

## TE Possible Alternative to Liver Biopsy

BY MIRIAM E. TUCKER

NEW YORK — Transient elastography correlated with aminotransferase levels in a cross-sectional study of 22 adolescent and young women with Turner's syndrome.

Transient elastography (TE), a novel technique for measuring liver stiffness, has been widely validated as a noninvasive alternative to liver biopsy for evaluating hepatic fibrosis in patients with chronic hepatitis C. It has not been used in Turner's syndrome (TS) patients, in whom liver involvement is common.

Although liver biopsy is the standard method for assessing liver fibrosis, it is an invasive and very expensive procedure that can incur life-threatening complications, and therefore can't be used as a tool to screen or monitor liver function in all TS patients.

TE is a painless procedure in which an ultrasound transducer probe mounted on a vibrator issues a wave through underlying tissues. Pulse-echo ultrasound acquisition is used to follow the propagation of the shear wave and to measure its velocity, which is directly related to tissue stiffness. The stiffer the tissue, the faster the shear wave propagates (*J. Hepatol.* 2008;48:835-47).

The findings from this small study—which will require replication in a larger number of patients—suggest that TE could be used to identify patients with elevated aminotransferase levels who might qualify for more invasive tests and possibly liver biopsy to better stage the etiology of liver involvement, Dr. Maria Francesca Messina said at a joint meeting of the Lawson Wilkins Pediatric Endocrine Society and the European Society for Pediatric Endocrinology.

The procedure could be used to monitor the progression of liver dysfunction in TS patients without exposing them to the significant clinical risks of more invasive procedures, Dr. Messina said.

The 22 TS patients had a mean age of 20.9 years and full pubertal development (spontaneous or pharmacologic). All fasted and underwent TE along with biochemical testing. Six patients were found to have elevated aminotransferase levels.

The mean liver stiffness for the entire group was 4.5 kilopascal (less than 7 kPa is generally considered mild or normal), and was significantly higher among those with elevated transaminase levels compared with those who had normal liver function (6 vs. 4 kPa), said Dr. Messina of the department of pediatrics at the University of Messina (Italy).

The TE device, called FibroScan, is marketed by France-based Echosens International ([www.echosens.com](http://www.echosens.com)). The company did not fund this study.

Dr. Messina stated that she has no relevant financial disclosures. ■

## Problems Seen in Type 1 Adolescents

BY MIRIAM E. TUCKER

NEW YORK — Early diabetes complications were seen in a significant proportion of 821 adolescents with type 1 diabetes for just 2-5 years.

Up to 1 in 5 of the adolescents had early indicators of eye, kidney, and/or nerve complications. The findings support early screening for diabetes complications as recommended by some—but not all—published consensus guidelines, Dr. Yoon

Hi Cho said at a joint meeting of the Lawson Wilkins Pediatric Endocrine Society and the European Society for Pediatric Endocrinology.

The 821 patients were all seen at the Children's Hospital at Westmead, Sydney, between 1990 and 2006. They were aged 11-17 years, with a type 1 diabetes duration of 2-5 years (median 3.8) and a median hemoglobin A<sub>1c</sub> level of 8.9%.

Early retinopathy, defined as one microaneurysm or hemorrhage on seven-

field stereoscopic fundus photography, was detected in 9% of the patients. Albumin excretion rate (AER) was measured for overnight urine collections. Early nephropathy, defined as a borderline elevation of AER of 7.5 to less than 20 mcg/min, was seen in 22% of the adolescents. Microalbuminuria, defined as an AER of 20 mcg/min or greater, was identified in 3%. Peripheral nerve abnormalities on thermal and vibration thresholds at the feet—mea-

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ONGLYZA is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

ONGLYZA should not be used for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis.

ONGLYZA has not been studied in combination with insulin.

