Abstract ID: 107 **Day / Time:** Monday, Nov 16, 12:00 PM – 12:15 PM

Efficacy and Safety of Vitamin E in Nonalcoholic Steatohepatitis Patients With and Without diabetes: Pooled analysis from the PIVENS and FLINT NIDDK NASH CRN Trials

Category: Steatosis and Steatohepatitis
Descriptor: QO2. Steatohepatitis: Clinical and Therapeutic
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Background: Vitamin E has been studied for the treatment for nonalcoholic steatohepatitis (NASH) in non-diabetic adult patients in the PIVENS randomized controlled trial (RCT). We present non-randomized safety/efficacy estimates for vitamin E in diabetic adult NASH patients from the placebo group in our recent FLINT RCT, which compared obeticholic acid (OCA) to placebo in diabetic and non-diabetic adult NASH. Results for vitamin E in diabetic NASH were compared to pooled results in non-diabetic NASH derived from the PIVENS vitamin E and placebo groups and from non-diabetics in the FLINT placebo group.

Methods: Two efficacy measures from FLINT were applied to our pooled data: histologic improvement, defined as ≥ 2 point improvement in NAS with no worsening of fibrosis or NASH resolution. Safety estimates paralleled those used in FLINT and included incidence of cardiac events and changes in lipid levels. Logistic regression models were used to summarize the odds ratio (OR) effects, confidence limits, and p-values on the pooled vitamin E treatment vs no vitamin E treatment efficacy estimates; Fisher's exact test was used to assess cardiac events.

Results: A total of 250 patients were randomized to vitamin E (n=80) or placebo (n=72) in PIVENS or to placebo (n=98) in FLINT and had both baseline and end-treatment liver biopsies; 53 had diabetes (21%) and 197 were non-diabetic (79%); 105 (42%) received vitamin E and 145 (58%) did not in the PIVENS or FLINT trials. Vitamin E use was associated with histologic improvement in diabetic (OR 4.4,

95% CI 1.1, 18.0, p=0.04) and non-diabetic patients (OR 3.1, 95% CI 1.7, 5.8, p<0.001) but not significantly greater rate of NASH resolution in diabetic (OR=1.8, 95% CI 0.3, 12.2, p=0.55) or non-diabetic patients (OR=1.7, 95% CI 0.9, 3.3, p=0.09). The incidence of cardiac events was not significantly different among diabetics taking vitamin E vs. not taking vitamin E (0% vs. 12%, p=0.19) nor among non-diabetics taking vitamin E vs. not taking vitamin E (12% vs. 9%, p=0.51). There were no significant differences in net change from baseline in total cholesterol, HDL cholesterol, LDL cholesterol, or triglycerides.

Conclusions: Vitamin E treatment was associated with similar significant improvement in NASH histology in both diabetic and non-diabetic patients. There was no association of vitamin E use with important adverse safety measures using a pooled analysis of patients from two RCTs of adult NASH. These preliminary findings from pooled data support RCTs in diabetic NASH to establish whether the promising safety and efficacy profiles for vitamin E in diabetic NASH are confirmed.

Sponsored by: Sponsored by the NIH NIDDK (National Institute of Diabetes and Digestive and Kidney Diseases).
Disclosures: Kris Kowdley: Yes conflict of interest;Evidera:Grant/Research Support;Gilead:Grant/Research Support;Immuron:Grant/Research Support;Intercept:Grant/Research Support;Tobira:Grant/Research Support;Abbvie:Speaking and Teaching;Achillion:Advisory Committees or Review Panels;BMS:Advisory Committees or Review Panels;Evidera:Advisory Committees or Review Panels;Gilead:Speaking and Teaching;Gilead:Advisory Committees or Review Panels;Merck:Advisory Committees or Review Panels;Novartis:Advisory Committees or Review Panels;Trio Health:Advisory Committees or Review Panels;Abbvie:Advisory Committees or Review Panels; Laura Wilson: No Answer.; Mark Van Natta: No conflict of interest; Rish Pai: No Answer.; Arun Sanyal: Yes conflict of interest;UpToDate:Independent Contractor;Salix:Consulting;Salix:Grant/Research Support;Bristol Myers:Advisory Committees or Review Panels;Immuron:Consulting;Gilead:Advisory Committees or Review