LIFE 21® apheresis unit Instructions for double column immunoadsorption

User Manual

Software version from 7.3



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User Manual

Software version from 7.3

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For U.S. CAUTION: Investigational Device. Limited by Federal (or United States) Law to Investigational Use or under an FDA Approval.

Essential information

This user manual provides instructions, warnings, precautions, and other important information for double column immunoadsorption on the LIFE 21 apheresis unit (instrument). For further details on the instrument, warnings, precautions and troubleshooting as well as specifications, see the user manuals issued for the respective matter and instructions for use of the respective adsorber (or to the clinical investigation documentation, if applicable).

In general, the TheraSorb® LIFE 21 therapeutic apheresis platform (LIFE 21 apheresis platform) is intended for professional operators in health care settings and should only be used by persons who have been trained by Miltenyi Biotec authorized personnel.

⚠ WARNING

Before putting the instrument into operation, the operator must read and understand the safety information, warnings, precautions, and instructions for proper operation provided in the LIFE 21 user manuals (including without limitation the safety information in chapter 3 "Important safety information" of the user manual LIFE 21 apheresis unit "General information – Instrument") and in any safety-related recommendations issued by Miltenyi Biotec. Pay special attention to all warnings displayed on the instrument or provided with consumables and accessories. Confirm all safety information, warnings, precautions, and instructions are observed at all times while the instrument is in operation.

Retain the user manuals for future reference. They should be kept accessible and readily available together with all other safety and operating documentation during the entire life cycle of the instrument for all personnel responsible for installation, operation, and maintenance.

Disregard of any instructions, warnings or cautions at any time can endanger patients, operator and others due to possible instrument damage or malfunction and may compromise the electrical, electronical, electromagnetic and mechanical safety. This might result in the risk of electrical shock, physical injuries, fluid imbalances or loss, vascular damage, hemolysis or embolism. Disregard also excludes the manufacturer from any liability.

If the operator is concerned about the safe use of the LIFE 21 apheresis platform or requires any information about the instrument and its consumables, contact the authorized local Miltenyi Biotec service provider or call the Miltenyi Biotec Technical Support.

IMPORTANT

Before using any products of the LIFE 21 apheresis platform for clinical treatments outside the European Economic Area, the regulatory approval of the products in your country must be confirmed.

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1 Introduction

1.1 General information

This user manual provides instructions, warnings, precautions, and other important information for double column immunoadsorption on the LIFE 21 apheresis unit (instrument). For further details on the instrument, warnings, precautions and troubleshooting as well as specifications, see the user manuals issued for the respective matter and instructions for use of the respective adsorber (or to the clinical investigation documentation, if applicable).

1.2 General description – immunoadsorption

The double column immunoadsorption is used for therapeutic removal of specific components from human blood plasma using two adsorbers (adsorber pair). The term “immunoadsorption” refers to the specific binding of defined molecules by means of antibody or peptide recognition of their antigens. The procedure follows a standardized scheme, which is identical for all double column immunoadsorptions using multiple pass adsorbers. “Multiple pass” refers to repeated cycles of plasma loading and regeneration of an adsorber pair during a treatment.
An adsorber pair is allocated to only one patient. Depending on the procedure, the adsorber pair can be regenerated at the end of a treatment and used for several treatment sessions (multiple use), or is disposed of after one treatment (single use).

More in detail, blood is drawn from the patient through a venous access, anticoagulated and separated into its liquid and cellular components using the disk separator as part of the tubing set. The separated plasma is perfused through the first adsorber where the target substances are then bound by the specific

ligand on the adsorber matrix. The depleted plasma is reunited with the cellular blood constituents and returned to the patient via the blood return line (see Figure 1.1).

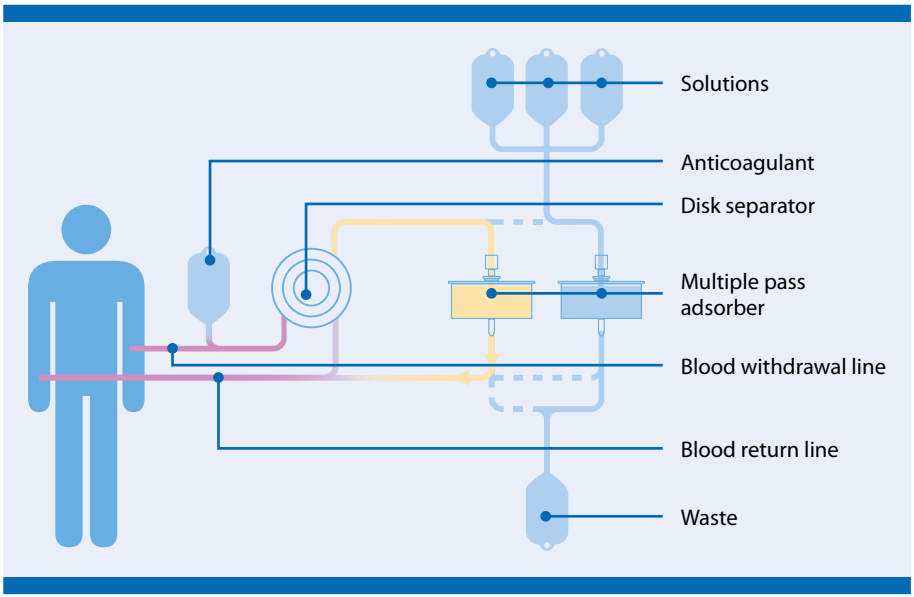


Figure 1.1: General scheme of a double column immunoadsorption

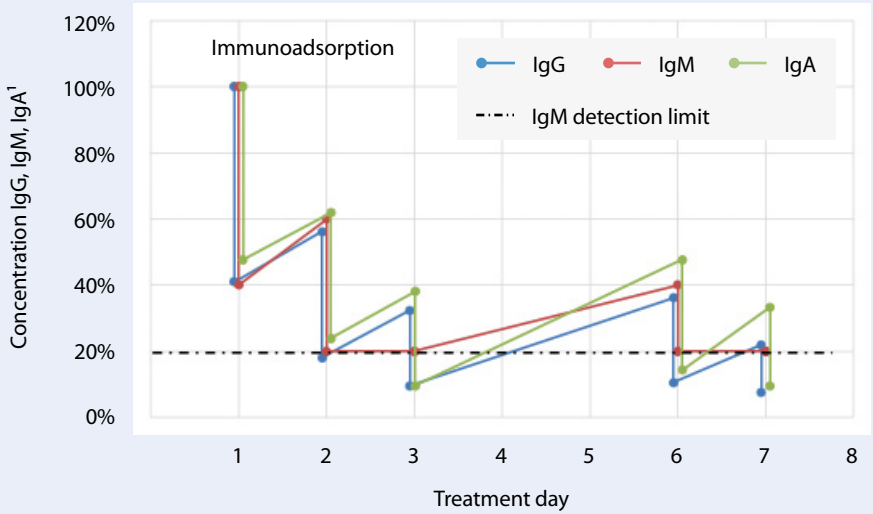
When the first adsorber has processed a predefined volume of plasma, the plasma is directed to the second adsorber for processing. During this time the first adsorber is regenerated by removing the target molecules from the matrix. During regeneration an adsorber is first flushed with priming solution to displace the plasma and return it to the patient, then target molecules are eluted (pH shift), followed by neutralization (pH adjustment) of the adsorber and a final rinse again with priming solution to remove the neutralization buffer. The regeneration of each adsorber can be repeated as often as necessary during a treatment, with the number of processing/regeneration cycles per session depending on the adsorber type and depletion level desired. During a treatment, approximately 2–2.5 times the patient's plasma volume is processed.

After the treatment is finished, the adsorber pair is either discarded (single use) or regenerated and preserved for storage until the next treatment (multiple use). Before final regeneration, the adsorber pair and the extracorporeal blood circuit are flushed with priming solution to return plasma, cell concentrate and whole blood to the patient. Afterwards, the patient is disconnected from the tubing set.

The final regeneration of an adsorber pair (multiple use) is performed with the elution buffer, immediately followed by rinsing each adsorber with preservation buffer to achieve neutralization and preservation in one step. Before re-use the

adsorber pair is extensively rinsed with priming solution to remove the preservation buffer, which is used for storage between treatments to prevent microbial growth.

After initial efficient elimination of the target molecule a general observation is a fast overnight rebound of the molecule concentration in the blood (see Figure 1.2). This increase is generally due to a redistribution of the molecules from the tissue or from binding sites (e.g., of endothelial cells) into the blood stream. In order to eliminate a significant amount of the target molecule from the body of the patient, repeated treatments are therefore recommended.



1 From initial value on first treatment day

Figure 1.2: Example of elimination with redistribution of immunoglobulins upon repetitive treatment sessions with TheraSorb - Ig omni 5 adsorber pair

2
Glossary

2.1 Graphical depiction

The following section lists and explains the panels depicting the potential consequences of hazardous situations which can occur if instructions, warnings or precautions outlined are not followed.

⚠ WARNING

Indicates a hazard or hazardous situation which could result in death or persisting or life-threatening medical conditions, ailments, and injuries that require stationary medical intervention and observation.

⚠ CAUTION

Indicates a hazard or hazardous situation which could result in temporary and reversible medical conditions, ailments, and injuries that require ambulatory medical intervention and observation.

NOTICE

Indicates a hazardous situation which, if not avoided, could lead to property damage, but not to an injury.

IMPORTANT

Indicates other situations which may occur if particular instructions or information are not followed or observed.

2.2 Glossary of symbols and terms

An overview of symbols and terms is provided in the user manual “General information – Instrument” or in the appropriate package insert of the products used.

3 Materials required

The following sections describe the materials needed for a double column immunoadsorption.

3.1 Materials required

In general, a double column immunoadsorption requires a combination of different products comprising a specific adsorber kit allocated to only one patient and disposables used for one treatment (see Table 3.1).
For further information on adsorber and treatment specifications see adsorber-related package insert.

Material[1]	Quantity	Components
LIFE 21 apheresis unit (Software version from 7.3)	1	–
Adsorber kit	1	• one adsorber pair • one patient chip card (PCC) • one adsorber holder
Disposables set	1	• TheraSorb - TS IA 100 • TheraSorb neutralization buffer • TheraSorb elution buffer • TheraSorb priming solution See adsorber-related package insert for treatment-specific quantities and consumables.
Spare parts[2]: TheraSorb - Spare Part Package	1	• two hydrophobic filter • one particle filter • one deaeration/particle filter
TheraSorb - DS 100	1	• disk separator

1 For order information refer to www.miltenyibiotec.com or contact your local representative.
2 It is recommended to have spare parts available during a treatment.

Table 3.1: Treatment components

⚠ WARNING

Risk of compromised safety and perfomance. Unauthorized materials or equipment may compromise the safety and performance of a therapeutic apheresis procedure due to risks of infection, cell loss, toxicity, adverse immune reactions, embolism, coagulation impairment, blood or plasma loss, metabolic acidosis, hyperphosphatemia or incomplete or insufficient apheresis. Only use authorized materials or equipment.

3.1.1 Additional materials

Besides the components described above, additional materials are required for the treatment.

Material	Description
ACD-A, anticoagulant solution	1,000 mL bag, spike connector or female Luer Lock connector
Heparin (anticoagulant solution) or equivalent	5,000 IU/mL, 5 mL solution
Infusion pump	for additional anticoagulant administration
(Optional) Waste bag, sterile	1-5, 10,000 mL bag, female Luer Lock connector
16 G needle, or equivalent	1 or 2 for venous access

Table 3.2: List of additional materials

IMPORTANT

The additional materials are not part of the LIFE 21 apheresis platform. Therefore, use only recommended materials that are certified for medical use in the country of operation.

3.2 General description - Adsorber

The cylindrical housing of each adsorber is manufactured from polycarbonate and is provided with a female inflow and outflow connector. The adsorber matrix is retained in the cylindrical housing between a double membrane above and below the matrix.
The adsorber (DV3 or DV4 housing) is connected through the female connectors to the inflow and outflow line of the tubing set. An adsorber pair is always used for a treatment (see Figure 3.1).

⚠ WARNING

Risk of embolism or infection. Opening the lateral connector will cause irreversible spillage of the adsorber matrix into the open (or into the tubing set). The lateral adsorber connector should not be opened at any time.

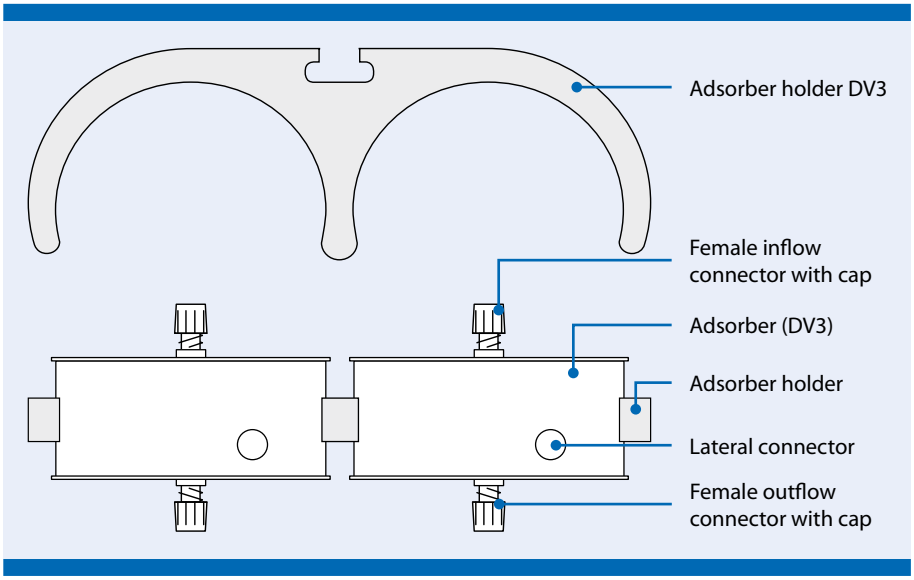


Figure 3.1: Example of adsorber pair (DV3, 100 mL) with adsorber holder

3.3 General description - TheraSorb solutions

All TheraSorb solutions, except for TheraSorb preservation buffer, are delivered in 5 liter bags. The preservation buffer is delivered in a glass bottle.

⚠ WARNING

Risk of infection. Loss of sterility and microbial contamination may result in the risk of infection of a patient. TheraSorb solutions may only be used if the solutions are clear and the bags or bottles and their caps are undamaged.

⚠ CAUTION

Risk of metabolic acidosis, hyperphosphatemia, adverse immune reactions and incomplete apheresis. Connection of a wrong or unauthorized solution can not be detected by the LIFE 21 apheresis unit. This may cause insufficient regeneration of an adsorber with the risk of metabolic acidosis, hyperphosphatemia, adverse immune reactions and incomplete apheresis. Only connect the correct and authorized solutions.

IMPORTANT

See the adsorber-related package insert for solutions allocated to a specific treatment and amounts needed for a certain number of cycles performed. If more cycles are planned, additional solutions may be required.

3.3.1 TheraSorb priming solution

TheraSorb - priming solution, an isotonic NaCl (0.9%) solution is intended to be used for the rinsing of the tubing set and the adsorber pair in all phases of a treatment. During the return of plasma to the patient and the mixing with blood components a transfer of priming solution to the patient occurs.

Connector: spike port, imprint color coded in green

3.3.2 TheraSorb elution buffer

TheraSorb elution buffers have either a pH value of 1.6 (TheraSorb - PA pro) or 2.8 (TheraSorb - Gly-HCl pro) and are intended to be used to regenerate the adsorber pair. Due to the pH value, the substances bound in the adsorber pair will be released and discarded with the elution buffer into the waste.

Connector: male Luer Lock, break-off tip for fluid-pass, imprint color coded in yellow

⚠ CAUTION

Risk of metabolic acidosis. Regeneration of the adsorber pair with an elution buffer not allocated to the specific treatment will cause incomplete regeneration of the adsorber pair and continuously compromise its performance and neutralization. Insufficient neutralization can cause metabolic acidosis in the patient. See the adsorber-related package insert for details on the treatment-specific elution buffer. Only use an elution buffer allocated to the specific treatment for regeneration of the adsorber pair.

3.3.3 TheraSorb neutralization buffer

TheraSorb neutralization buffer, a 30 mM PO_4 phosphate-buffered sodium chloride solution (pH 7.4), neutralizes the acidic effects of the elution buffer by increasing the pH value in the adsorber to a physiological level.

Connector: female Luer Lock, break-off tip for fluid-pass, imprint color coded in black

3.3.4 TheraSorb preservation buffer

After the patient is disconnected, the TheraSorb preservation buffer, a PBS, 0.01% (w/v) NaN_3/15% (v/v) EtOH solution, is needed for the preservation of the adsorber pair (only multiple use). The adsorber pair can then be stored until the next treatment session.

Connector: spike port

⚠ WARNING

Risk of toxicity. The TheraSorb preservation buffer is acutely toxic and may cause severe complications if infused unintentionally to the patient. In order to prevent an unintended infusion into the patient, the preservation solution TheraSorb - PBS-Azide must not be brought into the treatment room before the complete disconnection of the patient from the instrument. Adherence to this procedure should prevent an unintentional infusion of the solution into the patient.

IMPORTANT

Further information on toxicity and safe handling of the TheraSorb preservation buffer can be found in subsection 4.2.3 "Precautions".

3.4 General description - Tubing set

See subsection 6.2.1 "Tubing set components and connectors".

4

Warnings and precautions

4.1 General warnings and precautions

General warnings and precautions regarding the use of the LIFE 21 apheresis platform can be found in the user manual “Warnings, precautions and troubleshooting”.

⚠ WARNING

Risk of electrical shock, physical injuries, fluid imbalances or loss, vascular damage, hemolysis or embolism. Disregard of any instructions, warnings or cautions at any time can endanger patients, operator and others due to possible instrument damage or malfunction and may compromise the electrical, electronical, electromagnetic and mechanical safety. Always follow the instructions, warnings or cautions at any time.

4.2 Double column immunoadsorption

4.2.1 Intended purpose

The double column immunoadsorption is intended for the therapeutic removal of specific components from human blood plasma. See package insert for the specific intended purpose of the adsorber used.

4.2.2 Side effects

For detailed information read the package insert delivered with the individual adsorber kit and disposable set. Read the relevant section in the user manual “Warnings, precautions and troubleshooting” for general risks and hazards related to therapeutic plasmapheresis.

Very limited information is currently available regarding the use of TheraSorb adsorbers in pregnant women and nursing mothers. In such cases, the treatment should be carried out only after rigorous assessment of the indication. When treating small children, particular attention must be paid to the extracorporeal volume required for the treatment.

4.2.3 Precautions

For detailed information read the package insert delivered with the individual adsorber kit and disposable set. Read the relevant section in the user manual "Warnings, precautions and troubleshooting" for general risks and hazards related to apheresis.

TheraSorb preservation buffer

Sodium azide (NaN_3) and ethanol are the active components of the TheraSorb preservation buffer (PBS, 0.01% (w/v) NaN_3/15% (v/v) EtOH). Sodium azide at the denoted concentration inhibits the growth of inadvertently introduced microorganisms during storage of the adsorber pair between treatment sessions. Sodium azide is generally accepted as an antimicrobial preservative and has been used continually for many years for the preservation of adsorbers.

⚠ WARNING

Risk of toxicity. NaN_3 can be hazardous or even lethal after incorporation into the body. Pre-treatment rinsing or preservation of the adsorber pair should generally only be started when the patient is not yet, or no longer connected to the instrument to prevent a risk of adverse immune reactions or toxicity. Take special care when handling the preservation buffer:

- **Do not drink, eat or smoke while handling the preservation buffer.**
- **Always wear protective gloves.**
- **In case of skin contact, rinse immediately with water.**
- **In case of contact with mucosa or eyes, rinse immediately with large amounts of water and seek medical advice.**

If any of the following symptoms occur after exposition to the solution, immediately consult a physician: headache, nausea, vomiting, diarrhea, restlessness, shortness of breath, faintness, dizziness, drop in blood pressure, bradycardia or tachycardia.

Additional toxicological information	
After inhalation of dust/aerosol	Severe irritations of mucous membranes and respiratory tract
Possible consequences	Pulmonary edema. Latency, no immediate effect
After contact with skin	Severe irritations
After contact with eyes	Severe irritations
After ingestion	Irritations of the mucous membranes of mouth, throat, esophagus and gastrointestinal tract
Systemic effects	
Dysfunction of the central nervous system, failure of the cardiovascular system, tachycardia, decline of blood pressure, coughing, respiratory depression, spasms, headache, dizziness (vertigo), nausea, vomiting, collapse, unconsciousness.	

Table 4.1: Additional toxicological information and systemic effects

IMPORTANT

Any serious incident that has occurred in relation to this product should be reported to Miltenyi Biotec B.V. & Co. KG – using the contact information provided – and the competent authority of the member state in which the operator of this product is established and in which the patient has been treated.

5 Preparative steps

The treatment on the instrument is fully automated and requires only a few preparative steps.

⚠ WARNING

Risk of infection. Loss of sterility and microbial contamination may result in the risk of infection of a patient. Observe adequate hygienic measures for aseptic handling for all preparative steps.

5.1 Anticoagulation

In order to prevent blood or plasma coagulation in the extracorporeal circuit during the treatment, the blood must be anticoagulated. Anticoagulation should be individually adapted for each patient in accordance with the instructions given by the attending physician.
See user manual “Warnings, precautions and troubleshooting” for the recommended combination of the anticoagulation solutions ACD-A and Heparin. Recommendations regarding calcium substitution can also be found there.

5.2 Adsorber pair

Remove the adsorber pair from the refrigerator to bring the adsorber, to room temperature before preparing the instrument for the treatment. This step shall be omitted for adsorbers stored at room temperature.

⚠ WARNING

Risk of microbial contamination and infection or blood or plasma loss. Untight connections may result in microbial contamination and infection or leakage of the extracorporeal fluid path with the risk of blood or plasma loss. The adsorber pair must have reached room temperature by the time they are connected with the tubing set. This will avoid damage to the Luer Lock connectors on opening.

6

Preparation of the instrument

This chapter describes step-by-step how to prepare the instrument for a double column immunoadsorption. As a representative treatment the use of the TheraSorb - Ig omni 5 adsorber pair for multiple use is described. The preparation is divided into the following steps:

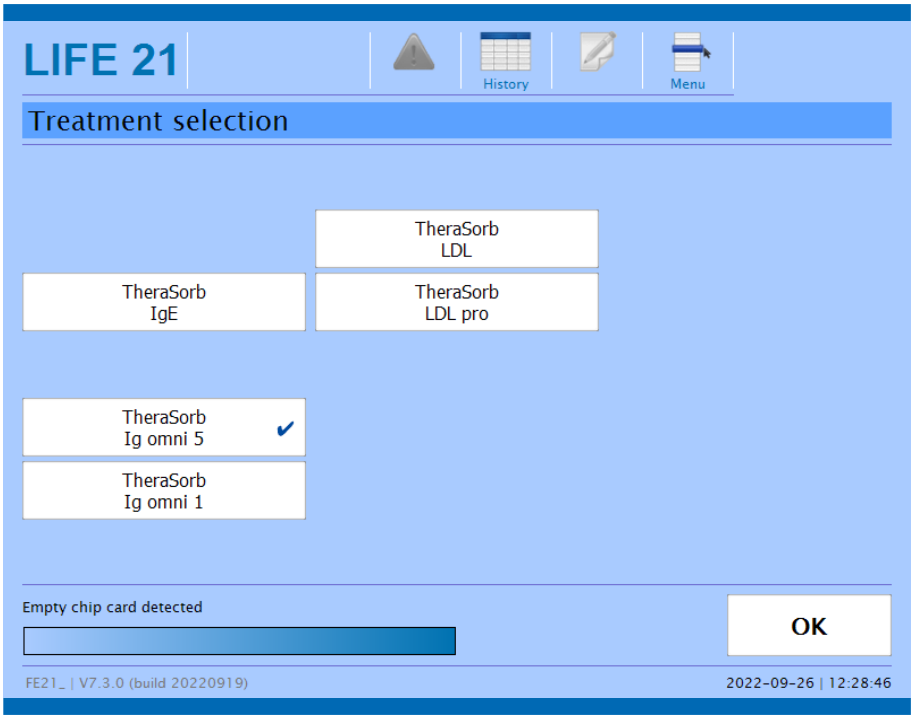
- initialization of the instrument
- tubing set installation – Part 1
- settings for patient and treatment parameters
- tubing set installation – Part 2
- automatic priming of extracorporeal system
- adsorber pair connection and rinsing
- connection of patient (selection of Single Needle/Double Needle mode)

The different steps will be elucidated by displaying the appropriate software screens and by stating specific operator actions required.
The treatment described reflects the first usage of an adsorber pair with a new patient chip card.
The graphical user interface (GUI) allows the operator to interact with the instrument via software screens using touch-sensitive functions.

6.1 Initialization

Operator action: Switch on the instrument by attaching the power cable to a suitable power outlet and activating the power switch located on the rear panel of the instrument.

After the initialization phase, the first screen is displayed showing different treatment options (see Screen 6.1).



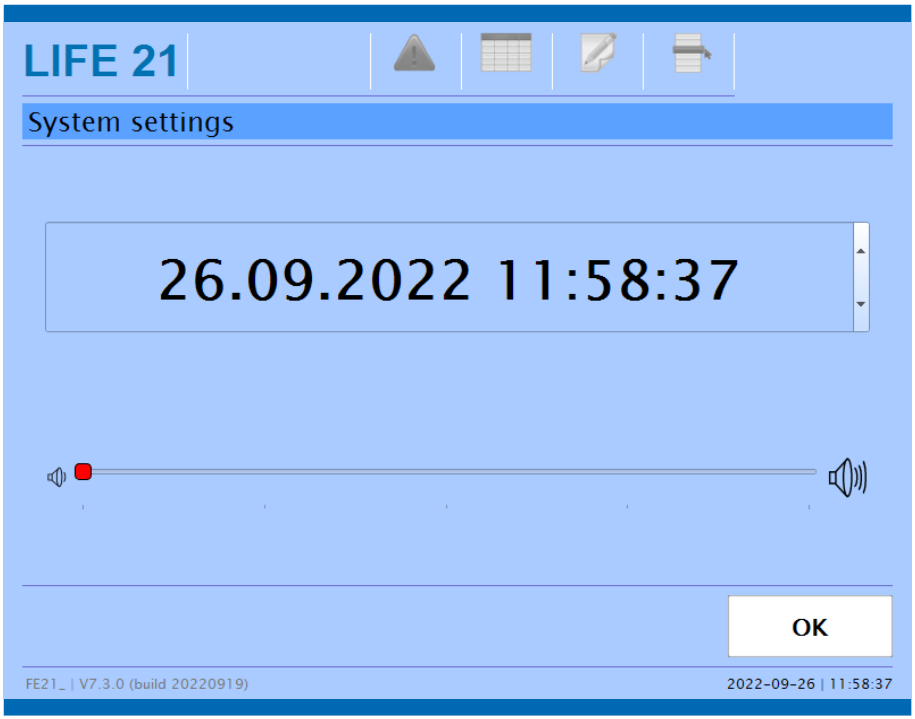
Screen 6.1: Main screen to select a treatment

IMPORTANT

The user interface will guide the operator through the treatment. For details regarding the graphical user interface, see user manual "General information – Instrument". The pictures presented in this manual are representative treatment screens and in some instances may differ slightly from screens displayed on the instrument during the treatment.

Optional operator action:

- By pressing **Menu** followed by **System settings** the time and date as well as the volume of the warning tone can be adjusted (see Screen 6.2).
- By pressing **Menu** followed by **Transfer protocol data** the protocol of the last treatment can be transferred to a USB flash drive.



Screen 6.2: System settings

Operator action: Insert patient chip card with the side of the golden chip, into the card drive. Select **TheraSorb - Ig omni 5** treatment by pressing the respective button.
Treatment relevant data and material information is transferred to the patient chip card during the treatment to prevent any patient/adsorber pair mismatch in future treatments.

At the end of the treatment, process and patient-related information will be transferred to the chip card. After every treatment the previous information on the card will be overwritten by the current treatment-related information.

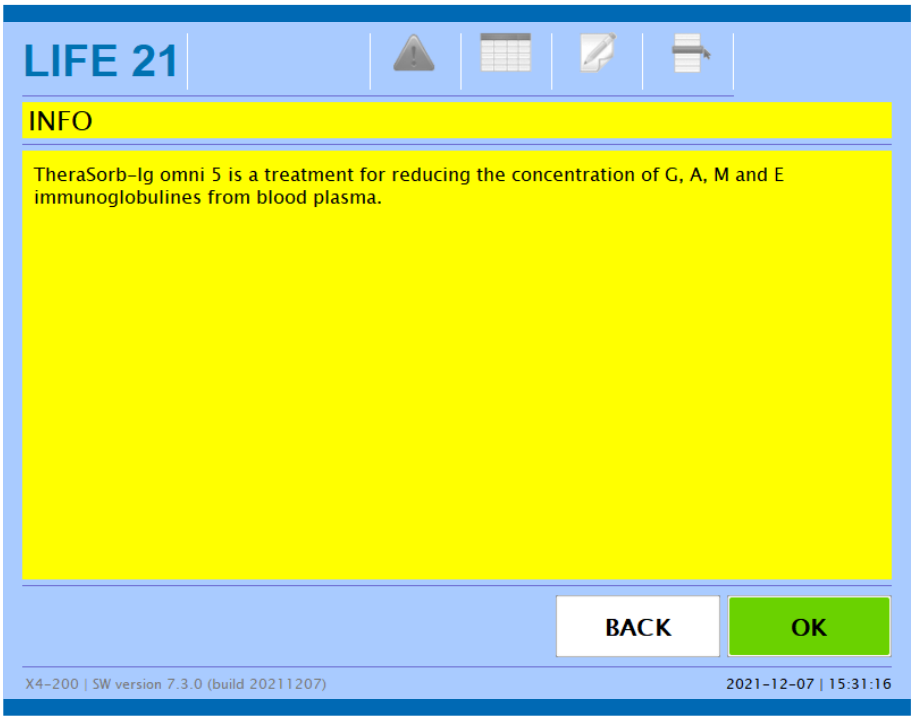
IMPORTANT

For consecutive treatments the last treatment-related information saved on the patient chip card is displayed by the instrument.

⚠ WARNING

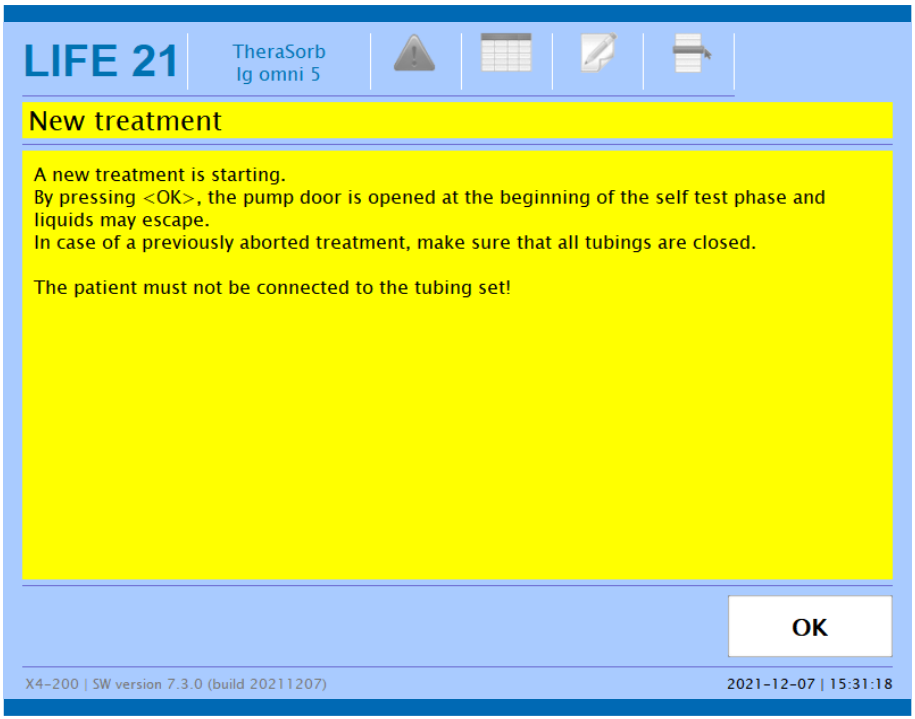
Risk of data loss or data corruption. To select and to continue the treatment, the patient chip card is required. Do not remove the chip card unless prompted by the instrument. Incorrect insertion or removal may lead to data loss or data corruption. Make sure the correct patient chip card is used. To avoid any mistaken identity it is highly recommended that the patient chip card is labeled with pseudonymized patient information before the first treatment. Mismatching of a re-usable adsorber and the corresponding patient may cause cross-contamination with the risk of bacterial or viral infection as well as a prionopathy.

