Efficacy and Safety of Taspoglutide Monotherapy in Drug-Naive Type 2 Diabetic Patients After 24 Weeks of Treatment

Results of a randomized, double-blind, placebo-controlled phase 3 study (T-emerge 1)

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OBJECTIVE—To evaluate the efficacy and safety of taspoglutide monotherapy in drug-naive patients with type 2 diabetes inadequately controlled.

RESEARCH DESIGN AND METHODS—In this 24-week double-blind, placebo-controlled, multicenter trial, 373 patients with type 2 diabetes naive to antihyperglycemic medication were randomized to weekly subcutaneous taspoglutide 10 or 20 mg or placebo.

RESULTS—HbA1c reductions from baseline were greater with taspoglutide 10 and 20 mg than placebo (least squares mean [SE] changes: −1.01 ± 0.07% vs. placebo, −1.18 ± 0.06%, and −0.99 ± 0.07%, respectively; both P < 0.0001 vs. placebo). Decreases in bodyweight were greater with taspoglutide 10 mg (−1.45 ± 0.32 kg) and with 20 mg (−2.25 ± 0.30 kg) than placebo (−1.23 ± 0.31 kg; P = 0.61 and P = 0.02 for taspoglutide 10 and 20 mg vs. placebo, respectively). Gastrointestinal adverse events and injection site reactions were more common with taspoglutide than placebo.

CONCLUSIONS—In drug-naive patients, once-weekly taspoglutide improved glycemic control, reduced body weight, and was generally well tolerated.

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Taspoglutide is a human glucagon-like peptide 1 analog with a pharmacokinetic profile suitable for once-weekly subcutaneous administration (1). In a phase 2 clinical trial, once-weekly taspoglutide added to metformin lowered HbA1c by up to 1%, reduced body weight, and was generally well tolerated (2). The efficacy and safety of taspoglutide monotherapy as a first-line agent was investigated in a phase 3 trial in patients with early type 2 diabetes who were inadequately controlled with diet and exercise and naive to antihyperglycemic therapy.

RESEARCH DESIGN AND METHODS—This 24-week, randomized, double-blind, placebo-controlled study (clinical trial reg. no. NCT00744926) was conducted at 53 centers internationally and in accordance with the principles of the Declaration of Helsinki. An institutional review/ethics board at each center approved the protocol, and written informed consent was obtained from all patients.

Eligible patients were adults (aged ≥18 and ≤80 years) with type 2 diabetes naive to antihyperglycemic therapy and controlled with diet and exercise (HbA1c 6.5–10%; BMI 25–45 kg/m²).

Patients were excluded if they had significant complications associated with type 2 diabetes, symptomatic gastrointestinal diseases, history of bariatric surgery, pancreatic disease, cardiac disease within the past 6 months, history of unstable hypertension, treatment with chronic corticosteroids within the past month, and treatment with weight-lowering agents within the past 12 weeks.

Patients were randomly assigned (1:1:1) to subcutaneous taspoglutide 10 mg weekly, taspoglutide 20 mg weekly (after 10 mg weekly for the initial 4 weeks), or placebo. Patients were stratified by baseline HbA1c (≤8.0 or ≥8.0%). If glycemic control deteriorated, additional antihyperglycemic rescue medication was prescribed and the patient could continue in the study.

The primary efficacy end point was absolute change from baseline in HbA1c after 24 weeks. Secondary efficacy end points included HbA1c response rates (≤6.5% and ≤7%) and changes in fasting plasma glucose (FPG), fructosamine, body weight, fasting proinsulin, fasting proinsulin-to-insulin ratio, and homeostasis model...
Table 1—AEs (safety population)

| AEs leading to withdrawal | Placebo (n = 123) | Taspoglutide 10 mg (n = 116) | Taspoglutide 20 mg (n = 129) |
|---------------------------|------------------|-----------------------------|-----------------------------|
| Vomiting                  | 0 (0.8)          | 2 (1.7)                     | 0                           |
| Nausea                    | 0 (0.8)          | 2 (1.7)                     | 0                           |
| Diarrhea                  | 1 (0.8)          | 2 (1.7)                     | 0                           |
| Other gastrointestinal events | 0 (0.8)         | 2 (1.7)                     | 0                           |
| Injection site reaction   | 0 (0.8)          | 2 (1.7)                     | 0                           |
| Hyperglycemia             | 2 (1.6)          | 2 (1.7)                     | 0                           |
| Hypersensitivity          | 0 (0.8)          | 2 (1.7)                     | 0                           |
| Liver enzyme elevations   | 1 (0.8)          | 0 (0.8)                     | 0                           |
| Palpitations              | 0 (0.8)          | 0 (0.8)                     | 0                           |
| Headache                  | 0 (0.8)          | 0 (0.8)                     | 0                           |
| Total patients withdrawn  | 4 (13)           | 13 (40)                     | 17 (45)                     |
| Treatment-emergent AEs*   |                  |                             |                             |
| Total gastrointestinal events | 13 (10.6)  | 44 (37.9)                   | 58 (45.0)                   |
| Nausea                    | 5 (4.1)          | 30 (25.9)                   | 40 (31.0)                   |
| Vomiting                  | 0 (0.8)          | 20 (17.2)                   | 23 (18.7)                   |
| Diarrhea                  | 5 (4.1)          | 16 (13.8)                   | 12 (9.3)                    |
| General disorders and administration site conditions | 13 (10.6) | 42 (36.2) | 44 (34.1) |
| Injection site nodule     | 1 (0.8)          | 14 (12.1)                   | 12 (9.3)                    |
| Injection site reaction   | 0 (0.8)          | 8 (6.9)                     | 9 (7.0)                     |
| Injection site in duration | 1 (0.8)        | 6 (5.2)                     | 7 (5.4)                     |
| Injection site pruritus   | 0 (0.8)          | 5 (4.3)                     | 7 (5.4)                     |
| Total nervous system disorders | 6 (4.9)  | 19 (16.4)                   | 15 (11.6)                   |
| Headache                  | 2 (1.6)          | 13 (11.2)                   | 8 (6.2)                     |
| Dizziness                 | 2 (1.6)          | 6 (5.2)                     | 8 (6.2)                     |
| Total metabolism and nutrition | 4 (3.3)  | 14 (12.1)                   | 7 (5.4)                     |
| Hypoglycemia              | 1 (0.8)          | 6 (5.2)                     | 5 (3.9)                     |

Data are n or n (%)....

Fig. 1. Treatment groups were well matched in...
than placebo. No cases of severe hypoglycemia were reported.

Withdrawal from treatment as a result of AEs occurred in 3.3, 11.2, and 13.2% of the placebo, taspoglutide 10-mg, and taspoglutide 20-mg groups, respectively (Table 1).

CONCLUSIONS—Once-weekly taspoglutide monotherapy improved HbA1c, FPG, and HOMA-B and reduced body weight during a 24-week period in patients with newly diagnosed type 2 diabetes who were naive to antihyperglycemic agents. Notable findings included a mean reduction in HbA1c of nearly 1.2% in patients with a mean baseline of 7.7% treated with taspoglutide 20 mg. In patients with baseline HbA1c of ~7.0%, patients achieved an HbA1c of 6.1% with 20 mg and 6.3% with 10 mg after 24 weeks of treatment with taspoglutide.

Taspoglutide monotherapy was generally well tolerated; the most frequently reported AEs were nausea and vomiting. Hypersensitivity reactions occurred in four patients; two patients withdrew. In summary, once-weekly taspoglutide given as monotherapy was efficacious and generally well tolerated in patients with type 2 diabetes naive to treatment with antidiabetic agents.

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