THE NEXT HORIZON IN DIALYSIS IS CLOSER THAN YOU THINK

HDx by THERANOVA EXPANDS YOUR RENAL POSSIBILITIES

The new HDx therapy (expanded HD) is the next evolution in hemodialysis, as it effectively targets the removal of large middle molecules. Indeed, many of them are linked to the development of inflammation, cardiovascular disease, and other co-morbidities in dialysis patients.

Not only can HDx therapy provide HDF performance and beyond in the removal of conventional middle and large middle molecules, it does so using regular HD workflow and infrastructure.

The HDx therapy is enabled by the THERANOVA® dialyzer featuring an innovative membrane that combines a higher permeability than regular high-flux dialyzers with effective selectivity for large proteins.

This new therapy opens up a new option for dialysis patients who are believed to benefit from effective removal of large uremic toxins, for clinics that want expanded dialysis performance without the added burden of HDF.

*Do not use THERANOVA dialyzers in HDF or HF mode.
Mortality from cardiovascular and infectious events in HD remains unsatisfactorily high with current dialytic therapies.6 Large middle molecules have been associated with inflammation, cardiovascular events and other dialysis-related comorbidities.2 Current dialytic therapies, though efficient in removing small solutes, have limited capability in removing large middle molecules.3

HDx is a new therapy targeting an efficient removal of large middle molecules, without the need for a more complex setup than in regular HD. The HDx therapy is delivered with an innovative dialyzer featuring a new type of membrane, combining a higher permeability than high-flux dialyzers with effective selectivity to retain essential proteins.4,5
There is growing evidence showing a link between large middle molecules and the development of different outcome-related morbidities:

- Complement factor D (24 kDa)
- α1-microglobulin (33 kDa)
- YKL-40 (40 kDa)
- Immunoglobulin Free Light Chains (22.5 and 45 kDa)

More than the specific impact that each and every large middle molecule may have on the health of chronic kidney disease patients, it is critical to understand and address their collective effect. Uremia related to the retention of large middle molecules is indeed associated with inflammation and cardiovascular events.8,9,10

**LARGE MIDDLE MOLECULES ARE ASSOCIATED WITH INFLAMMATION AND CARDIOVASCULAR EVENTS**

- Comorbidities
- Retention of uremic solutes
- Infectious complications
- Inflammation
- Oxidative stress
- Reduced appetite
- Increased catabolism
- Endothelial dysfunction
- Vascular calcification
- Progression of cardiovascular diseases
- Protein-energy wasting
A STEP CLOSER TO THE NATURAL KIDNEY

TURNING INNOVATIVE DESIGN INTO A CLINICAL SOLUTION

The THERANOVA dialyzer enables the HDx therapy by combining 4 therapeutic principles: permeability, selectivity, retention and internal filtration — into a single dialyzer design.

Its innovative medium-cut-off (MCO) membrane expands the range of solutes removed during regular dialysis, while retaining essential proteins at a safe and controlled level. This unique cut-off and retention onset profile allows for filtration close to that of the natural kidney.4,5

<table>
<thead>
<tr>
<th>Number of pores [a.u.]</th>
<th>Pore radius [nm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>High flux</td>
<td>2.0</td>
</tr>
<tr>
<td>THERANOVA</td>
<td>4.0</td>
</tr>
<tr>
<td>High cut-off</td>
<td>6.0</td>
</tr>
<tr>
<td></td>
<td>8.0</td>
</tr>
<tr>
<td></td>
<td>10.0</td>
</tr>
</tbody>
</table>

HIGHER PERMEABILITY

With an increased nominal pore size, the THERANOVA dialyzer has a significantly higher permeability for large middle molecules compared to regular high-flux membranes, before and after blood contact.

EFFECTIVE SELECTIVITY FOR LARGE PROTEINS

By combining a unique asymmetric 3-layer structure with a carefully controlled distribution of the pore size, the THERANOVA dialyzer enables a stable separation profile and selectivity throughout the treatment, keeping albumin removal at a controlled level.

<table>
<thead>
<tr>
<th>Dextran molecular weight [g/mol]</th>
<th>Sieving coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>10^4</td>
<td>0.6</td>
</tr>
<tr>
<td>10^5</td>
<td>0.8</td>
</tr>
<tr>
<td>10^6</td>
<td>1.0</td>
</tr>
</tbody>
</table>

RETENTION

The adsorption properties of the THERANOVA membrane maintain the same level of bacteria and endotoxin retention as other standard dialysis membranes.11 Despite its higher permeability, the THERANOVA membrane appears to be a safe and effective barrier to potential dialysis fluid contaminants. It is compatible with standard fluid quality (ISO 11663:2014) and does not require any additional fluid quality control measures.12

INTERNAL FILTRATION

The inner diameter of the THERANOVA membrane has been carefully reduced in order to increase internal filtration along the membrane, conducive to an enhanced removal of large middle molecules.

