Economic evaluation of expanded hemodialysis with the Theranova 400 dialyzer: A post hoc evaluation of a randomized clinical trial in the United States

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BACKGROUND

In 2018, approximately 485,000 people in the US received maintenance dialysis for kidney failure, a number that has doubled in the last 20 years. Medicare funds about three fourths of patients requiring dialysis; although dialysis is required by <1% of Medicare enrollees, these patients account for 7.2% of paid Medicare claims.

Despite dialysis, uremic toxins may accumulate over time and increase patient morbidity and mortality. Conventional dialysis modalities such as high-flux hemodialysis (HD) typically remove small molecules (<0.5 kDa) and smaller middle molecules (0.5-25 kDa), but not larger middle molecules (25-60 kDa). To address this unmet need, the **Theranova** 400 dialyzer (Baxter Healthcare Corporation, Deerfield, IL) has been developed and was approved by the FDA in August 2020. The **Theranova** 400 has an expanded solute removal profile up to 45 kDa and may be used in expanded hemodialysis, a technique that combines diffusion and convection in a hollow-fiber dialyzer with a medium cut-off membrane. In the original analysis, this randomized, controlled trial has shown **HDx** therapy with **Theranova** to be superior to high-flux HD in terms of the removal of larger middle molecules such as lambda-free light chains, while maintaining adequate serum albumin levels. This secondary analysis aimed to determine if use of **HDx** therapy could also reduce healthcare costs for this patient population, particularly if, as expected, removal of larger middle molecules is associated with improved clinical outcomes.

OBJECTIVE

This post-hoc analysis therefore reviewed trial data regarding clinical outcomes in particular hospitalization rates, and healthcare costs of patients treated with either **HDx** therapy with **Theranova** or high-flux HD.

METHODOLOGY

This prospective, randomized, open-label, parallel study (NCT03257410) in patients receiving maintenance dialysis treatment compared results of those treated with **HDx** therapy with the **Theranova** 400 dialyzer to those dialyzed with a high-flux HD dialyzer of the same size, with thrice-weekly sessions over 24 weeks. Patients were clinically stable adults who had received HD with a high-flux dialyzer for ≥3 months; all had stable vascular access and maintained an acceptable urea clearance. Patients were excluded if they had had an acute infection in the previous 4 weeks or if they had certain chronic diseases (i.e., cancer, HIV, hepatitis, chronic liver disease, paraprotein-associated disease, monoclonal/polyclonal gammopathy).

- Hospitalization – any SAE which contained a hospitalization admission date. Hospitalization rate - total number of hospitalizations/total person years of follow up during the trial period.
- Erythropoietic stimulating agents (ESA) use was captured in the study but data were incomplete so use and dose were assumed to be equal between 2 arms.
- Cost of hospitalization – taken from Kaiser Family Foundation USA average in 2018.

This analysis examined hospitalization, hospitalization rate (number of hospitalizations divided by total person-years of follow up), hospital length of stay, total cost of hospitalization, and cost of dialyzers. The cost per high-flux dialyzer was assumed to be $6.50, and the cost per **Theranova** dialyzer was $15.00; other costs associated with dialysis were assumed to be equal and were excluded from the model, as were patient medications and medication doses.

Statistical Analysis

Mean length of hospitalization was estimated using a Poisson (log-count) general linear model. A univariate sensitivity analysis was included to evaluate the impact of observed variability on cost differences between treatments. Itemized and total costs per group were calculated through random sampling of all input parameters based on the closest approximations of their observed distributions; repetition over 10,000 simulations generated the mean and 95% confidence intervals (CI).

RESULTS

Study Population

A total of 172 patients were randomized, and 171 were treated at 21 US centers between September 2017 and October 2018; 86 were treated with **HDx** therapy using **Theranova** (389 patient-months), and 85 with a high-flux dialyzer (366 patient-months). Baseline demographics and clinical characteristics were similar between groups; 39% of patients were female, and the mean age was 59±13 years.

Clinical outcomes: hospitalization and length of stay

Clinical outcomes are shown in Table 1. Hospitalization was 45% lower in patients treated with **HDx** therapy with **Theranova** compared with high-flux HD (IRR=0.55; 95% CI: 0.30, 1.00; P=0.042). There was no significant difference in length of hospital stay.

TABLE1. Clinical Outcomes

Health resource utilization	Theranova (n=86)	High-flux HD (n=85)	P-value
Hospitalization events	18	31	--
Total hospital days	74	139	--
Total patient-years (PY)	32.4	30.5	--
Hospitalization rate per PY	0.56 (0.13)	1.02 (0.12)	0.042
Hospital length of stay (mean days [SE])	4.11 (0.57)	4.63 (0.58)	0.406

HD, hemodialysis; PY, patient year; SE, standard error.
Adapted from Blackowicz et al.

