

# PharmaCE™

a continuing education program for *JPT* readers

## July/August CE Questions

### Educational Consultants

David A Riley EdD, Chairman, PharmaCE Panel, School of Pharmacy, West Virginia University, Morgantown, WV; Michael C Shannon PhD, Vice-Chairman, PharmaCE Panel, Nicholasville, KY; Ginger G Scott PhD, School of Pharmacy, West Virginia University, Morgantown, WV; Robert B Supernaw PharmD, School of Pharmacy, Wingate University, Wingate, NC.



### ACCREDITATION

PharmaCE is approved by the American Council on Pharmaceutical Education as a provider of continuing pharmaceutical education.

► THIS TEST PROVIDES 1.0 CREDIT HOUR ◀

ACPE Universal Program Number 407-000-05-053-H01  
Expires: 8/31/08

## EXENATIDE FOR TYPE 2 DIABETES

(see page 191)

### Goal

To review the pharmacology, pharmacokinetics, clinical efficacy, and safety studies of exenatide and provide information available to aid in the proper clinical use of exenatide in patients with type 2 diabetes.

### Objectives

After reviewing this article, the reader should be able to:

1. identify the pharmacologic activities of GLP-1 and exenatide in humans;
2. identify the pharmacokinetic properties of GLP-1 and exenatide in humans and apply these principles to proper dosage and administration of the exenatide compound;
3. select appropriate patients with type 2 diabetes for treatment with exenatide based on characteristics such as age, comorbidities, and glucose abnormalities;
4. identify expected outcomes of therapy for patients on exenatide, including efficacy and safety;
5. identify potential adverse effects of exenatide and clinically relevant strategies for reducing their incidence.

### Test Questions

1. GLP-1 is an incretin hormone known to:
    - (a) stimulate glucagon secretion.
    - (b) elevate postprandial plasma glucose concentration.
    - (c) increase the rate of gastric emptying.
    - (d) stimulate insulin secretion.
    - (e) stimulate hepatic glucose output.
  2. GLP-1 activity is stimulated by:
    - (a) increased plasma glucose concentration.
    - (b) increased plasma insulin concentration.
    - (c) decreased plasma glucose concentration.
    - (d) decreased plasma insulin concentration.
    - (e) increased plasma glucagon concentration.
  3. Which of the following statements is *true*?
    - (a) Exenatide is a GLP-1 analog.
    - (b) Exenatide is a GLP-1 receptor agonist.
    - (c) Exenatide is a GLP-1 receptor antagonist.
    - (d) Exenatide is a glucagon receptor agonist.
    - (e) Exenatide is a glucagon receptor antagonist.
  4. The longer half-life of exenatide compared with GLP-1 is due to:
    - (a) increased renal elimination of exenatide.
    - (b) DPP IV resistance of exenatide.
    - (c) increased fat solubility of exenatide.
    - (d) increased glomerular filtration rate.
    - (e) All of the above are correct.
- Questions 5–7 refer to the following case:
- A 54-year-old male presents with type 2 diabetes. His current medications include metformin 1000 mg twice daily, glyburide 10 mg twice daily, and lisinopril 20 mg daily. Current laboratory findings reveal fasting plasma glucose 140 mg/dL, 2-hour postprandial glucose 240 mg/dL, HbA<sub>1c</sub> 7.6%, and blood pressure 126/78 mm Hg. He is very hesitant to start insulin therapy.
5. Based on available clinical trial data, which of the following clinical changes would be a *least* likely result of exenatide therapy in this patient?
    - (a) decreased postprandial glucose
    - (b) decreased HbA<sub>1c</sub>
    - (c) increased high-density lipoprotein cholesterol
    - (d) decreased fasting plasma glucose
    - (e) decreased weight
  6. Which of the following would be a likely adverse effect due to exenatide?
    - (a) hypoglycemia
    - (b) hyperglycemia
    - (c) headache
    - (d) tachycardia
    - (e) elevated blood pressure
  7. Which of the following dosing regimens for exenatide would be *most* appropriate for the patient based on available clinical trial data?
    - (a) 10 µg subcutaneously at bedtime
    - (b) 5 µg subcutaneously in the morning
    - (c) 5 µg subcutaneously 3 times daily before meals
    - (d) 10 µg orally 3 times daily
    - (e) 5 µg orally 3 times daily
  8. Which of the following patients would be a good candidate for exenatide?
    - (a) 35-year-old lean female with type 1 diabetes with normal fasting blood glucose level, elevated postprandial blood glucose, and HbA<sub>1c</sub> 7.7%
    - (b) 43-year-old obese male with type 2 diabetes with elevated fasting blood glucose, normal postprandial blood glucose, and HbA<sub>1c</sub> 7.7%
    - (c) 85-year-old obese female with type 2 diabetes with normal fasting blood glucose, elevated postprandial blood glucose, and HbA<sub>1c</sub> 7.7%

Answer sheet appears on page 240.