Operator action: To continue press **OK** after the button in the treatment selection screen is activated. An information screen is displayed (see Screen 6.3).



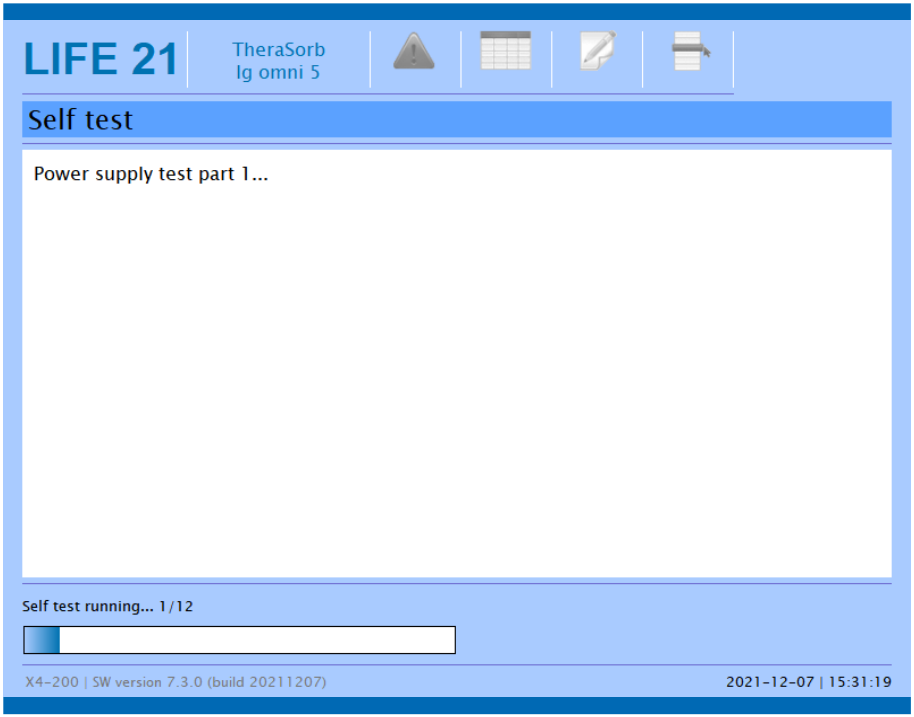
Screen 6.3: Information screen on selected treatment

Operator action: To continue press **OK**. Follow the instructions and press **OK** (see Screen 6.4).



Screen 6.4: Instruction screen to start self-test phase

The selected treatment is initialized and self tests are performed (see Screen 6.5).



Screen 6.5: Representative screen for performed self tests

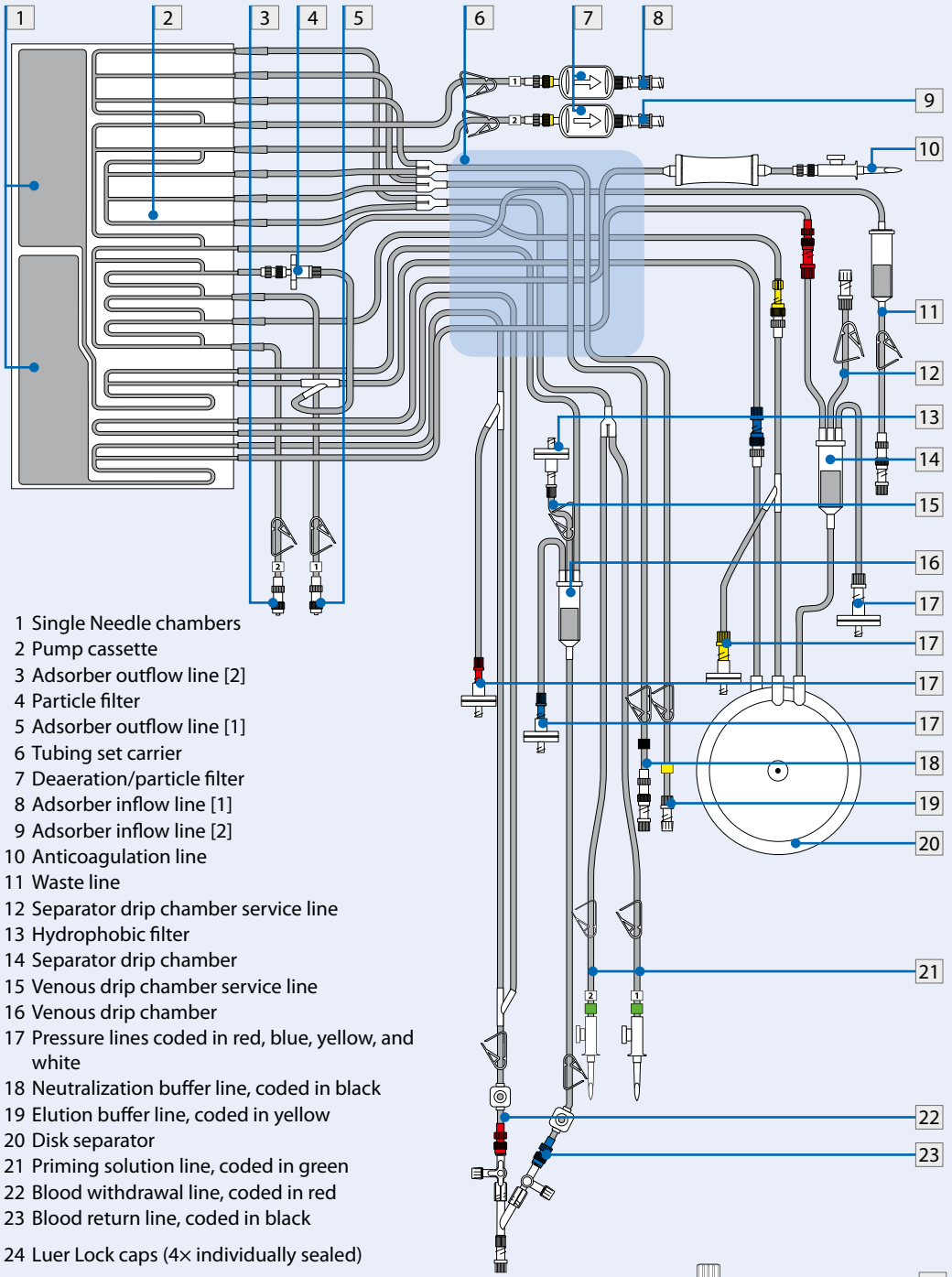
6.2 Tubing set installation – Part 1

The following section guides the operator through the first part of the tubing set installation starting with an overview on the tubing set components followed by a detailed description of the installation process of the tubing set components.

6.2.1 Tubing set components and connectors

The tubing set represents the extracorporeal blood and fluid path during the treatment. It connects the patient with the anticoagulant, the specific adsorber pair, and delivers the eluted proteins and rinsing solutions to the waste. It is composed of a pump cassette, a disk separator (for plasma separation), a tubing set carrier and tubing lines with connectors to the adsorber pair, solutions, external pressure sensors and the vascular access points of the patient.
In addition, the tubing set comes with four sterile Luer Lock caps used to close the inflow and outflow connectors of the adsorber pair after the treatment. The components of the TheraSorb - TS IA 100 tubing set are provided in a sealed and sterilized package. The tubing set components are illustrated in Figure 6.1 and Figure 6.2.

IMPORTANT
Do not connect components to the tubing set (such as adsorbers or solutions) unless prompted by the instrument.



1 Single Needle chambers
2 Pump cassette
3 Adsorber outflow line [2]
4 Particle filter
5 Adsorber outflow line [1]
6 Tubing set carrier
7 Deaeration/particle filter
8 Adsorber inflow line [1]
9 Adsorber inflow line [2]
10 Anticoagulation line
11 Waste line
12 Separator drip chamber service line
13 Hydrophobic filter
14 Separator drip chamber
15 Venous drip chamber service line
16 Venous drip chamber
17 Pressure lines coded in red, blue, yellow, and white
18 Neutralization buffer line, coded in black
19 Elution buffer line, coded in yellow
20 Disk separator
21 Priming solution line, coded in green
22 Blood withdrawal line, coded in red
23 Blood return line, coded in black

24 Luer Lock caps (4× individually sealed)

Figure 6.1: Components of the tubing set (upon delivery adsorber inflow and outflow lines are connected)

The allocation of tubing paths to the pumps, type of connectors and color codes used are summarized in Figure 6.1 and Table 6.1.

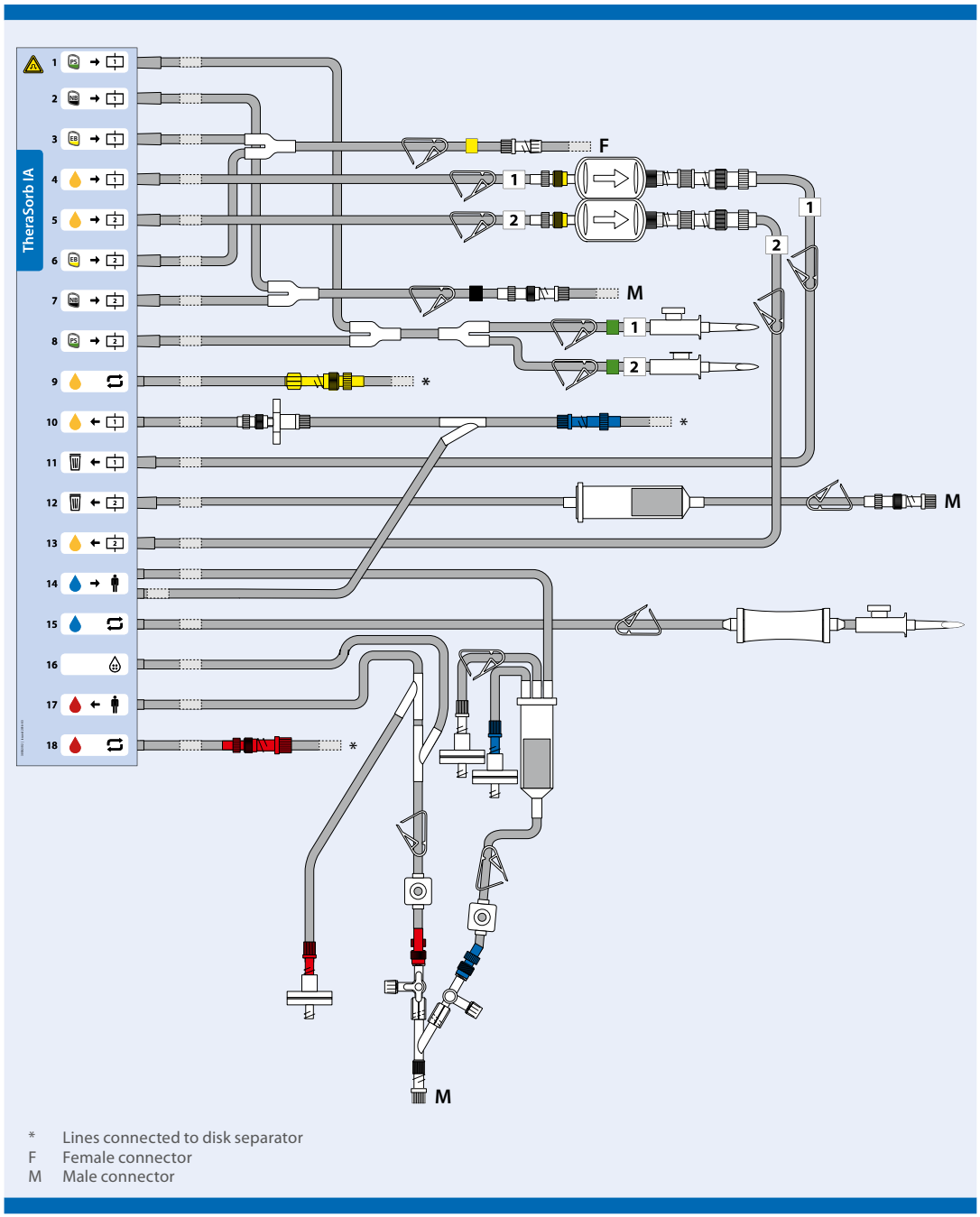


Figure 6.2: Allocation of tubing lines and connectors, schematic view neither showing full length of tubing nor all components.

Symbol	Explanation
	**pump 1:** a) Priming solution from bag to adsorber 1 (preparation, treatment and reinfusion) b) Preservation solution from bottle to adsorber 1 (preservation only)
	**pump 2:** Neutralization buffer from bag to adsorber 1
	**pump 3:** Elution buffer from bag to adsorber 1
	**pump 4:** Plasma from disk separator to adsorber 1
	**pump 5:** Plasma from disk separator to adsorber 2
	**pump 6:** Elution buffer from bag to adsorber 2
	**pump 7:** Neutralization buffer from bag to adsorber 2
	**pump 8:** a) Priming solution from bag to adsorber 2 (preparation, treatment and reinfusion) b) Preservation buffer from bottle to adsorber 2 (preservation only)
	**pump 9:** Plasma from disk separator to blood cell concentrate (adsorber bypass) and treated plasma of the adsorber to be loaded in the adsorber exchange step
	**pump 10:** Plasma from adsorber 1 to blood cell concentrate
	**pump 11:** Fluid from adsorber 1 to waste
	**pump 12:** Fluid from adsorber 2 to waste
	**pump 13:** Plasma from adsorber 2 to blood cell concentrate
	**pump 14:** Whole blood from blood return line to patient

Symbol	Explanation
	**pump 15**: Single Needle OUT chamber In/Out (in Single Needle mode only): a) Single Needle withdrawal step: Blood cell concentrate from disc separator to Single Needle OUT chamber; b) Single Needle return step: Blood cell concentrate from Single Needle OUT chamber to blood return line
	**pump 16:** Anticoagulant from bag to blood withdrawal line
	**pump 17:** Whole blood from blood withdrawal line to disk separator
	**pump 18:** Single Needle IN chamber In/Out (in Single Needle mode only): a) Single Needle withdrawal step: whole blood from blood withdrawal line to Single Needle IN chamber; b) Single Needle return step: whole blood from Single Needle IN chamber to disk separator

Table 6.1: Explanation of symbols on pump door label

6.2.2 Deaeration/particle filter

The filter in Figure 6.3 is included in the two adsorber inflow lines of the tubing set. It ensures removal of air from the adsorber tubing line and removal of particles or aggregates from the plasma or solutions that may pass the adsorber. The filter can be replaced in case of clogging.

IMPORTANT

The TheraSorb - Spare Part Package contains a sterile deaeration/particle filter, individually sealed. The spare filter can be used in case a filter exchange has to be performed during a treatment.

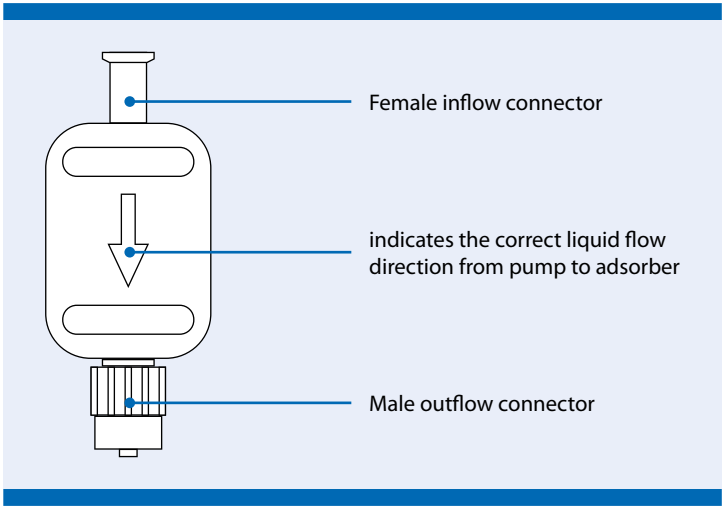


Figure 6.3: Deaeration/particle filter with connectors

6.2.3 Particle filter

The particle filter in Figure 6.4, as part of the tubing set, is integrated in the central plasma return line to the patient in the segment of the tubing set between pump No. 10 and pump No. 14 of the installed tubing set. The particle filter ensures the safety of the patient in the unlikely event that the adsorber membranes rupture and Sepharose™ is released. In addition, the filter retains any particles that may pass the adsorber membranes due to their small size. The filter can be replaced in case of clogging.

⚠ WARNING

Risk of embolism. A double column immunoadsorption performed without the particle filter present in the central plasma return line can lead to embolism by particles. Performing a treatment without a particle filter in place results in the exclusion of any liability by the manufacturer. Only perform a double column immunoadsorption with the particle filter present in the central plasma return line.

IMPORTANT

The TheraSorb - Spare Part Package contains a sterile particle filter, individually sealed. The spare filter can be used in case a filter exchange has to be performed during a treatment.

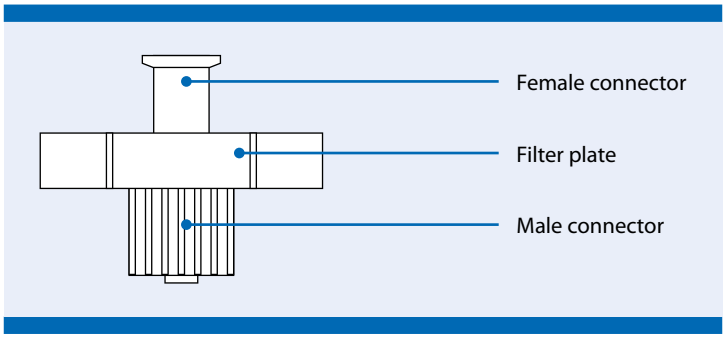


Figure 6.4: Particle filter with connectors

6.2.4 Hydrophobic filter

The 0.2 µm filter in Figure 6.5 is included at the end of the four pressure tubing lines (red, blue, yellow, and white) of the tubing set and connects the pressure lines to the external pressure sensors of the instrument. The filter prevents liquid from passing and ensures that the sensors remain dry. In addition, the filter is included at the end of the venous drip champer service line. The filter shall be replaced in case it got wet.

IMPORTANT

The TheraSorb - Spare Part Package contains two sterile hydrophobic filters, individually sealed. The spare filter can be used in case a filter exchange has to be performed during a treatment.

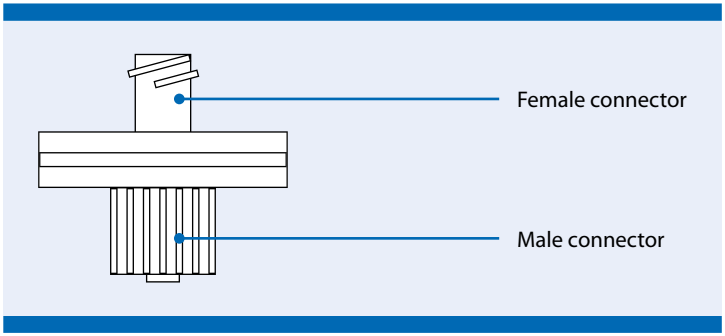


Figure 6.5: Hydrophobic filter with connectors

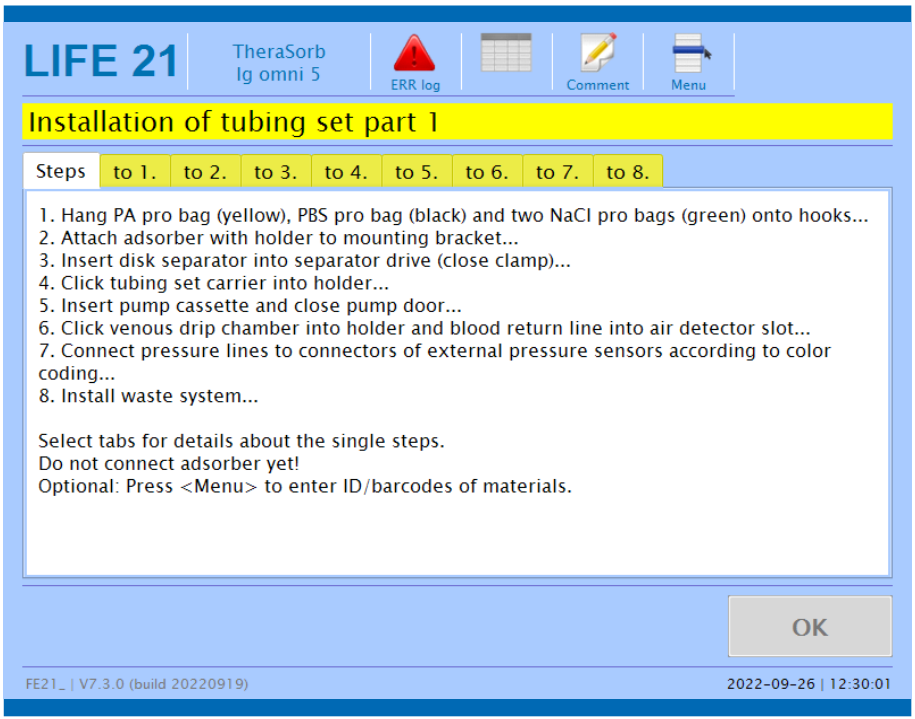
6.2.5 Installation steps

This subsection guides the operator step-by-step through the first part for the tubing set installation.

⚠ WARNING

Risk of infection. Loss of sterility may result in microbial contamination with the risk of infection of a patient. Damaged packaging could indicate that the tubing set is no longer sterile and therefore must not be used. Carefully inspect the packaging for damage, puncture or tears. Use the tubing set only if package is undamaged and sealed. The Luer Lock connections must be closed tightly before use.

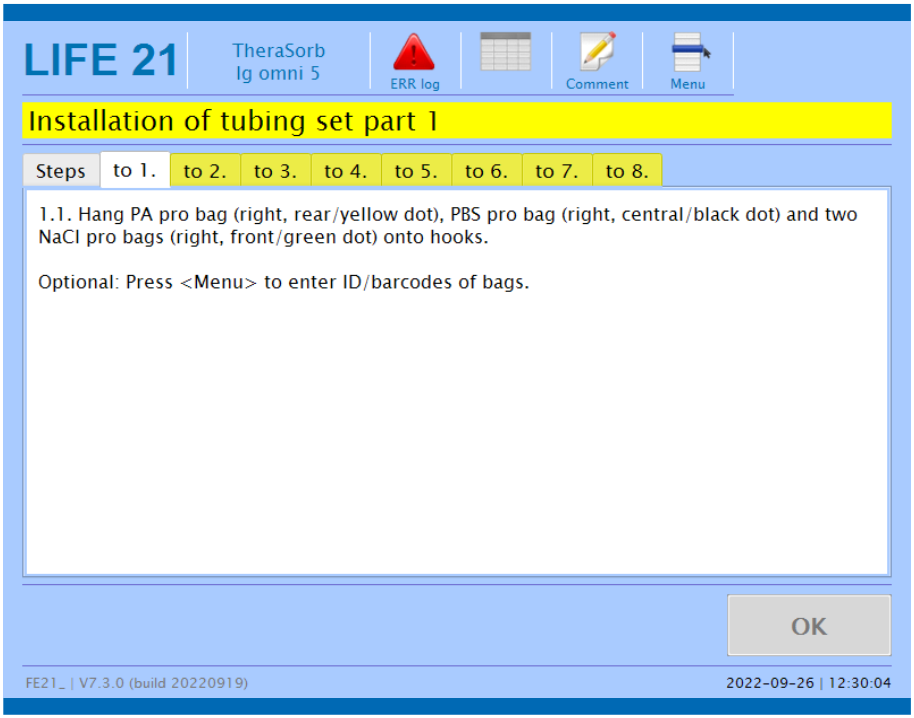
After the initialization steps are completed, the overview screen for the first part of the tubing set installation is displayed (see Screen 6.6). A summary of all required steps is given under **Steps**.



Screen 6.6: Short instruction of installation steps

It is highly recommended to follow the detailed instructions under **to 1.** through **to 8.** to enable the correct installation of the tubing set.

Operator action: Select to 1. and follow the instructions (see Screen 6.7).



Screen 6.7: Placing solution bags on hooks

Figure 6.6 displays the recommended position of bags on hooks.

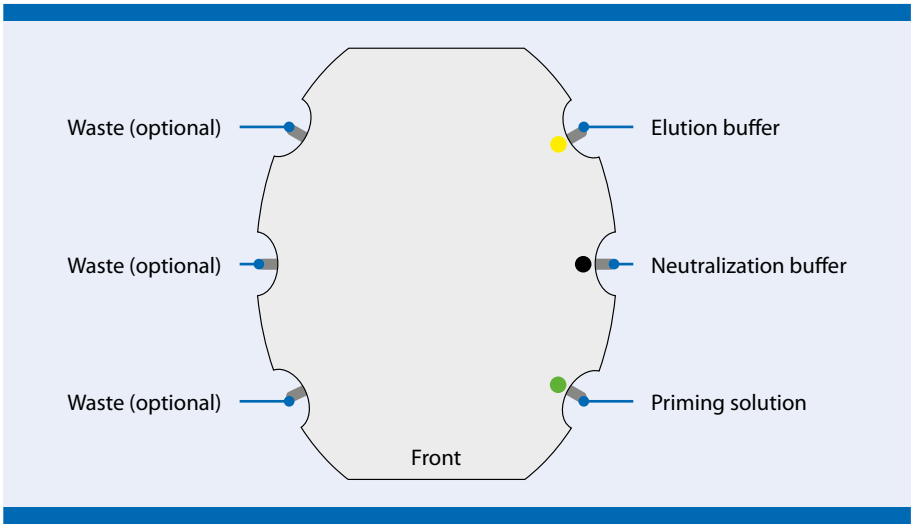
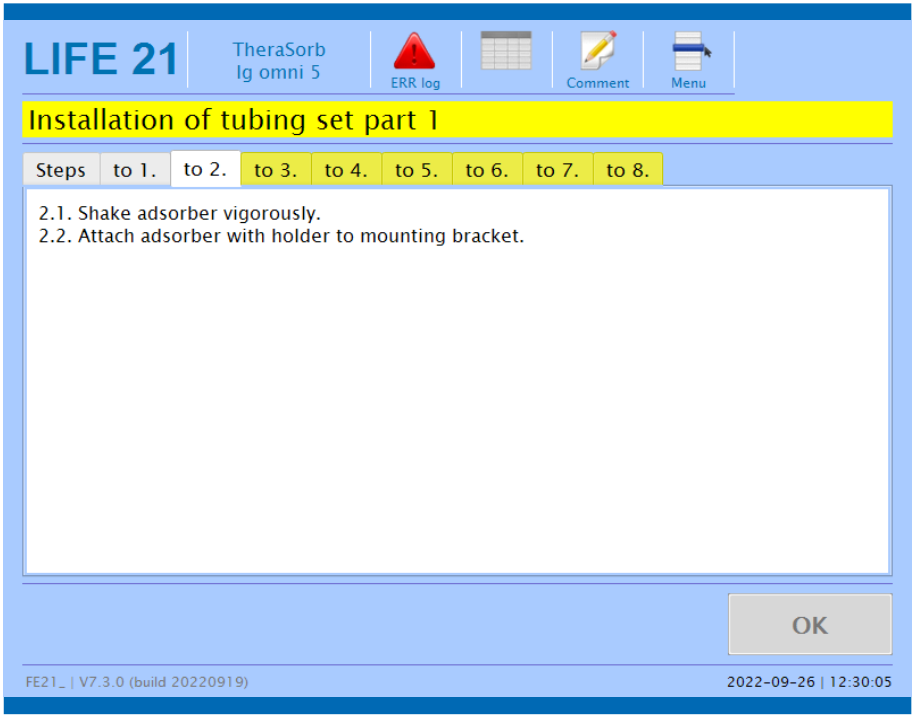


Figure 6.6: Recommended positions of solution bags on the instrument

Operator action: Select to 2. and follow the instructions (see Screen 6.8).



Screen 6.8: Installation of adsorber pair

Figure 6.7 shows the correct installation of the adsorber pair onto the mounting bracket. For a first treatment unpack the adsorber pair and click each adsorber into the adsorber holder.

⚠ WARNING

Risk of toxicity or adverse immune reactions. Premature connection may cause insufficient priming and rinsing of the extracorporeal fluid path with the risk of toxicity (NaN_3/Ethanol) or adverse immune reactions. Do not connect the adsorber pair to the tubing set yet!

IMPORTANT

Shake adsorbers vigorously before clicking them into the adsorber holder.

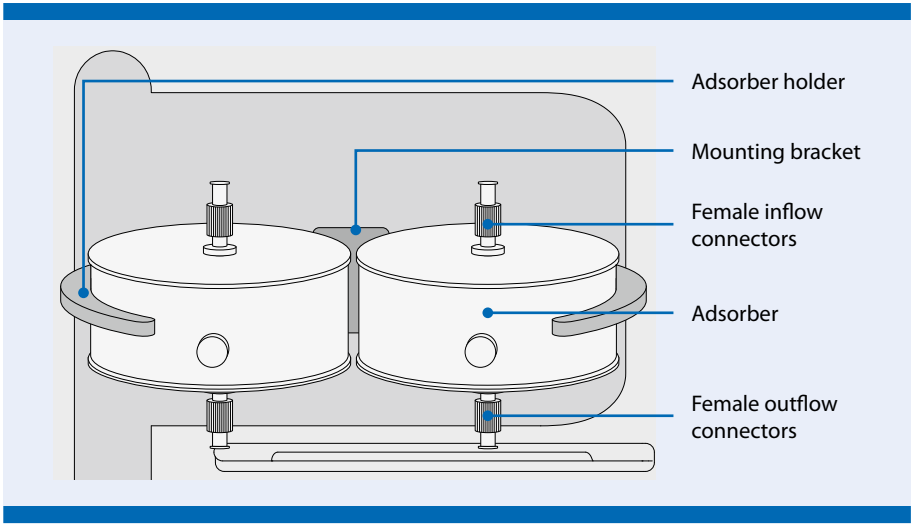
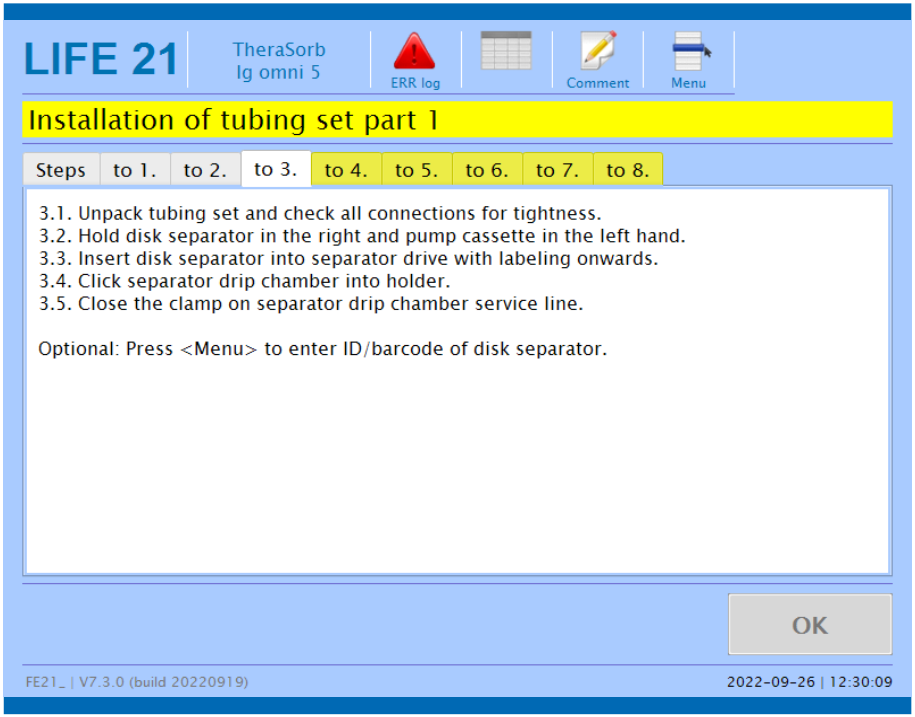


Figure 6.7: Correct installation of the adsorbers onto the mounting bracket

⚠ WARNING

Risk of infection. Loss of sterility and microbial contamination may result in the risk of infection of a patient. Do not use the adsorber pair after the use-by date indicated on the label. The adsorber pair should not be used if damaged (e.g., cracks in the housing, leaking connectors) or if microbial contamination is suspected.

