

**Baxter**

**CHANGE ONE THING.**


**CHANGE EVERYTHING.**

**HDx Clinical Evidence Series 1**  
**: Patient Reported Outcomes**




**INTRODUCING THERANOVA FOR  
EXPANDED HEMODIALYSIS [HDx]**


# Theranova를 통한 확장된 혈액투석: NOW IS THE TIME TO CHANGE EVERYTHING



중/대분자(500-45,000 Da) 요독소는 염증, 심혈관질환 (Cardiovascular disease, CVD) 및 기타 투석 관련 동반 질환의 발생과 관련이 있습니다.<sup>1-3</sup>



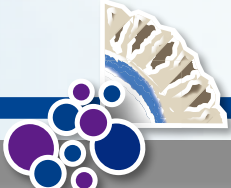
심혈관질환은 염증, 죽상동맥 경화증 및 석회화와 연관성이 있습니다. 신부전(Kidney failure) 환자의 약 50%가 심혈관질환으로 사망합니다.<sup>4-6</sup>




기존의 고유량 투석막은 중/대분자 요독소 (최대 45,000 Da)의 제거에 제한적입니다.<sup>7</sup>

**CHANGE ONE THING.**


혈액투석 (HD)의 차세대 투석막, Theranova는 기존 HD 방식 대비 염증 및 심혈관질환과 관련된 중/대분자 (최대 45,000 Da) 제거율을 개선하여 정상 신장 기능에 한층 더 가까워졌습니다.<sup>3,8-11</sup>



Theranova 투석막의 차별화된 디자인은 고유량 투석막에 비해 중/대분자(최대 45,000 Da)를 효과적으로 제거하는 동시에 필수 단백질을 선택적으로 유지하고 알부민 수치를 안정적으로 유지합니다.<sup>2,3,8-10,12,13</sup>



후향적 분석(n=81) 결과, HDx 요법은 입원 일수 및 센터 내 약제 사용을 크게 감소시켰습니다.<sup>14</sup> 무작위 대조 연구(n=171)에서 all-cause hospitalization이 43% 감소한 것으로 나타났습니다.<sup>15</sup> 일부 환자에서는 특정 염증 지표의 개선이 관찰되었습니다(n=41).<sup>16</sup>



HDx 요법은 환자의 증상부담, 하지불안증후군(Restless leg syndrome), 요독성 소양증(Uremic pruritus) 및 투석 회복 시간 등 환자가 보고한 신질환 관련 삶의 질 결과를 개선할 수 있습니다.<sup>8,9,17,18</sup>

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투석막 하나를 변경하여 혈액투석 치료 결과들의 많은 부분을 바꿀 수 있습니다.<sup>10</sup>

테라노바는 혈액투석 환자의 삶의 질과 연관된 Patient Reported Outcome을 개선시킵니다.

Safety > Performance > Effectiveness > **Patient-reported outcome** > Hard outcome and economics

Q1.

선생님의 혈액투석 환자 중,  
**하지불안증후군(Restless legs syndrome, RLS)**을  
호소하는 환자가 있으십니까?

RLS는 말기 신부전과 연관성을 보이는 질환 중 하나로,  
투석 환자의 최대 70%에서 RLS가 발생합니다.<sup>19</sup>

[ Prevalence of RLS among patients on dialysis<sup>19</sup> ]



- 투석 환자에서 RLS로 인해 투석 치료를 조기에 중단하는 환자 비율은 20%로 예측됩니다.<sup>19</sup>
- RLS가 있는 투석 환자의 경우, RLS가 없는 투석 환자 대비 수면의 질 및 낮 시간의 활동이 저하되는 것으로 나타났습니다.<sup>19</sup>

혈액투석을 받는 말기 신부전 환자 (ESRD)에서 삶의 질과 Patient-reported outcome (PRO)에  
대한 관심 및 중요성이 증가하고 있습니다. 보다 효과적으로 큰 증분자 물질을 제거하는  
MCO 투석막의 사용은 혈액투석 환자의 RLS를 개선시킬 수 있습니다.<sup>17,20</sup>

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Impact of Medium Cut-Off Dialyzers on Patient-Reported Outcomes: **COREXH Registry**

