

No Benefit of ACE Inhibitors/Statin for Teens with Type 1 Diabetes

Treatment with angiotensin-converting enzyme (ACE) inhibitors, statins, or both does not affect albumin excretion in adolescents with type 1 diabetes, concludes a trial in *The New England Journal of Medicine*.

In a screening study of 4407 adolescents with type 1 diabetes, 1287 had increased albumin excretion, defined as the upper third of the albumin-to-creatinine ratio. Of these, 443 were randomly assigned to treatment with an ACE inhibitor, statin, or matching placebo in a 2-by-2 factorial design. The

main outcome of interest was change in albumin excretion, assessed every 6 months over 2 to 4 years. Secondary outcomes included microalbuminuria, retinopathy, lipid levels, and other cardiovascular risk markers.

Change in albumin-to-creatinine ratio over time was unaffected by treatment with ACE inhibitor and/or statin. The incidence of microalbuminuria was lower with ACE inhibitor compared to placebo, but this difference was not considered significant. Statin treatment was associated with expected

changes in lipid levels. However, there were no between-treatment differences in carotid intima-media thickness, other cardiovascular risk markers, glomerular filtration rate, or retinopathy progression. No serious unexpected adverse reactions occurred.

In adolescents with type 1 diabetes, puberty-associated increases in albumin excretion occur before the development of microalbuminuria and macroalbuminuria. This suggests that ACE inhibitors or statins might have beneficial effects for young diabetics with high albumin excretion.

However, the randomized, placebo-controlled trial shows no significant difference in albumin-to-creatinine ratio for young patients with type 1 diabetes taking ACE inhibitors or statins. Aside from statin-induced changes in lipid profiles, secondary outcomes are also similar between groups. The authors plan continued follow-up to assess any delayed “legacy effect” of early treatment [Marcovecchio ML, et al. ACE inhibitors and statins in adolescents with type 1 diabetes. *N Engl J Med* 2017; 377: 1733–1745]. ■

Lactation:

Risk Summary

There are no human data regarding the effect of AURYXIA in human milk, the effects on the breastfed child, or the effects on milk production. Data from rat studies have shown the transfer of iron into milk by divalent metal transporter-1 (DMT-1) and ferroportin-1 (FPN-1). Hence, there is a possibility of infant exposure when AURYXIA is administered to a nursing woman. The development and health benefits of breastfeeding should be considered along with the mother's clinical need for AURYXIA and any potential adverse effects on the breastfed child from AURYXIA or from the underlying maternal condition.

Pediatric Use: The safety and efficacy of AURYXIA have not been established in pediatric patients.

Geriatric Use: Clinical studies of AURYXIA included 292 subjects aged 65 years and older (104 subjects aged 75 years and older). Overall, the clinical study experience has not identified any obvious differences in responses between the elderly and younger patients in the tolerability or efficacy of AURYXIA.

OVERDOSAGE

No data are available regarding overdose of AURYXIA in patients. In patients with chronic kidney disease, the maximum dose studied was 2,520 mg ferric iron (12 tablets of AURYXIA) per day. Iron absorption from AURYXIA may lead to excessive elevations in iron stores, especially when concomitant intravenous iron is used.

In clinical trials, one case of elevated iron in the liver as confirmed by biopsy was reported in a patient on dialysis administered IV iron and AURYXIA.

PATIENT COUNSELING INFORMATION

Dosing Recommendations: Instruct patients to take AURYXIA as directed with meals and adhere to their prescribed diets. Instruct patients on concomitant medications that should be dosed apart from AURYXIA. Advise patients not to chew or crush AURYXIA because tablets may cause discoloration of mouth and teeth.

Adverse Reactions: Advise patients that AURYXIA may cause discolored (dark) stools, but this staining of the stool is considered normal with oral medications containing iron.

AURYXIA may cause diarrhea, nausea, constipation, vomiting, hyperkalemia, abdominal pain, and cough. Advise patients to report severe or persistent gastrointestinal symptoms to their physician.

Accidental Ingestion: Advise patients to keep this product out of the reach of children and to seek immediate medical attention in case of accidental ingestion by a child.

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Race Modifies HIV's Impact on Dialysis Survival

Even with modern antiretroviral therapy (ART), survival on dialysis is significantly lower for non-white patients with HIV infection, according to a study in *Kidney International*.

Using data from a nationwide dialysis provider, the researchers identified two groups of HIV-positive dialysis patients: 5348 patients who had HIV only and 1863 patients with HIV and hepatitis C virus (HCV) coinfection. In both groups, a large majority of patients were African American: 74.3% of the HIV-positive group and 81.6% of the HIV/HCV-positive group. Percentages of Caucasian patients were 13.2% and 9.0%, respectively.

A cohort of 410,545 HIV/HCV-negative patients were studied for comparison: 47.6% Caucasian and 29.0% African American. The effects of HIV- and HIV/HCV-positive status on mortality were assessed, along with the possible modifying effects of race.

In Caucasians, HIV status was not significantly related to mortality, but HIV/HCV infection was: hazard ratio (HR) 1.48. For non-Caucasians, both HIV- and HIV/HCV-positive status were associated with higher mortality: HR 1.44 and 1.77, respectively. The results were similar in secondary analyses using matched propensity scores.

The effects of HIV infection on dialysis outcomes are unclear, particularly in the era of widespread ART use. The new analysis suggests a “very concerning” reduction in survival associated with HIV-positive status in non-Caucasian patients: African American, Latino, Asian, and “other.”

Across racial/ethnic group, dialysis survival is reduced for patients with HIV/HCV coinfection. The authors discuss the need for interventions targeting these vulnerable populations, possibly including early nephrology referral and therapy for HCV [Sawinski D, et al. Race but not hepatitis C co-infection affects survival of HIV+ individuals on dialysis in contemporary practice. *Kidney Int* 2017; <http://dx.doi.org/10.1016/j.kint.2017.08.015>]. ■