Operator action: Select to 3. and follow the instructions (see Screen 6.9).



Screen 6.9: Installation of disk separator and separator drip chamber

⚠ WARNING

Risk of infection. Loss of sterility and microbial contamination may result in the risk of infection of a patient. To prevent damage to the tubing set or loss of sterility of the interior fluid path do not drop the tubing set and avoid prolonged exposure or contact of open connectors to the environment during the preparation and treatment phase!

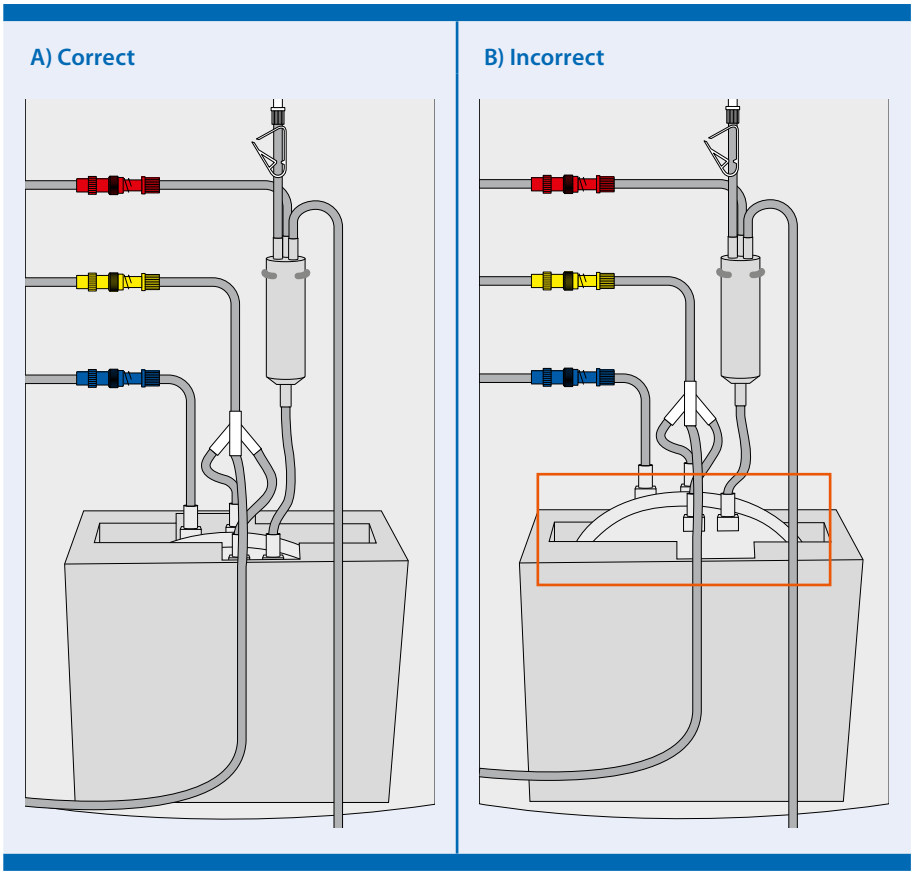
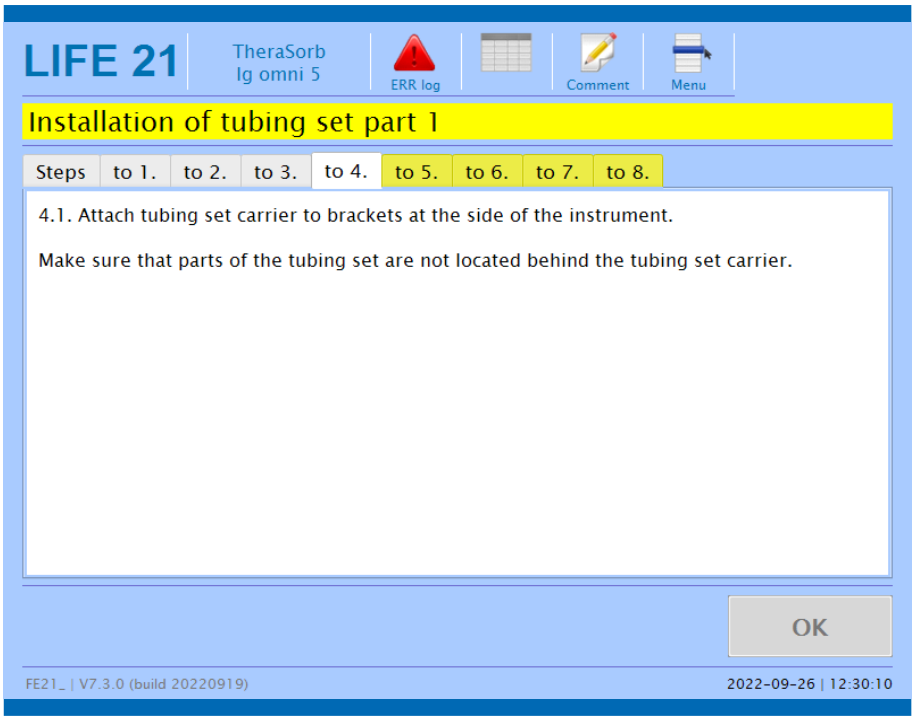


Figure 6.8: Correct position of disk separator in separator drive

Operator action: Select to 4. and follow the instructions (see Screen 6.10). The correct installation of the tubing set carrier is shown in Figure 6.9.



Screen 6.10: Installation of tubing set carrier

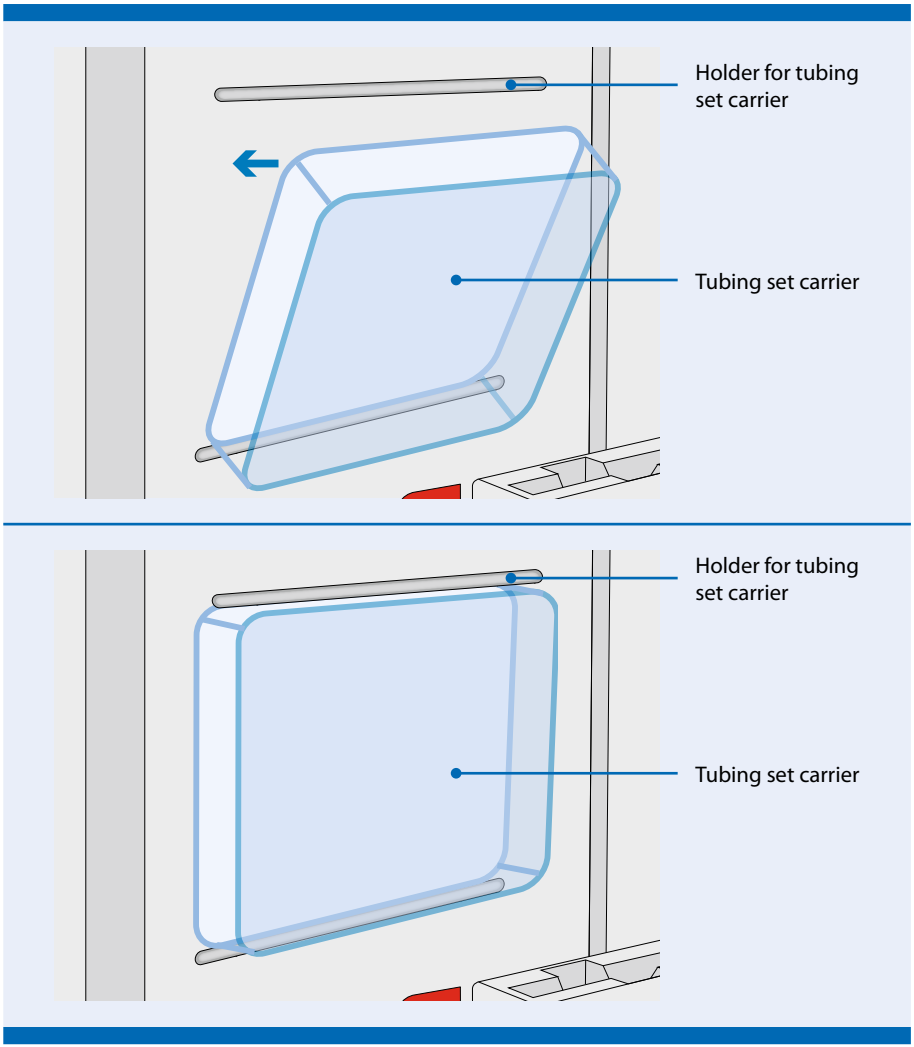
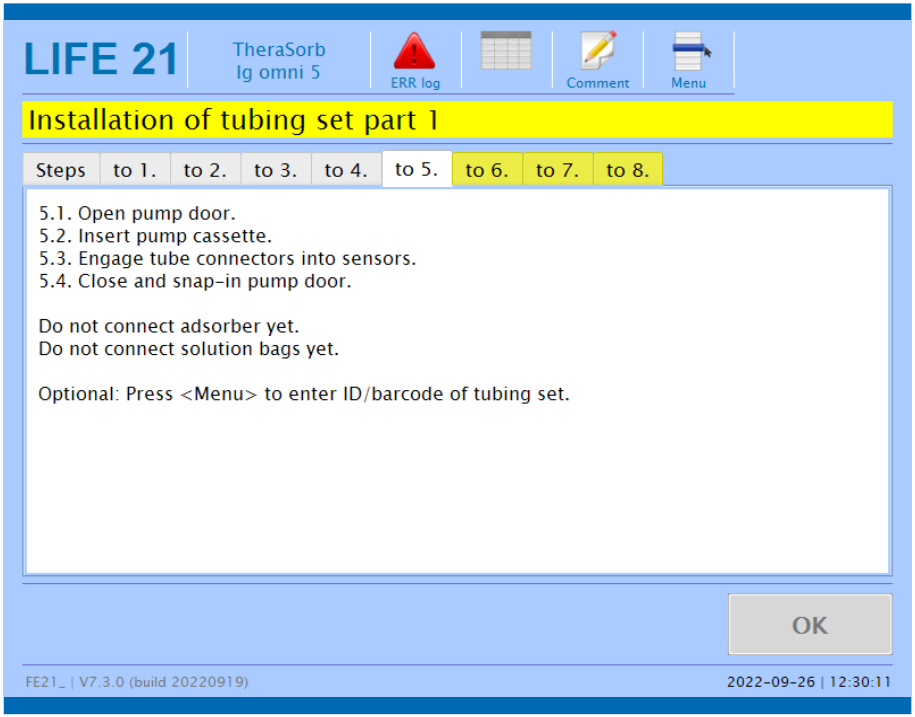


Figure 6.9: Insertion of tubing set carrier into holder (schematic view without tubing)

Operator action: Select to 5. and follow the instructions (see Screen 6.11).



Screen 6.11: Installation of pump cassette

⚠ WARNING

Risk of toxity or adverse immune reactions. Premature connection may cause insufficient priming and rinsing of the extracorporeal fluid path with the risk of toxicity (NaN_3/Ethanol) or adverse immune reactions. Do not connect adorbers pair and solutions bags to the tubing set yet.

Figure 6.10 shows how the pump cassette is placed into the pump module. Make sure that the tubings fit correctly into the light and pressure sensors.

IMPORTANT

Make sure that the pump cassette label position is bottom left and upfront for correct installation.

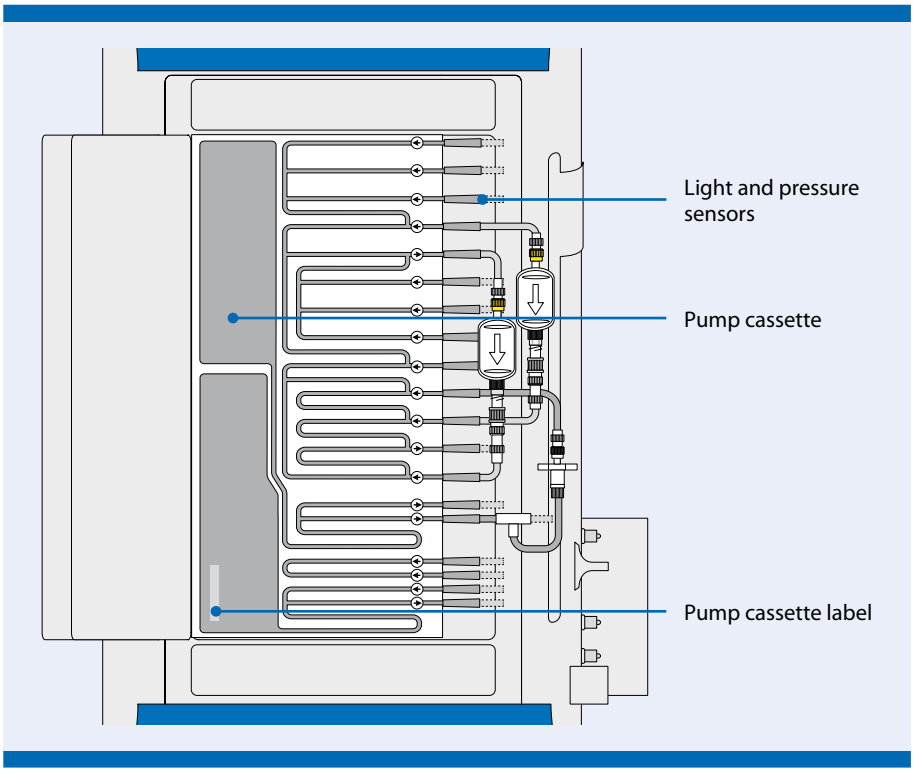
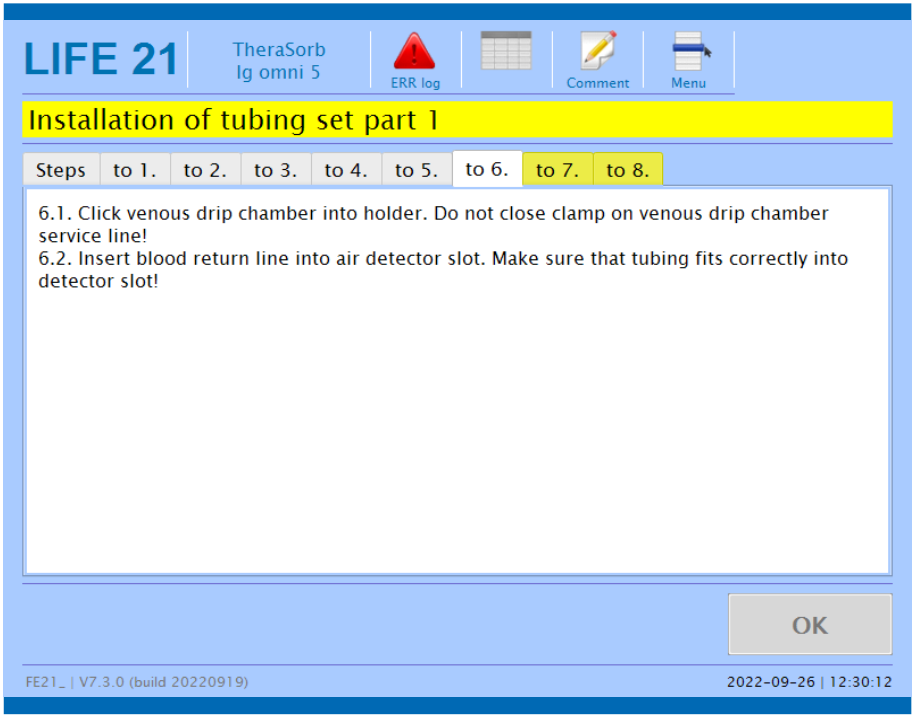


Figure 6.10: Correct placement of pump cassette into pump module

Operator action: Select to 6. and follow the instructions (see Screen 6.12).



Screen 6.12: Installation of venous drip chamber

Figure 6.11 shows the correct position oft the venous drip chamber and the blood return line in the air detector.

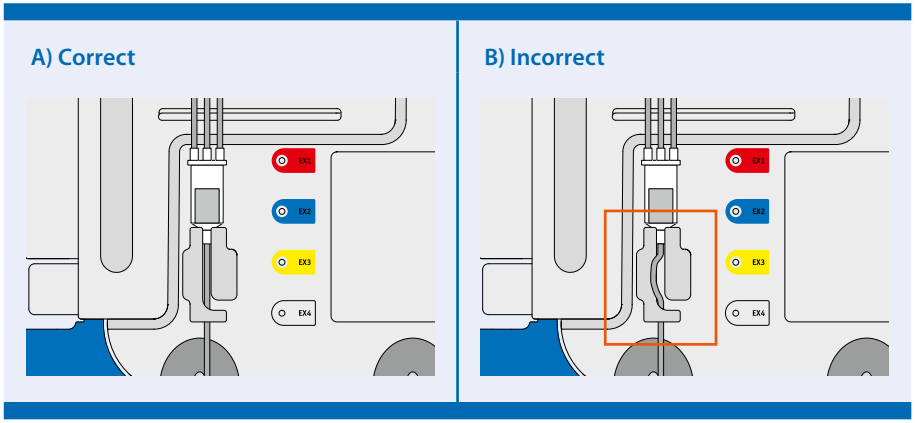
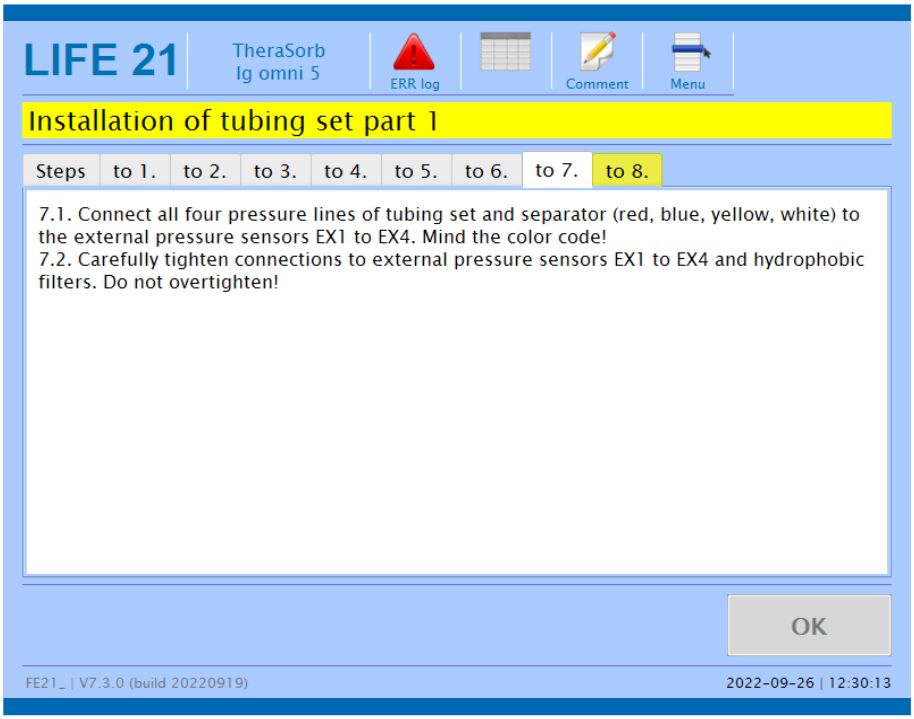


Figure 6.11: Correct position of venous drip chamber and blood return line

⚠ WARNING

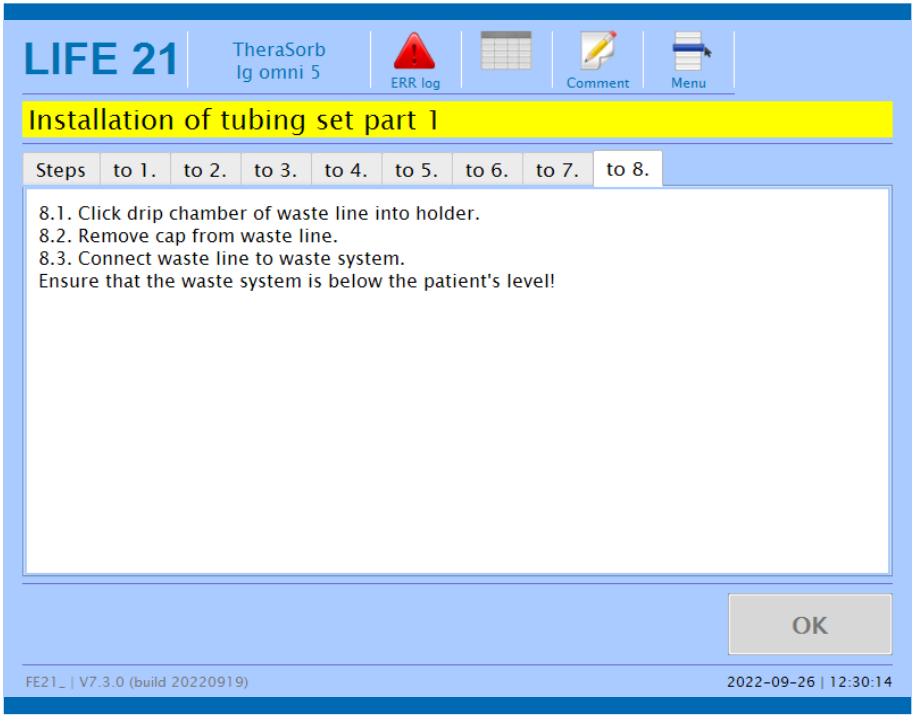
Risk of embolism. In case the blood return is connected incorrectly, the returned blood cannot be monitored for the occurrence of air bubbles. Do not to confuse the blood return line with other lines of the tubing set when placing the tubing into the air detector.

Operator action: Select **to 7.** and follow the instructions (see Screen 6.13).



Screen 6.13: Connection of pressure lines to EX1-EX4

Operator action: Select to 8. and follow the instructions (see Screen 6.14).



Screen 6.14: Connection of waste line

Operator action: For step 8.3 on Screen 6.14 using a waste bag follow the instructions below:

- Unfold and place the waste bag onto the hooks located on the left side of the housing.
- Make sure that the bag is placed onto two separate hooks with one eyelet each.
- The markers on the bag indicating the approximate fill volume must be visible to the operator.
- Check that the outlet at the bottom of the bag is completely closed to avoid spillage of the potentially infectious waste fluids.
- Connect the waste line of the TheraSorb - TS IA 100 tubing set (male Luer Lock connector) securely to the female Luer Lock connector of the waste bag.
- Open all clamps and press OK to continue.

⚠ WARNING

Risk of infection. Exceeding the fill volume of 10 L specified by the bag manufacturer can cause a rupture of the bag and spillage of potentially infectious material. Spillage may contain microbial or viral contamination which may lead to a risk of infection. Overfilling may also cause the bag to slip off the hook or cause a breakage of the hook itself. Carefully monitor the fill level of the waste bag as indicated by the markers on the bag surface. In case of spillage, observe local precautions and regulations for the handling of infectious materials.

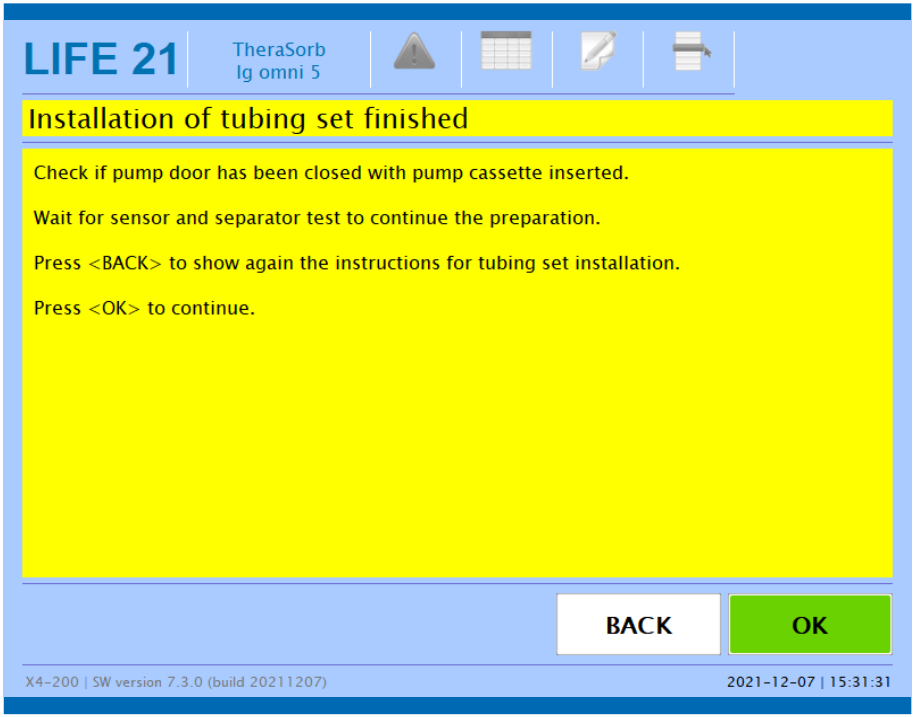
⚠ WARNING

Risk of infection. The drip chamber of the waste line has to be in an upright position and the waste bag or the connection to the central waste line should not be higher than level of patient, to avoid any retrograde contamination. Loss of sterility and microbial contamination may result in the risk of infection of a patient. If correct installation and orientation cannot be guaranteed an independent back flow prevention must be installed.

NOTICE

Risk of damage to the hooks. The maximum weight of a bag hanger is limited to 10 kg. Do not overload the hooks.

Operator action: Press **OK** and follow the instructions (see Screen 6.15).



Screen 6.15: Finalization of tubing set installation

The instrument performs internal tests before the next screen is shown (see Screen 6.16).

6.3 Input of patient and treatment-related settings

The following section guides the operator through the entry of patient and treatment-related settings for a first TheraSorb - Ig omni 5 treatment using a new adsorber pair and patient chip card.

6.3.1 General parameters

Operator action: Enter patient-relevant data by pressing the respective buttons on the screen as well as treatment-related settings, for example, blood flow and hematocrit (see Screen 6.16). A data entry mask allows the operator to enter the data using an on-screen keyboard, and to confirm the entry by pressing **OK** (see Screen 6.17).

The first and last name of a patient can be entered in a pseudonymous form, e.g., patient identification number. The entry fields for name and first name allow up to 30 alphanumeric characters.

⚠ WARNING

Risk of cross-contamination. Mismatching of adsorber and patient can cause cross-contamination. Patient identification must be unambiguous and consistent over treatments.

Patient identification is used for the specific allocation and matching of a reusable adsorber to the patient in question either directly or via the patient chip card.

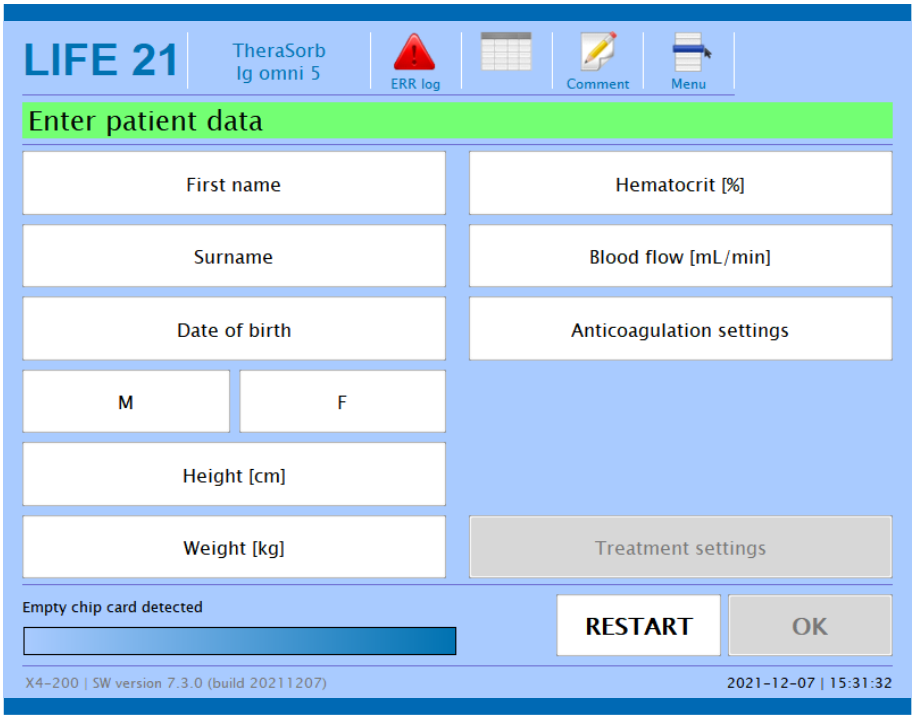
The entry of the sex of a patient designates the biological genetically determined sex and does not reflect gender preferences. The biological sex (female or male) is used for the calculation of the plasma volume of a patient, in combination with the age, height and weight of the patient. If a patient is a transsexual undergoing a sex change, the treating physician must determine the most adequate biological sex for the most correct determination of the plasma volume.

⚠ CAUTION

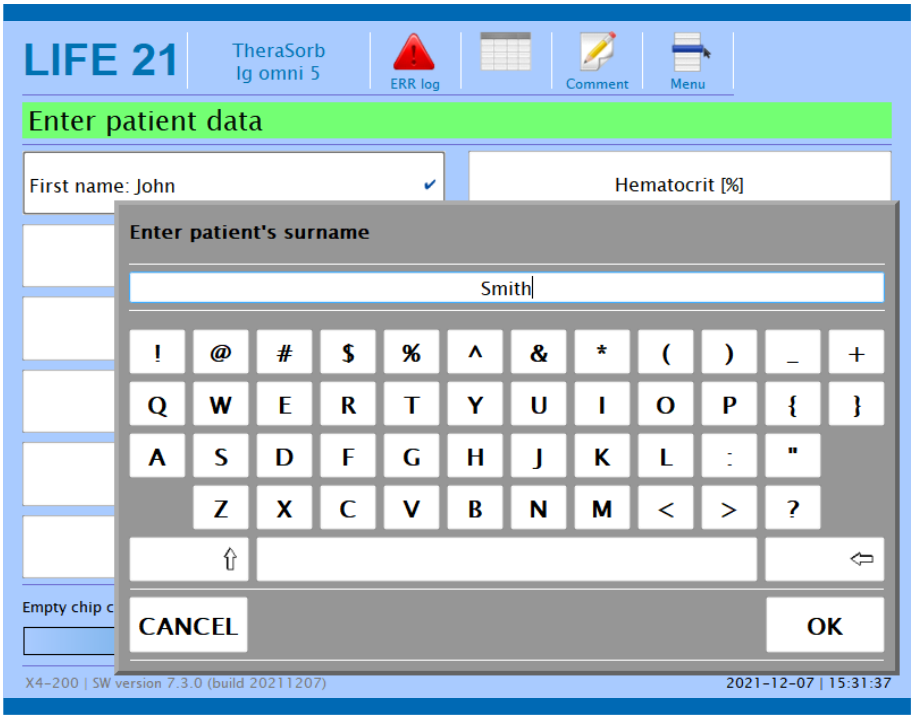
Incorrect entry of sex, weight, height, and age can cause erroneous calculation of the plasma volume of a patient. This can cause insufficient or excessive apheresis treatment with insufficient or excessive lowering of the target molecule(s).

IMPORTANT

In case of consecutive patient treatments, parameters from the patient chip card will be displayed on the screen automatically. Parameters to be confirmed or modified need to be entered as described above.



Screen 6.16: Entry of patient-relevant data (first treatment)



Screen 6.17: Representative data entry mask with an on-screen keyboard

Completed fields are displayed with a check mark (tick).

