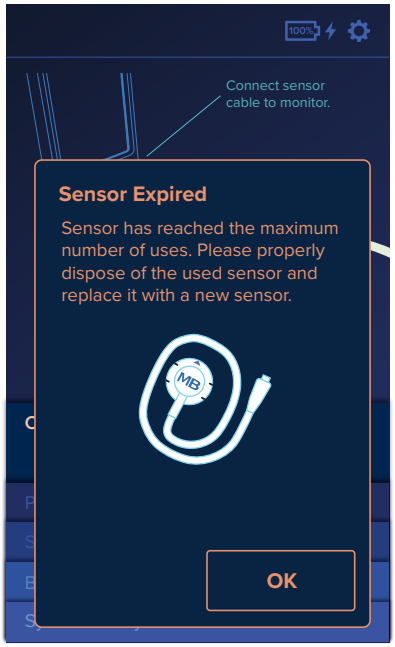


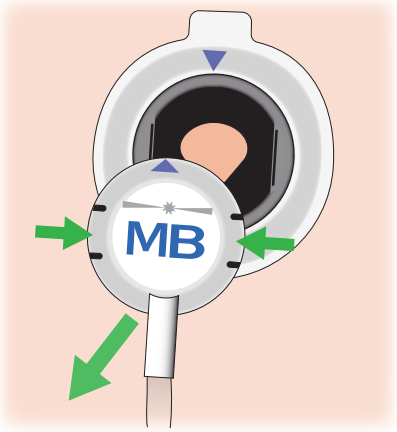
Figure 8. Connect Sensor screen and location point on monitor

IMPORTANT: TGFR Reusable Sensors can perform 20 sessions: The monitor will log the connection and briefly display the number of uses remaining on that sensor with a “Sensor Uses Remaining” counter (Figure 9), indicating how many more uses before sensor expiration.

Figure 9. Sensor Uses Remaining

- If starting a session and the TGFR Reusable Sensor shows one use remaining, discard the sensor at the end of that session.
- If an expired TGFR Reusable Sensor is connected to the monitor, a ‘Sensor Expired’ screen will appear (see Figure 10). Press “OK” and unplug the cable from the monitor to return to the ‘Connect Sensor’ screen and discard the expired sensor. Obtain a new or different clean sensor and a new disposable ring, following the site preparation steps above. Attach the sensor to the patient, anchor the cable, connect the sensor cable to the monitor, and follow the on-screen instructions.





1. Remove expired sensor from disposable ring by pressing the clips in and lift the sensor from the ring and discard.
2. Press OK on the monitor.
3. Attach a new TGFR Reusable Sensor to a new disposable ring.
4. Follow the sensor placement instructions.
5. Connect the new sensor to the monitor and continue.

Figure 10. Sensor expired – reusable sensor replacement steps

Patient Information Screen

Once a sensor is connected, the monitor will automatically transition to the 'Patient Information' screen (Figure 11a). 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 12).

Note: If starting a new session with the same patient ID, a patient ID confirmation dialog will display. Upon confirming that Patient ID, a display will provide a countdown until the previous injection will be adequately cleared to start a new session (Figure 11b).

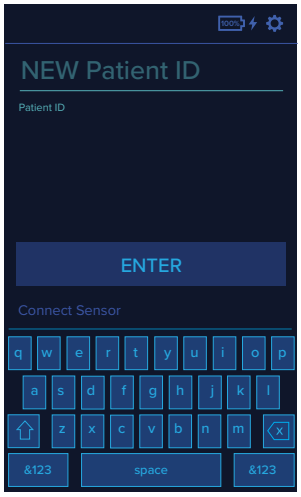


Figure 11a. Patient Information screen

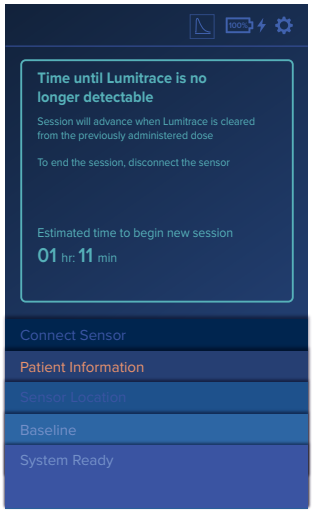


Figure 11b. If entering the same Patient ID, a timer may appear, indicating clearance time until the next session may be started with a new sensor.

Sensor Location Screen

After entering a patient's ID to start a new session, the monitor will display the 'Sensor Location' screen (Figure 12).

Two options for sensor location are available: Pectoralis Major or Sternum/Manubrium.

Press the selected site location on the Sensor Location screen ONCE to confirm where the sensor was placed. The sensor icon will highlight when selected and then the user will be prompted to ensure that the patient remains as still as possible for the next 20 minutes. After confirming that prompt, the monitor will advance to the 'Skin Tone Adjustment' screen.

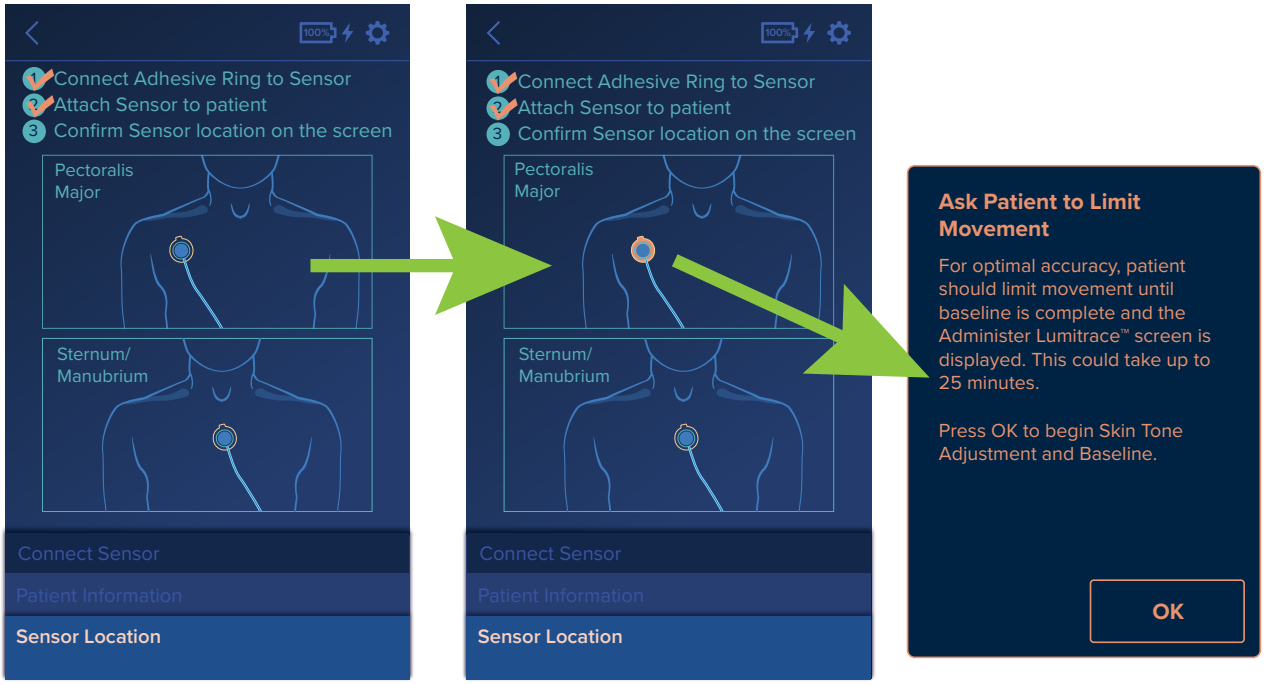


Figure 12. Selecting sensor location

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 and the user confirms that the patient has been asked to limit movement, 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 return 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' 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 (Figure 13). The TGFR cycles the sensor LED power and selects the LED power level that provides an optimal signal for that individual sensor location. The sensor is now adjusted to the patient's skin and the 'Establishing Baseline' screen (Figure 14) will appear and begin counting down the time until baseline is complete.

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

Note: Do not change the room lighting conditions during skin tone adjustment. If a Skin Tone Adjustment error is received, repeat the skin tone adjustment keeping the ambient light in the room consistent.

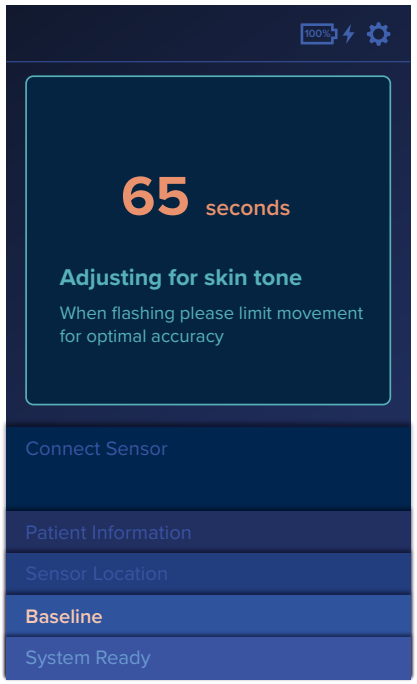


Figure 13. Skin Tone Adjustment screen

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, hands, or tape 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 14) will display the estimated time to baseline acquisition completion.

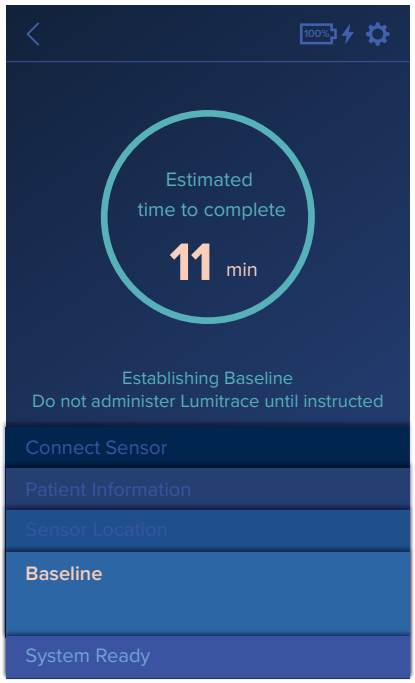


Figure 14. Establishing Baseline screen

Note: If the system cannot establish a baseline within approximately 21 minutes, a Baseline Timeout screen will display (Figure 15). Depending on the issue with establishing a baseline, the user may be prompted to replace the sensor or restart baseline acquisition (See, Section XI Troubleshooting: 'Baseline Timeout').