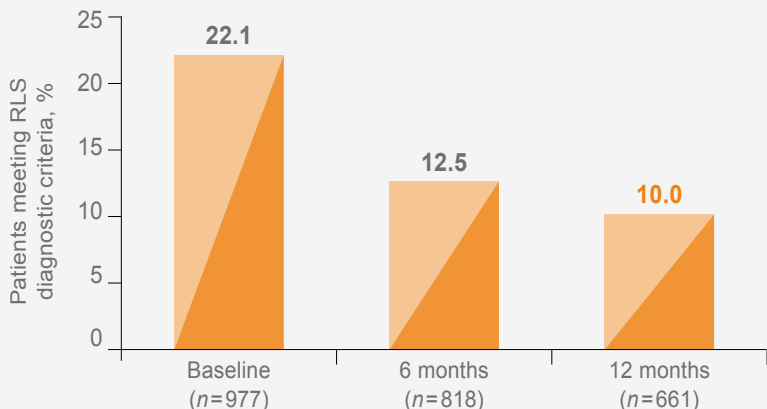
Alarcon JC, et al. Blood Purif. 2021;50(1):110-118.

High-Flux 투석막에서 MCO 투석막으로 변경한 경우, HDx 환자의 PRO에 미치는 영향을 평가한 대규모 다기관 COREXH Registry 연구 결과

테라노바로 변경하고 12개월 차 RLS 진단 환자의 비율은 baseline 기준 22.1%에서 10%로 50% 이상 유의한 감소가 관찰되었습니다 ( $p < 0.0001$ ).<sup>17</sup>

$\alpha$ 1-microglobulin과 같은 큰 중분자 물질들의 제거가 RLS의 호전과 연관성이 있다고 알려져 있습니다.<sup>21</sup>

[ Longitudinal changes in patients meeting RLS diagnosis<sup>17</sup> ]



Adapted from Alarcon JC, et al. 2021.

• A removal rate of 35% of  $\alpha$ 1-microglobulin ( $\alpha$ 1-MG; a heme scavenger) is associated with an improvement in RLS symptoms<sup>21</sup>

테라노바를 통한 큰 중분자 물질의 보다 효과적인 제거는 RLS를 개선시킬 수 있습니다.<sup>17</sup>

Proportion of patients meeting the RLS diagnostic criteria at baseline as well as 6 and 12 months of follow-up after switching to the medium cut-off membrane.

**Study design:** A prospective, multicenter, observational cohort study of 992 patients from 12 renal clinics in Colombia who were switched from high-flux HD to MCO therapy and observed for 12 months. Changes in Kidney Disease Quality of Life 36-Item Short Form Survey (KDQoL-SF36) domains, Dialysis Symptom Index (DSI), and restless legs syndrome (RLS) 12 months after switching to MCO membranes were compared with time on high-flux membranes. Repeated measures of ANOVA were used to evaluate changes in KDQoL-SF36 scores; severity scoring was used to assess DSI changes over time; Cochran's Q test was used to evaluate changes in frequency of diagnostic criteria of RLS.



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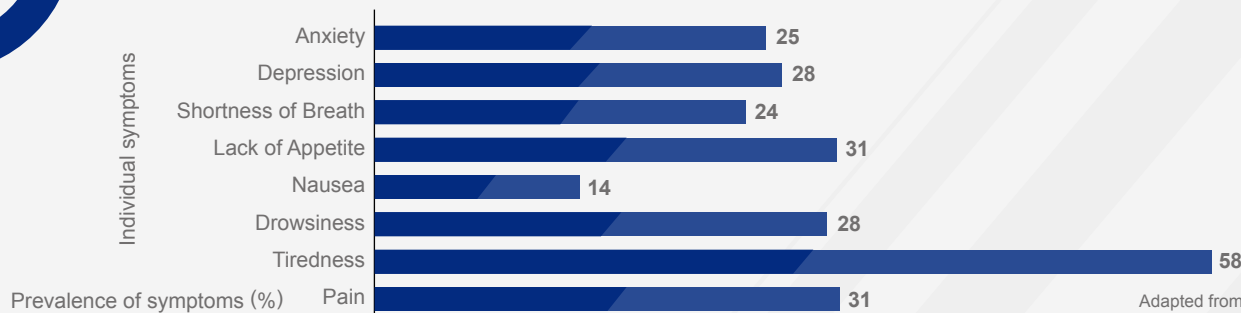
Q2.

선생님의 혈액투석 환자 중, 호흡곤란, 어지러움/현기증 등 신체적, 정신적 증상부담 (Symptom burden)을 경험하고 있는 환자가 있으십니까?