6.3.2 Anticoagulation settings

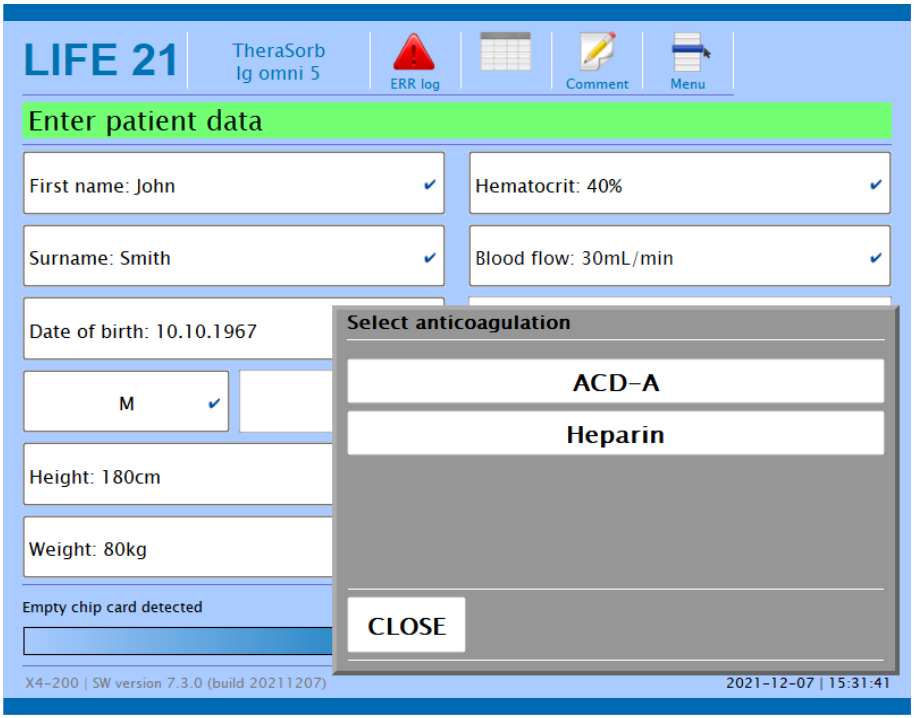
Operator action: After selecting the button **Anticoagulation settings** make sure that further options will be selected for anticoagulation (see Screen 6.18). Settings for ACD-A (see Screen 6.19 and Screen 6.20) or heparin (see Screen 6.21 and Screen 6.22) are required. ACD-A can be entered as the ratio of ACD-A to blood flow (e.g., 1:18) or in percentage to blood flow (e.g., 5%).

IMPORTANT

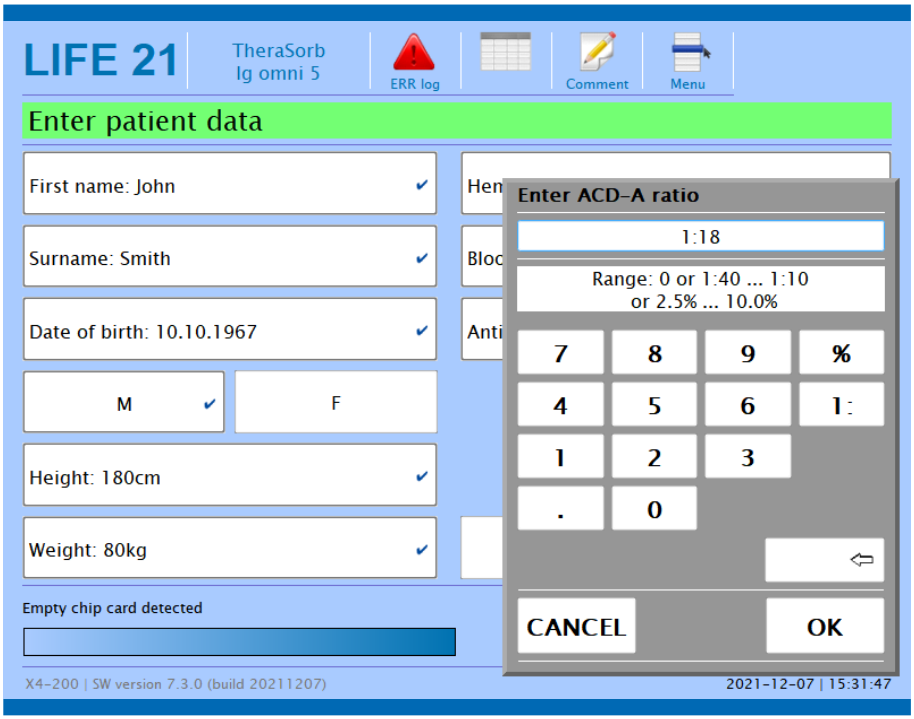
For the following treatments, a third button can be selected that shows automatically the anticoagulation setting of the last treatment (e.g., ACD-A 1:18).

⚠ WARNING

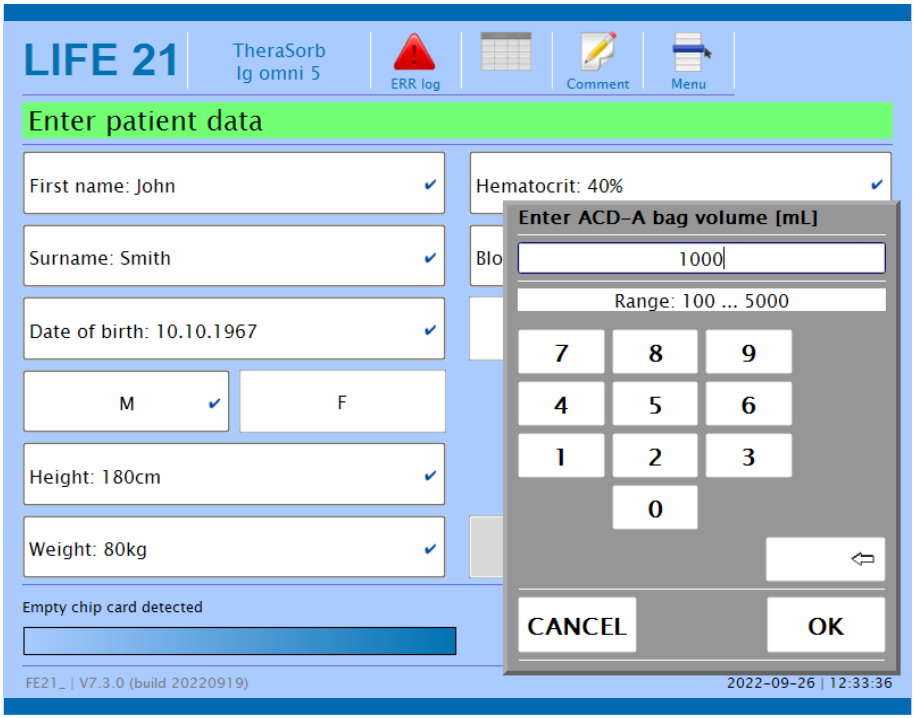
Risk of embolism, bleeding, or mineral imbalances. The instrument cannot monitor the connection of wrong or incorrectly concentrated anticoagulation solutions. Impaired anticoagulation in the extracorporeal fluid path may cause bleeding or mineral imbalances and embolism caused by extracorporeal blood clotting. It is essential to read the recommendations for anticoagulation settings given in the user manual "Warnings, precautions and troubleshooting". If the patient experiences symptoms of hypocalcaemia (a risk if ACD-A is administered) countermeasures have to be taken (e.g., calcium administration). The patient must be informed about symptoms of physiological reactions to citrate.



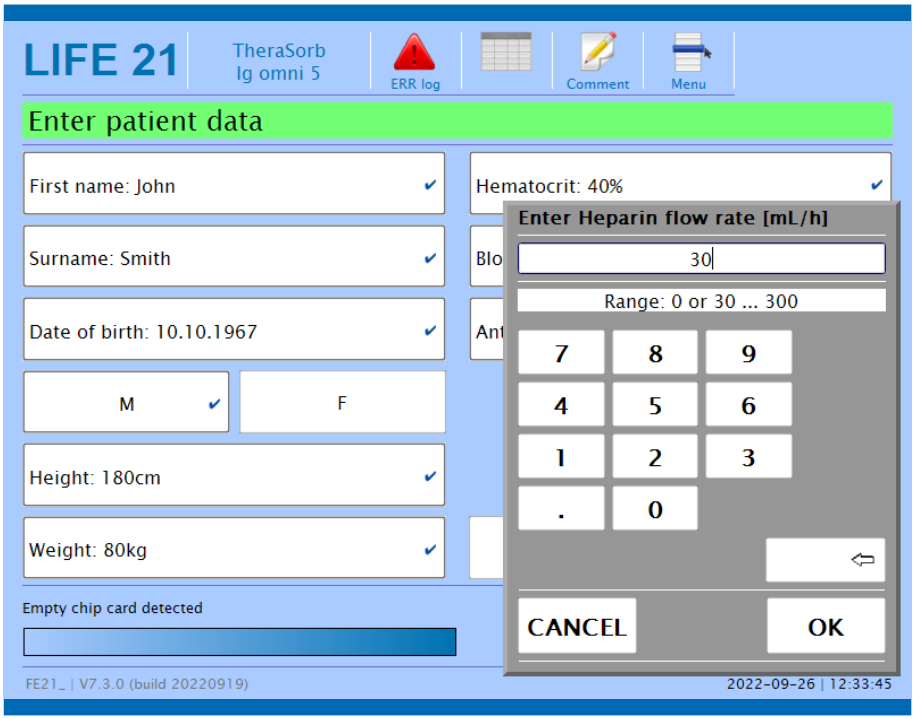
Screen 6.18: Anticoagulation settings



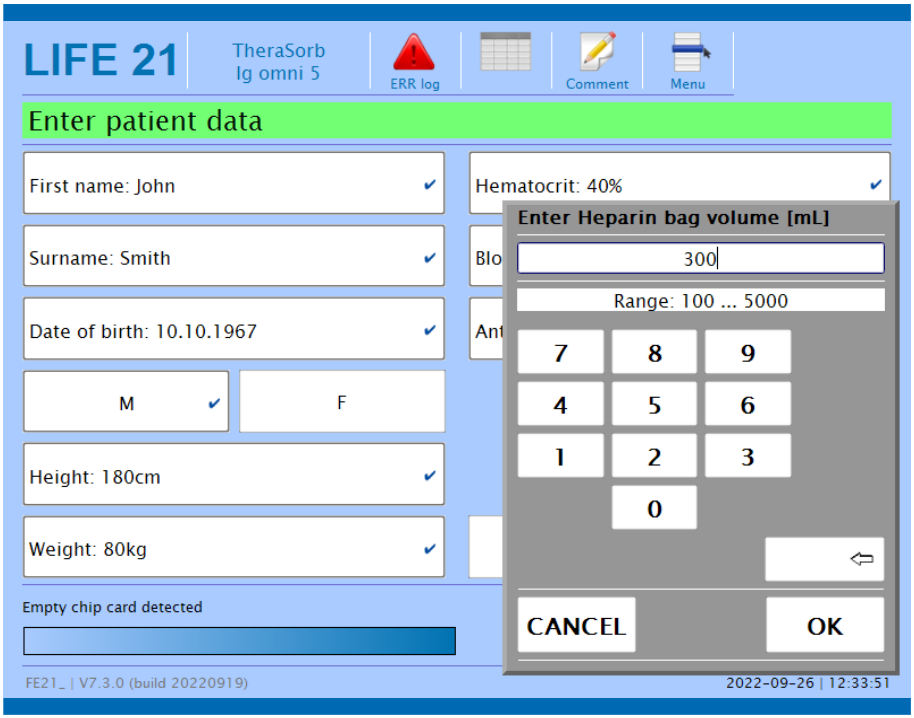
Screen 6.19: Ratio ACD-A to blood flow



Screen 6.20: ACD-A bag volume

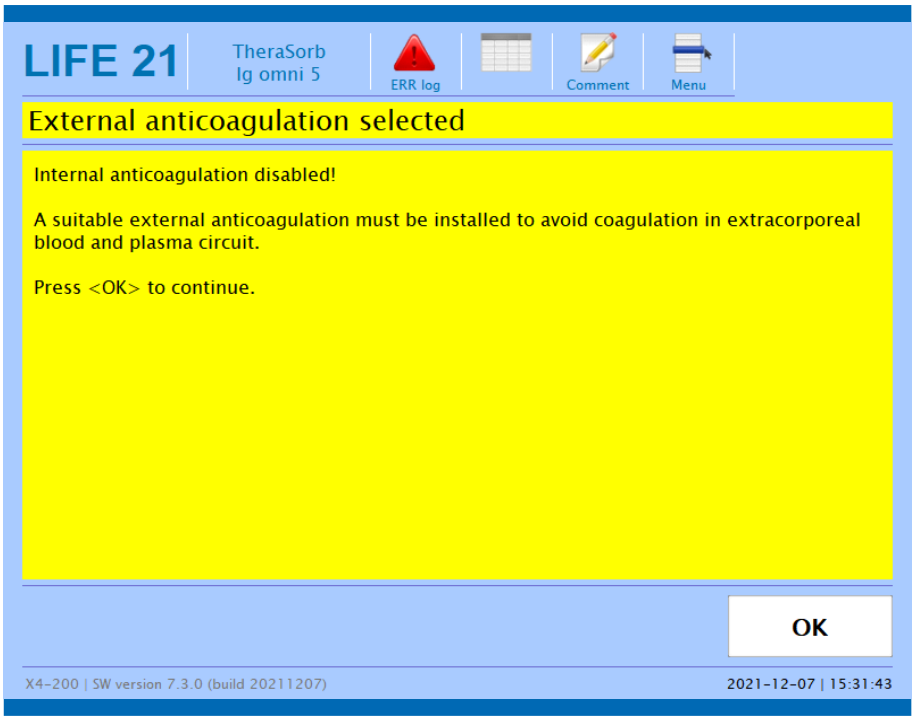


Screen 6.21: Heparin settings - flow rate



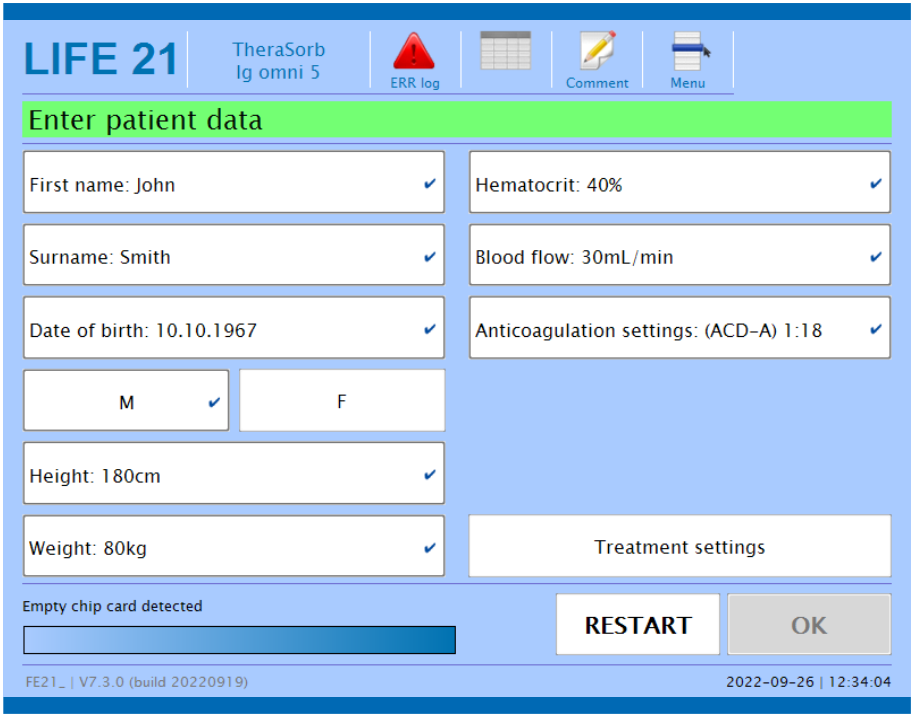
Screen 6.22: Heparin bag volume

Operator action: If the anticoagulation setting for ACD-A or heparin was set to zero follow the instruction below (see Screen 6.23).



Screen 6.23: Connection of external antigoagulation needed

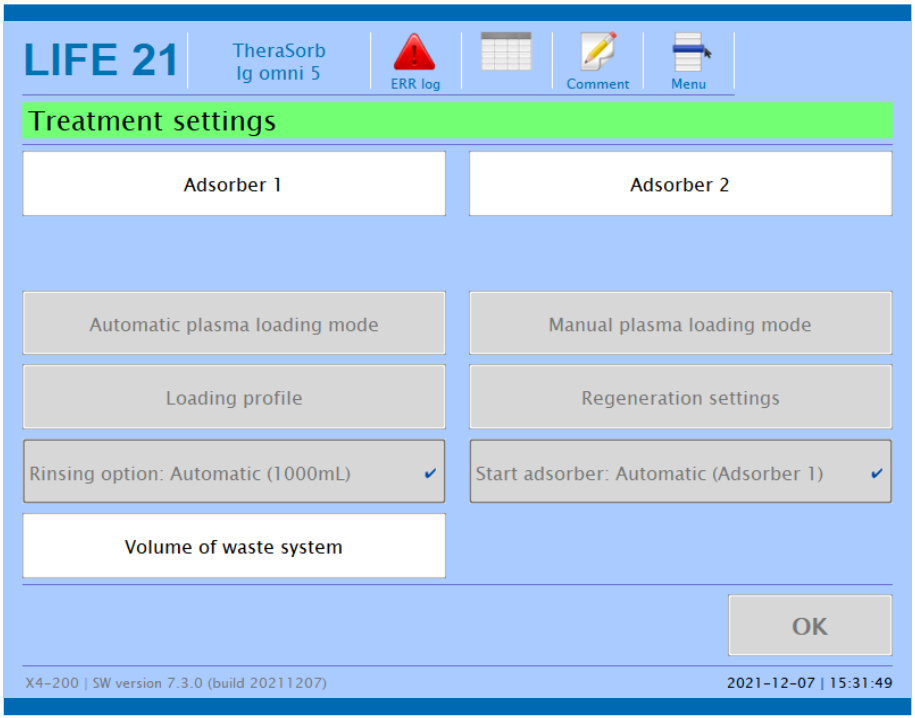
After completion of the anticoagulation settings a summary of the patient data is shown (see Screen 6.24).



Screen 6.24: Patient data set completed

6.3.3 Treatment settings

Operator action: After selecting the button **Treatment settings** all treatment-relevant parameters must be entered by the operator (see Screen 6.25).



Screen 6.25: Treatment settings screen

Fields that need data entry are displayed with a white background, completed fields are displayed with a check mark and still inactive fields are displayed with a grey background.

A summary and explanation of each button displayed on the treatment-setting screen can be found in Table 6.2.

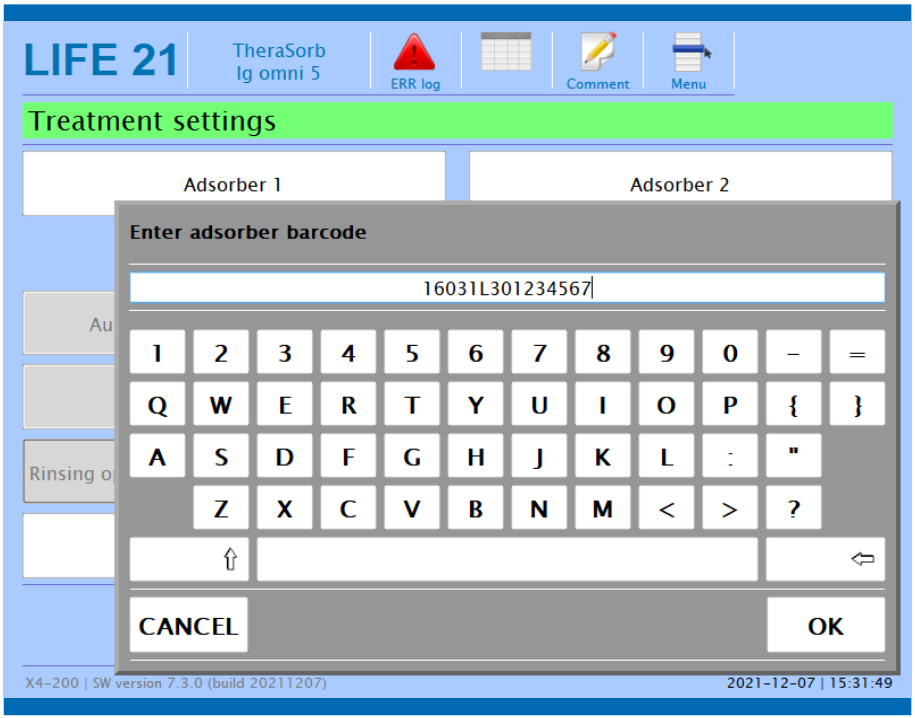
Display element	Function
Adsorber 1	The bar code of adsorber 1 has to be scanned with the barcode scanner. Only in case of malfunction enter the barcode manually.
Adsorber 2	The bar code of adsorber 2 has to be scanned with the barcode scanner. Only in case of malfunction enter the barcode manually.
Automatic plasma loading mode	Optimal plasma loading of the adsorber pair in each cycle and blood/plasma processing speed will be calculated and adjusted automatically by the instrument. This is the recommended option in most treatments.
Manual plasma loading mode	Plasma loading of the adsorber pair in each cycle and blood/plasma processing speed can be entered manually by the operator.
Loading profile	Only active in manual plasma loading mode. The plasma loading volume in each cycle can be entered manually.
Regeneration settings	Only active in manual plasma loading mode. The volume of the regeneration solutions can be changed within a defined range given by the instrument.
Rinsing option: automatic (1,000 mL)	Default setting for the rinsing of the adsorber pair is 1,000 mL before treatment. Different options can be selected.
Start adsorber: Automatic (Adsorber 1)	First plasma loading on adsorber 1.
Volume of waste system	Handling of the waste has to be entered. The three options are: 10,000 mL = standard bag, Central = connection to central waste system or Custom setting = free input of bag volume, range 100…10,000 mL

Table 6.2: Function of elements displayed on treatment settings screen

IMPORTANT

Refer to the recommendations of the treating physician regarding the chosen treatment settings for the patient, and all related parameters.

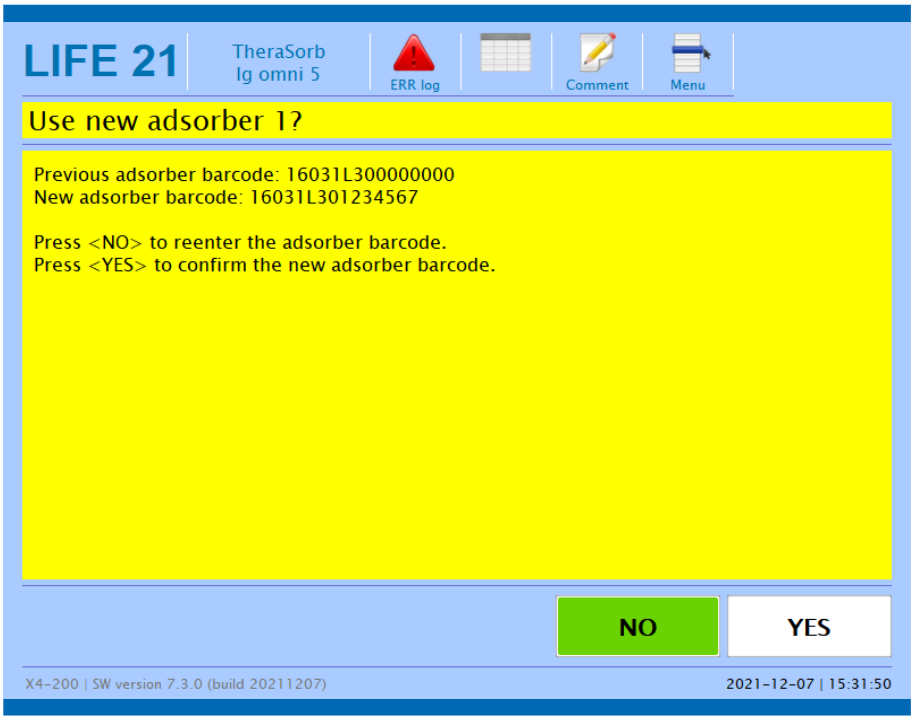
Operator action: After selecting the field **Adsorber 1** (see Screen 6.26) the operator can either scan the barcode on the bottom of the adsorber housing or enter the 15- digit adsorber code manually. Repeat the steps for the second adsorber and press **OK** to continue.



Screen 6.26: Entry of adsorber barcode

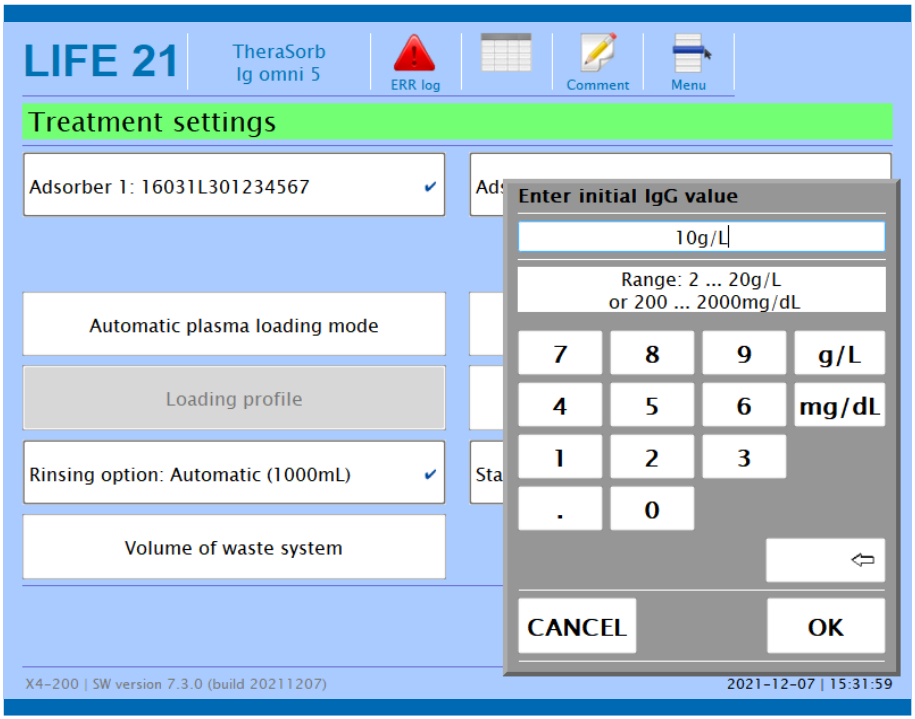
IMPORTANT

For consecutive treatments Screen 6.27 will be displayed when an existing adsorber must be replaced by a new adsorber.



Screen 6.27: Request to confirm new adsorber

Operator action: Select **Automatic plasma loading mode** and enter the initial target molecule concentration (see Screen 6.28). Press **OK** to continue and the Ig removal graph will be displayed (see Screen 6.29).



Screen 6.28: Entry of initial target molecule concentration (IgG)

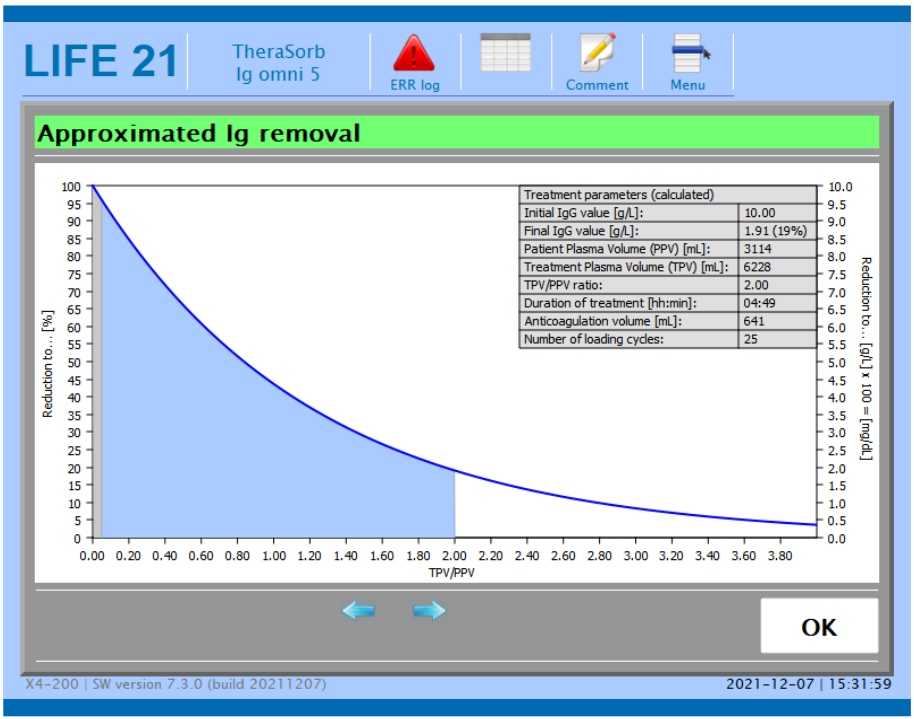
Operator action:

- Set plasma volume to be treated by using the arrow-buttons ⬅ ➡ or set the plasma volume by touching the curve at the desired reduction level.
- Press **OK** to continue.

In automatic treatment mode, the software requires the target molecule concentration IgG for elemination calculation of optimal adsorber loading and optimal plasma flow. See details on specific parameters for the TheraSorb - Ig omni 5 adsorber or other adsorber types in the adsorber-related package insert.

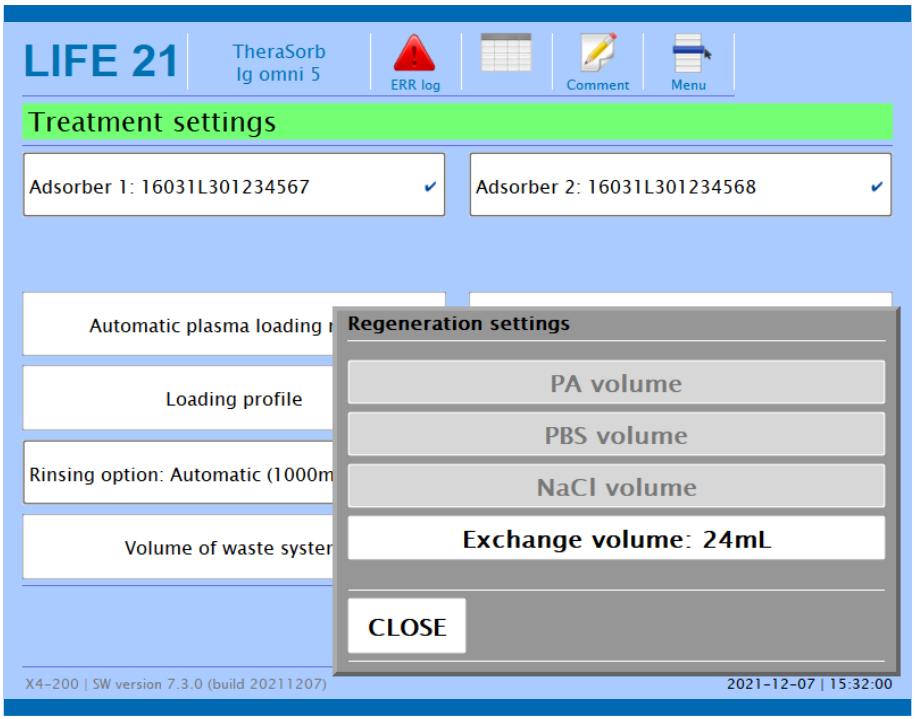
IMPORTANT

In order to check the success of the treatment, target molecule concentration in plasma or serum should be measured before and after each treatment session.