Figure 15. 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 16). 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.

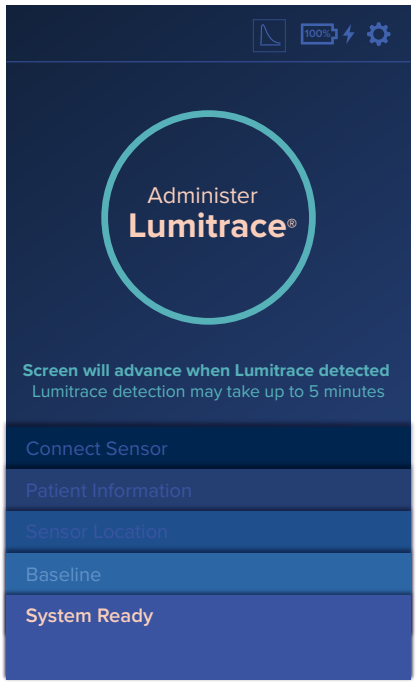


Figure 16. Administer Lumitrace screen

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 17). If the sensor does not detect the Lumitrace injection, the 'Lumitrace Administered?' or 'Lumitrace Not Detected' screens will appear (See Figures 45-46, or Section XI Troubleshooting: 'Lumitrace Not Detected').

Starburst appears after a minimum threshold of Lumitrace is detected – typically within 2-5 minutes of injection

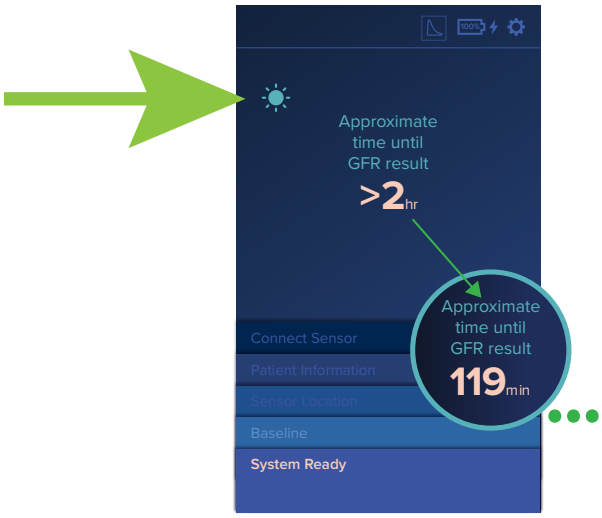


Figure 17. Approximate Time until GFR Result screen

System Ready - Approximate Time until GFR Result Screen

During the ‘System Ready’ process, the ‘Approximate Time until GFR Result’ screen (Figure 17) 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 interim assessments of GFR 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 17). This informs the user that the GFRs will be reported. The approximate time to the first GFR is shown on the screen.

The ‘System Ready’ process is complete when the first tGFR 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 18).

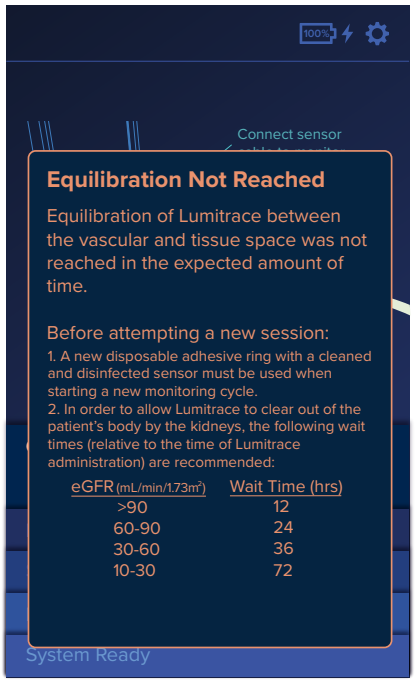


Figure 18. Equilibration Not Reached screen

Monitoring Screen

The image below shows the 'Monitoring' screen (Figure 19) of a typical monitoring session that has been running for approximately 7 hours.

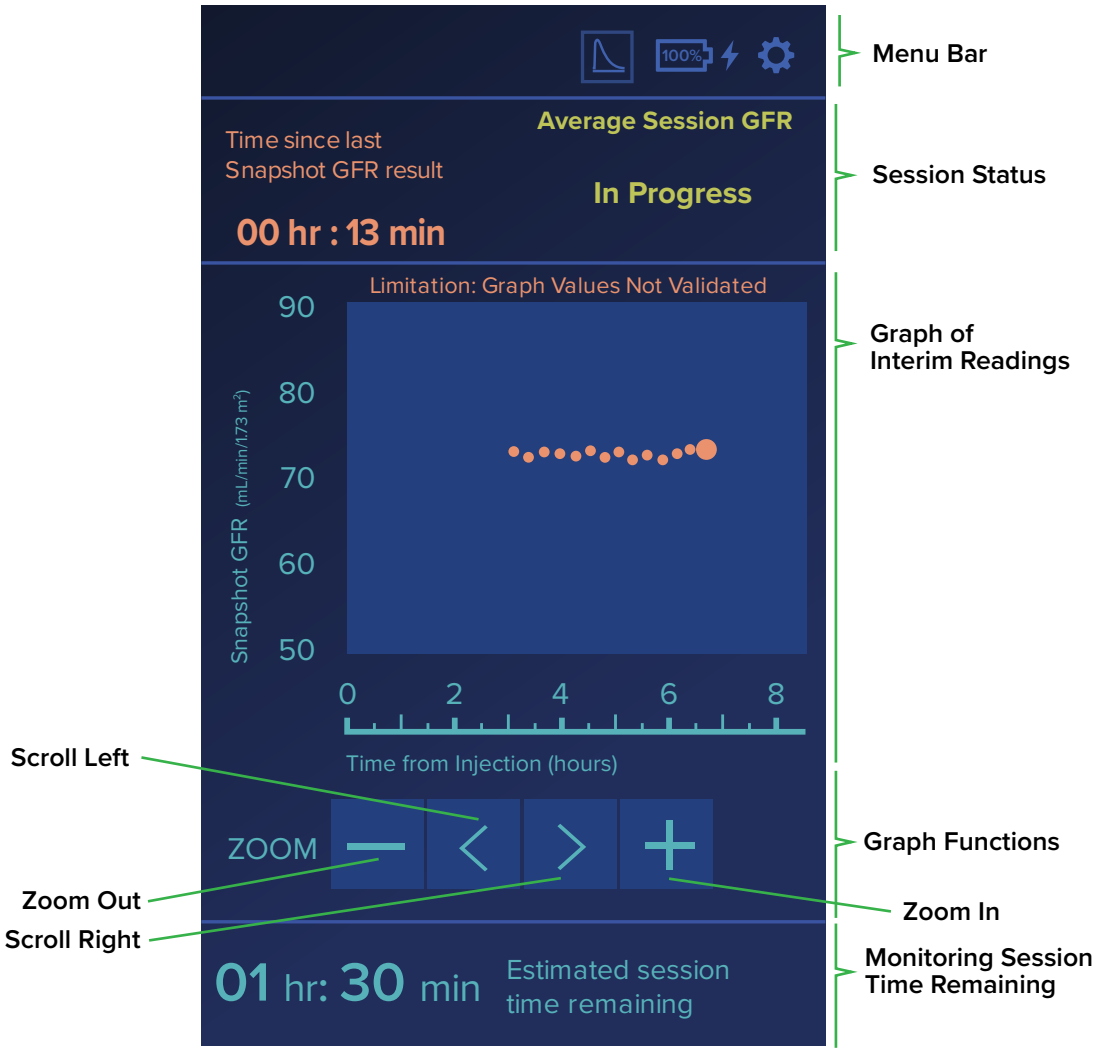


Figure 19. Monitoring screen – graph view

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 Function 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 20). Lows and highs are noted as “below” or “above” in the List View, which is only available at the end of a full session.

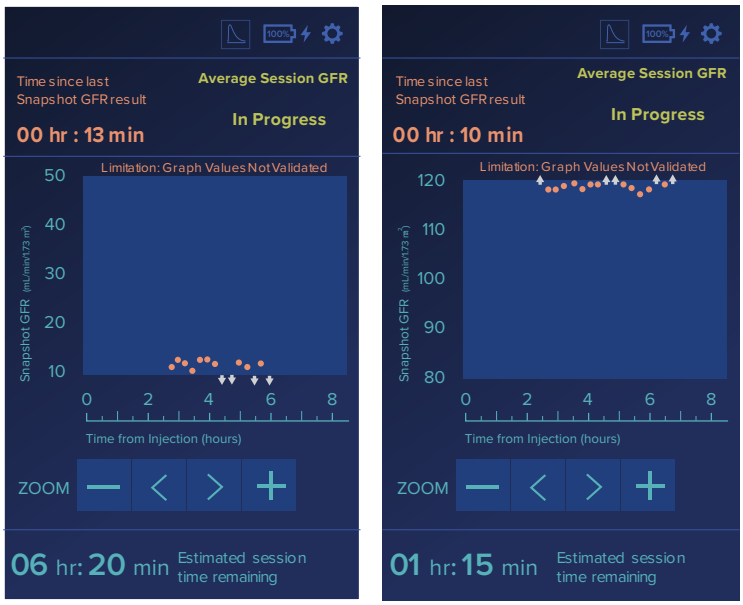


Figure 20. Low and High tGFR points on graph and list views.

Lumitrace Clearance Graphs

Pressing the menu bar graph button displays the Lumitrace Clearance Graph (Figure 21, left). 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 21, right). Press the menu bar graph button again to return to the Monitoring screen graph view.).

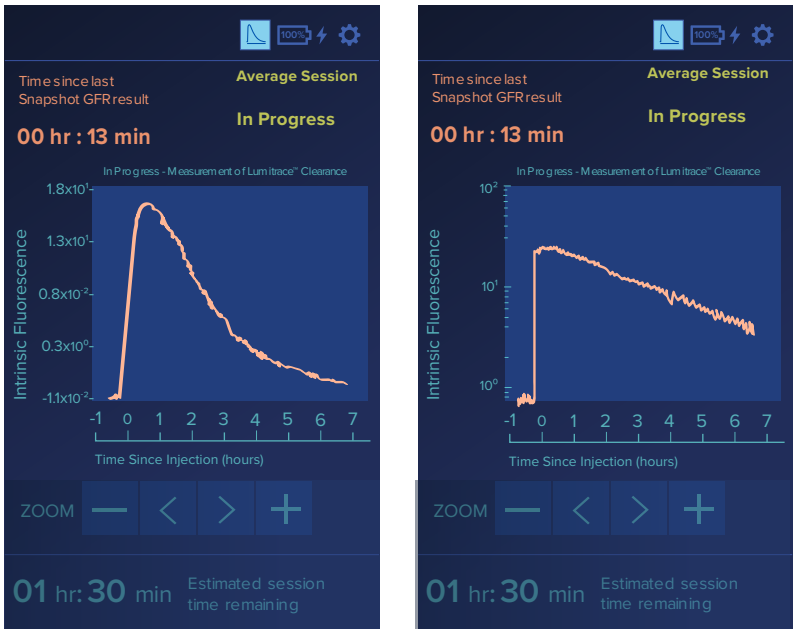


Figure 21. Lumitrace clearance linear (left) and semi-log scale (right).