- (d) 50-year-old lean male with type 2 diabetes with elevated fasting blood glucose, normal postprandial blood glucose, and HbA<sub>1c</sub> 7.7%
- (e) 40-year-old obese male with type 2 diabetes with elevated postprandial blood glucose and HbA<sub>1c</sub> 7.7%
9. Which of the following statements regarding the adverse effects associated with exenatide is *true*?
- Nausea is dose dependent.
  - Slow dose titration decreases incidence of nausea.
  - Hypoglycemia is uncommon.
  - Increased blood pressure is uncommon.
  - All of the above are correct.
10. What is the suggested dosage and administration of exenatide based on the clinical trial data?
- 1–2 µg subcutaneously 2 times daily before meals
  - 1–2 µg subcutaneously 3 times daily after meals
  - 5–10 µg subcutaneously 2 times daily before meals
  - 5–10 µg subcutaneously 4 times daily before meals
  - 5–10 µg subcutaneously 2 times daily after meals
11. A 45-year-old obese male with type 2 diabetes is currently on metformin 1000 mg 2 times daily and diet therapy. His HbA<sub>1c</sub> is 8.3% after 6 months of this therapy. His fasting blood glucose level is under control; however, the postprandial values are elevated. Is this patient a potential candidate for combination exenatide therapy?
- No. He has not been on this strength of metformin long enough to determine whether it is working.
  - Yes. His postprandial levels and HbA<sub>1c</sub> are elevated and there is possible weight reduction with exenatide therapy.
  - Yes. Metformin does not work unless it is used as combination therapy in type 2 diabetes.
  - No. Exenatide affects the fasting blood glucose levels, but not postprandial levels.
  - No. Patients on metformin cannot use exenatide.
12. Clinical trial data have indicated safety and efficacy of exenatide when used in combination with:
- sulfonylurea.
  - metformin.
  - meglitinide.
- I only
  - II only
  - I and II
  - II and III
  - I, II, and III
13. A 35-year-old slightly obese female is receiving glyburide 5 mg daily and metformin 500 mg twice daily. She currently has an HbA<sub>1c</sub> of 7.2%, and her postprandial values are always elevated. She and her husband are getting ready to have another child and she wants to know what she is supposed to do about her diabetes medication therapy. Is she a potential candidate for exenatide?
- No. No clinical data are currently available on exenatide and pregnancy.
  - Yes. She should not be on metformin or glyburide when she is pregnant, so exenatide would be a good alternative.
  - No. Her HbA<sub>1c</sub> level is only slightly elevated, so she does not need exenatide to help lower it.
  - Yes. She has elevated HbA<sub>1c</sub> and postprandial levels.
  - No. Metformin and glyburide are safe in pregnancy, and there is no reason to change therapy.

14. The primary reason for patients withdrawing from the clinical trials was:
- lost to follow-up.
  - adverse event.
  - loss of glycemic control.
  - investigator decision.
  - protocol violation.
15. In clinical trials, exenatide has shown all of the following results *except*:
- decreased fasting insulin levels.
  - decreased HbA<sub>1c</sub>.
  - decreased low-density lipoprotein cholesterol.
  - decreased body weight.
  - decreased postprandial glucose levels.

► THIS TEST PROVIDES 2.0 CREDIT HOURS ◀

ACPE Universal Program Number 407-000-05-054-H01  
Expires: 8/31/08

### ATORVASTATIN

(see page 197)

#### Goal

To review the development program for atorvastatin in the context of a changing healthcare environment such that pharmacists can appreciate trial design that supports more relevant therapeutic decisions.

#### Objectives

After reviewing this article, the reader should be able to:

- understand the differences between trial types based on surrogate measures versus those with clinically relevant endpoints;
- acknowledge that actions of a drug therapy may be determined well beyond their primary pharmacology;
- understand that clinical trial programs in cardiovascular medicine must evaluate a broad base of patients, often with significant differences in baseline risk;
- understand that surrogate measures of therapy, which include biochemical and technological assessments of disease pathology, must be validated with respect to clinical outcomes;
- understand that clinical trials using comparator agents are critical in determining true differences in overall effectiveness.

