Newly reported data representing nearly all US outpatient dialysis facilities reveal that most bloodstream infections in dialysis patients continue to occur in those with central venous catheters used for vascular access. The findings, which are published in a recent Clinical Journal of the American Society of Nephrology study, come from the first year of data used by the Centers for Medicare & Medicaid Services to assess facility performance based on bloodstream infections.

Increasing attention is being paid to reducing vascular access-related infections in dialysis patients. “Hemodialysis patients are at high risk for infections, which increase mortality, hospitalization, and healthcare costs. Therefore, surveillance of infectious adverse events among hemodialysis patients is very important,” said the Centers for Disease Control and Prevention’s (CDC’s) Duc Bui Nguyen, MD, lead author of the study. “Tracking infections helps guide intervention and prevention efforts to reduce severe events.”

In the late 1990s, the CDC initiated a system to help facilities track infections. The new data were generated by expanding that system.

“We still have to teach people to put the patient’s voice first,” Dishman told attendees at the May 2017 Kidney Health Initiative (KHI) meeting in Silver Spring, MD. KHI is a public-private partnership between the American Society of Nephrology, US Food and Drug Administration, and over 75 companies and organizations focused on enhancing patient safety and fostering innovation in kidney disease.

Dishman said his kidney transplant care was the first time he received truly comprehensive care. But if All of Us is successful in its goals, it may help accelerate the shift toward personalized medicine.

**Beta testing**

Already more than 300 participants age 18 and older have enrolled in the All of Us Research Program, according to Akinlolu Ojo, MD, MPH, PhD, MBA, a nephrologist at the University of Arizona and one of the project’s principle investigators.

**Findings**

Early diabetic kidney disease shortens life expectancy.

**Fellows Corner**

With political, societal changes linked to diseases seen today, how should docs respond?

**Policy Update**

NIH gains in budget process still fall short of need.

**Kidney Disease Biomarkers**

Some progress, more work needed to identify AKI in radiocontrast nephropathy, oncology, and for progression to CKD.

**Practice Pointers**

Primary and secondary FSGS, plus recurrent FSGS after transplant.

**New JASN Editor-in-Chief**

Jocelyn P. Briggs, MD, takes the helm.

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**All of Us Research Program Aims to Catapult Personalized Medicine Forward**

May Help Define Both Good Kidney Health and Disease Contributors

By Bridget M. Kuehn

In late May, the more than $200 million project began enrolling the first of what will eventually be 1 million study participants, making it one of the largest research programs ever attempted. Participants will represent a broad range of health statuses, ages, and walks of life. Investigators plan to follow participants for decades and collect reams of biological, lifestyle, and healthcare data. This trove of data will provide a rich resource for researchers trying to better understand risk factors for disease, find ways to more precisely target treatments, reduce health disparities, and advance personalized care.

“The more we understand about individual differences, the better able we will be to effectively prevent and treat illness,” said NIH Director Francis S. Collins, MD, PhD, in a statement about the program.

Fully engaged and empowered patients will be essential to the massive program’s success.

“As a cancer patient for 23 years—who was eventually cured with the help of precision medicine—Eric Dishman brings a very patient-centric view to his work leading the National Institutes of Health’s (NIH) ambitious All of Us Research Program.

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**Catheters Continue to Be Linked to Most Bloodstream Infections in Dialysis Patients**

By Tracy Hampton

Newly reported data representing nearly all US outpatient dialysis facilities reveal that most bloodstream infections in dialysis patients continue to occur in those with central venous catheters used for vascular access. The findings, which are published in a recent clinical study, come from the first year of data used by the Centers for Medicare & Medicaid Services to assess facility performance based on bloodstream infections.

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Catheters

Continued from page 1

fections among dialysis patients. In the early years, a relatively small number of dialysis facilities participated. Today, thousands of facilities report to the CDC’s National Healthcare Safety Network (NHSN) Dialysis Event Surveillance. This is in part due to requirements set in 2012 that all Medicare-licensed outpatient dialysis facilities report access-related infections to the NHSN.

Also, in 2014, bloodstream infections were added to the Centers for Medicare & Medicaid Services’ End-Stage Renal Disease Quality Incentive Program to assess dialysis facility performance.