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 advance to the 'Measurement Session Ended' screen. The monitor will calculate an Average Session GFR and display it in green in the upper right of the screen (Figure 22, left).

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

Figure 22. An Average Session GFR value appears in green on the display (left). A Session Interrupted message will appear in orange if the session was stopped before Lumitrace clearance was completed (right).

For a complete session, 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.

3. Select "END SESSION" button (Figure 23). A confirmation screen will appear. Selecting "END SESSION" confirmation will clear the session data from the screen, and it will no longer be displayed. **Be sure the Average Session GFR 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 disposable ring 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 the sensor (Figure 24, right).
7. The system is ready to start a new session when the 'Connect Sensor' screen appears.
8. If you are starting a session, place a cleaned/disinfected sensor with a new disposable ring 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.

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.

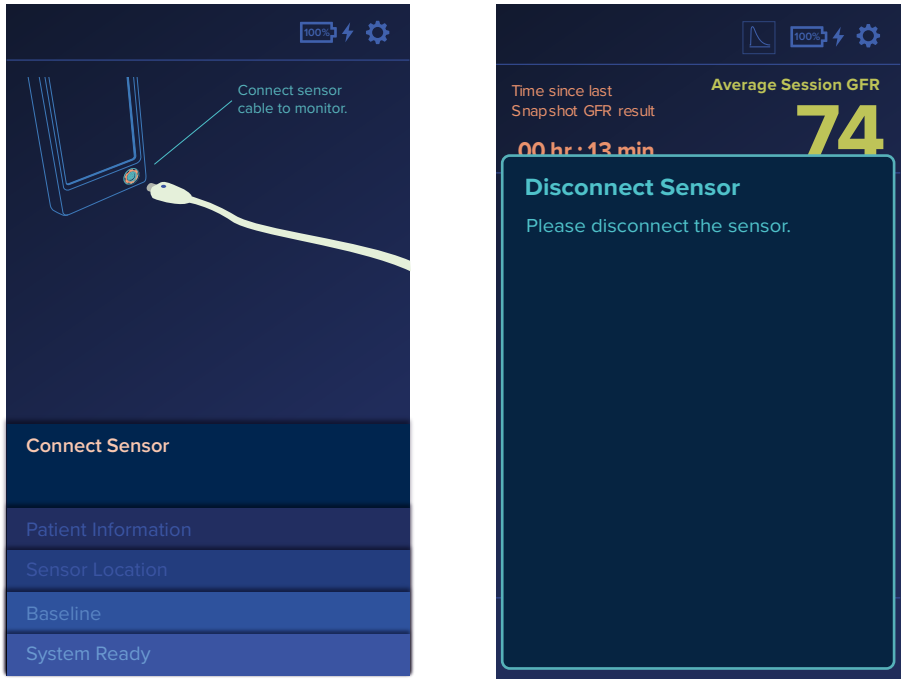


Figure 24. Workflow after session ends. The monitor will either go to the 'Connect Sensor' screen (left) if the sensor is already unplugged from the monitor, or the 'Disconnect Sensor' screen (right) if the sensor is still connected to the monitor.

Workflow Following a Completed Session

Session For a New Patient

Connect the cleaned and disinfected sensor to a new TGFR Disposable Ring. Prepare the patient and sensor as described in the “Starting a New TGFR Session” section. The monitor will return to the initial startup sequence for a new patient. Once the sensor is reconnected, the number of sessions remaining for that sensor will briefly display. Enter the Patient ID on the ‘Patient Information’ screen and continue following the instructions on the monitor.

New Session For the Same Patient

If a new session is necessary on the same patient, clean & disinfect the sensor, secure a new disposable ring, and prepare the patient, sensor, and ring as described in the “Starting a New TGFR Session” section on page 14.

Once the sensor is reconnected to the monitor, the number of sessions remaining will display. Confirm the patient matches the Patient ID on the prompt by pressing “YES”. Confirm the “New” session (Figure 25) to start a new session for the same patient.

Figure 25. Notification prompts to confirm starting a new session on the same patient if the sensor is still connected to the monitor.

Note: If there is uncleared Lumitrace injection remaining from the previous session, the monitor will enter a countdown to clear any detectable Lumitrace injection from the patient before a new session can be started (Figure 26, left) on this patient. The ‘Sensor Location’ screen will appear once this countdown is completed (Figure 26, right). If Lumitrace injection has already cleared, the monitor will automatically transition to the ‘Sensor Location’ screen.

Note: When confirming the patient ID, if “NO” is errantly chosen, simply reenter the patient ID and follow the prompts.

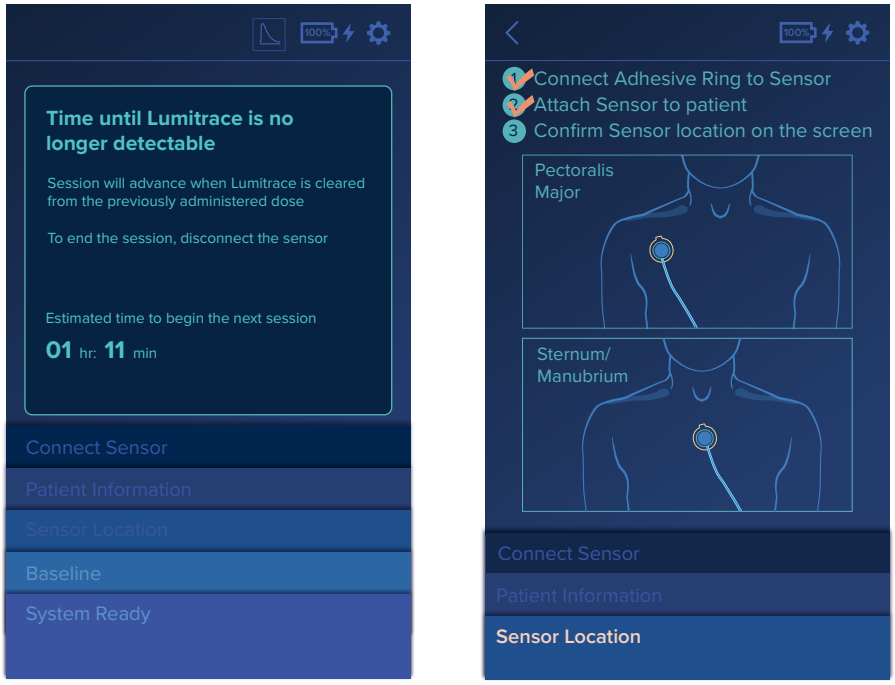


Figure 26. Session for the same patient. The TGFR Monitor will initiate a countdown before the next injection if the previous Lumitrace injection has not been cleared (left). Wait until the countdown is complete and workflow will automatically transition to the 'Sensor Location' screen (right).

Moving a Patient

If the patient must be moved during a session, temporarily unplug the power source from the back of the monitor and roll the IV pole holding the monitor with the patient. Use care to keep the sensor on the patient's skin from being pulled or dislodged. The monitor must be plugged back in upon return.

Sensor Detachment from the Patient

The adhesive on the disposable ring is single-use and cannot be reapplied. If a sensor is removed or dislodged from the patient's skin for any reason, a new disposable ring is needed and a new session must be 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 XI: Troubleshooting, or estimated clearance times in Table 1).

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.

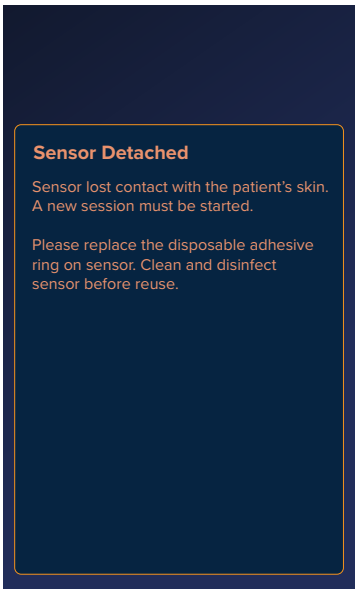


Figure 27. Detached sensor PRIOR to injection

1. Remove the sensor completely from the patient and disconnect from the monitor. Discard the disposable adhesive ring, clean and disinfect the reusable sensor, and replace the used disposable ring with a new disposable ring.
2. Once the sensor is disconnected from the monitor, the alert screen will advance to the 'Connect Sensor' screen (Figure 8). 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. Separate the sensor from the adhesive ring, discard the ring, and disconnect the cable from the monitor. Then clean and disinfect the sensor so it is ready for a new session.
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).

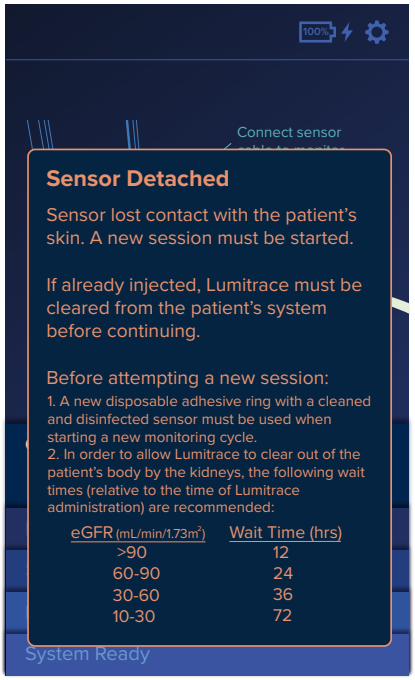


Figure 28. Detached sensor AFTER injection, PRIOR to first reading result

Detachment After Readings are Plotted

If the sensor becomes detached from the patient **after reading values have been plotted**, the end session message will be displayed as shown in Figure 29. Select OK. A "Session Interrupted" message will be displayed and the Average Session GFR will not be displayed.