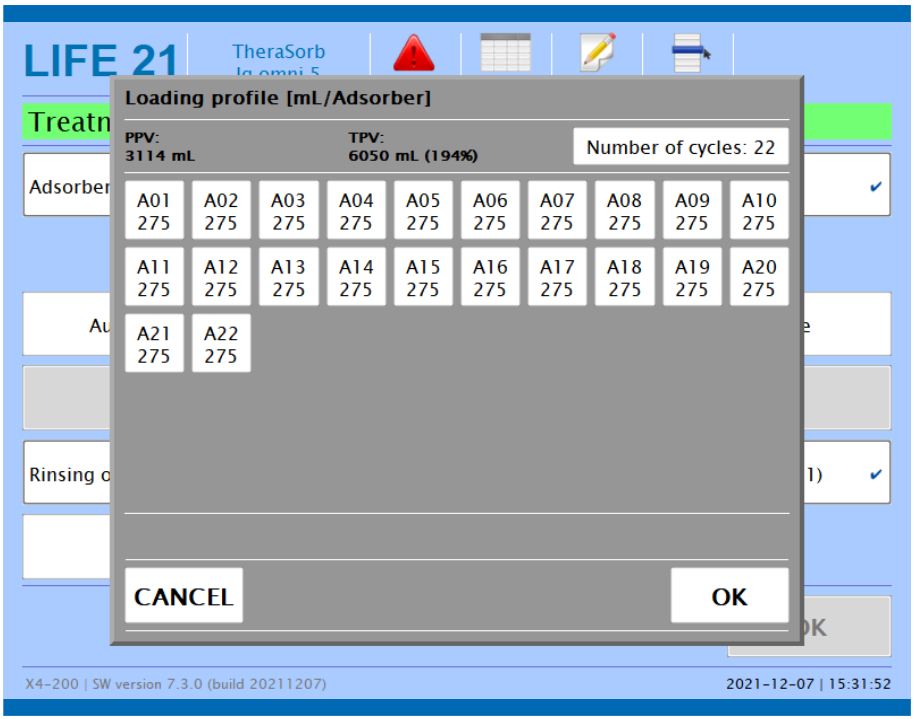
Screen 6.29: Removal graph with different treatment parameters

In the automatic plasma loading mode the loading profile and regeneration settings are preset. Only the exchange volume can be adjusted (see Screen 6.30).



Screen 6.30: Adjustment of the exchange volume in the automatic plasma loading mode

Optional operator action: Select **Manual plasma loading mode** to open the loading profile summary (see Screen 6.31).

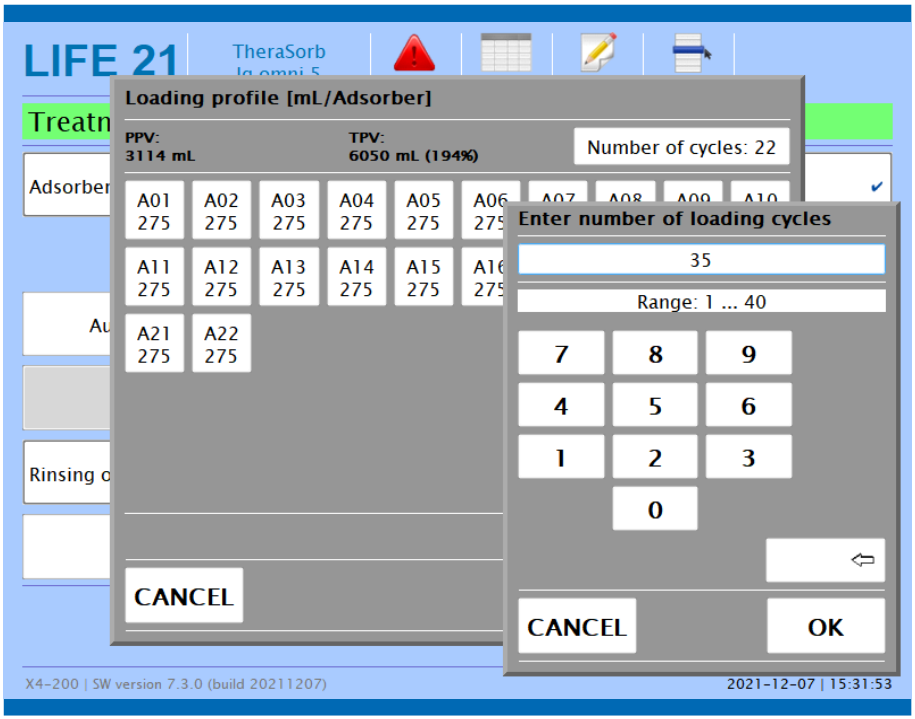


Screen 6.31: Loading profile summary

The parameters are displayed:

- **PPV:** Patient plasma volume (calculated)
- **TPV:** Treated plasma volume = plasma volume to be processed
- **A01–A60:** Cycles and corresponding loading volumes in mL

Operator action: Select **Number of cycles** and enter the number of loading cycles (see Screen 6.32). Press **OK** to return to previous screen with the updated number of cycles for the manual mode.

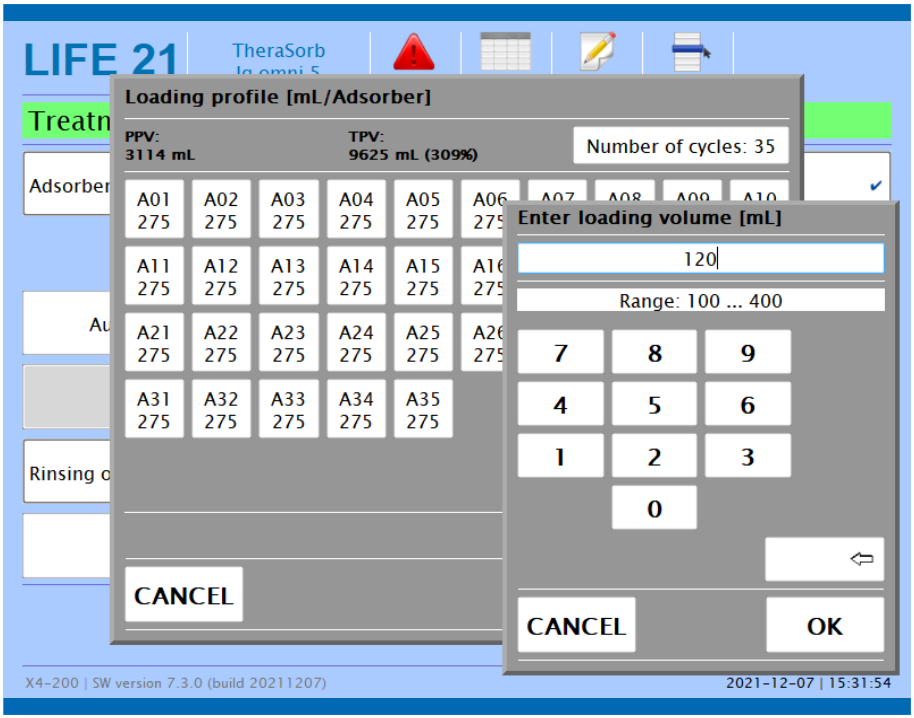


Screen 6.32: Entry of loading cycles

Operator action: To change the plasma loading per cycle in the manual mode (see Screen 6.33):

- Select the relevant button (e.g., A01 for the first cycle).
- Enter the desired plasma loading of this cycle.
- Press OK to confirm the value.

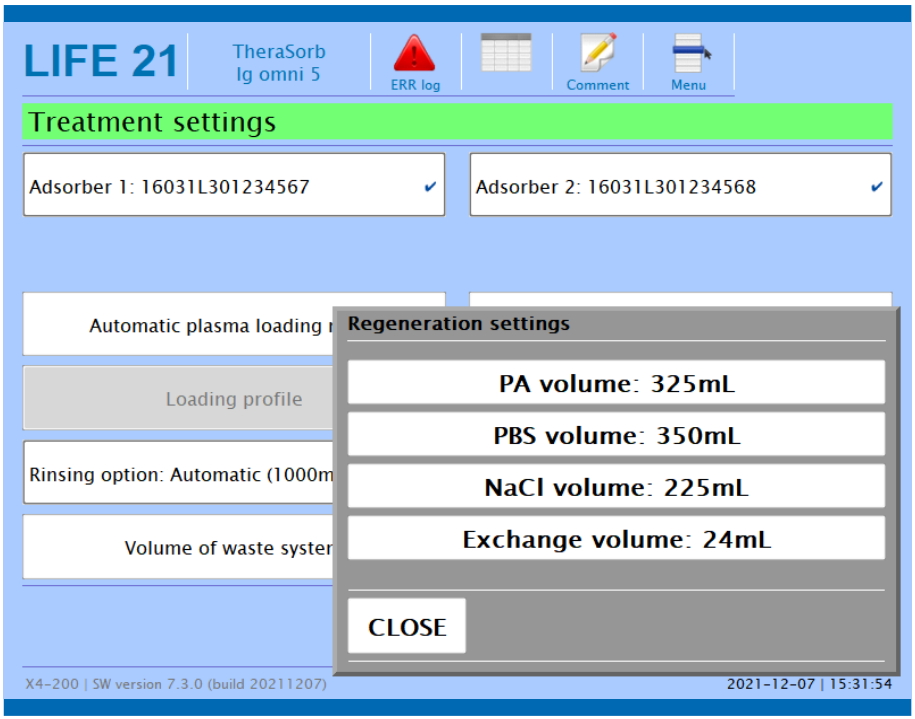
All subsequent cycles will be displayed with the new loading volume.



Screen 6.33: Change of plasma loading volume

Operator action: Press OK to get back to the Screen 6.25 "Treatment settings screen".

Operator action: Select **Regeneration settings** to proceed to the regeneration settings in the manual mode (see Screen 6.34).

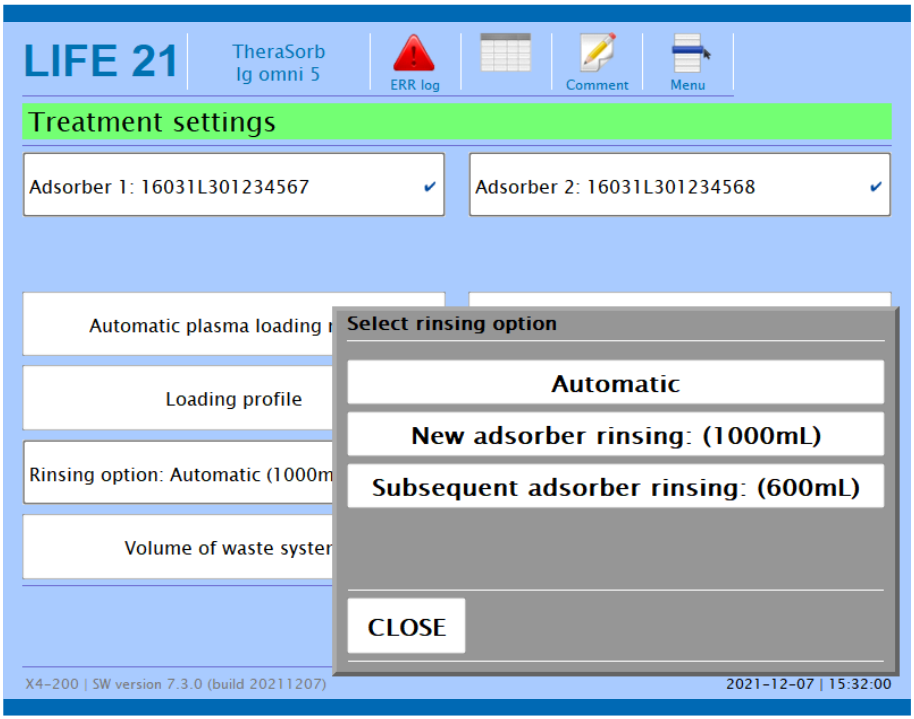


Screen 6.34: Regeneration settings with default values

Operator action: Confirm the preset rinsing volumes by pressing **CLOSE**.

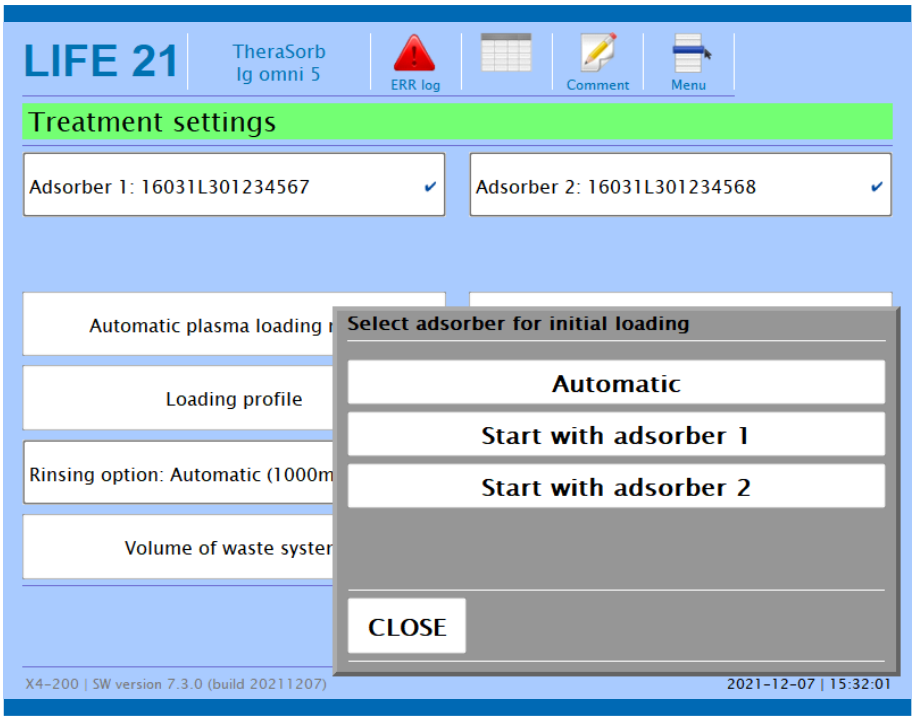
Individual volumes can be adjusted in the manual mode by selecting the respective button.

Optional operator action: Select **Rinsing option: Automatic (1000 mL)** to change the default by choosing another option displayed (see Screen 6.35). To continue press **OK**.



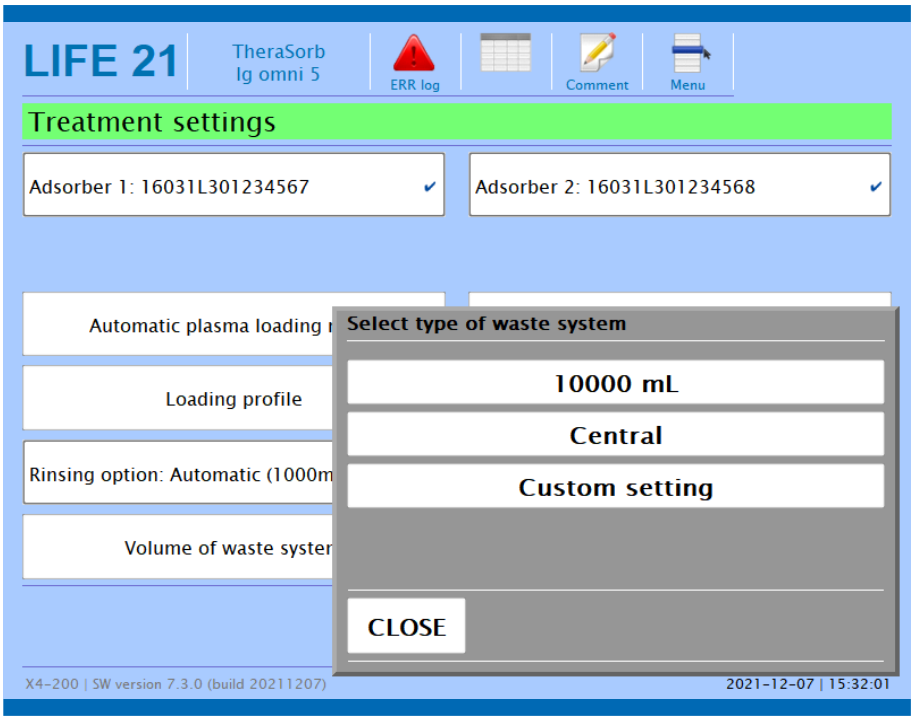
Screen 6.35: Rinsing volume screen

Optional operator action: Select **Start adsorber: Automatic (Adsorber 1)** to change the default by choosing another option displayed (see Screen 6.36).



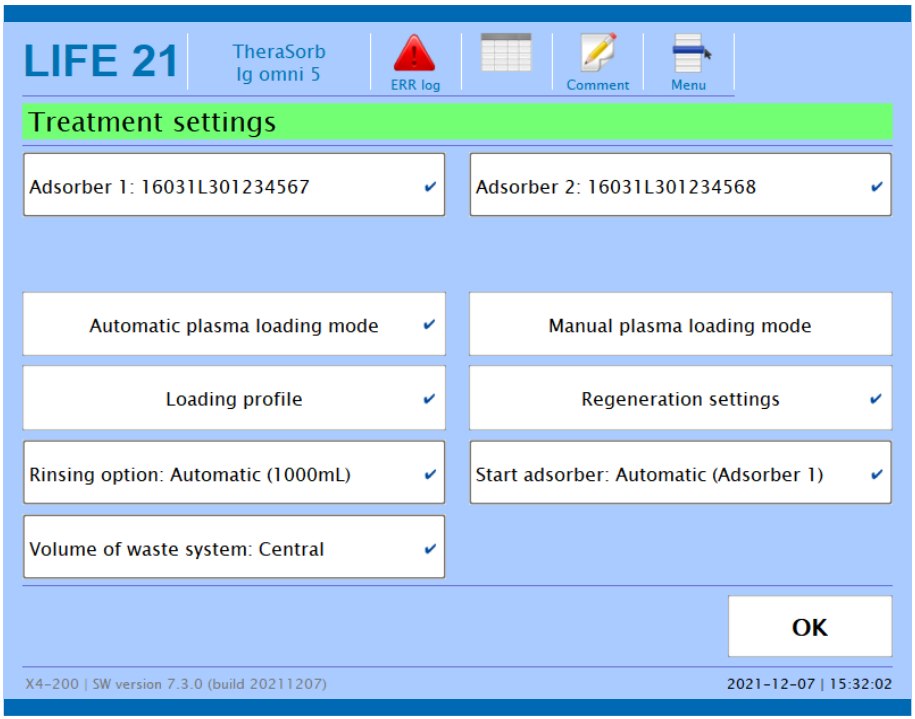
Screen 6.36: Select adsorber for initial loading

Operator action: Press **Volume of waste system** to select one of the options (see Screen 6.37).



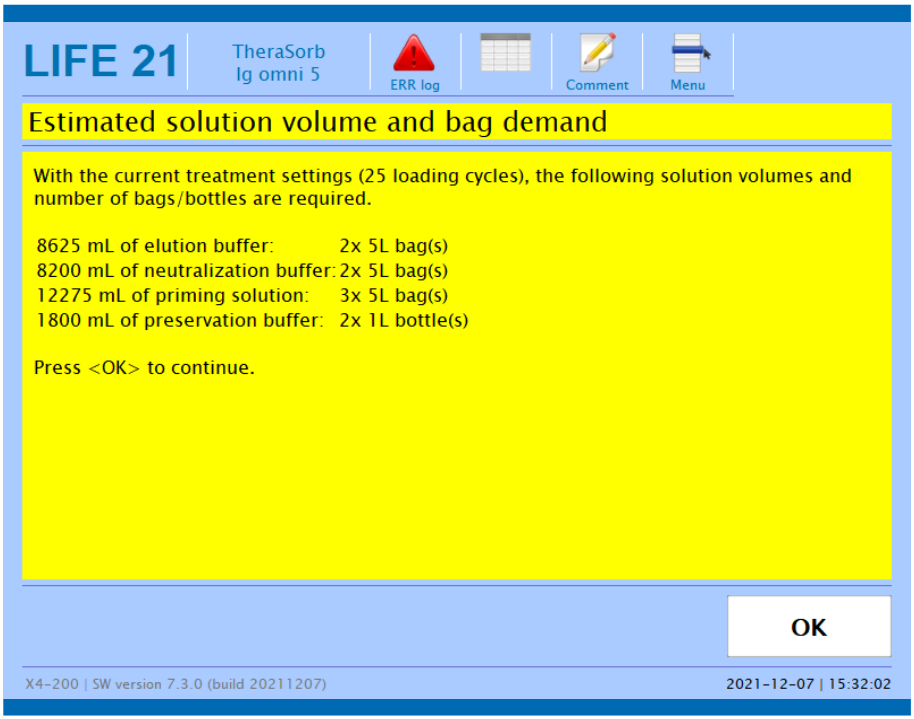
Screen 6.37: Waste bag volume screen

After pressing OK the summary screen for the treatment settings is displayed (see Screen 6.38). Check all entries for correctness.



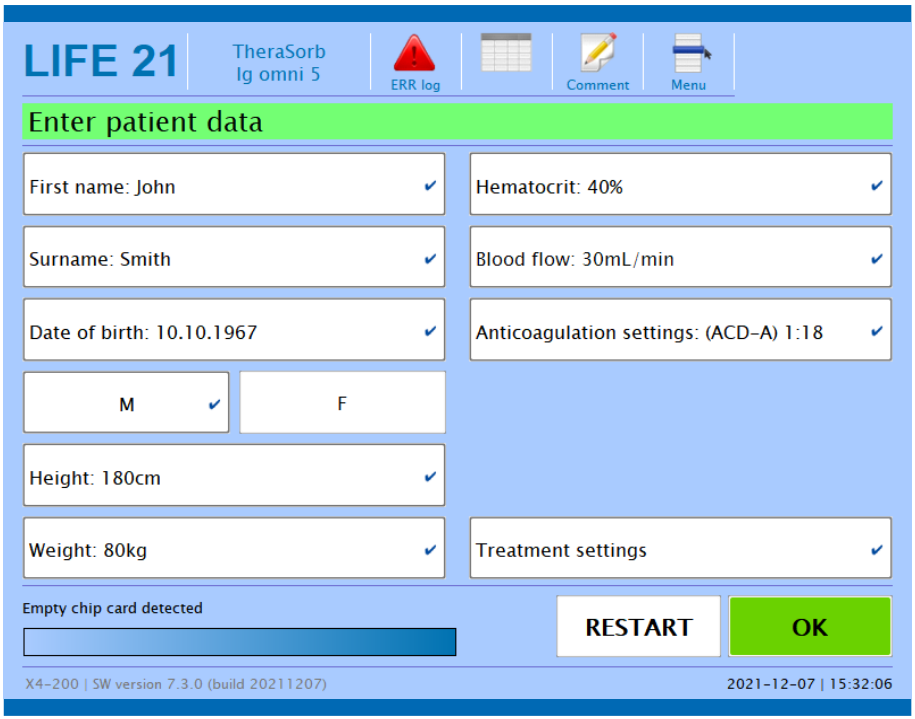
Screen 6.38: Summary of all treatment settings in automatic mode

Operator action: Press **OK** to continue. A summary screen is displayed showing the required solution volumes and bag demands for the current treatment settings (see Screen 6.39). Press **OK** to continue.



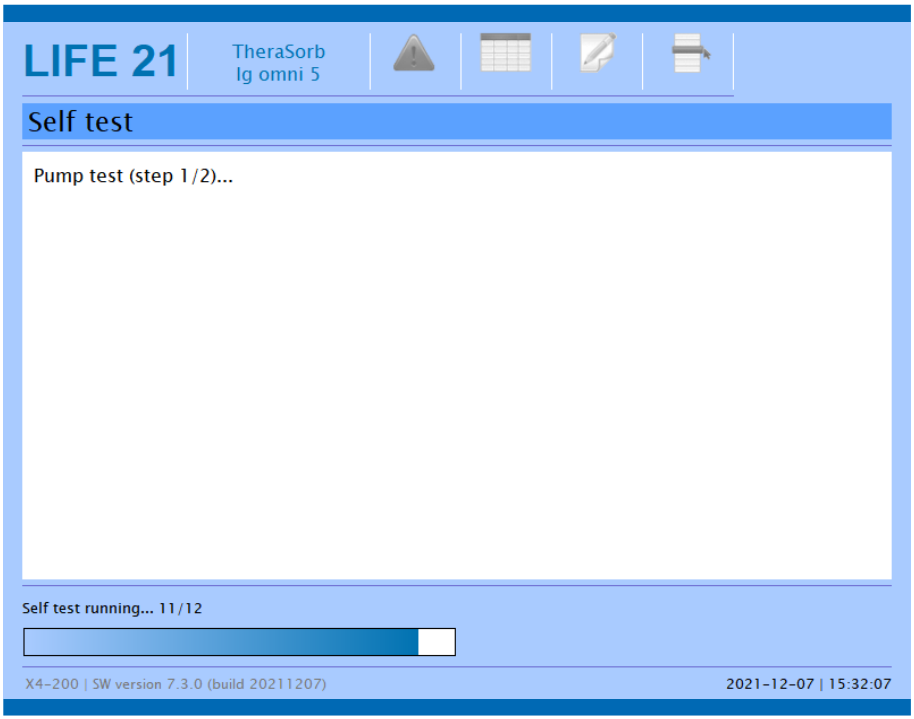
Screen 6.39: Estimated solution volume and bag demand for current treatment settings

Operator action: Press **OK** to continue and the completed patient data screen is displayed (see Screen 6.40). Check entries for correctness.



Screen 6.40: Completed data set

Operator action: Press **OK** to continue. All treatment and patient relevant settings will be transferred to the patient chip card and the instrument starts internal tests (see Screen 6.41).



Screen 6.41: Representative status screen for self tests

NOTICE

Risk of data loss or data corruption. Incorrect insertion or removal of chip card may lead to data loss or data corruption. Do not remove the chip card unless prompted by the instrument.

6.4 Tubing set installation – Part 2

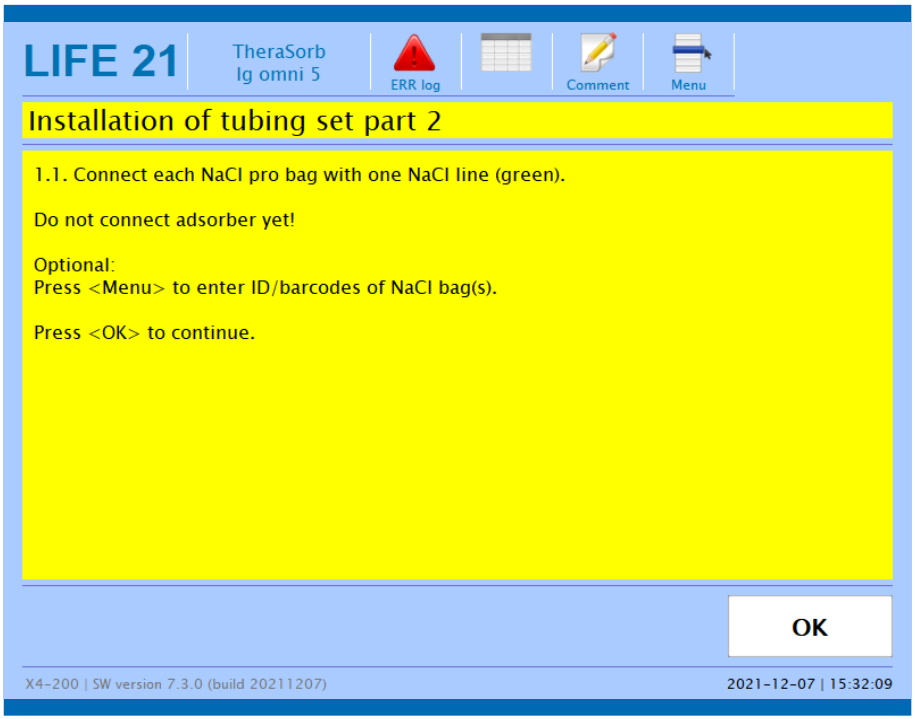
The following section guides the operator through the tubing set installation – Part 2. Connection of solutions as well as the connection of the adsorber pair and the patient to the tubing set are described.

⚠ WARNING

Risk of infection. Loss of sterility and microbial contamination may result in the risk of infection of a patient. Observe adequate hygienic measures for aseptic handling for all preparative steps.

6.4.1 Connecting the solutions

Operator action: Follow the instructions for the connection of the TheraSorb - NaCl pro priming solution bags (see Screen 6.42). Press **OK** to continue and to start the priming solution suction test.

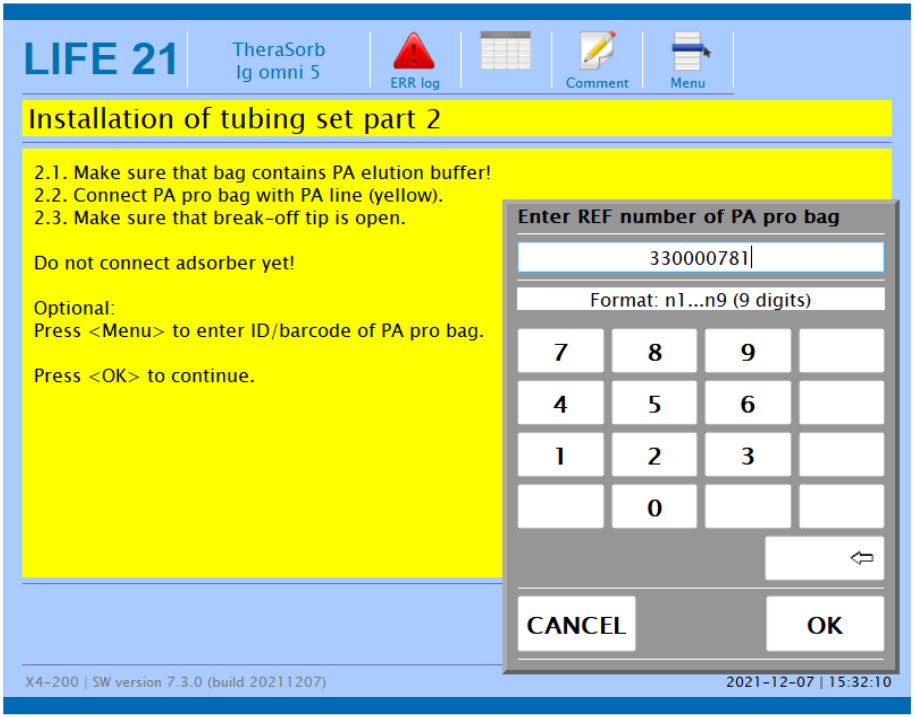


Screen 6.42: Connection of the priming solution bags

Operator action: Follow the instructions for the connection of the TheraSorb - PA pro elution buffer bag (see Screen 6.43). Enter the REF number of the elution buffer and press **OK** to continue.
The REF number can be found on the bag imprint and must be entered without hyphens as a 9-digit numeric value. Press **OK** to start the elution buffer suction test.

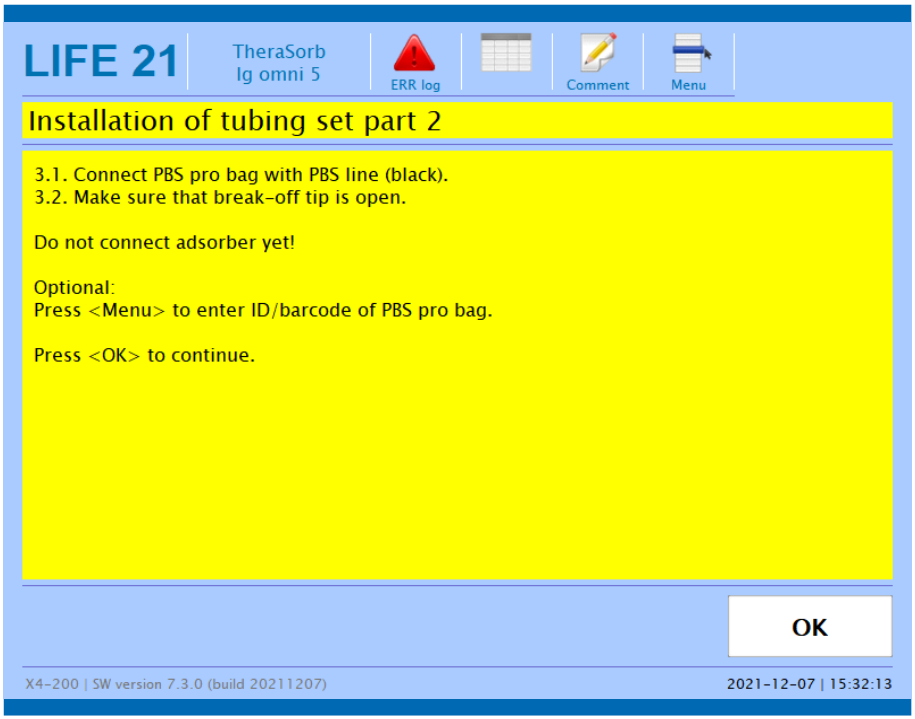
⚠ CAUTION

Risk of metabolic acidosis, hyperphosphatemia, adverse immune immune reactions and incomplete apheresis. Connection of a wrong or unauthorized solution can not be detected by the instrument and may cause insufficient regeneration of the adsorber pair. Do not connect any wrong or unauthorized solution.



