Table 1. Patient Characteristics at Admission

	TBI (n = 111)	Non-TBI (n = 52)
Men, n (%)	83 (75)	28 (54)
Age at admission, y	42.7 ± 18.5	47.9 ± 16.0
Glasgow Coma Scale score at admission	10.2 ± 3.1	11.3 ± 2.3
Time from trauma to rehabilitation, d	20.7 ± 13.0	28.6 ± 18.6
Length of rehabilitation, d	113.1 ± 67.2	93.7 ± 40.5
CT and MRI findings (TBI)		
Shearing lesions	30 (27)	—
Traumatic subarachnoid hemorrhage	64 (57)	—
Cerebral edema	26 (23)	—
Cranial fracture	42 (38)	—
Cause of Injury (non-TBI)		
Subarachnoid hemorrhage	—	16 (31)
Intracerebral hemorrhage	—	12 (23)
Anoxic brain injury	—	9 (17)
Other	—	15 (29)
FIM score at admission	18 (18 to 44)	18 (18 to 25)
Posttraumatic amnesia, d	80 (26 to 365)	—
> 28 d	98 (88)	—
< 28 d	13 (12)	—

Data expressed as n (%), mean ± standard deviation, or median (range, 10% to 90%).

CT=computed tomography; TBI=traumatic brain injury; FIM=Functional Independence Measure; MRI=magnetic resonance imaging.

Table 2. GOS-E Scores Distribution[a]

	TBI		Non-TBI	
	Discharge	Follow-up	Discharge	Follow-up
Lower capability of independent activity	75%	53%	85%	64%
Higher capability of independent activity	30%	50%	15%	38%

[a]Percentage of patients in the scoring group.

TBI=traumatic brain injury; GOS-E=Extended Glasgow Outcome Scale.

discharge, low GOS-E scores indicated a low degree of independent activities. The improvements in the capability of independent activity at the 1-year follow-up were not as marked in these patients, compared with patients who were more capable of independent activities at discharge (Table 2).

Thirty-two percent of all patients had suppressed gonadal or thyroidal function. The majority (68%) of all patients had elevated stress hormones. One-quarter of all patients displayed both features.

Secondary hypogonadism and elevated stress-related hormones were related to worse 1-year FIM scores in univariate analyses (p = .001 and p = .01, respectively). These associations remained following multivariate analysis (p = .01). Reduced gonadal or thyroid hormones and elevated stress-related hormones were related to a worse 1-year GOS-E score in univariate analyses (p = .04 and p = .006, respectively). Elevated stress-related hormones remained independently associated with a worse 1-year GOS-E score in multivariate analysis (p = .01).

The results indicate that endocrine changes occurring in brain injury may not necessarily be a consequence of brain damage. Rather, the endocrine alterations may represent physiological stress adaptations to the acute illness, and a subsequent prolonged stress response. The data do not support the routine use of pituitary assessment soon after TBI. This assessment should be reserved for patients with clinical features indicative of hypopituitarism.

Greater HbA_{1c} Reduction in Uncontrolled Type 2 Diabetes With Once-Weekly Exenatide Autoinjection

Written by Brian Hoyle

Patients with uncontrolled type 2 diabetes display greater reductions in HbA_{1c} using a regimen of a once-weekly autoinjection of exenatide as compared with twice-daily injections of exenatide. The results of the randomized, double-blind Efficacy and Safety of Exenatide Once Weekly Suspension in Subjects With Type 2 Diabetes study [DURATION-NEO-1; NCT01652716] were presented by Carol H. Wysham, MD, Rockwood Clinic, Spokane, Washington, USA.

A once-weekly administration of the glucagon-like peptide-1 receptor agonist exenatide provides glycemic control and helps with weight loss in individuals with type 2 diabetes [Russell-Jones D et al. *Diabetes Care* 2012; Blevins T et al. *J Clin Endocrinol Metab* 2011; Bergenstal RM et al. *Lancet* 2010; Diamant M et al. *Lancet* 2010; Drucker DJ et al. *Lancet* 2008]. However, the current

Table 1. Demographics and Baseline Characteristics

	Once-Weekly Exenatide (n = 229)	Twice-Daily Exenatide (n = 146)	All Patients (n = 375)
Sex, male	148 (65)	92 (63)	240 (64)
Age, y	56 ± 10	57 ± 9	56 ± 10
Race			
Caucasian	168 (73)	110 (75)	278 (74)
Black	38 (17)	23 (16)	61 (16)
Asian	17 (7)	8 (5)	25 (7)
Other	6 (3)	5 (3)	11 (3)
Ethnicity: Hispanic or Latino	54 (24)	34 (23)	88 (23)
Body weight, kg	97 ± 23	97 ± 18	97 ± 21
Body mass index, kg/m^2	33 ± 6	33 ± 5	33 ± 6
HbA_{1c}%	8.5 ± 1.0	8.5 ± 1.0	8.5 ± 1.0
Fasting plasma glucose, mg/dL	181 ± 45	184 ± 47	182 ± 45
Duration of diabetes, y	9 ± 6	8 ± 6	9 ± 6
Renal impairment			
None	85 (37)	55 (38)	140 (37)
Mild	113 (49)	76 (52)	189 (50)
Moderate	29 (13)	15 (10)	44 (12)
Severe	0	0	0

Data are number (% of total) or mean ± standard deviation.

need for reconstitution of the formulation has hindered its use. The present study evaluated a new formulation that does not require reconstitution and that can be administered by a single-use autoinjection pen.