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

1. Once the end of session is confirmed, remove the sensor completely from the patient and disconnect from the monitor. Remove and clean/disinfect the reusable sensor and discard the used disposable adhesive ring.
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).

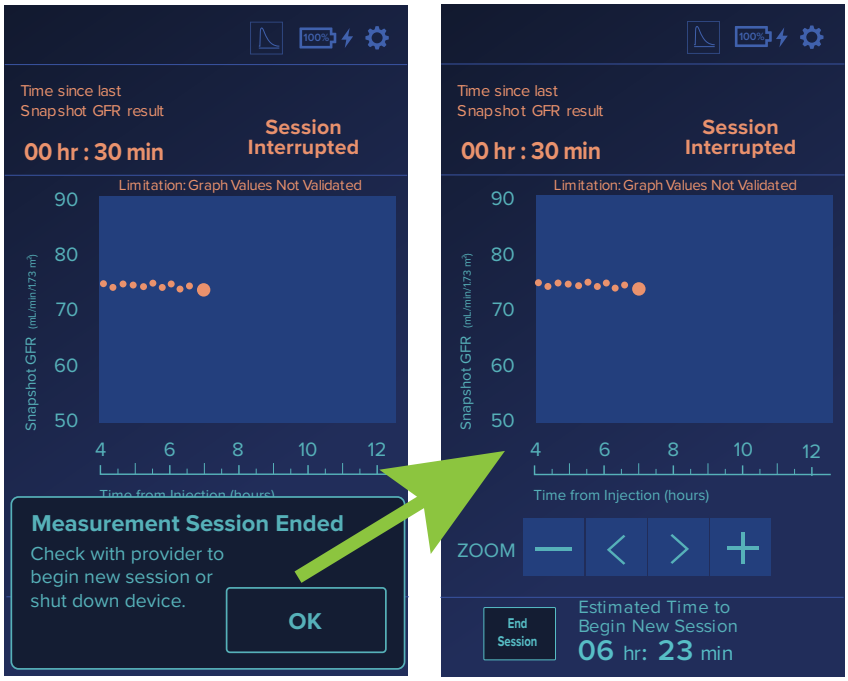


Figure 29. Detached sensor AFTER first reading.
The graph data will be cleared when the "End Session" button is pressed.

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).

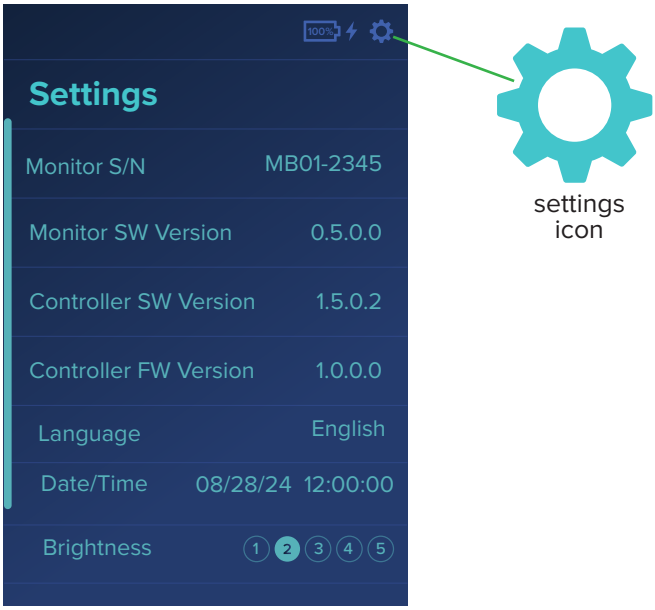


Figure 30. Settings screen.

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 – 52.

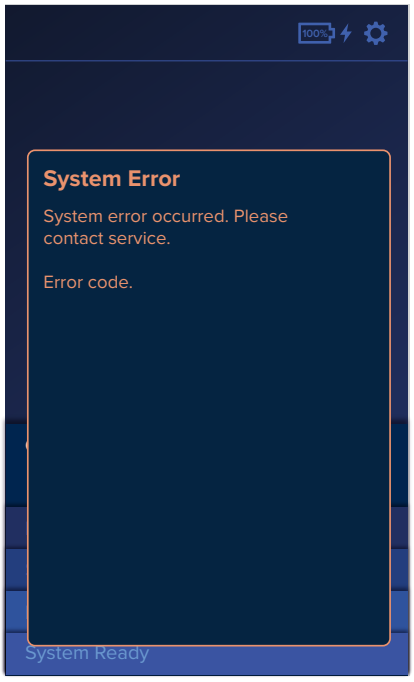


Figure 31. System Error

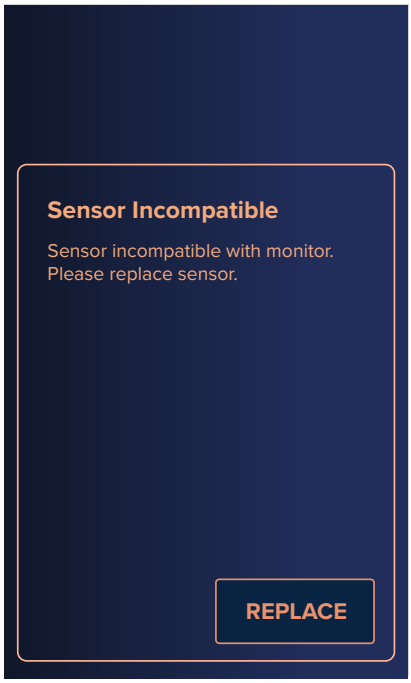


Figure 32. Sensor Incompatible

Figure 33. Sensor Error

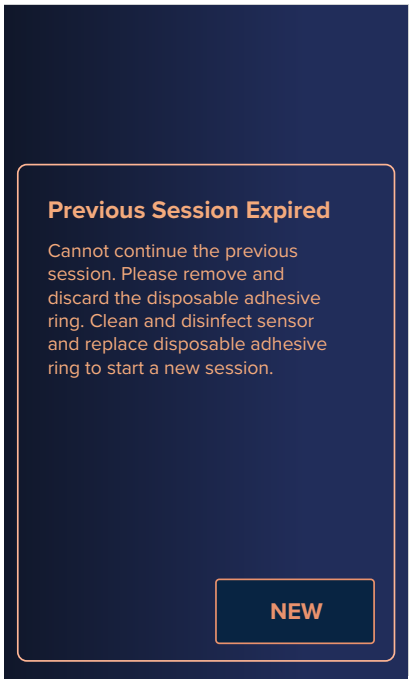


Figure 34. Previous Session Expired

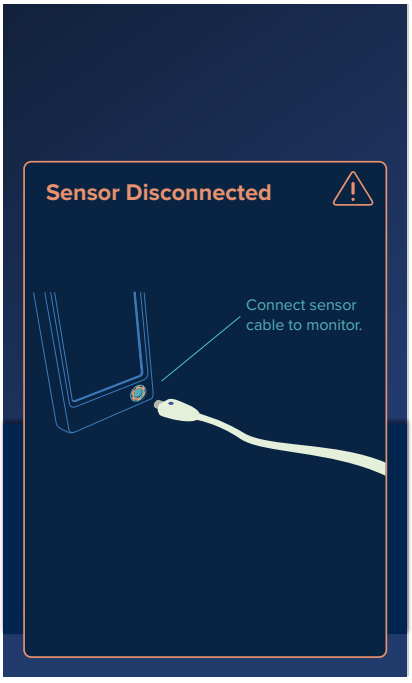


Figure 35. Sensor Disconnected

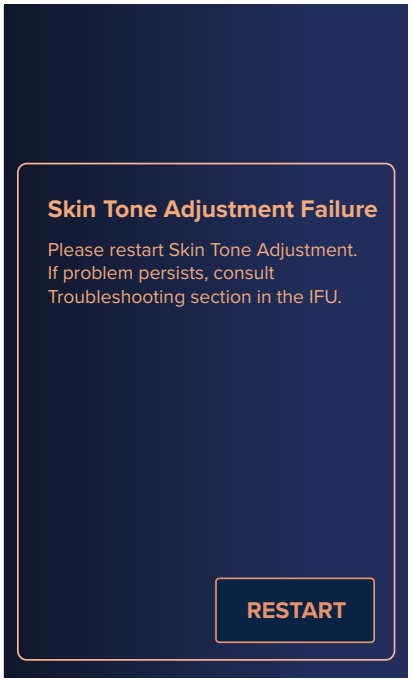


Figure 36. Skin Tone Adjustment Failed

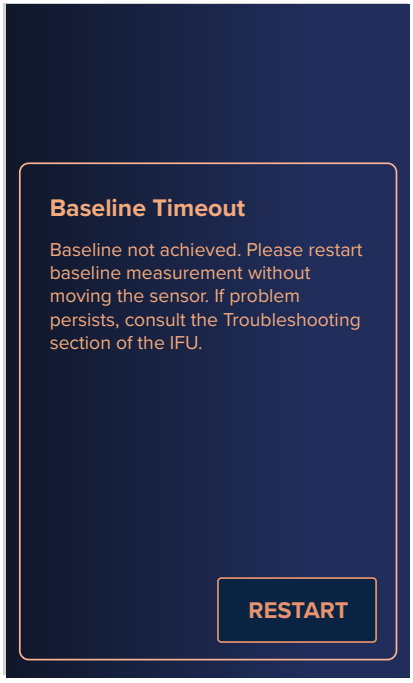


Figure 37. Baseline Timeout

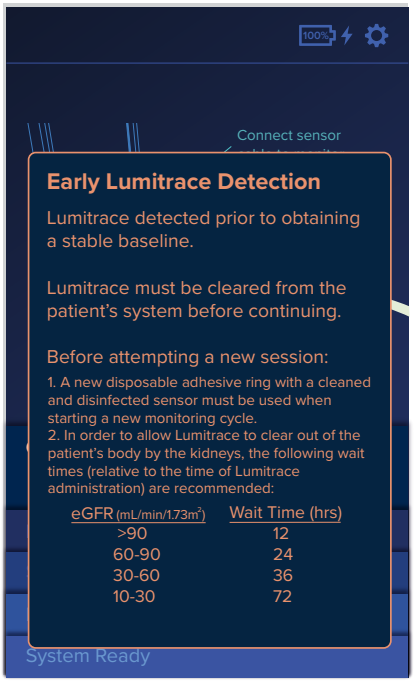


Figure 38. Early Lumitrace Detection

Figure 39. Lumitrace Administered?