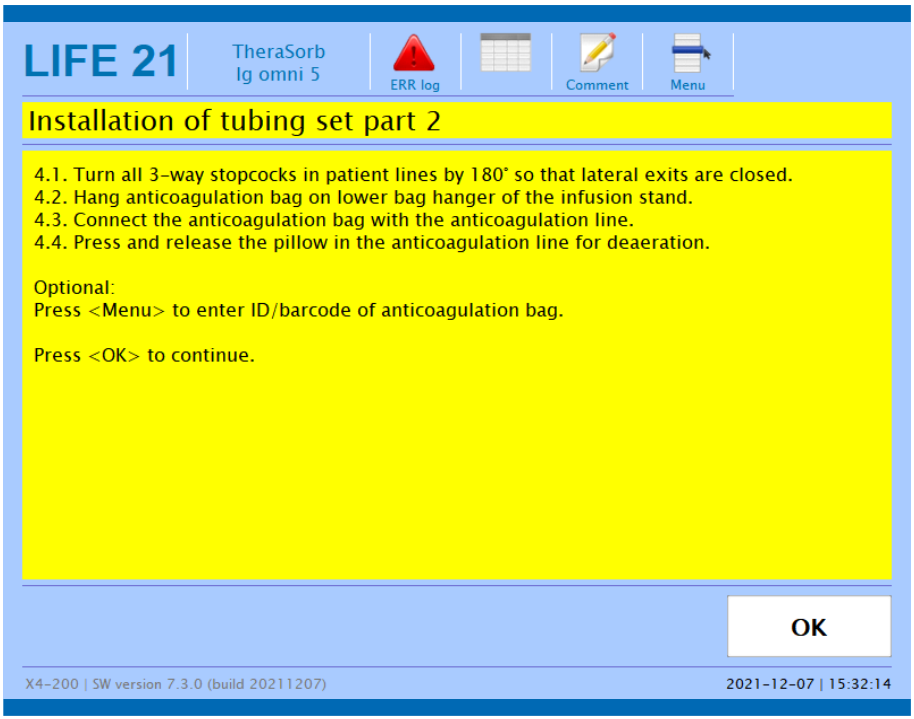
Screen 6.43: Connection of the elution buffer bag

Operator action: Follow the instructions for the connection of the TheraSorb - PBS pro neutralization buffer bag (see Screen 6.44). Press **OK** to continue and to start the neutralization buffer suction test.



Screen 6.44: Connection of neutralization buffer bag

Operator action: Follow the instructions (see Screen 6.45) and press **OK** to start the suction test for the anticoagulant followed by the priming procedure.



Screen 6.45: Instruction screen on patient line and connection of anticoagulation bag

Figure 6.12 shows the correct position of the 3-way stopcocks after turning. The lateral exit of the blood withdrawal line can be used, for example, as a heparin or calcium infusion line. The injection ports are solely for sampling (for instance, to monitor the albumin concentration) during the treatment.

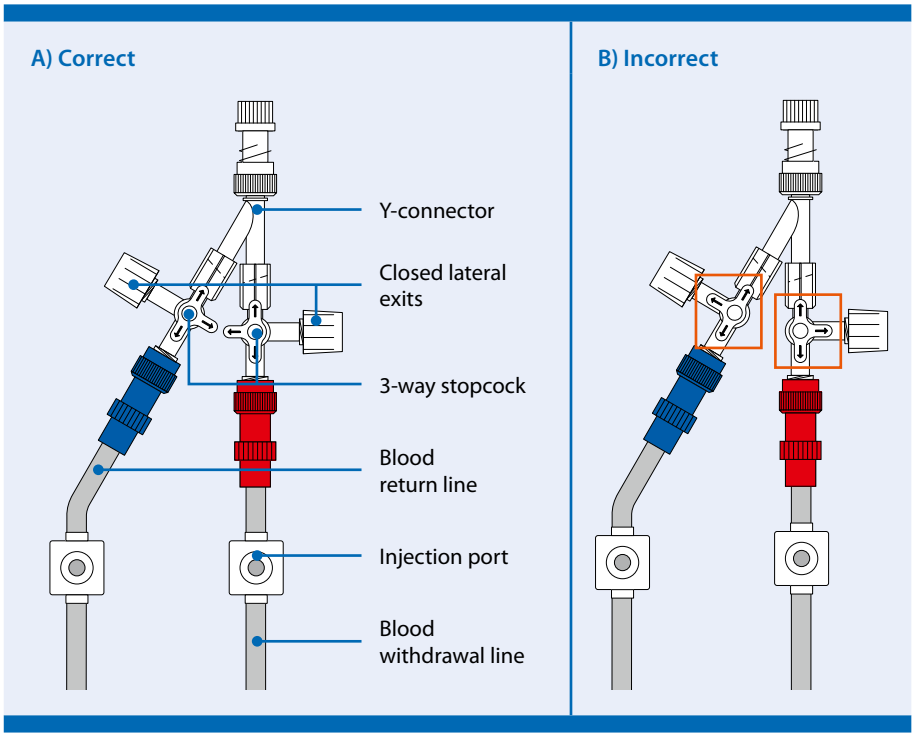
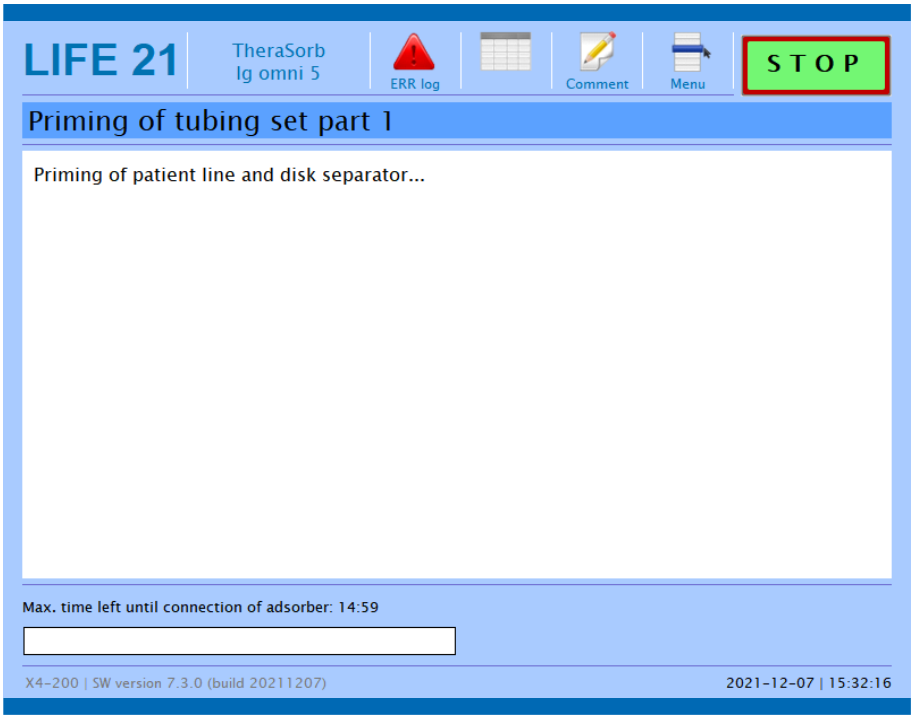


Figure 6.12: Correct position of the 3-way stopcocks in patient line

The instrument performs different tests and a status screen informs about the remaining time until continuation (see Screen 6.46).

- suction test anticoagulant
- priming of single-needle chambers
- priming of patient line, separator and tubing set
- test of external pressure sensors
- pressure test part 2 and 3
- pump calibration

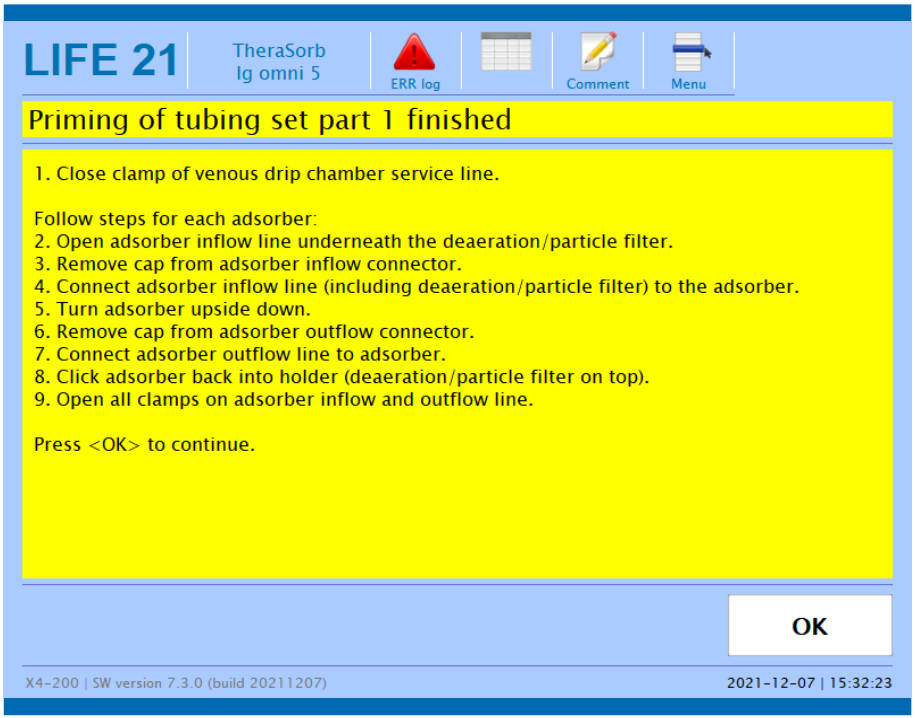


Screen 6.46: Priming of tubing set and self-tests

After successful completion of the tubing set deaeration, the Screen 6.47 is displayed describing the connection of the adsorber pair to the tubing set.

6.4.2 Connecting the adsorber pair

Operator action: Follow the instructions and press **OK** to continue (see Screen 6.47).



Screen 6.47: Connection of the adsorber pair

The venous drip chamber with the service line is located above the air detector. Each adsorber has to be connected underneath the deaeration/particle filter (see Figure 6.13).

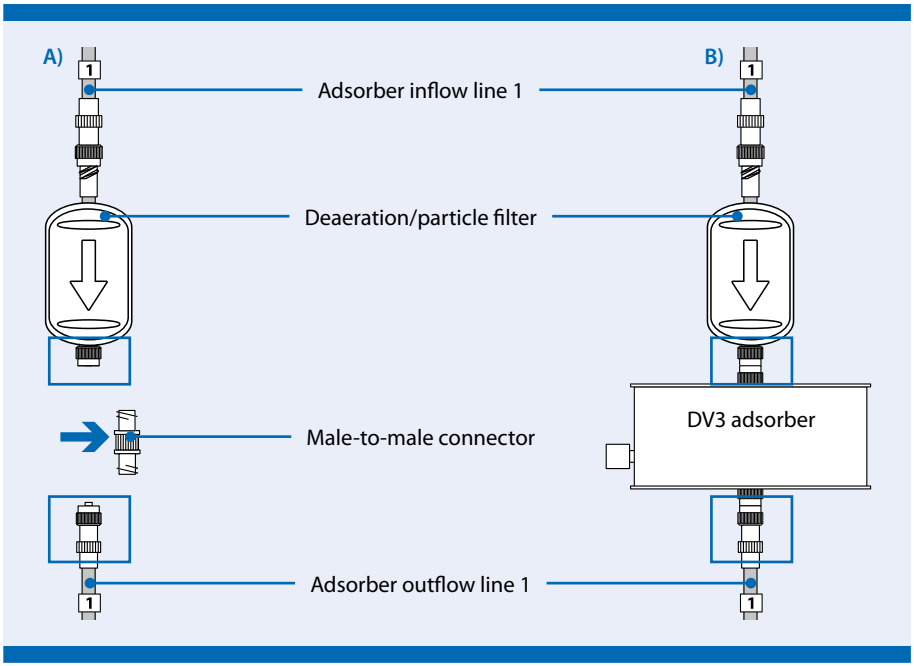


Figure 6.13: Example, connection of a DV3 adsorber with adsorber inflow and outflow line 1

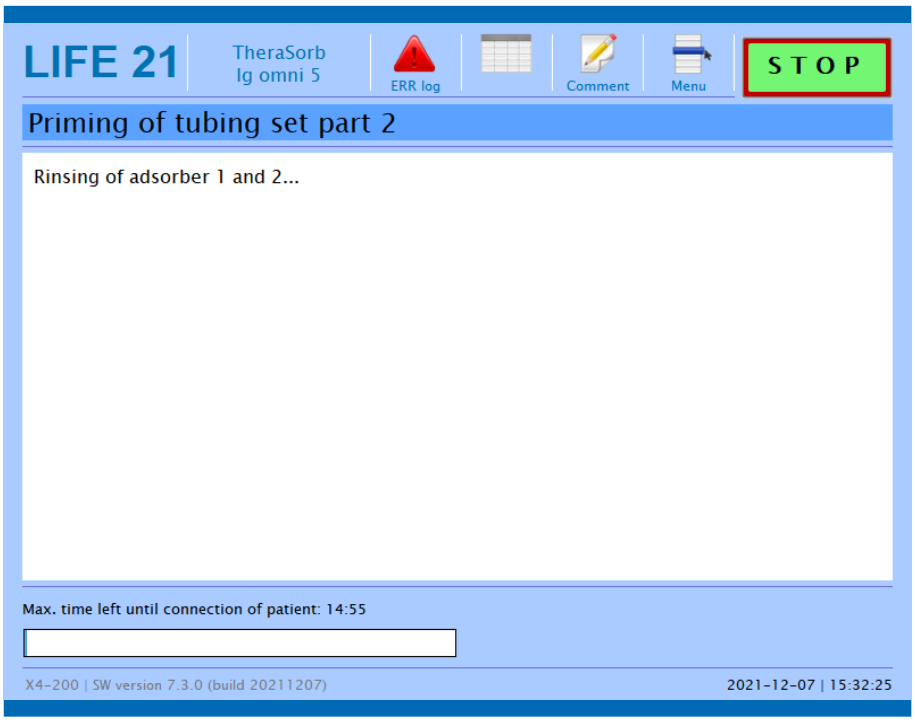
IMPORTANT

If you plan to take samples for sterility tests and/or pH control later on in the treatment phase, insert a sterile 3-way stopcock below each adsorber (between outflow connector and outflow line).

⚠ WARNING

Risk of blood or plasma loss. Untight connections may result in microbial contamination and infection or leakage of the extracorporeal fluid path with the risk of blood or plasma loss. Make sure that the adsorber pair is correctly connected.

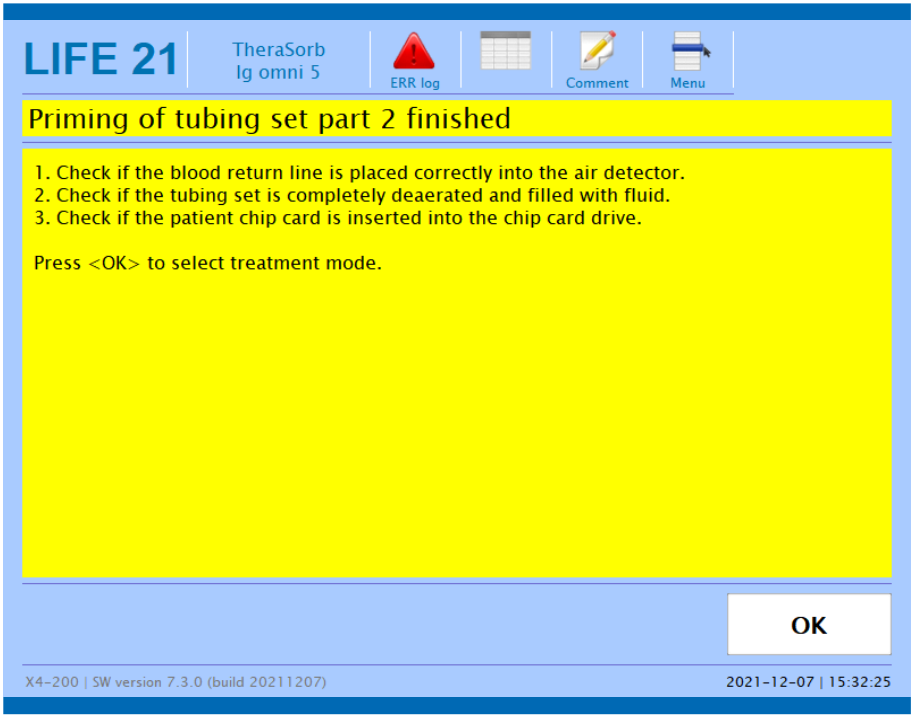
The instrument rinses the adsorber pair and performs final tests. Make sure that the clamp in the service line of the venous drip chamber located in the blood return line is closed. A status screen displays the time remaining for the final tests before the patient can be connected to the tubing set (see Screen 6.48).



Screen 6.48: Status screen for adsorber tests

6.5 Connecting the patient

Operator action: Follow the instructions and press **OK** to continue (see Screen 6.49).



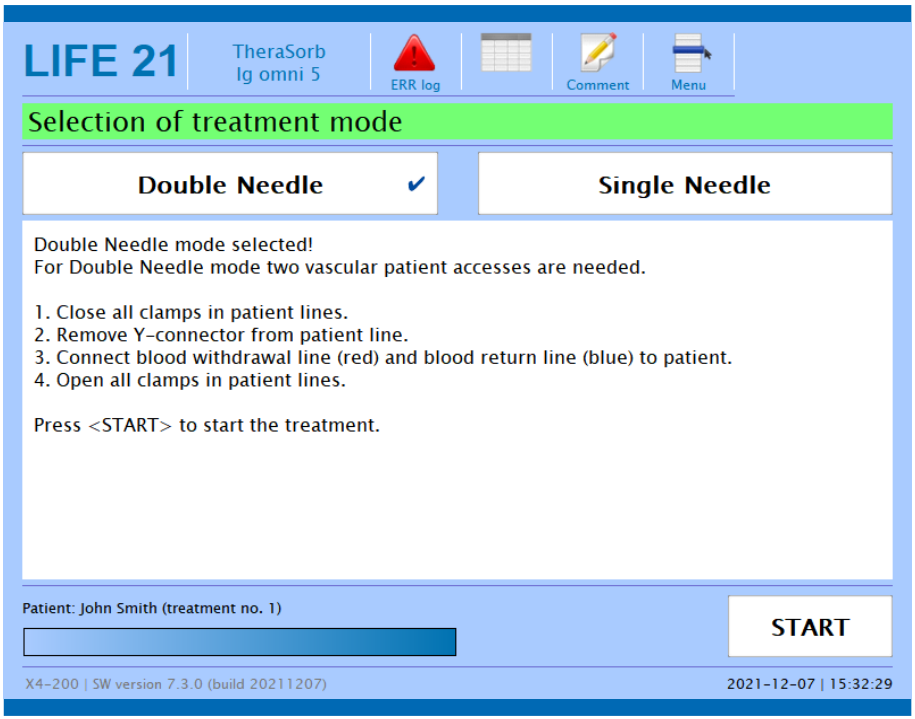
Screen 6.49: Last check points before patient connection

Operator action: The operator has to choose between Double Needle or Single Needle mode to connect the patient to the tubing set.
Select **Double Needle** (see Screen 6.50) or **Single Needle** (see Screen 6.51) and follow the instructions.

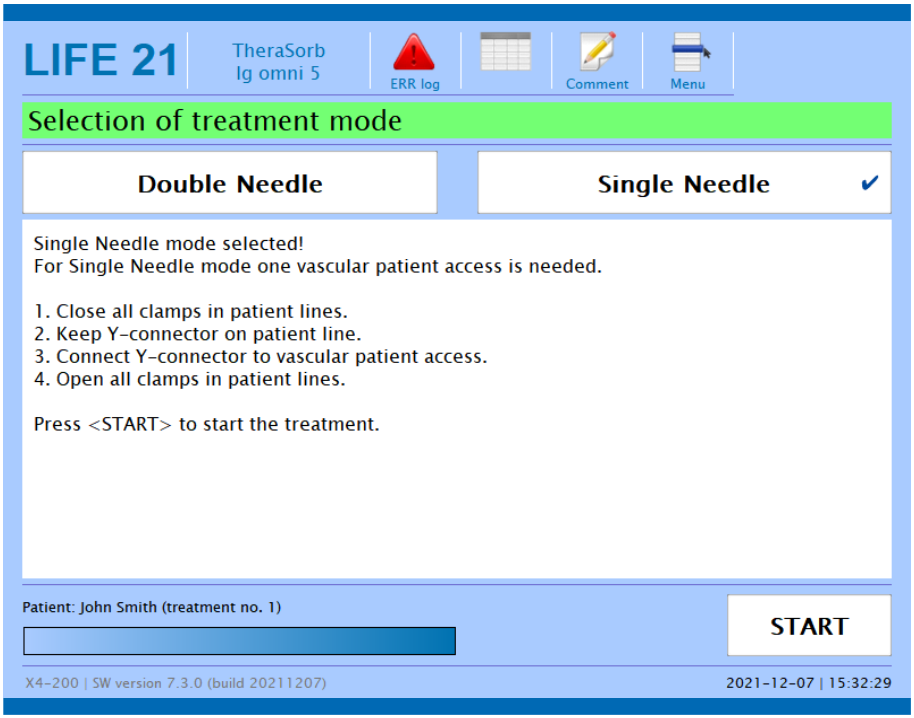
In case of the Double Needle mode, two independent venous accesses have to be established for the patient, and the Y-connector of the patient line needs to be removed above the 3-way stopcock (see Figure 6.12 "Correct position of the 3-way stopcocks in patient line").

⚠ CAUTION

Risk of vascular damage. Dislocation of the needles can lead to vasular damage. Patient access must be carefully monitored in order to avoid dislocation of the needles. To avoid inflammation and sclerotization of punctured veins, inject heparin bolus into the venous access, if required.



Screen 6.50: Instructions for Double Needle mode



Screen 6.51: Instructions for Single Needle mode

Operator action: Press START to start the treatment.

In case the treatment of the patient cannot be performed the adsorber pair can be preserved by pressing MENU and Cancel treatment (reinfusion).

⚠ CAUTION

Risk of bleeding or mineral imbalances and extracorporeal blood clotting. Impaired anticoagulation in the extracorporeal fluid path may cause bleeding or mineral imbalances and extracorporeal blood clotting. Do not administer any other medication via the tubing set because of the risk of an interaction with the anticoagulant! The access points in the tubing set are to be used solely for sampling (for instance, to monitor the albumin concentration) during the treatment.

7

Treatment run

This chapter describes how the operator can adjust or change parameters during the treatment. The automated process is divided into the following steps:

- Starting the blood withdrawal with default blood flow value.
- Filling of extracorporeal blood circuit (patient lines and disk separator) with blood, reinfusion of priming solution from disk separator into the patient (no plasma separation).
- Begin of plasma separation after complete filling of the disk separator with blood.
- Separated plasma directed to the adsorber (see Table 7.1).
- Priming solution from the adsorber is directed to the waste.
- Reinfusion of the depleted plasma back to the patient together with the blood cell concentrate from the disk separator.

⚠ CAUTION

Risk of vascular damage. Complications – including but not limited to the dislocation of the venous access – can cause vascular damage. During treatment, the patient must be monitored in order to ensure that any complications can be managed in a timely manner.

Phases of plasma loading and regeneration of the adsorber pair		
	Adsorber 1	**Adsorber 2**
Loading	1st cycle	Rinsed; waiting for 2nd cycle
	Plasma loading	
	Plasma loading completed	
Plasma transferred to adsorber 2, adsorber 1 rinsed with TheraSorb priming solution		
Regeneration	Rinsing with TheraSorb priming solution	2nd cycle; Plasma loading; Plasma loading completed
	Elution with TheraSorb elution buffer	
	Neutralization with TheraSorb neutralization buffer	
	Rinsing with TheraSorb priming solution	
	Finished; waiting for 3rd cycle	
Plasma transferred to adsorber 1, adsorber 2 rinsed with TheraSorb priming solution		
3rd until last cycle: consecutive loading and parallel regeneration		

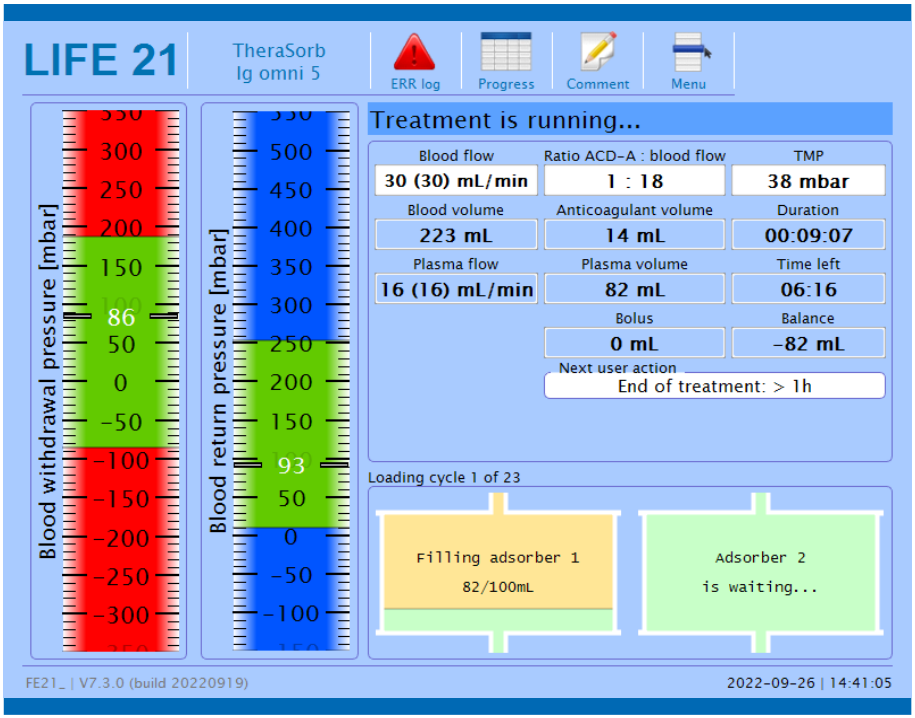
Table 7.1: Phases of plasma loading and regeneration of the adsorber pair

7.1 Treatment screen

During treatment, a status screen depicting the most important treatment-related information is displayed (see Screen 7.1). Several submenus can be accessed from this screen to change parameters (e.g., blood flow). During the treatment the residual volume and residual time before the next neccessary bag exchange is displayed below **Next user action**. If the remaining time is below one minute the information displayed will turn yellow.
If an immediate operator action is required a screen prompting, for example, the exchange of the waste bag, will overlay the treatment status screen.
If an error or malfunction occurs during treatment, an alarm screen accompanied by an audio signal will be displayed.
See user manual “Warnings, precautions and troubleshooting” for details on the alarms and alarm management.
The adsorber symbols in the lower right part of the treatemt screen (see Screen 7.1) visualize the adsorber status. The colors correspond to the fluids passing the adsorber (e.g., yellow for plasma, green for priming solution).

⚠ CAUTION

Risk of clotting in the extracorporeal fluid path. Prolonged interruption of treatment may affect anticoagulation effectiveness and causes clotting in the extracorporeal fluid path. Do not interrupt the treatment.



Screen 7.1: Representative treatment screen

A summary and explanation of each button displayed on the screen can be found in Table 7.2.

Display element	Function
STOP RESTART	Allows to interrupt the treatment temporarily. All pumps are stopped. This mode cannot be used for the exchange of the disk separator. Continues a temporarily interrupted treatment.
MENU	Gives access to menu options (see section 7.3 "Main menu").
Comment	Additional patient or treatment related data (e.g., blood pressure, pulse) can be entered (see section 7.4 "Comment input").
Progress	Displays a graph or a table with the progress of the treatment (see section 7.5 "Treatment progress").
ERR log	Displays the list of errors of the current treatment (see section 7.6 "Error logging").
Pressure bars	Displays the blood withdrawal pressure in the red bar and the blood return pressure in the blue. Adjustment of parameters: The allowed range for the withdrawal and return pressure is shown in green. The limits can be manually adjusted (upwards and downwards) by the drag and drop functionality. Pressure monitoring: The blood withdrawal and return pressures are monitored continuously by the instrument and are graphically displayed on the treatment screen. The operator-defined permissible range is displayed in green, whereas areas outside of the range, which cause an alarm, are displayed in red or blue. The instrument automatically sets the alarm thresholds after a short start-up period. In the Single Needle mode (SN mode) only one bar is depicted, a red bar during the blood withdrawal phase and a blue bar during the reinfusion phase. The alarm range of blood withdrawal pressure and blood reinfusion pressure will be widened due to the following events: • on start of treatment • after change of blood withdrawal flow • after stopping the treatment • after confirming an alarm • Restarting the treatment after solving an alarm occurance
Blood flow	Displays the current blood flow rate and gives access to modify the blood flow rate.
ACD-A:blood flow respectively heparin flow	Displays and gives access to modify the ACD-A:blood flow ratio or the heparin flow, respectively.

Display element	Function
TMP	Transmembrane pressure of the disk separator. Default value (Blood flow+50). If absolutely needed the value can be adjusted manually.
Status information	not adjustable
Blood volume Anticoag. vol. Duration Plasma flow Plasma volume Time left Balance	displays volume of blood processed displays volume of anticoagulant applied displays elapsed time of treatment displays current plasma flow displays current plasma volume processed displays calculated remaining treatment time displays current balance situation
Flow mode Pressure mode	***Flow mode*** is set by default. Blood withdrawal is performed at the pre-set flow rate and an ALARM is set off if the defined upper or lower blood withdrawal or blood return pressure limits are exceeded. ***Pressure mode*** is shown in the status line if the corresponding mode is selected via MENU. In pressure mode, the blood withdrawal rate is automatically adapted (increased or lowered) if the blood withdrawal pressure or blood return pressure reaches the upper or lower third of the allowed range (green coloured). Nevertheless, an ALARM is set off if the pressure reaches the limit of the allowed range despite of the flow rate adaption. Via the MENU button, the mode can be switched during the treatment.
Next user action	Displays residual time and residual volumes before next bag exchange is required. The background color changes to yellow if the time is below one minute.
Adsorber symbols	Visualization of loading cycle status of each adsorber
Loading cycles	Displays the number of plasma loading cycles in the current treatment
Status area	If the status area is displayed, additional hints are given or an operator action is required (yellow background).

