

# Industry Spotlight

## AKI Research News

Scientists are making strides in predicting occurrence of acute kidney injury (AKI) and in evaluating extensive data on patients who recover from AKI.

The Department of Veterans Affairs (VA) announced a year ago that it had signed a formal agreement with DeepMind to gather and analyze data on kidney disease and other conditions. Wired magazine caught up with the project's status recently, and noted that it drew on about 700,000 medical records from veterans. The VA has

been working with DeepMind (owned by Google's parent company, Alphabet) to create software that tries to predict when patients might develop AKI.

The VA's director of predictive analytics, Christopher Nielsen, told Wired that the project has "been fairly successful in predicting AKI at an early enough stage to prevent it."

The next step may be to use live data from the VA system to evaluate the accuracy of the AKI predictive factors over time, Wired noted. Then it would be possible to

introduce the system for use in a VA clinic to see if it helps improve care, a test that is at least one year away.

Dialysis and kidney care giant Fresenius also is interested in using its extensive patient data to learn more about AKI. Of 9000 patients diagnosed with AKI at Fresenius North America outpatient clinics, about one-third recovered kidney function within 90 days of beginning in-center hemodialysis, according to Fresenius.

Overall, 38% of patients recovered kidney function within 150 days of initiating

outpatient therapy, the company said in a press release.

The preliminary analysis of the Fresenius data included several clinical measures, such as type of vascular access used, ultrafiltration rates, and biochemical measures during the first 90 days of outpatient dialysis therapy.

The data also suggested that 20% of patients who begin outpatient in-center hemodialysis are diagnosed with AKI, and 44% of those patients transition to ESRD within 150 days of starting outpatient hemodialysis.

"This groundbreaking data holds enormous promise for developing further insights into the treatment of acute kidney injury," said Frank Maddux, MD, chief medical officer and executive vice president for clinical and scientific affairs at Fresenius Medical Care North America. ■

### VELTASSA® (patiomer) for Oral Suspension

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

#### INDICATION AND USAGE

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

**Worsening of Gastrointestinal Motility** Avoid use of VELTASSA in patients with severe constipation, bowel obstruction or impaction, including abnormal post-operative bowel motility 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 lead to hypomagnesemia. 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  $\geq 2\%$  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.

**Table 1: Adverse Reactions Reported in  $\geq 2\%$  of Patients**

Adverse Reactions	Patients treated with VELTASSA (N=666)
Constipation	7.2%
Hypomagnesemia	5.3%
Diarrhea	4.8%
Nausea	2.3%
Abdominal discomfort	2.0%
Flatulence	2.0%

During the clinical studies, the most commonly reported adverse reactions leading to discontinuation of VELTASSA were gastrointestinal adverse reactions (2.7%), including vomiting (0.8%), diarrhea (0.6%), constipation (0.5%) and flatulence (0.5%). Mild to moderate hypersensitivity reactions were reported in 0.3% of patients treated with VELTASSA in clinical trials. Reactions have included edema of the lips.

**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  $< 1.4$  mg/dL.

#### DRUG INTERACTIONS

In clinical studies, VELTASSA decreased systemic exposure of some coadministered oral medications. 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 3 hours before or 3 hours after VELTASSA.

#### 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** Of 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** Of the 666 patients treated with VELTASSA in clinical studies, 93% 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

**Drug Interactions** Advise patients who are taking other oral medication to separate the dosing of VELTASSA by at least 3 hours (before or after) [see *Drug Interactions*].

**Dosing Recommendations** Inform patients to take VELTASSA as directed with or without food and adhere to their prescribed diets. 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:

Relypsa, Inc.  
Redwood City, CA 94063  
Version 05; May 2018

**References:** 1. Weir MR, Bakris GL, Bushinsky DA, et al; for OPAL-HK Investigators. Patiomer in patients with kidney disease and hyperkalemia receiving RAAS inhibitors. *N Engl J Med*. 2015;372(3):211-221. 2. Data on file as of December 2017. Relypsa, Inc. 3. Data on file as of March 2018. Relypsa, Inc.

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## Different Fates for two RCC Treatments

One manufacturer has decided not to file for FDA approval of its renal cell carcinoma (RCC) treatment, while another manufacturer's combination of RCC drugs has won European approval.

Aveo Oncology, based in Cambridge, MA, decided against filing a new drug application for tivozanib (brand name Fotivda) in the United States. The FDA had informed Aveo that it was unsatisfied with the drug's overall survival data, and that the data failed to improve upon initial concerns the FDA had when it rejected the drug in 2013.

In that year, the FDA questioned the drug's benefits because data showed that tivozanib failed to beat the overall survival rate of Bayer's drug, Nexavar, FierceBiotech reported. An August 2018 analysis of required data will no longer be Aveo's final analysis but rather an interim analysis as the company continues toward FDA approval. Fotivda is approved for first-line treatment of advanced RCC in Europe.

Meanwhile, an RCC treatment that consists of a drug combination was approved for European patients. Bristol-Myers Squibb (Princeton, NJ) announced that the European Commission had approved the combination of its trademarked drugs Opdivo (nivolumab) 3 mg/kg plus Yervoy (ipilimumab) 1 mg/kg ("low-dose").

The combination therapy is a first-line therapy to treat patients with intermediate- and poor-risk advanced RCC. The European approval hinged on results from the CheckMate-214 trial, a phase 3, randomized, open-label study evaluating the combination of Opdivo plus Yervoy versus sunitinib in patients with previously untreated advanced renal cell carcinoma. The FDA has already approved the combination for certain patients whose cancer has metastasized. ■