Figure 40. Lumitrace Not Detected

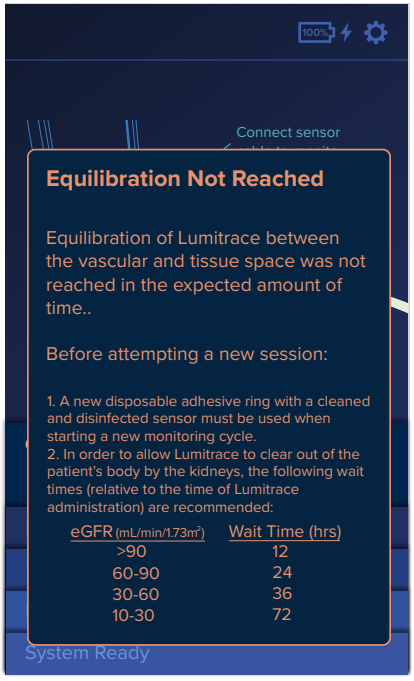


Figure 41. Equilibration Not Reached

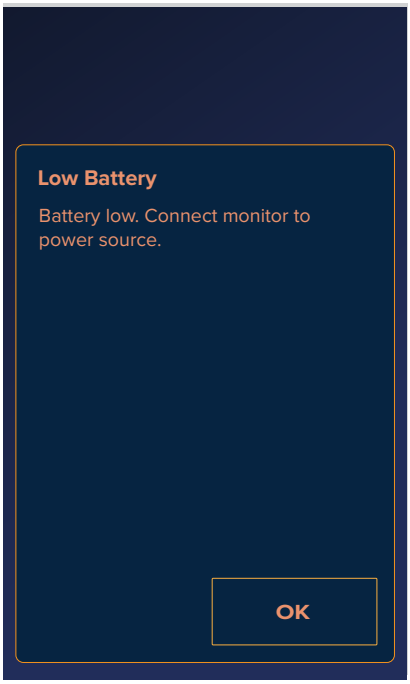


Figure 42. Low Battery

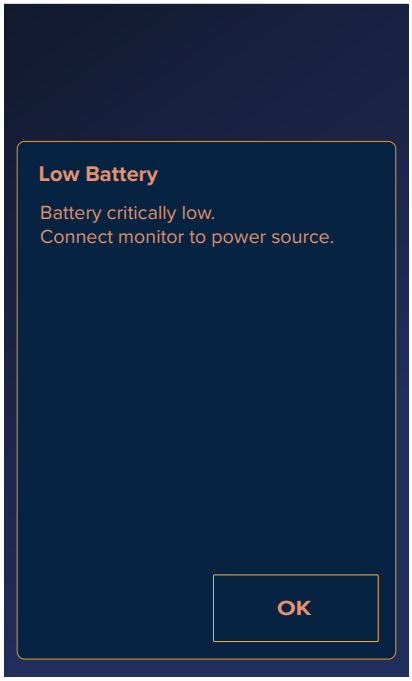


Figure 43. Critically Low Battery

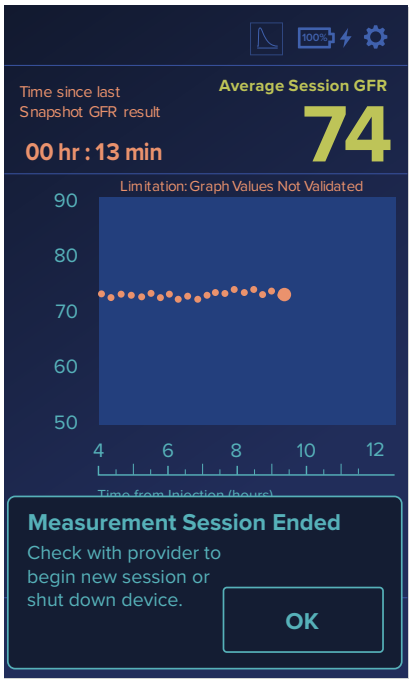


Figure 44. Measurement Session Ended

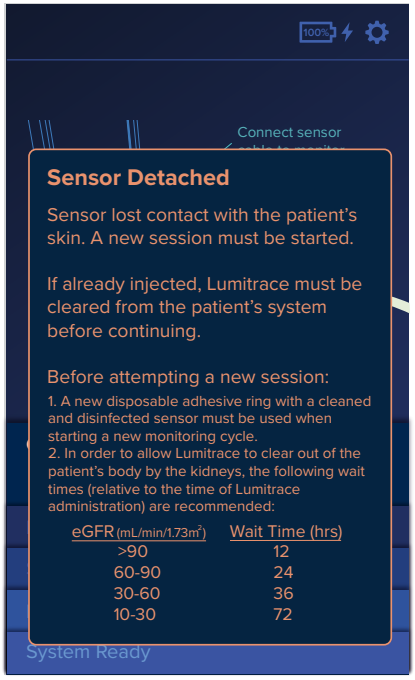


Figure 45. Sensor Detached - Post-Detection

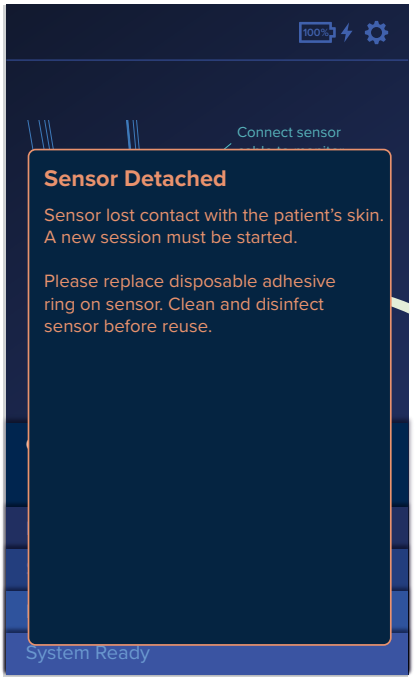


Figure 46. Sensor Detached - Pre-Detection

Figure 47. Unexpected Reboot Detected

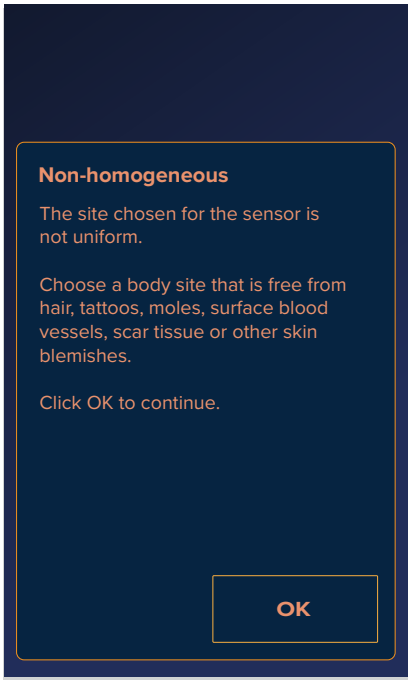


Figure 48. Sensor Site Non-homogeneous

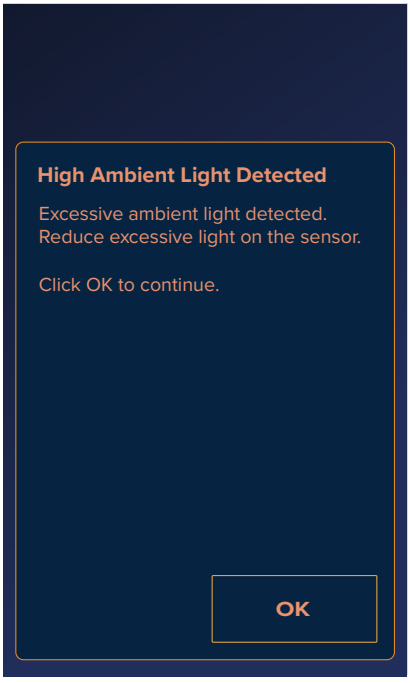


Figure 49. High Ambient Light

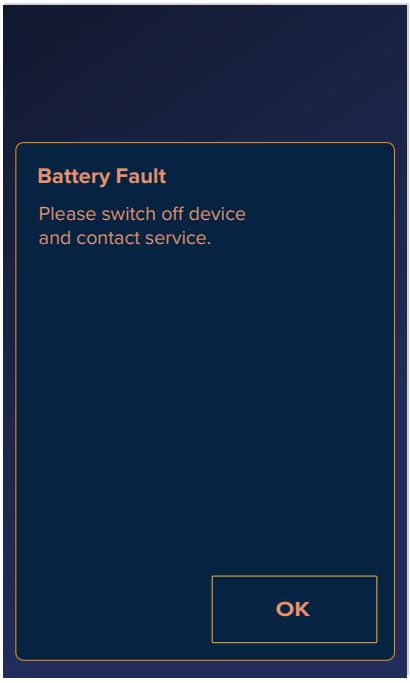


Figure 50. Battery Fault

Figure 51. Baseline Expired

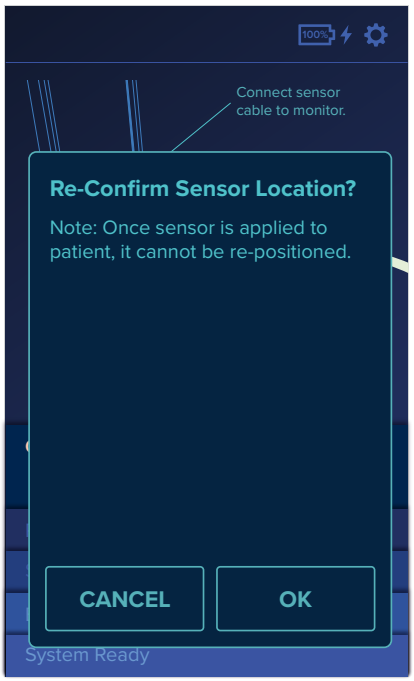


Figure 52. Re-confirm Sensor Location

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 25, left) 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 start a new session. If it does match the same patient and:

- A previous session exists for the patient, then the Sensor Location screen is displayed.
- 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.
- A previous session was interrupted after the Lumitrace injection, the user will only be allowed to continue the previous session, however no Average Session GFR will be displayed at the end of this session. If a new session is needed, a new disposable ring must be attached to the sensor and must be placed in a new location on the patient, after the first injection has been cleared by the kidneys (Table 1).
- 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 an error at the end of the skin tone adjustment sequence if there was excessive movement during the countdown, or if there was insufficient contact or the skin is non-homogenous, or if the ambient room lighting was changed during the Skin Tone Adjustment. Skin tone adjustment can be attempted again if this error occurs. Follow the steps below to reattempt Skin Tone Adjustment:

- Press “RESTART” and allow the system to attempt Skin Tone Adjustment again. Ensure the patient can remain still for the skin tone adjustment sequence.
- If you have attempted Skin Tone Adjustment multiple times, disconnect the sensor from the monitor, replace the disposable ring, and place the sensor in a new location on the patient’s chest according to the instructions for starting a new session.