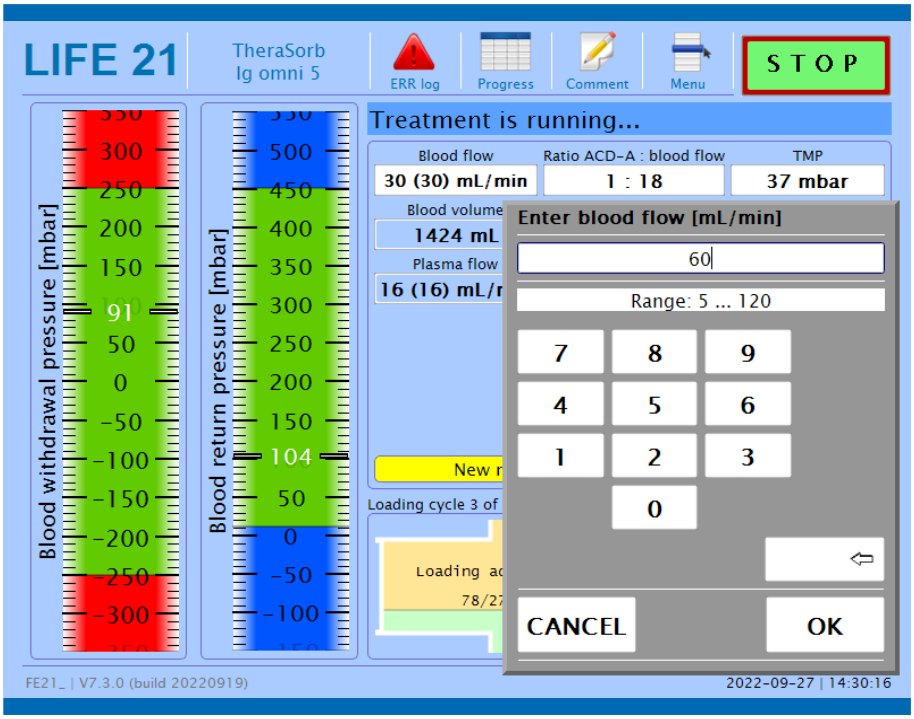
Table 7.2: Function of elements displayed on treatment status screen

7.2 Modification of main parameters

This section reflects the modification of parameters that might need attention during the treatment. The program will accept only values in between the permissible range displayed on the screen (see chapter 10 "Permissible range of treatment parameters" for details).

7.2.1 Modification of blood withdrawal flow

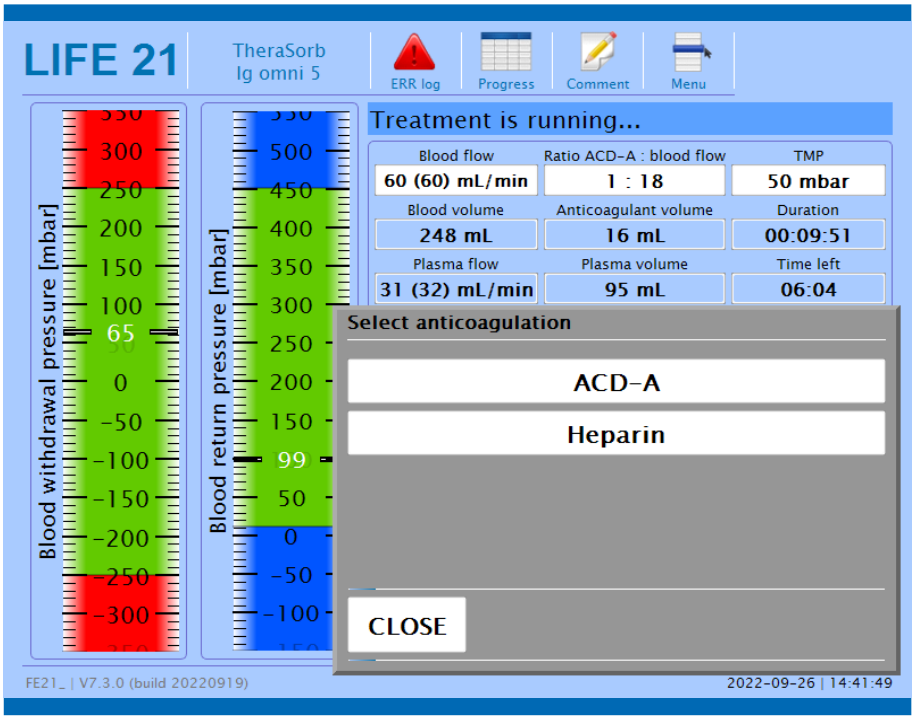
Operator action: Select **Blood flow** on treatment status screen to modify the blood flow to the required value (see Screen 7.3).
Press **OK** to return to the treatment status screen.



Screen 7.2: Adjustment of blood flow

7.2.2 Modification of anticoagulant settings

Operator action: Select **Ratio ACD-A:blood**, choose the new anticoagulant setting and change the respective value (see Screen 7.4).

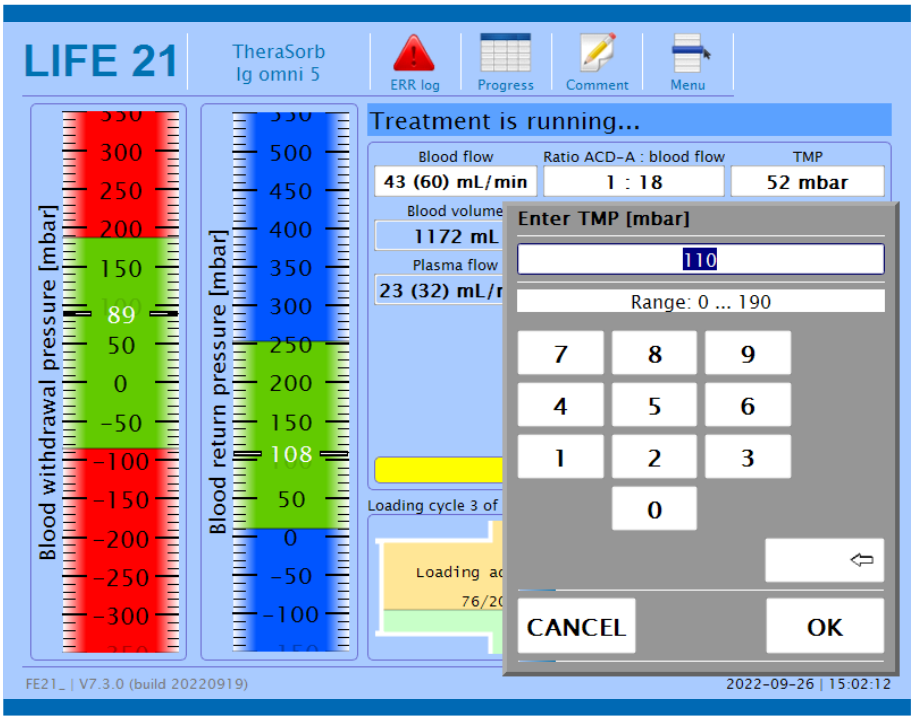


Screen 7.3: Adjustment of anticoagulation settings

7.2.3 Modification of transmembrane pressure (TMP)

The TMP is automatically adjusted to the value of the blood withdrawal flow (blood flow+50).

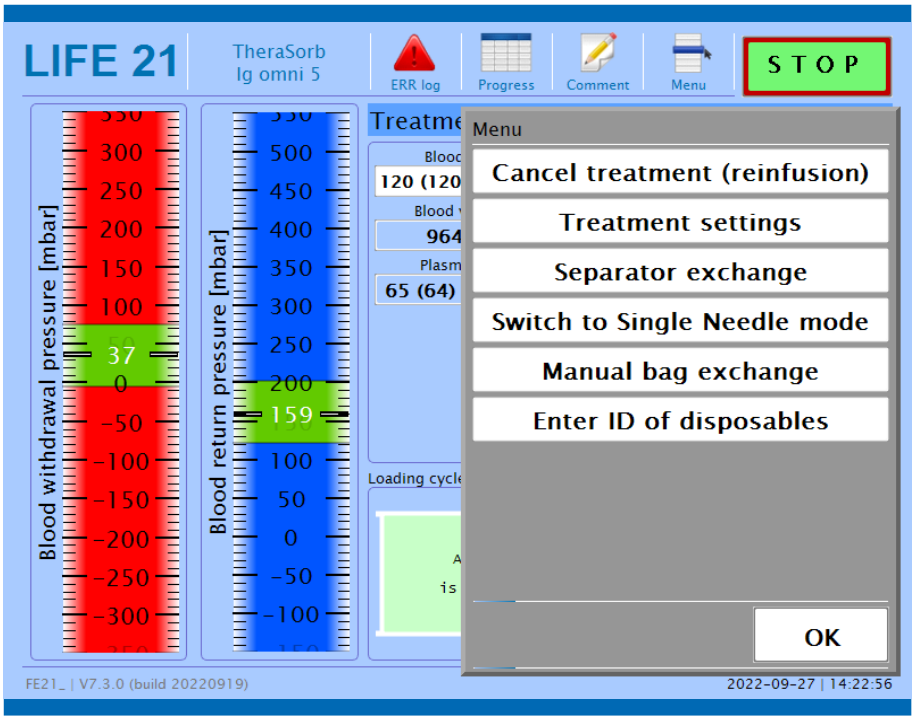
Operator action: Select **TMP** to change the default value, if absolutely necessary (see Screen 7.5).



Screen 7.4: Adjustment of TMP value

7.3 Main menu

A list is displayed after pressing the button **MENU** on the screen. It allows the operator to access more options, related to the current treatment (see Screen 7.6). A summary and explanation of each element displayed on the screen can be found in Table 7.3.



Screen 7.5: Representative menu screen

Display element	Function
Cancel treatment (reinfusion)	Facilitates a premature abortion of the treatment and initiates the reinfusion phase.
Treatment settings	Facilitates the access to, and the modification of, different treatment parameters (height, weight, hematocrit, date of birth, initial target molecule value, regeneration settings). Also the settings in the removal graph (only in automatic mode) and in the loading profile (only in manual mode) can be modified.
Separator exchange	Facilitates the exchange of the disk separator.
Switch to Single Needle mode	Switch to Single Needle or Double Needle mode.
Manual bag exchange	Facilitates the manual bag exchanges of a bag of any kind during treatment.
Enter ID of disposables	Opens sub-screen to enter different barcodes either by using the on-screen keyboard or by using the barcode scanner.
Switch to pressure mode	Allows to change from flow mode to pressure mode. Accessible only in manual loading mode.

Table 7.3: Function of elements displayed on menu screen

7.3.1 Premature cancellation of treatment

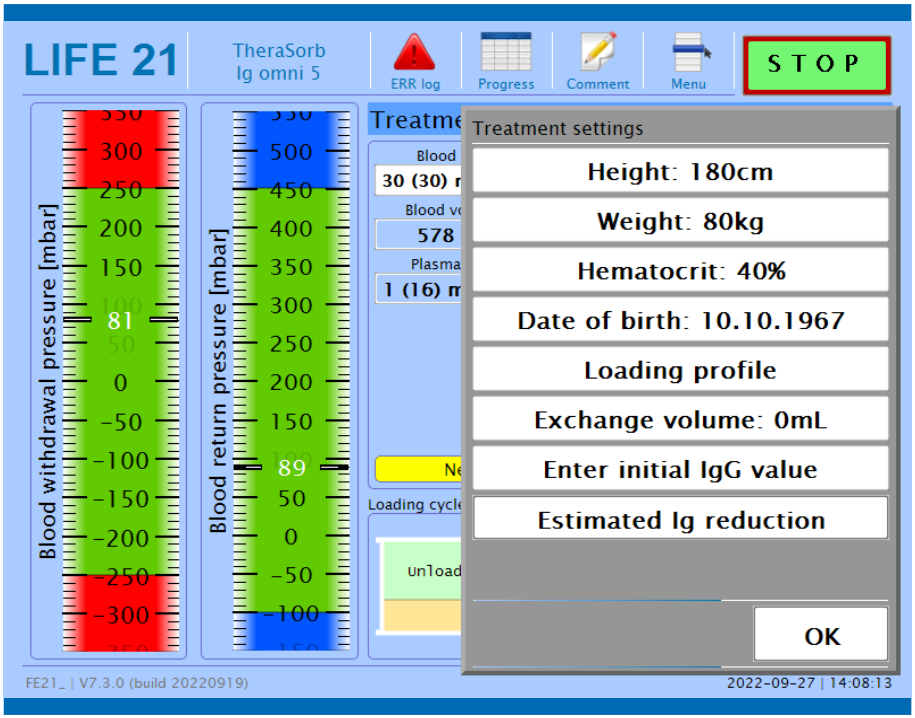
If a treatment needs to be canceled, the extracorporeal blood and plasma needs to be reinfused to the patient first before the disconnection of the patient prematurely.

Operator action: Select **MENU** on treatment status screen. Select **Cancel treatment (reinfusion)** on menu screen. Press **YES** to abort the current treatment. The operator is asked to continue with the reinfusion phase. See chapter 8 "Reinfusion, preservation and shutdown" for details. If needed, the reinfusion phase can be canceled to disconnect the patient immediately (see section 8.3 "Cancellation of reinfusion").

7.3.2 Modification of patient and treatment settings

Operator action: Select **MENU** on treatment status screen. Select **Treatment settings** for more details (see Screen 7.6). In case the manual mode is active additional settings are displayed:

- loading profile (when manual mode is active)
- regeneration settings (when manual mode is active)



Screen 7.6: Modification of treatment settings

7.3.3 Exchange of disk separator

If the disk separator needs to be exchanged during treatment, see user manual “Warnings, precautions and troubleshooting”.

7.3.4 Change of Single Needle/Double Needle mode

To change the treatment mode from double to Single Needle and vice versa see user manual “Warnings, precautions and troubleshooting”.

7.3.5 Manual bag exchange

If a bag, for example, the anticoagulation bag needs to be exchanged during treatment, see user manual “Warnings, precautions and troubleshooting”.

⚠ CAUTION

Risk of clotting in the extracorporeal fluid path. The anticoagulation bag has to be changed within the standby time given by the instrument to maintain anticoagulation of the blood in the system and to prevent the risk of clotting in the extracorporeal fluid path. Once the standby time ends, an alarm is displayed, and the operator is asked to continue the treatment. Change the anticoagulation bag within the standby time given by the instrument.

7.3.6 Barcode scan of disposables

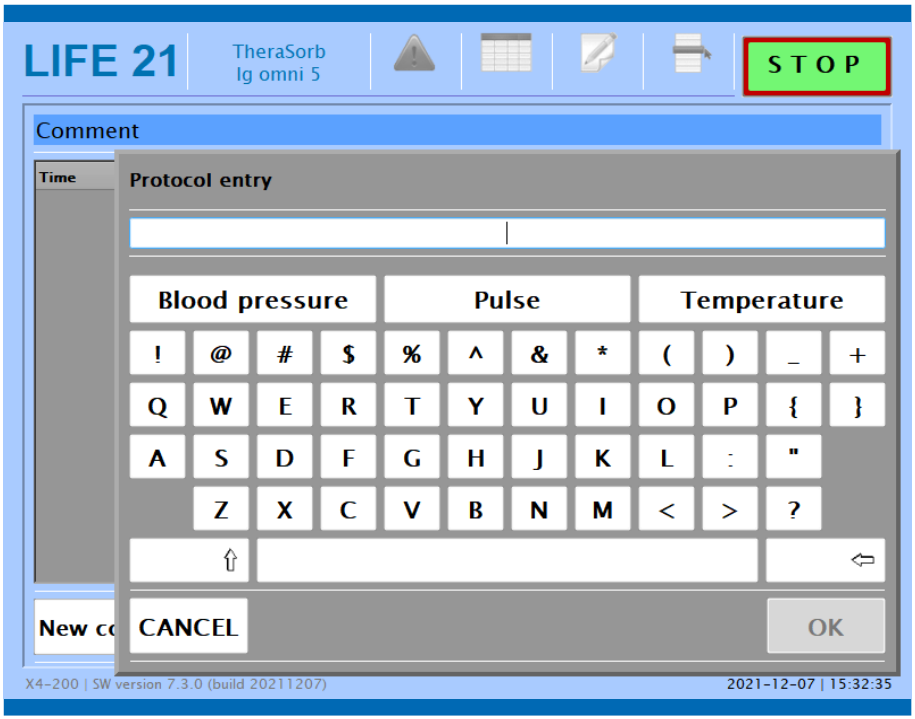
It is advisable to enter the barcodes of the disposables used, as the information is transferred to the treatment protocol.

7.3.7 Flow mode/pressure mode

For a description of this menu option see Table 7.2.

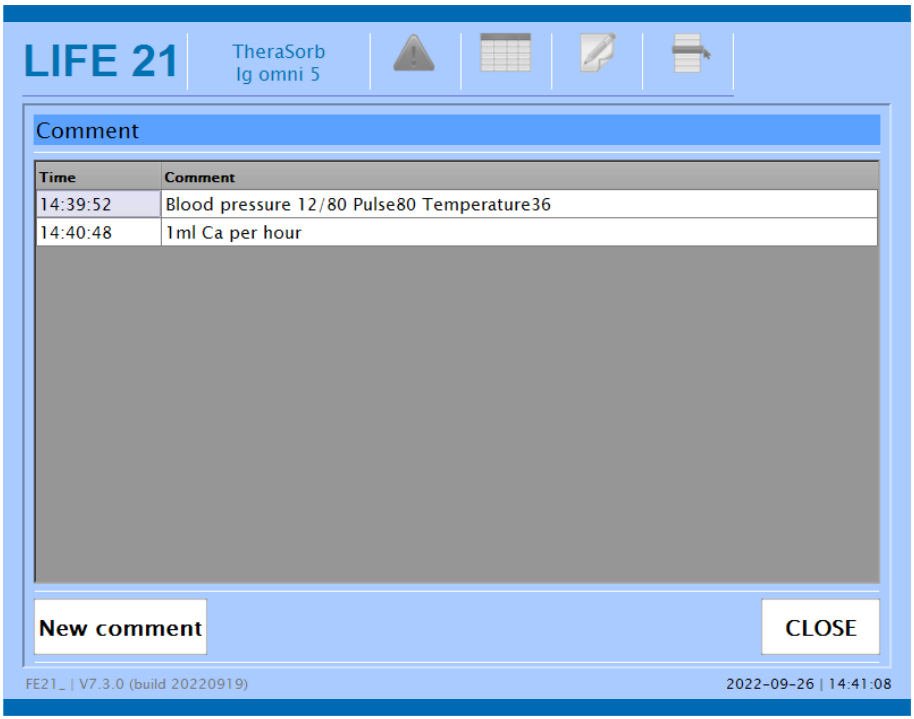
7.4 Comment input

Operator action: Select **Comment** (see Screen 7.7). Choose one of the default comment functions (**Blood pressure**, **Pulse**, **Temperature**) and add the measured patient value or enter a free alphanumeric comment string (up to 80 characters). Press **OK** to continue.



Screen 7.7: Comment input screen

The comments are saved in a comment list and transferred to the treatment protocol (see Screen 7.8).



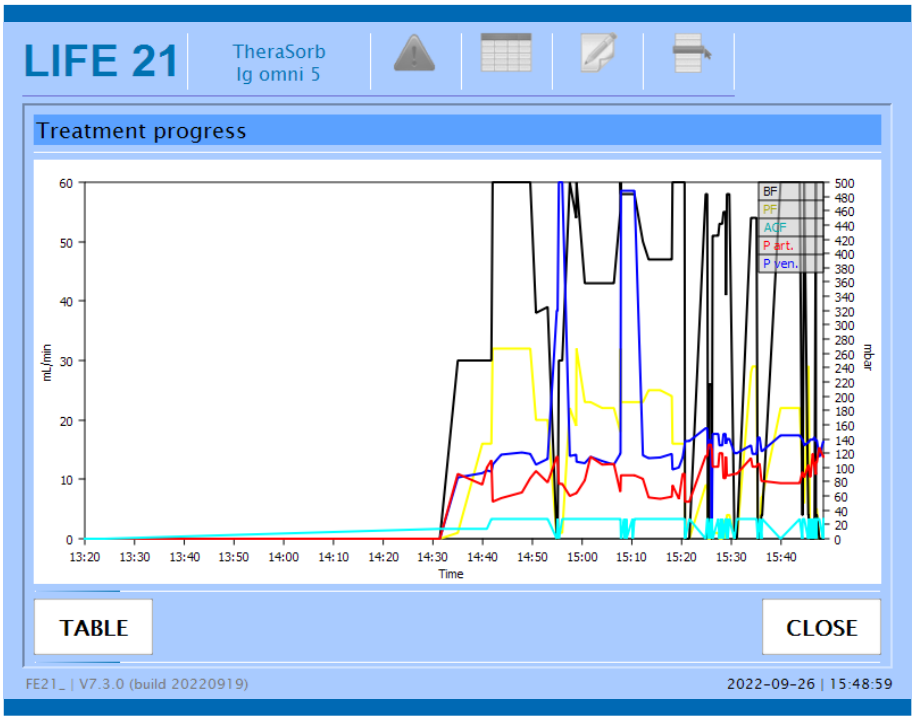
Screen 7.8: List of entered comments during treatment

7.5 Treatment progress

Operator action: Select **Progress** in treatment screen (see Screen 7.1). A tabular or graphic view of the course of the following patient/treatment parameter can be shown:

- blood flow (BF)
- plasma flow (PF)
- anticoagulant flow (ACF)
- TMP (only tabular view)
- pressure in blood removal line (P art.)
- pressure in blood return line (P ven.)
- total blood volume (only tabular view)
- total plasma volume (only tabular view)

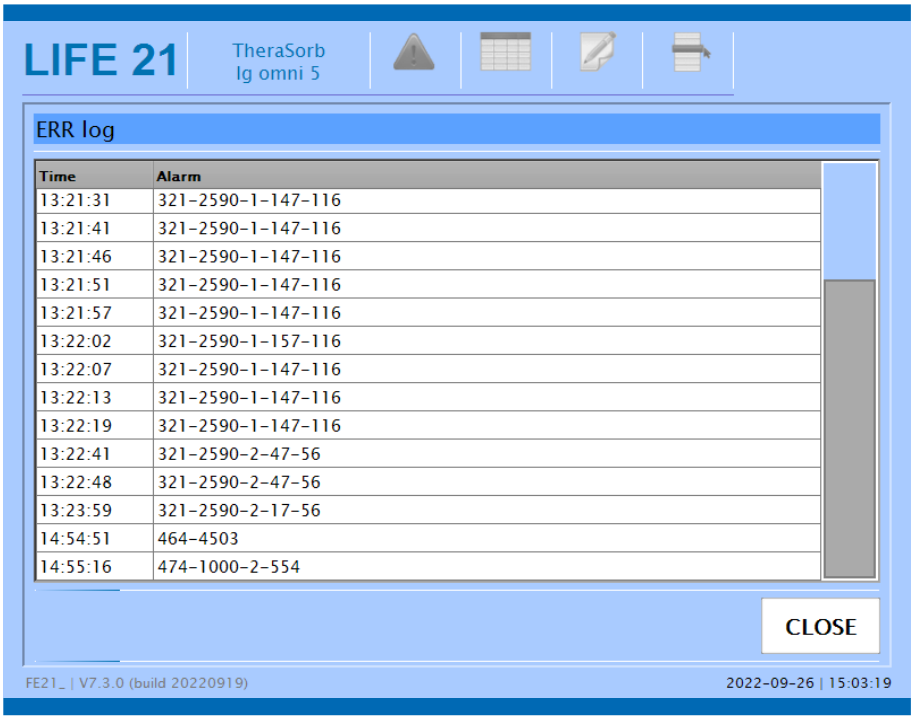
Select **GRAPH/TABLE** to switch between the different views. Press **OK** to return to treatment screen.



Screen 7.9: Display of treatment progress

7.6 Error logging

Operator action: Select **ERR log** on treatment screen (see Screen 7.1). A tabular view of all alarms occurred during the treatment is shown. This menu option is useful if an alarm ID shall be reported to Miltenyi Biotec Technical Support and the alarm ID and service info could not been noted down in the moment where the error occurred.



Screen 7.10: Display of Error log list

8

Reinfusion, preservation and shutdown

As soon as the previously defined number of cycles has been reached, the plasma separation will be stopped and the blood flow will be reduced to 10 mL/min. Blood is withdrawn from and returned to the patient at this blood flow to avoid coagulation in the extracorporeal circuit. The automated reinfusion phase will be started after acknowledgment of the treatment end by the operator and is divided into the following steps:

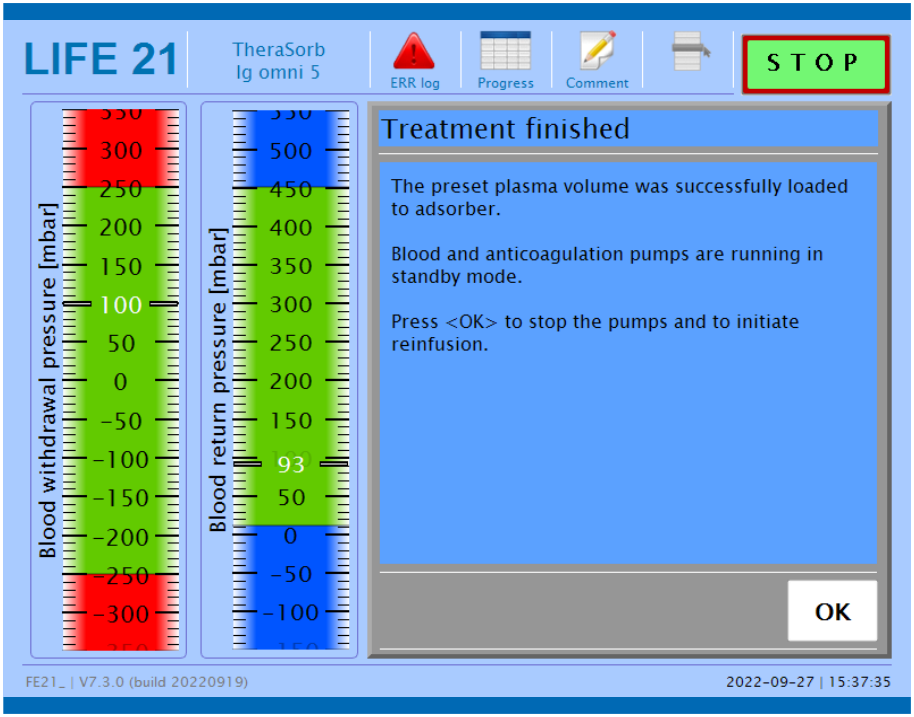
- return of blood/plasma from Single Needle chambers (only Single Needle mode)
- return of blood from withdrawal line
- return of blood/plasma from disk separator, rinsing of adsorber, and return of plasma from the adsorber
- disconnection of patient

The reinfusion balance starts at a negative volume which is the sum of adsorber and disk separator volume (see also the adsorber-related package insert)

.

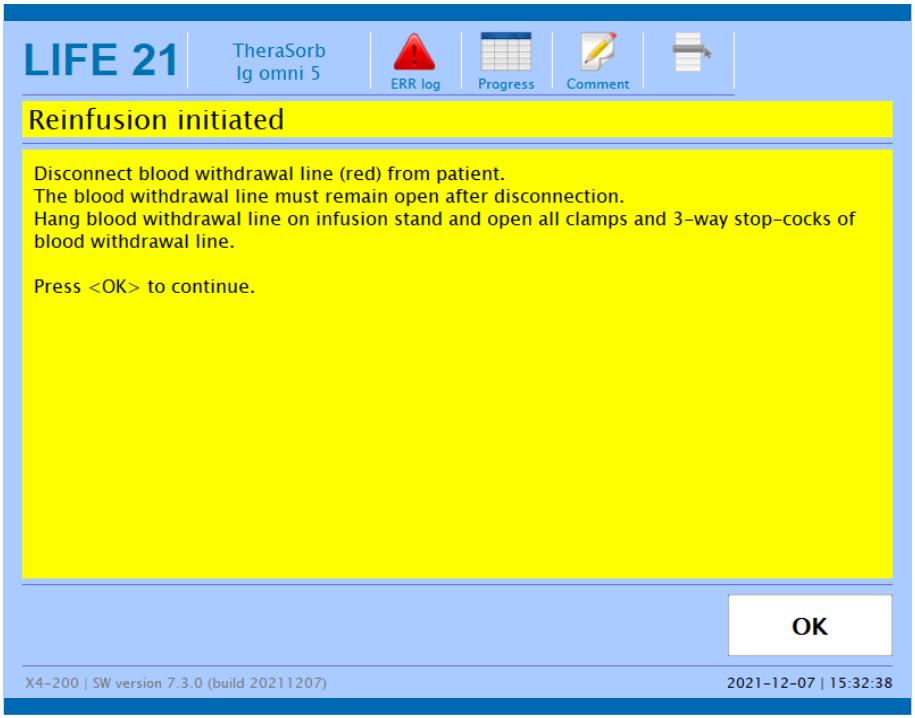
8.1 Reinfusion

Before the reinfusion can be started the operator is informed that the end of the treatment has been reached (see Screen 8.1).
Operator action: Press OK to stop the blood pumps.



Screen 8.1: End of treatment

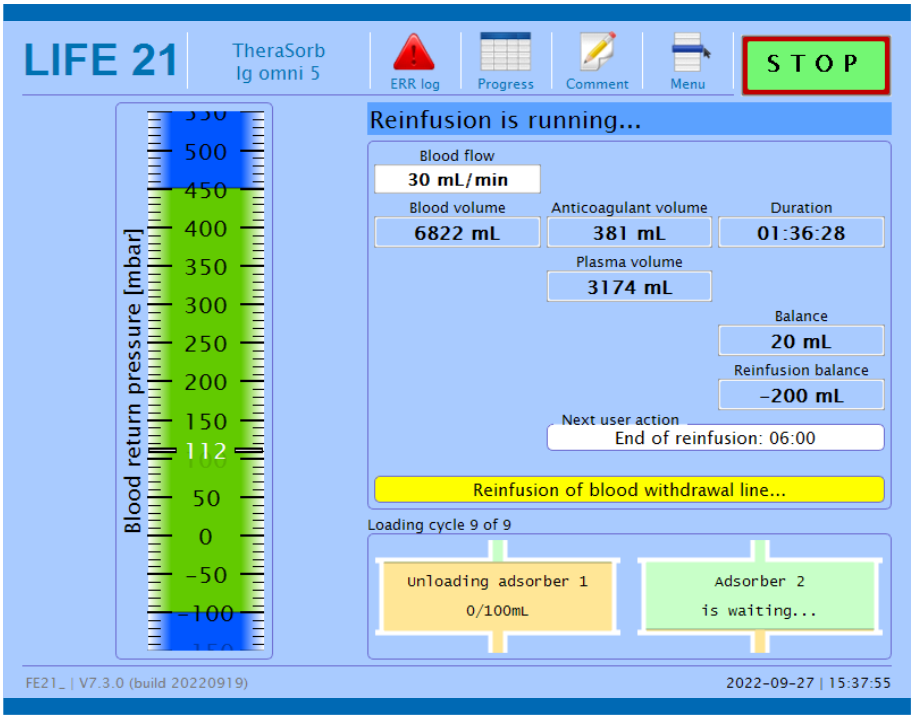
Operator action: Follow the instructions (see Screen 8.2).
In the Double Needle mode the reinfusion starts by emptying the blood withdrawal line. In the Single Needle mode the Single Needle chambers will be emptied first. The blood withdrawal line has to remain open after disconnection from the patient to enable emptying of that line.



Screen 8.2: Disconnection of patient

⚠ WARNING

Risk of infection. Loss of sterility and microbial contamination may result in the risk of infection of a patient. Observe adequate hygienic measures for aseptic handling to prevent contamination of the fluid path during emptying of the blood withdrawal line.



