

Berlin, 9/2/2015

Statement from the German Diabetic Association (DDG) on the termination of the "ENDO Trial" study (FDA study of the EndoBarrier in patients with Type 2 Diabetes mellitus)

On July 30, 2015, GI Dynamics (GID) announced that the clinical study ("Endo Trial") conducted in the USA would be terminated with immediate effect. The background to this decision was the recommendation issued by the FDA at the start of March that the recruitment of additional patients should be temporarily suspended. The reason for the FDA's recommendation to temporarily stop recruitment was the observation that in the current study, the defined tolerance threshold (2%) for the occurrence of liver abscesses had been exceeded. This complication occurred in 7 out of 217 patients (3.2%) in the intervention group and in 0 out of 108 patients in the Sham Group (control group: Endoscopy without EndoBarrier implantation). For all affected patients, the liver abscesses were cured using standard treatments (antibiotics and, if necessary, drainage) without consequences.

The key reason for the GID Management Team to now end the study completely was the incalculable prolongation to the study time resulting from the FDA recommendation and the associated significant increase in costs. However, all studies currently running outside of the USA will be continued.

The rate of liver abscesses is significantly higher in the Endo Trial than the rate observed around the world and in Germany. The global rate of liver abscesses is around 0.73% (3000 patients); in Germany it is 0.46% (651 patients, as at 8/24/2015). The national EndoBarrier register currently includes 3 cases of liver abscesses. In 202 documented cases, this corresponds to an event rate of 1.48%. The background to the increased complication rate observed in the USA is not known. However, it is possible that the high dose of proton pump inhibitors envisaged in the study protocol contributed to this. The effects of a reduction in the dosage of proton pump inhibitors over the course of the EndoBarrier implantation period are not being investigated at this time. In addition, all patients treated in the USA suffered from type 2 Diabetes mellitus. Liver abscesses occur more frequently in persons suffering from diabetes than in the normal population.

It is not currently known whether the prophylactic cyclical administration of antibiotics on two days per month would have a protective effect on the development of liver abscesses after EndoBarrier implantation. This measure cannot be recommended at this time.

On the basis of an initial review of the EndoTrial study data, a significant, and at 1.11 percentage points also greater, reduction in HbA1c can be seen in the intervention group after 12 months (absolute value: intervention group -1.25 percentage points; sham group -0.15 percentage points). HbA1c

Diabetes erforschen und verhindern, behandeln und heilen.

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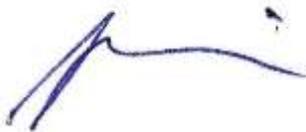
The initial value was 8.8 percent (duration of diabetes 7.6 years), the BMI was 38.4 kg/m². The HbA1c reduction recorded in the national register is 1.72 percentage points according to the latest analysis (initial value: 8.6 percent).

Since the effects on Diabetes mellitus and body weight were already significant nine to ten months after implantation according to the investigation results in Germany, in the future it will be necessary to consider whether the EndoBarrier® could routinely be explanted after just 10 months. A procedure of this type could prevent infectious complications, particularly liver abscesses, as the international registers show that liver abscesses occurred in particular in the later phase of the implantation period (months ten to twelve).

In view of the illustrated data, the German Diabetic Association adheres to the content of the recently published *Positionspapier der Fachgesellschaften zur Anwendungsempfehlung der endoskopischen biliodigestiven Diversion in Deutschland* [Position Paper by the Scientific Societies for Recommended Usage of Endoscopic Biliodigestive Diversion in Germany]:

http://www.dgvs.de/fileadmin/user_upload/Leitlinien/positionspapiere/s-0034-1366570.pdf

However, close attention should be paid to symptoms that indicate the occurrence of liver abscesses.



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