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. If the skin tone adjustment error is continuous and/or restarting does not resolve the error, contact Service or your MediBeacon representative.

Baseline Timeout

The TGFR Monitor may prompt a ‘Baseline Timeout’ at the end of baseline sequence if there was excessive movement during the countdown. 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 Reusable 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-Confirm Sensor Location” (Figure 52) message will appear. Press OK, choose the correct Sensor Location, and follow instruction on the prompts. If the baseline timeout error is continuous and/or restarting does not resolve the error, contact Service or your MediBeacon representative.

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

Baseline Expired

The TGFR Monitor may prompt a ‘Baseline Expired’ notification (Figure 51) 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 53). 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 54) informing the user that a new session must be started.

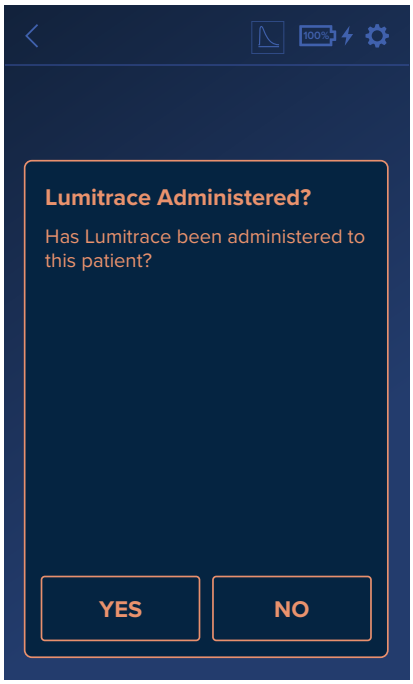


Figure 53. Lumitrace Administered?

Figure 54. 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 48) 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 (Table 1).

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 from the monitor. Carefully remove the sensor from the patient and from the disposable ring. Clean and disinfect the reusable sensor, attach it to a new disposable ring, and choose a new sensor site or wait until any discoloration has cleared from the original sensor site. Pay special attention to the Site Preparation instructions. If the error occurred after Lumitrace injection administration, wait until the advised clearance time has passed before re-administering the Lumitrace injection (Table 1).

Sensor Error

If a sensor error screen is encountered, disconnect the sensor from the monitor. Carefully remove the sensor from the patient and from the disposable ring. Discard the sensor. Obtain a new or different sensor, attach it to a new disposable ring, and choose a new sensor site on the patient's chest or wait until any discoloration has cleared from the original 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).

Unexpected Reboot

If an 'Unexpected Reboot' screen (Figure 47) 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 Reusable Sensor. Do not place tape, Tegaderm™, or other securement devices over the TGFR Reusable Sensor as this may push the sensor too far into the skin. Securing the TGFR Reusable Sensor cable to the body as shown in Figure 7 is encouraged to prevent cable movement from interfering with sensor data collection.

4. **Can the subject be active during the TGFR session?**
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 monitoring session?**
   The TGFR Reusable Sensor should not be removed from the skin until the session is complete. Removing the sensor from the skin will disrupt data collection 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 session 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 a maximum of 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 sessions 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 to clear. Also, refer to Table 1 for tracer 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 expected life of the battery is two to three years.

The monitor and sensors require no calibration. 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 Solution

A mild, common dish washing liquid detergent should be used to thoroughly clean the monitor body, power cord, and reusable sensor. 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 cleansers and disinfectants may cause significant damage to the TGFR components and may void warranty. Never use an abrasive pad on any surface of the TGFR Monitor or TGFR Reusable Sensor.

Cleaning Frequency

It is recommended that the TGFR Monitor, TGFR Reusable Sensor and power cord be cleaned after each use.

Note: If the sensor has been used 20 times, discard according to institutional policy for patient contacting leads.

Directions for Cleaning

TGFR Monitor and TGFR Reusable Sensor

Thoroughly clean the surfaces of the TGFR Monitor, TGFR Reusable Sensor, 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 or sensor and affect functionality. Inspect all components and repeat cleaning steps until there is no visible contamination. After cleaning the monitor, sensor, and power cord, wipe the monitor and sensor with a clean lint free damp cloth to remove the mild detergent mixture. Dry the monitor and sensor with a clean lint free cloth. Never use an abrasive pad or abrasive cleaner on the monitor or sensor.

TGFR Disposable Ring

The disposable ring is single-use and generally should not require cleaning. Should the ring 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 ring.

Directions for Disinfection

TGFR Monitor

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

TGFR Reusable Sensor

The TGFR Reusable Sensor is reusable and can be disinfected by dampening the surfaces with a 70% alcohol wipe or solution.

Disinfection Frequency

It is necessary to disinfect the TGFR Monitor, TGFR Reusable Sensor, sensor cord, 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.

Directions for Disinfecting the TGFR Reusable Sensor

Dampen the surfaces of the reusable sensor, including the cord, using a 70% alcohol wipe, or an equivalent lint free wipe wetted with 70% isopropyl alcohol. Wipe the reusable sensor as necessary to maintain visual wetness for a minimum duration of 2 minutes. After disinfecting the sensor, allow to air dry completely.

Caution: The TGFR Monitor and TGFR Reusable Sensors are not designed to be immersed, soaked, rinsed, or sprayed with water. Do not immerse, soak, rinse, or spray the monitor or sensors 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 Disposable Ring

The TGFR Disposable Ring is single-use and disposable. It generally should not require disinfection. Should the ring 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 ring.

Section XV: Product Complaints

Any complaint or dissatisfaction with product quality, performance, labeling, and/or safety should be reported to MediBeacon. If the device “malfunctions” (i.e., does not meet any of the performance specifications or does not perform as intended), MediBeacon should be notified immediately by phone, email, or written correspondence. When filing a complaint, please provide the product description, product number, lot number, your name/address/contact information, and the nature of the complaint.

MediBeacon Inc.
425 N. New Ballas Road
Suite 100
St. Louis, MO 63141 USA
Telephone - +1-800-669-8326
medibeacon.com

EC REP

MedEnvoy Global B.V.
Prinses Margrietplantsoen 33 - Suite 123
2595 AM The Hague
The Netherlands
SRN: NL-AR-000024028

Section XVI: Specifications

Compliance

Compliance	Standard
Product Safety	IEC 60601-1:2005, AMD 1:2012
Flammability	VR2
EMC	IEC 60601-1-2:2014 + A1:2020
Enclosure Protection	IPx0
Drop Test Compliance	Portable Equipment

Physical Specifications

Monitor	Height, Overall	12 in / 30.5 cm
	Width, Overall	10.75 in / 27.3 cm
	Depth, Overall	10 in / 25.4 cm
	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
Sensor and Ring	TGFR Reusable Sensor Service Life	20 uses within 5 years
	TGFR Disposable Ring 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 XVII: EMC Guidance and Manufacturer's Declarations

Guidance and Manufacturer's Declaration – Electromagnetic Emissions	
Emissions Test	
RF emissions	CISPR 11:2015 +A1:2016 +A2:2019
Harmonic emissions	IEC 61000-3-2:2018
Voltage fluctuations/flicker emissions	IEC 61000-3-3:2013 +A1:2017
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 61000-4-2:2008
Electrical fast transient/burst	IEC 61000-4-4:2012
Surge	IEC 61000-4-5:2014 +A1:2017
Voltage dips, short interruptions and voltage variations on power supply input lines	IEC 61000-4-11:2004 +A1:2017
Power frequency (60 Hz) magnetic field	IEC 61000-4-8:2009

Guidance and Manufacturer's Declaration – Radiofrequency Electromagnetic Immunity	
Conducted RF	IEC 61000-4-6:2013
Radiated RF	IEC 61000-4-3:2020

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 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 $d=2\sqrt{P}$	80 MHz to 800MHz $d=2\sqrt{P}$	800 MHz to 2700 MHz $d=2\sqrt{P}$
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 XVIII: Summary of Clinical Results

SUMMARY OF CLINICAL STUDIES

I. MediBeacon® TGFR Bridging Study with TGFR Reusable Sensor

The objectives of the MediBeacon TGFR bridging study utilizing the TGFR Reusable Sensor included the following:

- To establish that the Lumitrace injection transdermal fluorescence assessed GFR using the MediBeacon® Transdermal GFR System with the TGFR Reusable Sensor with disposable adhesive ring was comparable to the measured Lumitrace Injection plasma GFR.
- To evaluate the safety and effectiveness of the MediBeacon® Transdermal GFR System and the TGFR Reusable Sensor with disposable adhesive ring for the non-invasive transdermal fluorescence detection of Lumitrace injection in subjects.

A. Study Design – Bridging Study

This was a multi-center, open-label, adaptive bridging 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 Injection and the safety of the MediBeacon TGFR will also be evaluated.

A run-in cohort of up to 30 evaluable subjects commenced the study followed by the validation study portion to yield 140 evaluable subjects. After 75 evaluable subjects in the validation cohort was complete, an interim analysis was conducted to compare results against the primary endpoint specifications. To control alpha error in the interim analysis, alpha was lowered from 5% to 3% in the endpoint analysis. The study was designed to be terminated if the interim analysis met the endpoint.

The bridging study utilized the TGFR Reusable Sensor and TGFR Disposable Ring while the pivotal study utilized the single use TGFR Sensor.

1. CLINICAL INCLUSION AND EXCUSION CRITERIA

Enrollment in the MediBeacon TGFR bridging study was limited to subjects who met the eligibility criteria. The full list of selection criteria is provided here:

Inclusion Criteria:

- Age ≥ 18 years, male or female
- 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:

- Subjects positive for coronavirus disease 2019 at the time of dosing.
- 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 [AEs]) or anaphylactoid reaction to any allergen including drugs, Lumitrace or other related products (intolerance to a drug was 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 scaring, 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
- Use of tanning sprays, tanning products, etc. on the upper chest within 2 weeks of dosing day.
- Use of make-up, lotions, Vaseline, or other products on the area of the upper chest on the day prior to or the day of dosing.
- 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 subject's ability to complete study requirements or put the subject 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. To control the alpha error in the interim analysis, alpha was lowered from 5% to a value of 3% to calculate confidence intervals. Success for the study will be that the P30 lower limit of the 97% 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 System use (placement of the sensor assembly on the skin).