혈액투석 환자의 경우 피로, 호흡 곤란, 현기증 등의 Symptom burden을 겪고 있으며, 이러한 증상들을 혈액투석 환자의 삶의 질을 저하시킵니다.<sup>22</sup>



[ Frequency of moderate/severe distress of individual symptoms in patients with ESKD<sup>22</sup> ]



Adapted from Zhang JC, et al. 2020.

혈액투석 환자의 Symptom burden은 삶의 질의 저하, 우울증, 사망률의 증가 등으로 이어질 수 있습니다. 보다 효과적으로 큰 중분자 물질을 제거하는 MCO 투석막의 사용을 통해 혈액투석 환자의 Symptom burden의 개선을 도울 수 있습니다.<sup>17,22</sup>

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## Impact of Medium Cut-Off Dialyzers on Patient-Reported Outcomes: COREXH Registry

Alarcon JC, et al. Blood Purif. 2021;50(1):110-118.

High-Flux 투석막에서 MCO 투석막으로 변경한 경우, HDx 환자의 PRO에 미치는 영향을 평가한 대규모 다기관 COREXH Registry 연구 결과

12개월 차 KDQoL-36 조사 결과, 증상/문제, 신질환의 영향, 신질환 질병 부담 영역에서 유의한 개선이 관찰되었습니다.<sup>17</sup>

[ Changes in KDQoL-36 score over 12 months of follow-up<sup>17</sup> ]

KDQoL-36 domain	Statistic	Baseline (n=971)	6 months (n=808)	12 months (n=642)	p value <sup>a</sup>
Symptoms /problems	Mean	78.6	81.0	81.5	<0.0001
	SD	15.8	15.4	14.9	
Effects of kidney disease	Mean	69.7	72.8	75.1	<0.0001
	SD	22.3	22.0	21.0	
Burden of kidney disease	Mean	46.2	48.9	50.2	<0.001
	SD	27.5	29.9	32.3	

<sup>a</sup>For hypothesis testing, type-I error significance was set at p=0.01

Adapted from Alarcon JC, et al. 2021.

연구결과, Dialysis Symptom Index (DSI) 중 호흡곤란, 어지러움/현기증, 수면 장애 등 세가지 항목이 유의하게 개선되었습니다.<sup>7</sup>

[ Changes in DSI over 12 months of follow-up<sup>17</sup> ]

DSI domain	Statistic	Baseline (n=971)	6 months (n=808)	12 months (n=642)	p value
Number of symptoms	Mean	10.3	10.3	10	0.1 <sup>a</sup>
	SD	6.6	6.7	6.6	
Symptom severity score	Median	9	9	9	NA
	IQR	10	10	9	
Symptom severity score	Mean	30.7	29.9	28.5	0.009 <sup>b</sup>
	SD	22.3	32.0	21.7	
Symptom severity score	Median	26	26	23	NA
	IQR	32	30	31	

<sup>a</sup>By Friedman's test. <sup>b</sup>By ANOVA.

Adapted from Alarcon JC, et al. 2021.

[ Changes in frequency of DSI<sup>17</sup> ]

Item, n (%)	Baseline (n=989)	6 months (n=850)	12 months (n=600)	p value <sup>a</sup>
Shortness of breath	214 (21.64)	207 (24.32)	124 (20.63)	0.02 <sup>b</sup>
Dizziness/lightheadedness	268 (27.1)	207 (24.32)	127 (21.13)	0.01 <sup>b</sup>
Difficulty falling asleep	489 (49.44)	397 (46.71)	270 (45)	0.02 <sup>b</sup>

<sup>a</sup>Cochran's Q test for proportions at moments in time. <sup>b</sup>Considered to be marginally significant.

Adapted from Alarcon JC, et al. 2021.



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Q3.

선생님의 혈액투석 환자 중,  
**소양증(Pruritus)으로 인해 수면장애**가 있는  
환자가 있으십니까?