### Important Safety Information

- **Use with Medications Known to Cause Hypoglycemia:** Insulin secretagogues, such as sulfonylureas, cause hypoglycemia. Therefore, a lower dose of the insulin secretagogue may be required to reduce the risk of hypoglycemia when used in combination with ONGLYZA
- **Macrovascular Outcomes:** There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with ONGLYZA or any other antidiabetic drug

**Most common adverse reactions** (regardless of investigator assessment of causality) reported in ≥5% of patients treated with ONGLYZA and more commonly than in patients treated with control were upper respiratory tract infection (7.7%, 7.6%), headache (7.5%, 5.2%), nasopharyngitis (6.9%, 4.0%) and urinary tract infection (6.8%, 6.1%). When used as add-on combination therapy with a thiazolidinedione, the incidence of peripheral edema for ONGLYZA 2.5 mg, 5 mg, and placebo was 3.1%, 8.1% and 4.3%, respectively.

sured by thermal threshold tester and biothesiometer—were found in 22% of the patients, said Dr. Cho, a clinical endocrinology fellow at the hospital.

The proportions with borderline AER elevation rose from 16% of those aged 11-13 years to 23% of 13- to 15-year-olds to 25% of those aged 15-17 years. There was no significant effect of age for retinopathy (seen in 6%, 10%, and 11% of the three groups) or for peripheral nerve abnormalities (seen in 27%, 19%, and 22%). The rates of microalbuminuria remained low (4% or below). There was no significant difference in hemoglobin

A<sub>1c</sub> level between the three age groups (8.2%, 8.5%, and 8.6%), Dr. Cho said.

Retinopathy was significantly related to an elevated diastolic blood pressure level. A mean AER of 7.5 mcg/min or greater was associated with increased age, diabetes duration, and systolic BP. Peripheral nerve abnormalities were cor-

related with a higher BMI. There was no significant relationship between any of the complications and hemoglobin A<sub>1c</sub> level, cholesterol level, sex, insulin dose, or insulin regimen, she said.

Guidelines from the International Society for Pediatric and Adolescent Diabetes and from the Australian Pediatric Endocrinology Group

both advise screening children for diabetes complications after a diabetes duration of 5 years in prepubertal children and after 2 years in adolescents. The American Diabetes Association recommends retinopathy screening within 5 years of the onset of diabetes and nephropathy screening after a diabetes duration of 5 years in children aged 10 years and older.

“Longitudinal analysis will help define predictors of early complications and the potential for modifying [their] natural history,” said Dr. Cho, who had no relevant financial disclosures. ■

**In a study of 821 adolescents, up to 1 in 5 had early indicators of eye, kidney, and/or nerve complications. The findings support early screening for these conditions.**

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**Drug Interactions:** Because ketoconazole, a strong CYP3A4/5 inhibitor, increased saxagliptin exposure, the dose of ONGLYZA should be limited to 2.5 mg when coadministered with a strong CYP3A4/5 inhibitor (e.g., atazanavir, clarithromycin, indinavir, itraconazole, ketoconazole, nefazodone, nelfinavir, ritonavir, saquinavir, and telithromycin).

**Patients with Renal Impairment:** The dose of ONGLYZA is 2.5 mg once daily for patients with moderate or severe renal impairment, or with end-stage renal disease requiring hemodialysis (creatinine clearance [CrCl] ≤50 mL/min). ONGLYZA should be administered following hemodialysis. ONGLYZA has not been studied in patients undergoing peritoneal dialysis. Assessment of renal function is recommended prior to initiation of ONGLYZA and periodically thereafter.

**Pregnant and Nursing Women:** There are no adequate and well-controlled studies in pregnant women. ONGLYZA, like other antidiabetic medications, should be used during pregnancy only if clearly needed. It is not known whether saxagliptin is secreted in human milk. Because many drugs are secreted in human milk, caution should be exercised when ONGLYZA is administered to a nursing woman.

**Pediatric Patients:** Safety and effectiveness of ONGLYZA in pediatric patients have not been established.

\*metformin, glyburide, or thiazolidinedione (pioglitazone or rosiglitazone)

**Please read the adjacent Brief Summary of the Product Information.**

For more information about ONGLYZA visit [www.onglyza.com](http://www.onglyza.com).

Reference: 1. Fingertip Formulary® data as of October 2, 2009. Data on File, October 2009.

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