

## Findings

### Prediabetes linked to increased risk of hyperfiltration and albuminuria

Middle-aged adults with prediabetes are at increased risk of developing glomerular hyperfiltration and albuminuria, reports a study in *The American Journal of Kidney Diseases*.

The researchers analyzed prospective data on a general population sample of 1261 Norwegian adults drawn from the Renal Iohexol Clearance Survey in Tromsø

6 (RENIS-T6) Study and the RENIS Follow-Up Study. At baseline, subjects were 50 to 62 years old and free of diabetes. On the basis of fasting glucose and hemoglobin A1c levels, 595 participants had prediabetes according to American Diabetes Association criteria, and 169 participants had prediabetes according to International Expert Committee of 2009 (IEC) criteria.

At a median follow-up of 5.6 years, change in measured GFR (mGFR) was compared between groups; hyperfiltration was defined as mGFR above the 90th percentile adjusted for age, sex, height, and weight. Rates of high-normal urinary albumin-to-creatinine ratio (ACR; greater than 10 mg/g) were assessed as well.

On multivariable analysis, both sets of

prediabetes criteria predicted an increased mGFR at follow-up and a lower annual rate of decline in mGFR. Baseline fasting glucose and HbA1c were also significant predictors. In the smaller group of patients meeting IEC criteria, odds ratios were 1.92 for hyperfiltration and 1.83 for high-normal ACR. The associations remained significant after adjustment for baseline BP, use of antihypertensive medications, and other cardiovascular risk factors [Melsom T, et al. Prediabetes and risk of glomerular hyperfiltration and albuminuria in the general nondiabetic population: A prospective cohort study. *Am J Kidney Dis* 2016; 67:841–850]. ●

#### VELTASSA™ (patiomer) 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 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 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 ≥ 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 ≥ 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

No formal drug interaction studies have been conducted in humans.

In *in vitro* binding studies, VELTASSA was shown to bind 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** 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

Advise the patient to read 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. Instruct 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:

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Redwood City, CA 94063  
Version 01; October 2015

### What happens to kidney donors who develop ESRD?

A high proportion of living kidney donors who have developed ESRD are never waitlisted for kidney transplantation, reports a study in *Transplantation* that was part of a special issue on living organ donation.

Using data from the Scientific Registry of Transplant Recipients, the researchers identified 96,127 individuals who donated kidneys between 1994 and 2011. Of these, 99 developed ESRD. Median age at diagnosis of ESRD was 50 years old; 56 percent of patients were men, and 34 percent were black. Causes of ESRD were GN in 29.3 percent of donors, hypertension in 24.2 percent, diabetes in 5.1 percent, and other causes in 41.4 percent. Median times to developing ESRD in these groups were 7.4, 12.0, 9.9, and 9.6 years, respectively.

Initial treatment for ESRD was dialysis in 78 patients. Thirty-seven patients were waitlisted for kidney transplantation, and two received a live donor transplant without being listed. Twenty patients were listed pre-emptively, 19 of whom received a transplant. The remaining 39 patients were never listed and never received a transplant.

The donors were waitlisted earlier than a matched group of nondonors with ESRD (median of 14 versus 120 months) and transplanted earlier (2.8 versus 21.5 months). Donors were less likely than controls to receive a live donor kidney (13 versus 39 percent) and more likely to receive a standard criteria deceased donor kidney (87 versus 50 percent). The two groups had similar posttransplant graft and patient outcomes.

Living kidney donors have a “demonstrated, albeit low” risk of ESRD. This national study finds that living donors who develop ESRD are waitlisted and transplanted faster than matched nondonor controls. However, about 40 percent of donors with ESRD are never waitlisted, leading to very high mortality. This finding “warrants further study to ascertain why these donors with ESRD never gained access to the waiting list,” the researchers write [Muzaale AD, et al. Outcomes of live kidney donors who develop end-stage renal disease. *Transplantation* 2016; 100:1306–1312]. ●