The study involved 377 patients with type 2 diabetes. Other inclusion criteria were attempted control of diabetes using diet and exercise; the use of ≤2 of metformin, sulfonylurea, or thiazolidinediones; HbA_{1c} of 7.1% to 11.0%; body mass index ≤45 kg/m^2; and fasting plasma glucose <280 mg/dL. The patients were randomized to receive a once-weekly autoinjection of exenatide 2 mg (n = 229) or conventional twice-daily exenatide 10 µg (n = 148). The modified intention-to-treat population was 229 and 146, respectively. The primary end point was the change in HbA_{1c} after 28 weeks of treatment in the two study arms (197 and 118 subjects completed, respectively). The demographics and baseline characteristics were similar in both study arms (Table 1).

The change in HbA_{1c} over time for both study arms featured a similar sharp decline at Week 8, followed by divergent but stabilized levels thereafter. The primary outcome (change in HbA_{1c} between baseline and Week 28) significantly favored the once-weekly arm (–1.4%) compared with the twice-daily arm (–1.0%; p = .007). The proportion of subjects in the once-weekly exenatide and twice-daily exenatide arms who achieved HbA_{1c} reduction <7.0% were similar (49% and 43%, respectively; p = .23), but those who achieved a ≤6.5% reduction favored the once-weekly injection regimen (36% and 26%, respectively; p = .05). The decline in fasting plasma glucose was greater for the once-weekly arm from Weeks 6 to 24, but was not significant at Week 28 (-33 mg/dL vs –23 mg/dL for the twice-daily arm; p = .17). The change in postprandial glucose was similar between the study arms, as was the change in body weight (–1.5 ± 0.3 kg for once-weekly exenatide vs -1.9 ± 0.4 kg for twice-daily exenatide).

Table 2. Summary of Adverse Events

Category	Once-Weekly Exenatide	Twice-Daily Exenatide
All patients with AEs	162 (70.7)	108 (74.0)
AEs in ≥5% of patients		
Nausea	22 (9.6)	31 (21.2)
Injection site nodule	29 (12.7)	1 (0.7)
Diarrhea	12 (5.2)	17 (11.6)
Headache	13 (5.7)	9 (6.2)
Upper respiratory tract infection	13 (5.7)	5 (3.4)
Vomiting	8 (3.5)	9 (6.2)
Serious AEs	6 (2.6)	7 (4.8)
AEs leading to withdrawal	5 (2.2)	7 (4.8)

AEs=adverse events. Data are n (%).

The prevalence of adverse events (AEs) was overall similar between the study arms (Table 2). However, the prevalence of nausea and diarrhea was lower but the presence of an injection-site nodule was far more common in the once-weekly exenatide arm as compared with the twice-daily arm.

The present results were similar to those of the previous DURATION-5 study [Blevins T et al. *J Clin Endocrinol Metab* 2011]. This featured administration of exenatide QW, which required reconstitution and administration with a syringe. The researchers concluded that a weekly autoinjection of exenatide that does not require reconstitution provides statistically superior reduction in HbA_{1c} and fewer gastrointestinal AEs than the regimen of exenatide given by twice-daily injection.

Empagliflozin Reduces BP in Hypertensive Type 2 Diabetics

Written by Brian Hoyle

Empagliflozin, an investigational drug to treat type 2 diabetes that is being developed by Boehringer Ingelheim Pharma, lowered blood pressure (BP) in hypertensive type 2 diabetics and reduced blood glucose levels during 12 weeks of treatment. Afshin Salsali, MD, University of Medicine and Dentistry of New Jersey, Newark, New Jersey, USA, presented findings of the 12 Week Efficacy and Safety Study of Empagliflozin (BI 10773) in Hypertensive Patients With Type 2 Diabetes Mellitus [EMPA-REG BP; NCT01370005], a placebo-controlled Phase 3 trial (randomized, double-blind).

Prior 24-week Phase 3 clinical trials (randomized, double-blind) established the efficacy of empagliflozin (10 and 25 mg) in reducing systolic BP compared with placebo among patients with type 2 diabetes [Häring H-U et al. *Diabetes Care* 2014; Kovacs CS et al. *Diabetes Obes Metab* 2014; Häring H-U et al. *Diabetes Care* 2013; Roden M et al. *Lancet Diabetes Endocrinol* 2013]. The effect on blood sugar remained unclear.

The present study involved 823 subjects with type 2 diabetes and high BP (130/80 to 159/99 mm Hg) who were randomly assigned to receive placebo (n=271), empagliflozin–10 mg (n=276), and empagliflozin–25 mg (n=276). The baseline demographics and clinical characteristics of the randomized patients were similar (Table 1).

At baseline, the majority (63%) had an estimated glomerular filtration rate of 60 to 90 mL/min/1.73 m^2. All patients wore an ambulatory BP cuff that monitored systolic and diastolic BP every hour for 24 hours at baseline (before treatment) and after 12 weeks of treatment. Blood samples were also acquired at baseline and 12 weeks to determine HbA_{1c} levels as a measure of long-term blood sugar control.

The 24-hour pattern of systolic BP was almost identical for the 3 subject groups at baseline. At Week 12, while the 24-hour systolic BP curves for the 3 groups were similar in shape, the placebo group consistently displayed higher BP than either empagliflozin group.

Table 1. Baseline and Clinical Characteristics of the 3 Patient Groups

		Empagliflozin	
	Placebo	10 mg	25 mg
Subjects	271	276	276
Male	168 (62.0)	171 (62.0)	156 (56.5)
Age, y	60.3 ± 8.8	60.6 ± 8.5	59.9 ± 9.7
Body mass index, kg/m^2	32.4 ± 4.9	32.4 ± 5.3	33.0 ± 5.0
HbA_{1c}, %	7.9 ± 0.7	7.9 ± 0.8	7.9 ± 0.7

Values in number (%) or mean±standard deviation.