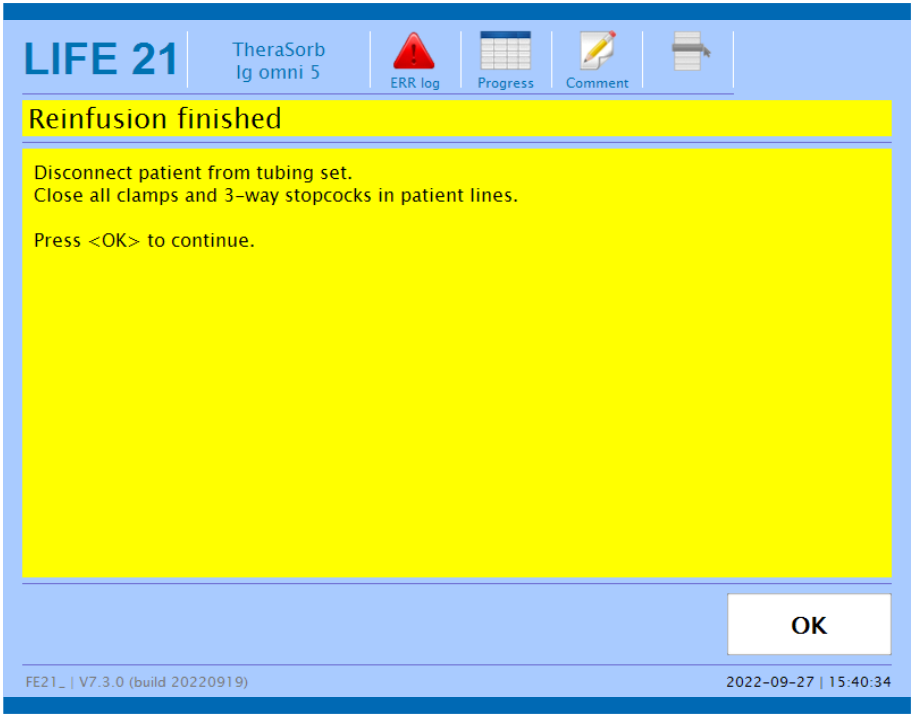
Screen 8.3: Reinfusion of plasma

Display element	Function
STOP RESTART	Allows to interrupt the reinfusion of plasma temporarily. All pumps are stopped. Continues a temporarily interrupted reinfusion.
Pressure bar	Displays the blood return pressure in blue. The limits can be manually adjusted (upwards and downwards) by the drag and drop functionality.
Blood flow	Displays the current blood flow rate and gives access to modify the reinfusion flow rate.
Status information Duration Reinfusion balance Balance	 displays elapsed time of treatment displays course of the balance during reinfusion displays current balance situation
Next user action	Displays residual time and residual volumes before next bag exchange is required. The background color changes to yellow if the time is below one minute.
Adsorber symbols	Visualization of loading cycle status of each adsorber
Loading cycles	Displays the number of plasma loading cycles in the current treatment
Status area	If the status area is displayed, additional hints are given or an operator action is required (yellow background).

Table 8.1: Function of elements displayed on reinfusion screen

Reinfusion phase ends automatically when the reinfusion volume defined for TheraSorb - Ig omni 5 has been reached. The information on the reinfusion volume of other treatments can be found in the adsorber-related package inserts.

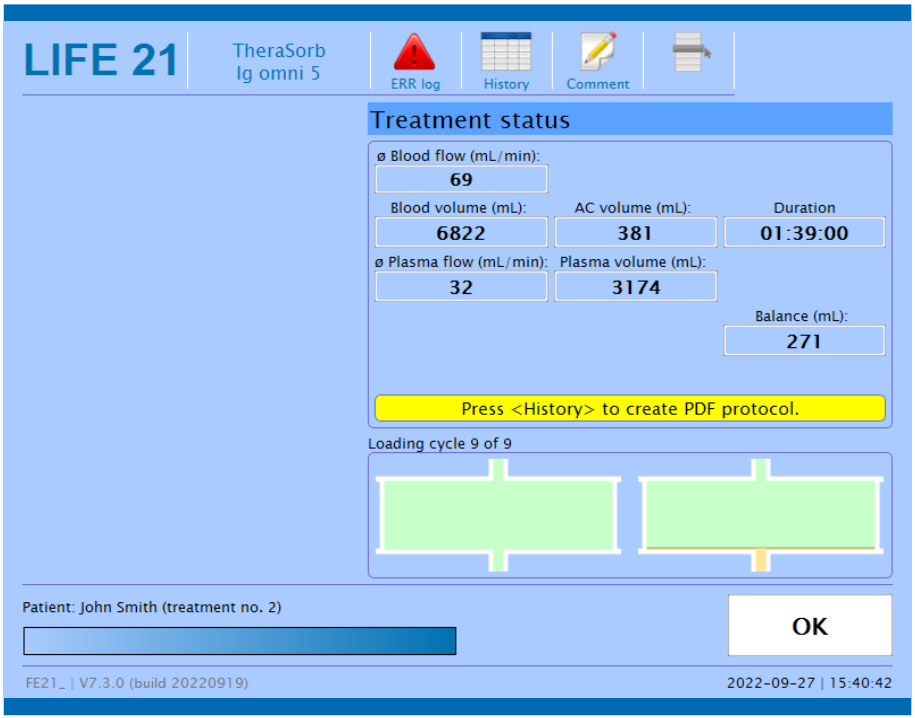
Operator action: Follow the instructions (see Screen 8.4) and press **OK**.



Screen 8.4: Disconnect patient from the tubing set

8.2 Treatment overview and options

After the end of the reinfusion phase and the disconnection of the patient a summary (see Screen 8.5) is shown.



Screen 8.5: Treatment status screen

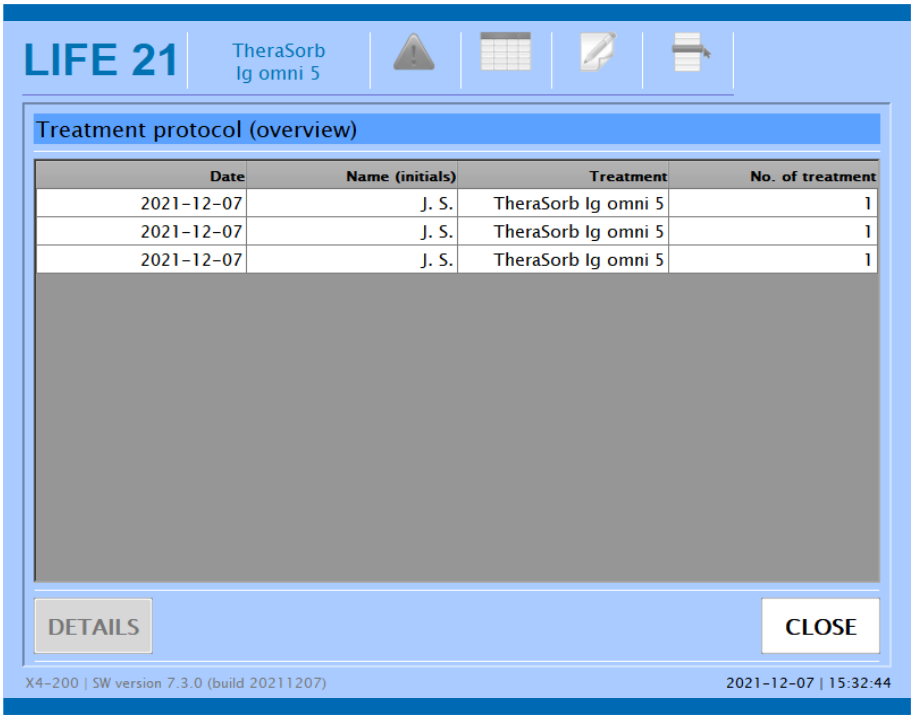
Before pressing **OK** the operator has further options described in the following chapters.

8.2.1 Entry of additional information for the treatment protocol

Operator action: Select **Comment** to enter additional information related to treatment parameters or patient.

8.2.2 Transfer of treatment protocol to USB flash drive

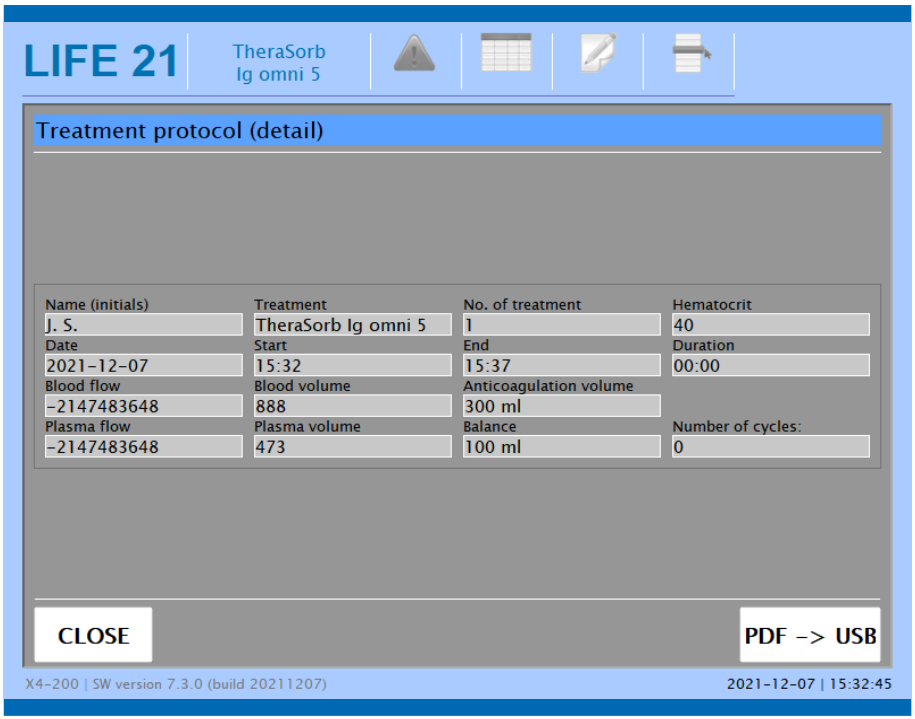
Operator action: The treatment protocol can be accessed after pressing **Progress** on the menu bar (see Screen 8.6).



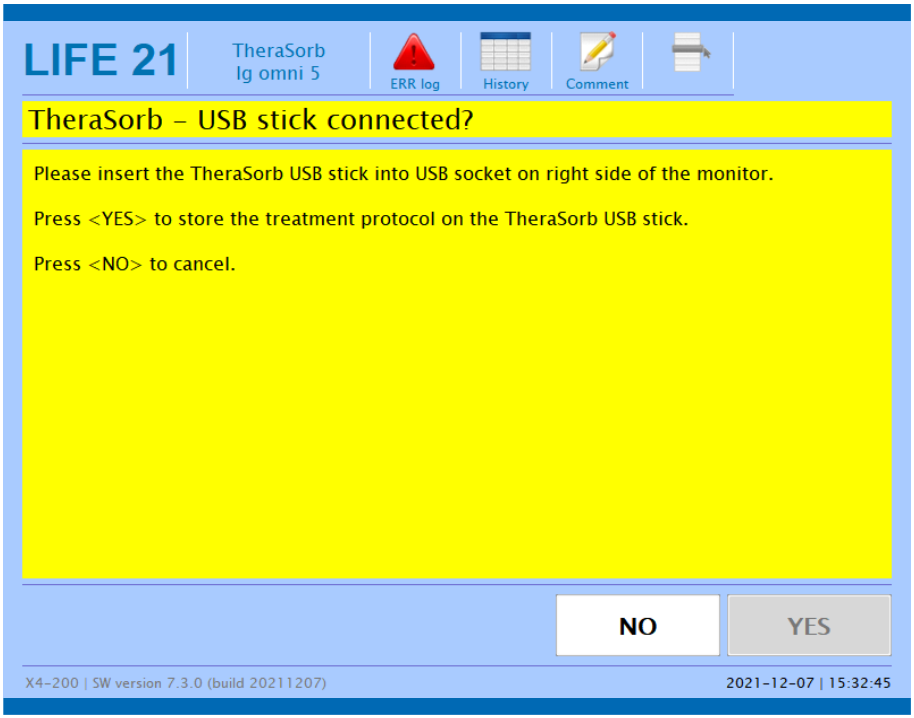
Screen 8.6: Display of treatment protocol

Operator action: After selecting the relevant treatment protocol press **OK** and the specific treatment summary screen is shown (see Screen 8.7).

Operator action: Select **PDF –> USB** and follow the instructions to transfer the treatment protocol to the USB flash drive (see Screen 8.8).



Screen 8.7: Treatment summary of selected protocol

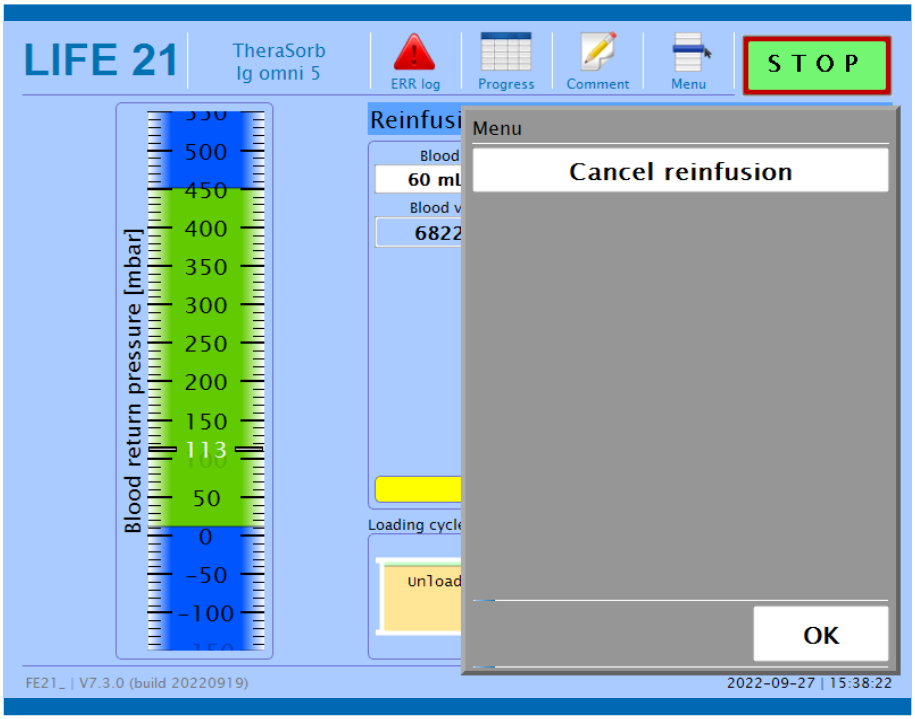


Screen 8.8: Transfer of treatment protocol to USB flash drive

Operator action: After transferring the protocol the treatment status screen is shown (see Screen 8.5). Press **OK** to start the regeneration and preservation of the adsorber pair. Continue with section 8.4 "Adsorber regeneration, preservation and storage".

8.3 Cancellation of reinfusion

The reinfusion phase can be ended prematurely if needed.
Operator action: Select **Menu** and choose **Cancel reinfusion** (see Screen 8.9). Confirm the selection by pressing **YES**. Afterwards the operator is instructed to disconnect the patient from the tubing set (see Screen 8.4). Continue with section 8.2 "Treatment overview and options".



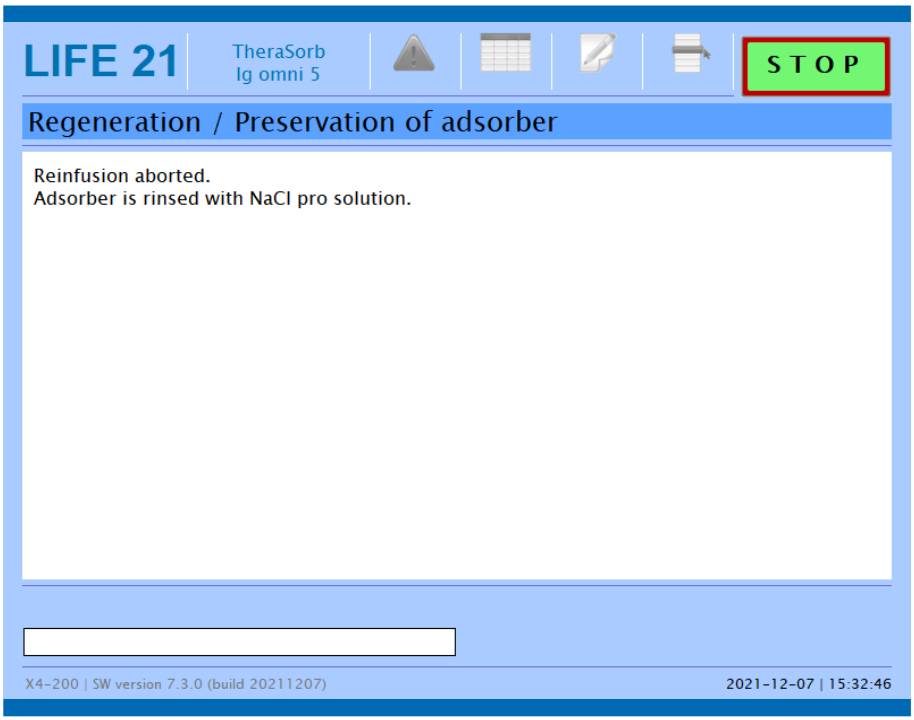
Screen 8.9: Premature ending of reinfusion phase

8.4 Adsorber regeneration, preservation and storage

After the reinfusion the multiple use adsorber pair is regenerated with TheraSorb elution buffer followed by preservation with TheraSorb preservation buffer. Afterwards, the adsorber pair is ready for storage until the next treatment. A status screen informs the operator about the time left for the regeneration step (see Screen 8.10).

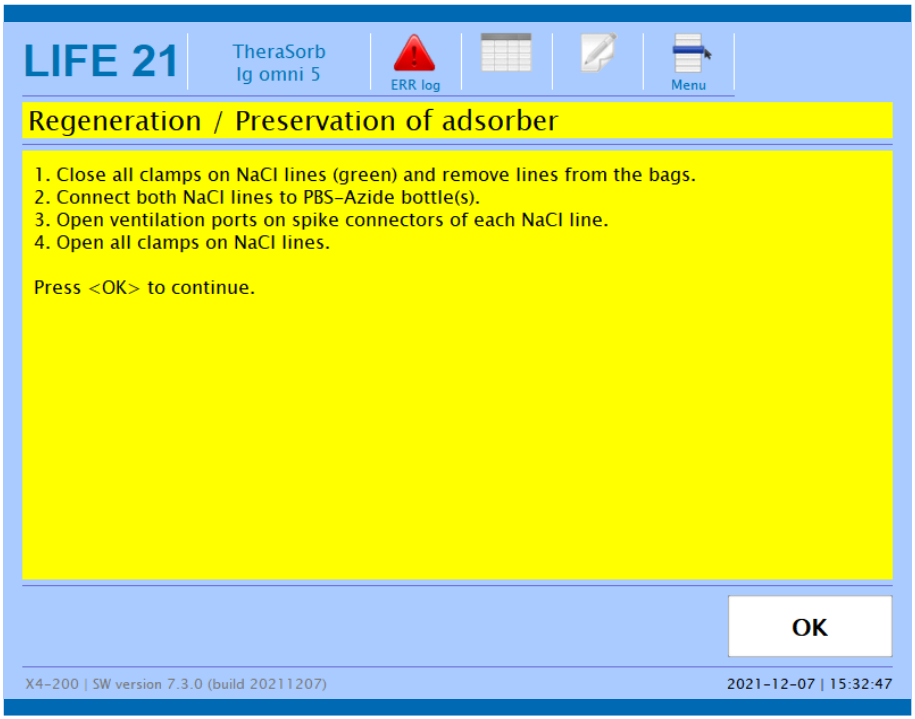
⚠ WARNING

Risk of toxicity. The TheraSorb preservation buffer is acutely toxic and may cause severe complications if infused unintentionally to the patient. In order to prevent an unintended infusion into the patient, the preservation solution TheraSorb - PBS-Azide must not be brought into the treatment room before the complete disconnection of the patient from the instrument. Adherence to this procedure should prevent an unintentional infusion of the solution into the patient.



Screen 8.10: Representative regeneration and preservation status screen

Operator action: After completion of the final regeneration, follow the instructions on the screen and press **OK** to start the preservation of the adsorber pair (see Screen 8.11).



Screen 8.11: Connection of TheraSorb preservation buffer to the tubing set

Operator action: After completion of the preservation step follow the instructions (see Screen 8.12) and press **OK** to continue. Use the sterile Luer Lock caps delivered with the tubing set to close the adsorber inflow and outflow connector.

⚠ WARNING

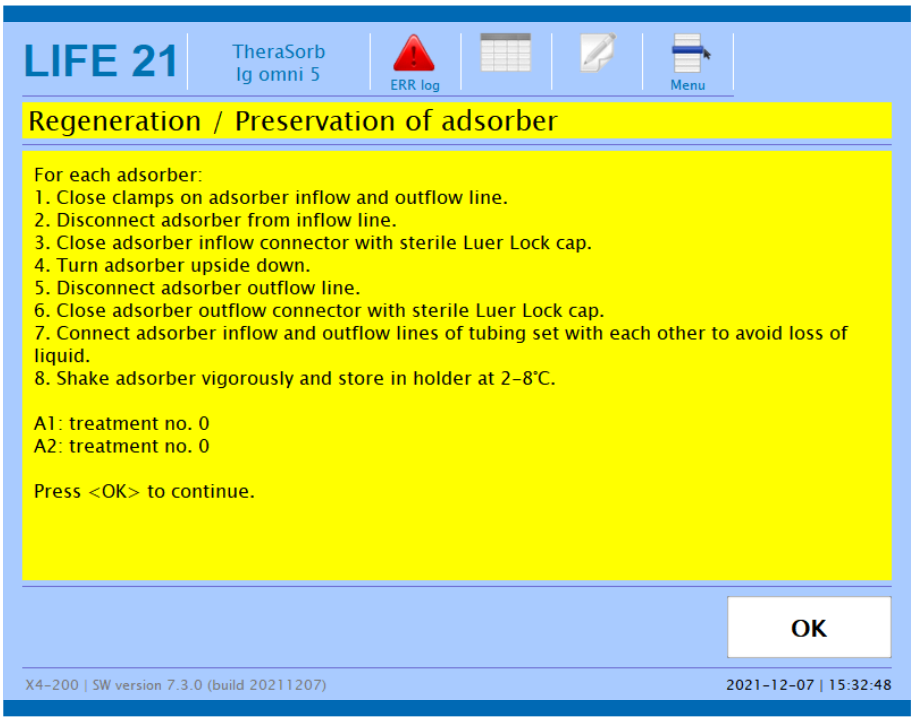
Risk of infection. Failure to preserve an adsorber and failure of cold storage may cause microbial contamination with a risk of infection at next use. The adsorber pair remains in the adsorber holder and is stored at +2 °C to +8 °C (+36 °F to +46 °F) until the next treatment.

⚠ WARNING

Risk of embolism. Freezing might cause damage to the adsorber matrix, which could lead to a possible risk of embolism for the patient. Make sure that the adsorber pair is not stored near the back of the refrigerator compartment to avoid any freezing.

IMPORTANT

Shake each adsorber vigorously before storage.



Screen 8.12: Removal and storage of adsorber pair after preservation

8.5 Shutdown

Operator action: To end the treatment and to shut down the instrument and follow the instructions (see Screen 8.13). After the adsorber pair is removed from the tubing set, follow the steps below:

- Clamp off all solution lines, patient lines, adsorber lines, and waste line.
- Remove patient the chip card.
- Remove all bags.
- Remove the tubing lines from the external pressure sensors with hydrophobic filters connected.
- Open the pump door by pressing **OK** and remove the pump cassette.
- Remove the disk separator from the separator drive and the remaining tubing from the instrument.
- Close the pump door.
- Press **OK** to shut down the instrument (see Screen 8.14).
- Turn off the instrument when prompted.

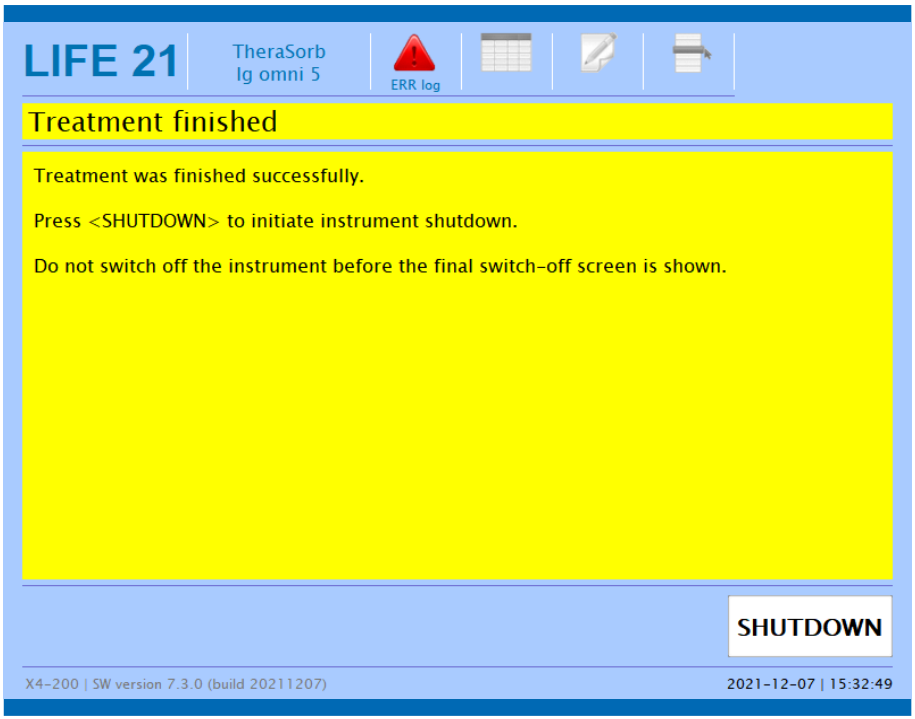
⚠ WARNING

Risk of infection. Incorrect treatment or disposal can lead to viral or microbial infection. All materials, which have been in contact with blood or plasma must be treated and disposed as biohazardous materials according to standard hospital or institutional requirements and national legislations.



Screen 8.13: Representative screen for a finished treatment

Operator action: Close the pump door and press **OK** (see Screen 8.14). Switch off the instrument at the rear panel as soon as the switch-off screen is diplayed.



Screen 8.14: Treatment finished screen

IMPORTANT

If the treatment protocol has not yet been saved on the TheraSorb USB flash drive, it can be saved at the beginning of the next treatment, by selecting **History** *in the treatment selection screen after the instrument has been switched on.*

8.5.1 Discard of used-up adsorber pair

Operator action:

- Use sterile Luer Lock caps (delivered with the tubing set) to close the adsorber inflow and outflow connector of each adsorber after disconnecting the adsorber pair from the tubing set.
- Dispose adsorber pair with respect to local standard hospital or institutional requirements.

⚠ WARNING

Risk of infection. Incorrect treatment or disposal can lead to viral or microbial infection. All materials, which have been in contact with blood or plasma must be treated and disposed as biohazardous materials according to standard hospital or institutional requirements and national legislations.

9 Additional settings/information

9.1 Testing the sterility of the adsorber

The procedure is recommended to test the sterility of each adsorber.

IMPORTANT

Test samples can only be taken if 3-way stopcocks have been installed below each adsorber.

To exclude microbial contamination, the microbiological investigation of the eluate from each adsorber is recommended. The chosen tests should allow for a determination of aerobic as well as of anaerobic microorganisms.
It is recommended to take the sample when the adsorber is filled with TheraSorb priming solution. This is best done at the end of the treatment just before the regeneration phase starts.

There are two options for collecting the samples:

Option A:
Collect the sample when the treatment is finished and the screen displayed requests to disconnect the tubing set from the patient.

Option B:
Collect the samples at the beginning of the treatment after rinsing of each adsorber is finished. This is possible, when the screen displays a decision on Single Needle- or Double Needle mode, or before connecting the patient.
It is not advisable to collect samples during the regeneration phase or after preservation of the adsorber as elution buffer or preservation buffer in the sample hinder microbial growth and lead to false negative results.

IMPORTANT

Observe aseptic handling to prevent contamination of the samples.

Operator action:

- Close clamps on adsorber inflow and outflow line.
- Connect a 3-way stopcock between the inflow connector of the adsorber and the inflow line (underneath the deaeration/particle filter).
- Position the 3-way stopcock to close the complete fluid path.
- Turn the adsorber upside-down and connect a 3-way stopcock between the outflow connector of the adsorber and the outflow line.
- Position the 3-way stopcock to close the complete fluid path.
- Turn the adsorber back in the right position (inflow connector above).
- Connect a 20 mL syringe filled with 20 ml sterile NaCl 0.9% infusion solution on the side port of the 3-way stopcock of the inflow line.
- Connect an empty 20 mL syringe to the side port of the 3-way stopcock of the outflow line.
- Position the 3-way stopcocks to allow for a fluid path towards the side ports (inflow and outflow line).
- Gently press the 20 ml sterile NaCl 0.9% infusion solution of the upper syringe into the adsorber. The empty syringe is automatically filled with the sample.
- Position the 3-way stopcocks to open the way for the adsorber fluid path and to close the side ports.
- Remove the syringes and place sterile caps on the side ports.
- Open all clamps on the inflow and outflow line of the tubing set.

Sampling size

Two 10 mL samples should be collected into tubes designed for microbiological samples, one for the testing on aerobic, the other for testing for anaerobic bacteria (at least 20 mL are needed in total).

⚠ WARNING

Risk of infection. Loss of sterility or microbial contamination may result in a risk of infection of a patient. The adsorber must be discarded if the microbiological test is positive. Do not use the adsorber for further treatments of the patient.

10

Permissible range of treatment parameters

A summary of all permissible ranges and values of parameters for a treatment is shown in Table 10.1.

Material	S, T, R[1]	Limits (Default setting)	Comment
Last name	S	up to 30 characters	–
First name	S	up to 30 characters	–
Date of birth	S	DD.MM.YYYY	–
Hematocrit	S	25 to 55	%
Height	S	<255	cm
Weight	S	<255	kg
Gender	S	Male (M), Female (F)	–
Blood withdrawal			
Flow SN DN	S, T	10 to 120 (30) 5 to 120 (30)	mL/min
Anticoagulation flow:			
ACD-A Heparin	S, T	0; 2.5 to 10 or 1:40 to 1:10 (1:18 resp. 5.5%) 0; 30 to 300	% Volume parts mL/h
Adsorber barcode	S	15 characters	–
Disposable barcodes	S, T, R	15 characters	–
Standby-flow	T	10	mL/min
AC-bag volume	T, R	100 to 5,000	mL

Material	S, T, R[1]	Limits (Default setting)	Comment
Volume of waste bag	T, R	Handling of the waste has to be entered. Selection between three options: 10,000 mL = standard bag, central = connection to central waste system or ??? = free input of bag volume, range 100…10,000 mL	mL
Blood withdrawal pressure	T, R	–188 to +188 –250 to +250	mmHg mbar
Blood reinfusion pressure	R	+8 to +338 (Single Needle: –188 to +338) +10 to +450 (Single Needle: –250 to +450)	mmHg mbar
Comment	T, R	<80 characters	–
Reinfusion blood flow	R	5 to 120 (30)	mL/min

1 S = Set-up, T = Treatment, R = Reinfusion

Table 10.1: Standard values and limits for the process

The first and last name of a patient can be entered in a pseudonymous form, e.g., patient identification number. The entry fields for name and first name allow up to 30 alphanumeric characters.

⚠ WARNING

Risk of cross-contamination. Mismatching of adsorber and patient can cause cross-contamination. Patient identification must be unambiguous and consistent over treatments.

Patient identification is used for the specific allocation and matching of a reusable adsorber to the patient in question either directly or via the patient chip card.

The entry of the sex of a patient designates the biological genetically determined sex and does not reflect gender preferences. The biological sex (female or male) is used for the calculation of the plasma volume of a patient, in combination with the age, height and weight of the patient. If a patient is a transsexual undergoing a sex change, the treating physician must determine the most adequate biological sex for the most correct determination of the plasma volume.

⚠ CAUTION

Incorrect entry of sex, weight, height, and age can cause erroneous calculation of the plasma volume of a patient. This can cause insufficient or excessive apheresis treatment with insufficient or excessive lowering of the target molecule(s).

11 Troubleshooting

For troubleshooting issues regarding the instrument see user manual “Warnings, precautions, and troubleshooting”.

If an error cannot be overcome by countermeasures described in the user manuals inform the Miltenyi Biotec Technical Support. Note the error code and service information on the screen for easier identification of the problem.

For filing a complaint submit the customer complaint form with all pertinent information to:

+49 3996 158-258
+49 3996 158-222
macstec@miltenyibiotec.de

Visit www.miltenyibiotec.com for local Miltenyi Biotec Technical Support contact information.

12 Legal notes

12.1 Limited warranty

Except as stated in a specific warranty statement, which may accompany the product, or unless otherwise agreed in writing by an authorized representative of Miltenyi Biotec, Miltenyi Biotec's warranty, if any, with respect to this product is subject to the terms and conditions of sale of the company within the Miltenyi Biotec group, which supplied the product. Copies are available on request or at www.miltenyibiotec.com. Terms and conditions of sale may vary by country and region. Copies of these terms are available on request or at www.miltenyibiotec.com. Nothing in this document should be construed as constituting an additional warranty.

Should the instrument be used in a manner not explicitly described in this manual, all warranties will be null and void.

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