말기 신부전 환자 (ESRD)의 약 40%가 중등증-중증의 소양증을 경험하는 것으로 나타났으며, **요독성 소양증 (Uremic pruritus, UP)**은 삶의 질 저하, 수면장애, 우울증 경험 등 임상적으로 중대한 영향을 미칠 수 있습니다.<sup>23</sup>

[ Prevalence of moderate to severe pruritus among patients with ESRD<sup>23</sup> ]



[ Major clinical impacts of UP<sup>23</sup> ]

- Poor quality of life
- Impaired sleep
- Depression
- Increased mortality

혈액투석 환자에서 피로, 전신 쇠약, 소양증과 같은 다양한 증상이 나타날 수 있으며, 이러한 증상은 기존의 투석 방식으로 제거되지 않는 중분자로 인한 것일 수 있습니다. 보다 효과적으로 큰 중분자 물질을 제거하는 MCO 투석막의 사용을 통해 혈액투석 환자의 삶의 질 및 소양증과 같은 **Patient reported outcome (PRO)**을 개선시킬 수 있습니다.<sup>8</sup>

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## Randomized controlled trial of medium cut-off versus high-flux dialyzers on quality of life outcomes in maintenance hemodialysis patients

Lim JH, et al. Sci Rep. 2020 May 8;10(1):7780

Medium cut-off (MCO) 투석막이 혈액투석 환자의 삶의 질 향상에 미치는 영향을 High-flux 투석막과 비교 평가한 연구 결과

12주 차 MCO군에서 High-flux군 대비 아침 소양증 점수\* 및 수면 중 긁는 행위의 빈도가 통계적으로 유의하게 낮았습니다.<sup>8</sup>

MCO군은 12주 차에 신체적 기능 및 신체적 역할 영역에서 High-flux 대비 개선을 보였습니다 (KDQOL-SF questionnaire).<sup>8</sup>

[ Assessment of uremic pruritus at baseline and 12 weeks<sup>8</sup> ]

	Baseline			12 weeks		
	MCO (n=24)	HF (n=25)	P	MCO (n=24)	HF (n=25)	P
<b>Distribution</b>						
Morning	1.42 ± 0.58	1.48 ± 0.71	0.736	1.29 ± 0.46	1.64 ± 0.64	0.034
<b>Sleep disturbance</b>						
Frequency of scratching during sleep	0.38 ± 0.92	0.24 ± 0.72	0.571	0.25 ± 0.53	1.00 ± 1.47	0.023

Adapted from Lim JH, et al. 2020.

[ Quality of life questionnaire scores at baseline and 12 weeks<sup>8</sup> ]

	Baseline			12 weeks		
	MCO (n=24)	HF (n=25)	P	MCO (n=24)	HF (n=25)	P
Physical functioning	72.1 ± 23.7	59.4 ± 28.3	0.096	75.2 ± 20.8	59.8 ± 30.1	0.042
Role-physical	56.3 ± 39.2	44.0 ± 40.4	0.287	61.5 ± 37.6	39.0 ± 39.6	0.047

Values are shown as the mean ± standard deviation

Adapted from Lim JH, et al. 2020.

\*Uremic pruritus was assessed using the scoring system modified by Pauli-Magnus. The pruritus scoring questionnaire was composed of severity, distribution, and sleep disturbance categories. Severity: Scores of 1, 2, 4, and 5 points were recorded for a slight itchy sensation without scratching, the need to scratch without excoriations, scratching with excoriation, and pruritus with total restlessness, respectively. Distribution: Itching at less than two sites, more than two sites, and generalized itching received 1, 2, and 3 points, respectively. The scores of severity and distribution were assessed in the morning and the afternoon. The two scores were multiplied separately to achieve a maximum of 30 points. Sleep disturbance: Each waking episode from itching received 2 points (maximum 10 points). Each nighttime scratching episode causing excoriations received 1 point (maximum 5 points). The final score was calculated as the addition of the sleep disturbance score and the severity-distribution product (maximum of 45 points). The VAS was used to evaluate the subjective intensity of pruritus. The patients reported their itching intensity on a 10-point VAS with 0 indicating no pruritus and 10 indicating unbearable pruritus.

**Study design:** A randomized, prospective, controlled, open-label, phase 4 trial to investigate the effect of an MCO dialyzer on the improvement of QOL in maintenance hemodialysis patients. Patients treated with maintenance HD at the Kyungpook National University Hospital were enrolled and randomized starting in July 2018, and the study was completed in January 2019. Forty nine HD patients with high-flux dialysis were randomly assigned to either an MCO (Theranova 400, Baxter) or a high-flux dialyzer and completed the study. The mean age of the MCO group patients switched from a high-flux membrane was 62.2 ± 13.7 years, and 75.0% were men. The high-flux group patients had a similar mean age and percentage of male participants (63.8 ± 15.2 years and 60.0%, respectively). QOL was assessed at baseline and after 12 weeks of treatment using the Kidney Disease Quality of Life Short Form-36, and pruritus was assessed using a questionnaire and visual analog scale. The reduction ratios of middle molecules were also evaluated.





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