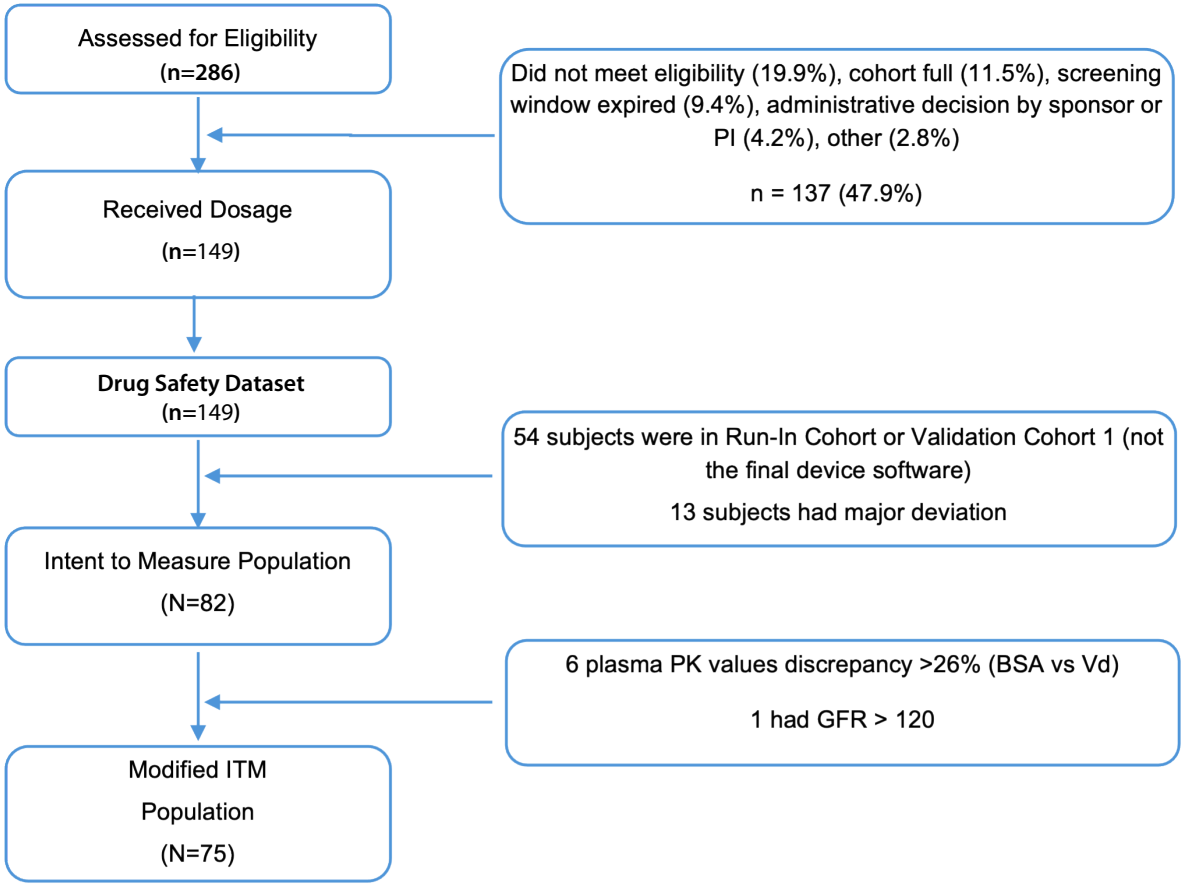
Additional safety variables include physical examinations, vital signs, clinical laboratory assessments, ECGs, and concomitant medication use. All safety analyses will be done for subjects receiving a single dose of Lumitrace injection.

B. Accountability of Bridging Study Cohort

A total of 286 subjects were screened and 149 (52.1%) subjects were enrolled and dosed, and 149 (52.1%) subjects completed the study. Reasons for not completing the study included did not meet eligibility (19.9%), cohort full (11.5%), screening window expired (9.4%), administrative decision by sponsor or PI (4.2%) and other (2.8%)

A total of 149 subjects were enrolled at 5 investigational sites in the United States.

Figure 55: Subject Accountability – Bridging Study



C. Study Population Demographics and Baseline Parameters – Bridging Study

Subject demographics and baseline characteristics are provided in Table 2. As targeted, the modified intent to treat (mITM) population of subjects had impaired and normal renal function in the study; 40/75 (53%) with an eGFR ≥ 70 mL/min/1.73m^2 and 35/75 (47%) with an eGFR < 70 mL/min/1.73m^2. Likewise, the modified intent to measure population was studied across the spectrum of the Fitzpatrick Skin Scale (FSS) with 42/75 (56%) of subjects with a FSS of I-III and 33/75 (44%) of subjects with a FSS of IV-VI.

Of 149 subjects included in the Safety Population, 123 (82.6%) subjects had at least one current medical history record. The most common (≥10% of subjects) medical histories were cardiovascular 94 (63.1%), genitourinary 91 (61.1%), endocrine metabolic 84 (56.4%), gastrointestinal 70 (47.0%), musculoskeletal 62 (41.6%), neurologic 46 (30.9%), head, eyes, ears, nose, and throat (HEENT) 45 (30.2%), respiratory 29 (19.5%), and psychological 22 (14.8%) conditions.

Table 2: Baseline Demographics

Characteristic Statistic	Stratum 1 (N = 40) n (%)	Stratum 2 (N = 35) n (%)	Total (N = 149) n (%)
Age at Screening (years)			
n	40	35	75
Mean (SD)	49.1 (13.0)	65.8 (9.51)	56.9 (14.2)
Median	51.0	68.0	59.0
Min, Max	24.0, 73.0	32.0, 77.0	24.0, 77.0
Sex, n (%)			
Male	19 (47.5)	19 (54.3)	38 (50.7)
Female	21 (52.5)	16 (45.7)	37 (49.3)
Race, n (%)			
White	21 (52.5)	18 (51.4)	39 (52.0)
Black or African American	15 (37.5)	14 (40.0)	29 (38.7)
Asian	1 (2.50)	1 (2.86)	2 (2.67)
Native Hawaiian or Other Pacific Islander	0	0	0
American Indian or Alaska Native	1 (2.50)	0	1 (1.33)
Other	2 (5.00)	1 (2.86)	3 (4.00)
Unknown or Not Reported	0	1 (2.86)	1 (1.33)
Ethnicity, n (%)			
Hispanic or Latino	13 (32.5)	16 (45.7)	29 (38.7)
Not Hispanic or Latino	27 (67.5)	19 (54.3)	46 (61.3)
Unknown or Not Reported	0	0	0
Height (cm)			
n	40	35	75
Mean (SD)	169 (9.31)	167 (8.62)	168 (8.98)
Median	166	167	166
Min, Max	153, 187	149, 184	149, 187
Weight at Baseline (kg)			
n	40	35	75
Mean (SD)	84.8 (18.9)	88.0 (14.5)	86.3 (17.0)
Median	85.8	86.3	86.1
Min, Max	49.2, 132	57.7, 116	49.2, 132

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Characteristic Statistic	Stratum 1 (N = 84) n (%)	Stratum 2 (N = 65) n (%)	Total (N = 149) n (%)
Body Mass Index at Baseline (kg/m^2) [a]			
N	40	35	75
Mean (SD)	29.6 (4.72)	31.7 (4.88)	30.9 (4.88)
Median	29.4	29.9	29.7
Min, Max	20.6, 38.6	24.7, 43.3	20.6, 43.3
eGFR Result Group			
≥90	25 (62.5)	0	25 (33.3)
60 - 89	15 (37.5)	7 (20.0)	22 (29.3)
45 - 59	0	12 (34.3)	12 (16.0)
30 - 44	0	10 (28.6)	10 (13.3)
15 - 29	0	6 (17.1)	6 (8.00)
Mexameter-Based Skin Color Type			
Type I	9 (22.5)	7 (20.0)	16 (21.3)
Type II	3 (7.50)	6 (17.1)	9 (12.0)
Type III	9 (22.5)	8 (22.9)	17 (22.7)
Type IV	5 (12.5)	4 (11.4)	9 (12.0)
Type V	3 (7.50)	6 (17.1)	9 (12.0)
Type VI	11 (27.5)	4 (11.4)	15 (20.0)
Mexameter-Based Skin Color Group			
Type I-III	21 (52.5)	21 (60.0)	42 (56.0)
Type IV-VI	19 (47.5)	14 (40.0)	33 (44.0)

D. Safety and Effectiveness Results – Bridging Study

A total of 149 patients were dosed including the run-in cohorts and 82 patients were considered in the Intent to Measure Population. After accounting for pre-determined exclusions there were 75 subjects evaluated 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 3. There were no adverse events related to the TGFR Monitor, TGFR Reusable Sensor, or TGFR Disposable Ring.

1. Safety Results

A total of 21 subjects had at least one adverse event reported 21/149 (14.1%), and of these adverse events, 0 (0.0%) were considered severe or serious adverse events.

One subject was considered discontinued from the study by the site following an extravasation that occurred during dosing. The subject was discontinued from PK and TGFR measurements, however they did complete the study through the follow-up visit.

A total of 8 subjects (5.4%) experienced a single moderate adverse event. Five of these subjects experienced a worsening of hypertension or other hypertensive event which was a pre-existing condition for these subjects. In one case, the PI considered a worsening hypertension as possibly related to Lumitrace when it occurred approximately 90 minutes after dosing and required medication for treatment. In review of this subject, the sponsor noted labile blood pressure readings at screening and baseline prior to dosing and unlikely related to the Lumitrace. All other cases of hypertension were not considered related to Lumitrace.

The other moderate events that were reported included a urinary tract infection treated with antibiotics, a vasovagal reaction, and worsening hyperkalemia. None of these events were considered related to Lumitrace by the PI.