#### Test Questions

- One of the initial trials in which atorvastatin was compared with other agents in the statin class, based on LDL-C effects, was:
  - L-EFFECT.
  - CURVES.
  - WOSCOPS.
  - RANDOM.
  - 4S.
- The ACCESS study was a comparison trial among statins to determine the ability of agents to reach what treatment goals?
  - Joint National Committee
  - American Heart Association Prevention Goals
  - National Cholesterol Education Program

- (d) American College of Physicians Practice Guidelines  
(e) American College of Cardiology Recommendations
3. Pooled safety data for atorvastatin demonstrate which of the following as the most common adverse event?
    - (a) persistent increase in liver enzymes
    - (b) elevations of creatine kinase to 10 times the upper limit of normal
    - (c) disorders of the digestive system
    - (d) myalgia
    - (e) visual disturbances
  4. All of the following are considered pleiotropic effects of the statin class *except*:
    - (a) triglyceride lowering.
    - (b) fibrinolytic effects.
    - (c) effect on nitric oxide metabolism.
    - (d) smooth muscle cell migration.
    - (e) lowering of inflammatory markers.
  5. High-sensitivity CRP has been established as:
    - (a) the target of treatment.
    - (b) being uniquely associated with atherosclerosis.
    - (c) a definitive marker to establish statin efficacy.
    - (d) a predictor of cardiovascular risk.
    - (e) a surrogate for outcomes in cardiovascular disease.
  6. Patients with acute coronary syndrome fall into which of the following risk strata?
    - (a) familial combined
    - (b) intermediate for cardiovascular events
    - (c) post-infarction event
    - (d) low risk for coronary calcification
    - (e) highest risk for death and recurrent ischemia
  7. The greatest benefit associated with statin treatment in the MIRACL study was found in:
    - (a) reduction of high-sensitivity CRP-mediated events.
    - (b) stroke.
    - (c) MI.
    - (d) worsening heart failure.
    - (e) peripheral vascular disease.
  8. Based on the findings of the PRISM study, pretreatment with a statin resulted in:
    - (a) standardization of drug therapy.
    - (b) reduction of event rates at 30 days' follow-up.
    - (c) statistical reduction in the number of deaths due to cardiovascular disease.
    - (d) increase of muscle-related adverse events.
    - (e) withdrawal of other lipid-regulating therapies.
  9. The ASCOT-LLA study evaluated all of the following *except*:
    - (a) benefits of lipid lowering in patients who had previously not been considered candidates for statin therapy.
    - (b) hypertensive patients with multiple risk factors.
    - (c) secondary prevention of cardiovascular events.
    - (d) benefits of lipid-lowering therapy within the first year of a planned 5-year study.
    - (e) All of the above factors were evaluated.
  10. Which of the following factors of the ALLIANCE study does *not* have practical implications for clinicians?
    - (a) it was a 4-year population-based, open-label, randomized trial
    - (b) included patients from managed care and VA facilities
    - (c) evaluated a high-risk population that could benefit from aggressive lipid lowering
    - (d) focused on patients with specific treatment goals
    - (e) reflected a real-world setting
  11. Which of the following factors was *not* part of the ASAP study?
    - (a) impact on clinical events
    - (b) treatment with active comparators
    - (c) surrogate measure
    - (d) unique patient population
    - (e) common approach as seen in the ARBITER study
  12. Based on studies presented in this paper, which of the following is *true* about IVUS?
    - (a) well-established surrogate for coronary disease events
    - (b) has no utility in determining atherosclerosis disease progression
    - (c) is a noninvasive technique
    - (d) requires baseline assessment and follow-up
    - (e) demonstrated no difference in treatment arms
  13. The use of composite endpoints in cardiovascular studies:
    - (a) is an atypical method to determine treatment effect.
    - (b) adds statistical rigor when interpreting trial results.
    - (c) must include only clinical events.
    - (d) requires a smaller number of patients for trial design.
    - (e) is limited to coronary events.
  14. Both REVERSAL and PROVE-IT included all of the following elements *except*:
    - (a) used interventional vascular assessment.
    - (b) was dependent on assessment of high-sensitivity CRP to assess treatment effect.
    - (c) used active comparators in the trial design.
    - (d) included acute coronary syndromes patient groups.
    - (e) contained aggressive LDL-C treatment targets.
  15. A major difference between the REVERSAL and PROVE-IT studies was:
    - (a) use of conventional versus intensive lipid-lowering treatment.
    - (b) comparison of specific statins in each study protocol.
    - (c) interpretation of atherosclerotic plaque burden results.
    - (d) interpretation of clinical endpoints.
    - (e) differences in LDL-C treatment effect between active comparators.