Economic evaluation

Table 2 shows the economic evaluation of **HDx** therapy with **Theranova** compared with high-flux HD. While the trial lasted 6 months, the economic model calculates values over one year of treatment. Although **HDx** therapy with **Theranova** is associated with a higher dialyzer cost, its lower all-cause hospitalization rate makes it a cost-efficient alternative. Compared with high-flux HD, **Theranova** offered an average annual estimated cost savings of $4772. Hospitalization rate and length of stay were the main drivers of cumulative cost.

TABLE 2. Economic Evaluation

		Per Patient Cost		
Item	Unit cost	Theranova	High-flux HD	Difference
All-cause hospitalization[a]	$2518 per day	$5756	$11,853	-$6097
Dialyzer cost[b]	$15.00 ea/ $6.50 ea	$2340	$1014	$1326
Cumulative		$8096	$12,867	-$4771

[a]All-cause hospitalization was defined as any serious adverse event that resulted in hospitalization. [b]**Theranova** dialyzer was priced at $15 in the United States and high-flux dialyzer was assumed to cost $6.50.
HD, hemodialysis.

Adapted from Blackowicz et al.

Probabilistic sensitivity analysis

A univariate sensitivity analysis (Figure 1) accounted for the observed variability in each model separately. Hospitalization rates were the main drivers of cost difference, particularly in the high-flux HD group. Results favored **Theranova** at the upper and lower thresholds for all inputs.

FIGURE 1. Univariate sensitivity analysis

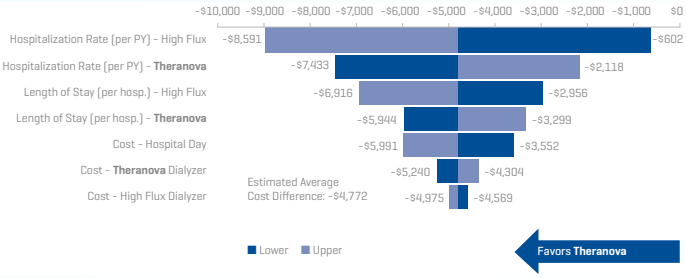

Figure adapted from Blackowicz et al.

Summary estimates were run with >10,000 simulations of costs to verify the mean difference in cost between treatments. Table 4 shows the probabilistic analysis, which determined that **HDx** therapy with **Theranova** was associated with lower costs in 96% of the simulations.

TABLE 3. Simulated summary of methods of mean cost difference

	Per Patient Cost Difference	
Item	Mean	(95% CI)
All-cause hospitalization (per day)	-$6103	(-$11,604 to -$601)
Dialyzer cost	$1326	--
Cumulative	-$4777	(-$10,278 to $725)
Proportion of simulations demonstrating **Theranova** cost-saving over high-flux HD	95.7%	

HD, hemodialysis
Adapted froackowicz et al.

Study Limitations

The 6-month trial had too few hospitalization events to draw sound statistical conclusions between categories (e.g., to eliminate trauma cases or assess infection- or cardiovascular-related events). Cost assumptions had to be made to complete the analysis; assuming that medications would be equivalent between arms was one such assumption. Also, study records on erythropoietin-stimulating agents and iron dosing were incomplete, and authors would have liked to incorporate that variable. Other potential study confounders seem to balance across treatment arms and are unlikely to affect study results.

DISCUSSION

There are few studies on health economics and patient outcomes regarding **HDx** therapy with **Theranova**, but this study supports the findings of two other studies, one showing that **HDx** therapy with **Theranova** was associated with lower hospitalization costs and the second (a retrospective, observational study) that showed that **HDx** therapy with **Theranova** was associated with a lower risk of hospitalization.

Authors add that the study entry criteria required that dialysis patients be medically stable so the study group tends to be younger than the average dialysis patient age in the USA. Since hospitalization costs drove healthcare costs in this relatively young and healthy population, cost differences could be greater still in a real-world setting, where patients may be older and less medically stable.

Findings are of potential importance in upcoming US payment models in kidney care, particularly the Comprehensive End-Stage Renal Disease Care Model (ESCO) and Kidney Care Choices, which consider hospitalization costs and the number of hospitalizations.

CONCLUSIONS

In this post-hoc analysis of a randomized clinical trial, the **HDx** therapy with **Theranova** dialyzer was associated with lower healthcare costs than standard high-flux HD. In addition to its superior removal of large middle molecules, the **Theranova** dialyzer is associated with a reduced hospitalization rate per patient year and is expected to be a cost-saving therapy, based on this significant reduction in hospitalization events.

CE 0123

Theranova dialyzers are indicated for treatment of chronic and acute renal failure by Hemodialysis. For single use only.

For safe and proper use of these devices refer to the Instructions for Use.

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