<table>
<thead>
<tr>
<th>Membrane Geometry</th>
<th>High-Flux</th>
<th>THERANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smaller inner diameter and reduced wall thickness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Greater packing-density</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improved undulation</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A STEP CLOSER TO THE NATURAL KIDNEY

By expanding the range of solutes removed in dialysis, while retaining selectivity towards albumin and other essential proteins, the THERANOVA dialyzer is coming a step closer to the natural kidney.
HD therapies have been the treatment of choice for many years — both for many patients and many clinics. The design and operating mode of the THERANOVA dialyzer enables the HDx therapy to be easily implemented on any HD monitor. This means by simply changing the dialyzer, any clinic can provide markedly greater clearances and intradialytic reduction ratios than regular HD — at ordinary blood flow rates.

### Overall Clearance: HDx vs. HD

<table>
<thead>
<tr>
<th></th>
<th>HDx THERANOVA 400</th>
<th>HD FX CORDIA 80</th>
<th>Standard error (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Beta 2 microglobulin</strong></td>
<td>80</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td><strong>Myoglobin</strong></td>
<td>20</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td><strong>Kappa free light chains</strong></td>
<td>40</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td><strong>Complement factor D</strong></td>
<td>60</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td><strong>Alpha 1 microglobulin</strong></td>
<td>20</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td><strong>Lambda free light chains</strong></td>
<td>40</td>
<td>30</td>
<td></td>
</tr>
</tbody>
</table>

### Reduction Ratio: HDx vs. HD

<table>
<thead>
<tr>
<th></th>
<th>HDx THERANOVA 400</th>
<th>HD FX CORDIA 80</th>
<th>Standard error (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Beta 2 microglobulin</strong></td>
<td>80</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td><strong>Myoglobin</strong></td>
<td>20</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td><strong>Kappa free light chains</strong></td>
<td>40</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td><strong>Complement factor D</strong></td>
<td>60</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td><strong>Alpha 1 microglobulin</strong></td>
<td>20</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td><strong>Lambda free light chains</strong></td>
<td>40</td>
<td>30</td>
<td></td>
</tr>
</tbody>
</table>
EXPANDED HEMODIALYSIS (HDx)

TREATMENT EFFECTS AND THERAPY IMPLICATIONS (VS. HDF)

HDx therapy enabled by the THERANOVA dialyzer provides an equivalent removal of small and conventional middle molecules, with the possibility of greater removal for large middle molecules when compared to high-volume HDF. HDx performance can be achieved in all regular HD environments: this simplicity removes the potential burden of patient eligibility or therapy specific delivery systems.

ALBUMIN REMOVAL PER SESSION:

- 3 grams on average in all cases, limited to between 1 and 4 grams per treatment.
- Similar removal compared to HDF on-line.
- Does not seem to have any impact on serum albumin levels after 6 months compared to HDF.

REMOVAL DURING CLINICAL TRIAL SESSIONS (IN GRAMS)

<table>
<thead>
<tr>
<th>Qb (mL/min)</th>
<th>T (h)</th>
<th>Mean (± SD)</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>300</td>
<td>4</td>
<td>2.3 ± 0.7</td>
<td>2.9</td>
<td>1.5-3.9</td>
</tr>
<tr>
<td>400</td>
<td>4.4</td>
<td>3.0 ± 0.7</td>
<td>3.2</td>
<td>1.2-3.9</td>
</tr>
</tbody>
</table>

Notes:
1. Qb = 400 mL/min; Treatment Time = 4.4 h; Vconv = 24L (Mean) – n = 20
HDF PERFORMANCE AND BEYOND*

- Equivalent removal of small and conventional middle molecules.
- Greater removal possible for large middle molecules.
- Applicable to all HD patients.

AS SIMPLE AS HD

- HD infrastructure: no need for HDF capable monitors nor specific water quality and fluid quality assurance measures.¹⁵
- Avoid HDF additional running costs: disposable infusion line, use of larger amounts of dialysis water and concentrates.¹⁶
- Avoid requirement for specialist training and extensive monitoring during therapy delivery.¹⁷

* Do not use THERANOVA dialyzers in HDF or HF mode
REFERENCES


For further information visit hdxtheranova.com

For further information visit hdxtheranova.com:

Baxter Healthcare Corporation
One Baxter Parkway
Deerfield, IL 60015
USA

MANUFACTURER

Gambro DIALYSEATOREN GMBH
Holger-Crafoord-Strasse 26
72379 Hechingen
Germany