In their recent analysis, Nguyen and his colleagues at the CDC summarized 2014 data submitted to the NHSN Dialysis Event Surveillance program. They noted that 6605 outpatient hemodialysis facilities reported data for a total of 160,971 dialysis events including 29,516 bloodstream infections (BSIs); 149,722 intravenous antimicrobial starts; and 38,310 episodes of pus, redness, or increased swelling at the hemodialysis access site. Across event types, pooled rates were highest for central venous catheters, lower for arteriovenous grafts, and lowest for arteriovenous fistulas.

The team found that 77% of BSIs were related to access-related infections—most—63% of BSIs and 70% of access-related BSIs—occurred in patients with a central venous catheter.

BSI and other dialysis event rates were also highest among patients using central venous catheters. Staphylococcus aureus was the most commonly isolated BSI pathogen (31%), and 40% of S. aureus isolates tested were resistant to the antibiotic methicillin. Vancomycin-resistant S. epidermidis patients started in 76% of intravenous antibiotic initiations.

Hospitalization was an outcome for 22% of all dialysis events, including 49% among central venous catheter events, 36% among arteriovenous fistula events, 15% among arteriovenous graft events, and 0.4% among other vascular access events. Hospitalizations occurred in 48% of BSIs, 46% of access-related BSIs, 25% of vascular access infections and 11% of local access site infections. Death occurred in 1352 (0.8%) of all dialysis events. Two percent of BSIs and 1.6% of access-related BSIs resulted in death.

“We now have a clearer picture of the rates and types of infections hemodialysis patients in the United States are experiencing—nearly all US outpatient hemodialysis facilities are participating in CDC’s NHSN Dialysis Event Surveillance,” said Nguyen. “Our findings emphasize the need for hemodialysis facilities to improve infection prevention and vascular access care practices.”

In an accompanying editorial, Dana Miskulin, MD, of the Tufts University School of Medicine, and Ambreen Gul, MD, of Dialysis Clinic Inc., noted that a major problem to the available data is that event reporting is based on an honors system, and dialysis units report their own information without any processes to ensure that events are reported accurately. “We make a plea to the dialysis community to ‘clean up’ the data and ensure that the Dialysis Event Improvement Program is fairer for all and to enable the full potential of these data, both for improving care now and for generating new evidence to provide future opportunities to improve care and outcomes, to be realized,” they wrote.

The authors of the editorial also noted that the nearly 50% decline in rates of bloodstream and localized vascular access infections observed from 2006 to 2014 reflects improved practices; however, several red flags suggest that underreporting of events is likely. They also pointed to several unanswered questions, including whether outcomes are superior with catheter removal/replacement vs. “treating through,” whether replacement over a wire is equivalent, and whether antibiotic locks have any role to play.


## Table 1: Adverse Reactions Reported in ≥ 2% of Patients

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>Patients treated with VELTASSA (N=680)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constipation</td>
<td>7.2%</td>
</tr>
<tr>
<td>Hypogammaglobulin</td>
<td>5.3%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4.8%</td>
</tr>
<tr>
<td>Nausea</td>
<td>2.3%</td>
</tr>
<tr>
<td>Abdominal discomfort</td>
<td>2.0%</td>
</tr>
<tr>
<td>Flatulence</td>
<td>2.0%</td>
</tr>
</tbody>
</table>

**VELTASSA** (patrovlome) for Oral Suspension

Brief Summary of Prescribing Information. Please see Full Prescribing Information for complete product information.

**WARNING: BINDING TO OTHER ORAL MEDICATIONS**

VELTASSA binds to many orally administered medications, which could decrease their absorption and reduce their effectiveness. Administer other oral medications at least 6 hours before or 6 hours after VELTASSA. Choose VELTASSA or the other oral medication if adequate dosing separation is not possible (see Warnings and Precautions and Drug Interactions).

**INDICATION AND LIMITATION OF USE**

VELTASSA is indicated for the treatment of hyperkalemia.

Limitation of Use: VELTASSA should not be used as an emergency treatment for life-threatening hyperkalemia because of its delayed onset of action.

**CONTRAINDICATIONS**

VELTASSA is contraindicated in patients with a history of a hypersensitivity reaction to VELTASSA or any of its components (see Adverse Reactions).

**WARNINGS AND PRECAUTIONS**

Binding to Other Orally Administered Medications

VELTASSA binds to many orally administered medications, which could decrease their gastrointestinal absorption and lead to reduced efficacy. Administer other oral medications at least 6 hours before or 6 hours after VELTASSA. Choose VELTASSA or the other oral medication if adequate dosing separation is not possible (see Drug Interactions).