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

Table 3: Lumitrace Injection Adverse Events by Type

Adverse Event Type	Events (N) Pilot 2 114 Subjects	Events (N) Pivotal Study 249 Subjects	Events (N) Bridging Study 149 Subjects	Subjects n (%) 512 Subjects
Injection site extravasation	6	3	2	11 (2%)
Headache	1	4	2	7(1%)
Hypertension	0	2	3	5 (1%)
Ecchymosis	0	3	0	3 (1%)
Cardiac Murmur	0	2	0	2 (<1%)
Urinary tract infection	0	1	1	2 (<1%)
Contusion	0	1	1	2 (<1%)
Fatigue	0	1	1	2 (<1%)
Cough	0	1	1	2 (<1%)
Oropharyngeal pain	1	0	0	1 (<1%)
Rash	1	0	0	1 (<1%)
Hot Flush	1	0	0	1 (<1%)
Oedema	0	1	0	1 (<1%)
Diarrhoea	0	1	0	1 (<1%)
Dyspepsia	0	1	0	1(<1%)
Nausea	0	1	0	1 (<1%)
Blood Glucose Increased	0	1	0	1 (<1%)
Weight Decreased	0	1	0	1 (<1%)
Pruritus	0	1	0	1 (<1%)
Haematoma	0	1	0	1 (<1%)
Hyperglycemia	0	1	0	1 (<1%)
Hypoglycemia	0	1	0	1 (<1%)
Nasal congestion	0	1	0	1 (<1%)
Glycosuria	0	1	0	1 (<1%)

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Adverse Event Type	Events (N) Pilot 2 114 Subjects	Events (N) Pivotal Study 249 Subjects	Events (N) Bridging Study 149 Subjects	Subjects n (%) 512 Subjects
Administration site haematoma	0	0	1	1 (<1%)
Administration site pain	0	0	1	1 (<1%)
Vessel puncture site hemorrhage	0	0	1	1 (<1%)
Dizziness	0	0	1	1 (<1%)
Presyncope	0	0	1	1 (<1%)
Hypertensive urgency	0	0	1	1 (<1%)
Photopsia	0	0	1	1 (<1%)
Gingival pain	0	0	1	1 (<1%)
Electrocardiogram change	0	0	1	1 (<1%)
Hypokalaemia	0	0	1	1 (<1%)
Flank Pain	0	0	1	1 (<1%)

There were no TGFR Monitor, TGFR Sensor, TGFR Reusable Sensor or TGFR Disposable Ring related adverse events.

2. Effectiveness Results Bridging Study (TGFR Reusable Sensor)

The primary endpoint was the performance measure of P30 for tGFR with respect to the nGFR, with a 97% confidence interval (CI). The performance goal and the success for the study was hypothesized when the lower limit of the 97% CI was greater than 85%. The primary endpoint was achieved.

Accuracy

Average Session GFR results comparison with measured GFR results:

Ninety-six percent of the transdermal GFR values obtained using this device were within 30% of the measured GFR values (with a confidence interval of 87.9-99.3%). This was the outcome of the bridging trial.

P30 Value	Upper 97% CI	Lower 97% CI
96.0%	99.3%	87.9%

A linear regression analysis found that mean of the difference tGFR - nGFR tended to decrease by -0.37 mL/min/1.73m² per year increase in age after adjustment for nGFR, Sex, Race and Fitzpatrick Skin Scale, which all had insignificant effects. For example, a 10-year increase in age will tend to decrease the difference by 3.7 mL/min/1.73m².

In the study tGFR tended to underestimate nGFR (mean difference -5.3, 95% CI -7.8, -2.9). For example, if the nGFR value is 30 ml/min/1.73m², then the TGFR reports a GFR value was on average about 25ml/min/1.73m².

Average Session GFR results comparison with estimated GFR (eGFR) results:
(using the creatinine-based 2009 CKD-EPI equation)

	Average Session GFR	eGFR*	Paired Difference
P30	96.0%	90.7%	6.67%
97% Confidence Interval	87.9 -99.3%	80.7% - 96.5%	-2.3% to 15.7%

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

In the bridging trial, 96.0% of the Average Session GFR values obtained using this device were within 30% of the measured GFR values and 90.7% 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/1.73m²) and Stratum 2 (eGFR < 70 mL/min/1.73m²).

Patient Population	P30 Value	Upper 97% CI	Lower 97% CI
Stratum 1 (eGFR ≥70 mL/min/1.73m²) N=40	95.0%	99.5%	81.7%
Stratum 2 (eGFR < 70 mL/min/1.73m²) N=35	97.1%	100%	83.6%

Primary Endpoint Evaluation by Fitzpatrick Skin Scale (FSS)

Patient Population	P30 Value	Upper 97% CI	Lower 97% CI
FSS Type I-II N=25	100%	100%	84.5%
FSS Type III-IV N=26	92.3%	99.3%	72.9%
FSS Type V-VI N=24	95.8%	99.9%	76.9%

3. Pediatric Extrapolation – Bridging Study

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

E. Financial Disclosure - Bridging Study

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 bridging clinical study included 5 investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

II. MediBeacon TGFR Pivotal Study – Single Use Sensor

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 – Pivotal Study

This was 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. Note that this study utilized the single use sensor.

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 scaring, 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 was 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 was 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 – Pivotal Study

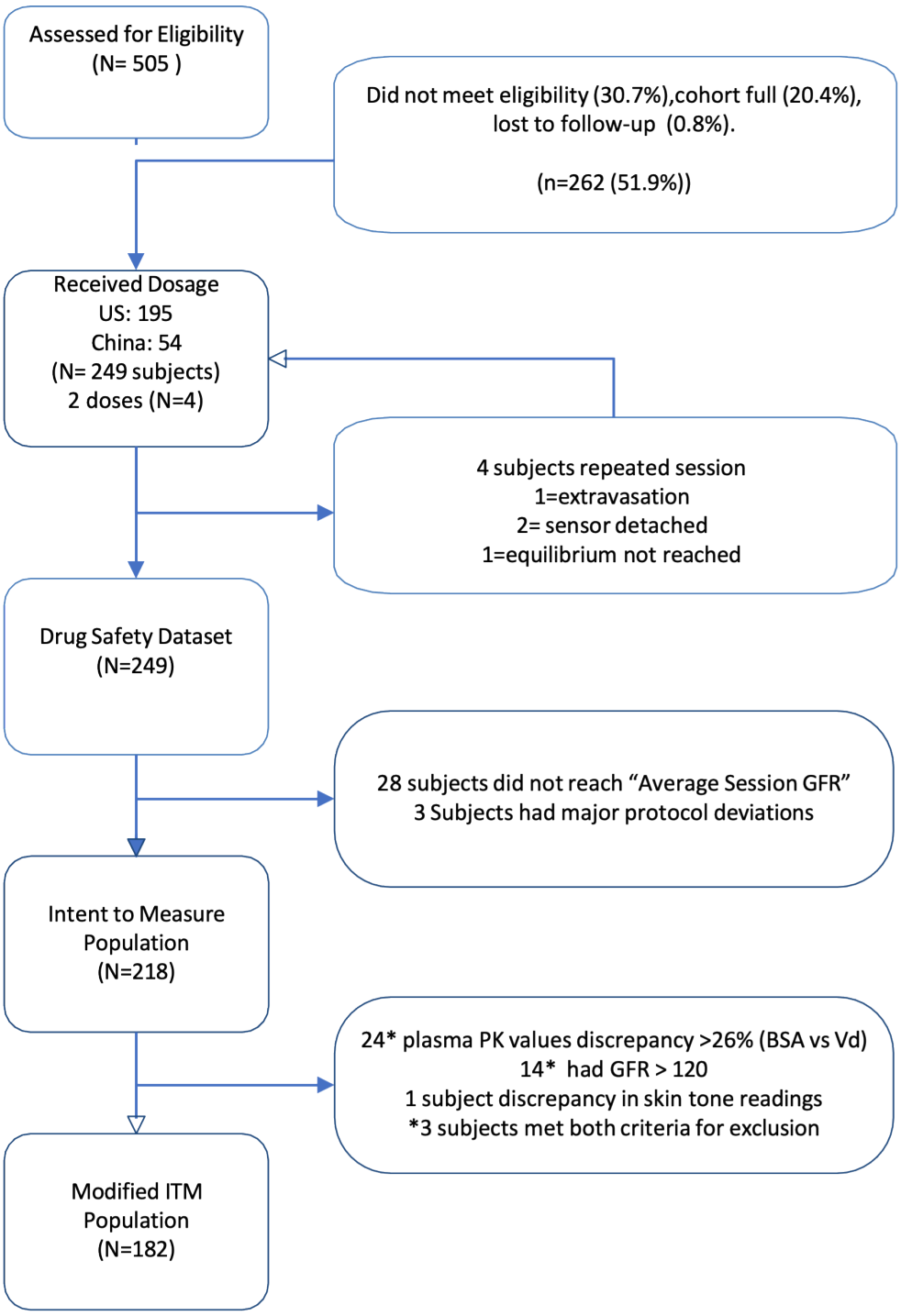
A total of 505 subjects were screened and enrolled globally, of whom 249 (49.3%) subjects were dosed and 243 (48.1%) subjects completed the study. Reasons for not completing the study included screen failure (30.7%), cohort full (20.4%), and lost to follow-up (0.8%)

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 4 and Figure 56.

Table 4: 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 56: Subject Accountability



C. Study Population Demographics and Baseline Parameters – Pivotal Study

Subject demographics and baseline characteristics are provided in Table 5. As targeted, the modified intent to treat population (mITM) of subjects had impaired and normal renal function in the study; 49% with an eGFR ≥ 70 mL/min/1.73m² and 50% with an eGFR < 70 mL/min/1.73m². 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 5: 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
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

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Characteristic Statistic	Stratum 1 (N=130) n (%)	Stratum 2 (N=119) n (%)	Total (N=24) n (%)
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 – Pivotal Study

A total of 249 patients were dosed and 182 patients completed the session obtaining an average tGFR reading and were 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 6. There were no device related adverse events reported.

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 severe or serious adverse events.

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 6: 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 TGFR Sensor or TGFR Monitor related adverse events reported in the pilot 2 study or pivotal study.

2. Effectiveness Results

The primary endpoint of the pivotal 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 transdermal 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 the table above).

Subgroup population results:

Patients were grouped into Stratum 1 (eGFR ≥70 mL/min/1.73m²) and Stratum 2 (eGFR < 70 mL/min/1.73m²).

Patient Population	P30 Value	Upper 95% CI	Lower 95% CI
Stratum 1 (eGFR ≥70 mL/min/1.73m²) N=90	95.6%	98.8%	89.0%
Stratum 2 (eGFR < 70 mL/min/1.73m²) 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 7: 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.

Subgroup Analyses

3. Pediatric Extrapolation

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

E. Financial Disclosure – Pivotal Study

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 in 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

MediBeacon®
Life, illuminated.

Manufactured for:
MediBeacon Inc.
425 N. New Ballas Road
Suite 100
St. Louis, MO 63141
United States

+1-800-669-8326

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