Worsening of Gastrointestinal Motility

Avoid use of VELTASSA in patients with severe constipation, bowel obstruction or impaction, including abnormal post-operative bowel mobility disorders, because VELTASSA may be ineffective and may worsen gastrointestinal conditions. Patients with a history of bowel obstruction or major gastrointestinal surgery, severe gastrointestinal disorders, or swallowing disorders were not included in the clinical studies.

Hypomagnesemia

VELTASSA binds to magnesium in the colon, which can increase serum magnesium. In clinical studies, hypomagnesemia was reported as an adverse reaction in 5.3% of patients treated with VELTASSA (see Adverse Reactions). Monitor serum magnesium. Consider magnesium supplementation in patients who develop low serum magnesium levels on VELTASSA.

**ADVERSE REACTIONS**

The following adverse reaction is discussed in greater detail elsewhere in the label:

- **Hypomagnesemia** (see Warnings and Precautions)

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of VELTASSA cannot be directly compared to rates in the clinical trials of other drugs and may not reflect the rates observed in practice. In the safety and efficacy clinical trials, 666 adult patients received at least one dose of VELTASSA, including 219 exposed for at least 6 months and 149 exposed for at least one year. Table 1 provides a summary of the most common adverse reactions (occurring in ≥ 2% of patients) in patients treated with VELTASSA in these clinical trials. Most adverse reactions were mild to moderate. Constipation generally resolved during the course of treatment.

**During the clinical studies, the most commonly reported adverse reactions leading to discontinuation of VELTASSA were gastrointestinal adverse reactions (2.7%), including vomiting (0.9%), diarrhea (0.6%), constipation (0.5%) and flatulence (0.5%). Mild to moderate hypomagnesemia reactions were reported in 0.3% of patients treated with VELTASSA in clinical trials. Reactions have included edema of the lips, mouth, and tongue. Laboratory Abnormalities

Approximately 4.7% of patients in clinical trials developed hypokalemia with a serum potassium value < 3.5 mEq/L. Approximately 9% of patients in clinical trials developed hypomagnesemia with a serum magnesium value < 1.4 mEq/L.

**DRUG INTERACTIONS**

No formal drug interaction studies have been conducted in humans. In vitro binding studies, VELTASSA was shown to bind to about half of the oral medications that were tested. Binding of VELTASSA to other oral medications could cause decreased gastrointestinal absorption and loss of efficacy when taken close to the time VELTASSA is administered. Administer other oral medications at least 6 hours before or 6 hours after VELTASSA. Monitor for clinical response and/or blood levels where possible.

**USE IN SPECIFIC POPULATIONS**

**Pregnancy**

Risk Summary

VELTASSA is not absorbed systemically following oral administration and maternal use is not expected to result in fetal risk.

Lactation

Risk Summary

VELTASSA is not absorbed systemically by the mother, so breastfeeding is not expected to result in risk to the infant.

**Pediatric Use**

Safety and efficacy in pediatric patients have not been established.

**Geriatric Use**

The 666 patients treated with VELTASSA in clinical studies, 59.8% were age 65 and over, and 19.8% were age 75 and over. No overall differences in effectiveness were observed between these patients and younger patients. Patients age 65 and older reported more gastrointestinal adverse reactions than younger patients.

**Renal Impairment**

The 666 patients treated with VELTASSA in clinical studies, 59% had chronic kidney disease (CKD). No special dosing adjustments are needed for patients with renal impairment.

**OVERDOSAGE**

Doses of VELTASSA in excess of 50.4 grams per day have not been tested. Excessive doses of VELTASSA may result in hypokalemia. Restore serum potassium if hypokalemia occurs.

**PATIENT COUNSELING INFORMATION**

Advise the patient to use the FDA-approved patient labeling (Medication Guide).

**Drug Interactions**

Advise patients who are taking other oral medication to separate the dosing of VELTASSA by at least 6 hours before or after (see Drug Interactions).

**Dosing Recommendations**

Inform patients to take VELTASSA as directed with food and adhere to their prescribed diets. Initiate patients to prepare each dose separately using the preparation instructions provided in the FDA-approved patient labeling (Medication Guide). Inform patients that VELTASSA should not be heated (e.g., microwaved) or added to heated foods or liquids and should not be taken in its dry form.

**Manufactured for:**

Relysia, Inc.

Redwood City, CA 94063

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