Auxora for the Treatment of Patients With Acute Pancreatitis and Accompanying Systemic Inflammatory Response Syndrome

Clinical Development of a Calcium Release-Activated Calcium Channel Inhibitor

SUPPLEMENTAL DIGITAL CONTENT

Study Inclusion Criteria

All patients were required to meet all of the following criteria to be included in the study:

1. A diagnosis of acute pancreatitis established by the presence of abdominal pain consistent with acute pancreatitis and 1 of the following 2 criteria:
   a. Serum lipase or serum amylase >3 times the upper limit of normal;
   b. Characteristic findings of acute pancreatitis on abdominal imaging;
2. The following 2 criteria:
   a. Hypoxia defined as an SpO_2 <96% with a FiO_2 of 21% (room air) to 27% or an SpO_2 <97% with a FiO_2 ≥28%; and
   b. A diagnosis of SIRS, defined by the presence of at least 2 of the following 4 criteria:
      i. Temperature <36°C or >38°C;
      ii. Heart rate >90 beats/minute;
      iii. Respiratory rate >20 breaths/minute or arterial carbon dioxide tension ($PaCO_2$) <32 mmHg;
      iv. White blood cell count >12,000 cells/mm^3, or <4000 cells/mm^3, or >10% immature (band) forms;
3. No evidence of pancreatic necrosis on CECT performed in the 18 hours prior to consent or after consent and before Day 1;
4. Adults ≥18 years of age;
5. A female patient of child-bearing potential who is sexually active with a male partner must be willing to practice acceptable methods of birth control for 365 days after the last dose of Auxora;
6. A male patient who is sexually active with a female partner of childbearing potential must be willing to practice acceptable methods of birth control for 365 days after the last dose of Auxora and must not donate sperm for 365 days;
7. Willing and able to or have a legally authorized representative that is willing and able to, provide informed consent to participate, and to cooperate with all aspects of the protocol.

Exclusion Criteria

All patients with any of the following conditions or characteristics were excluded from the study:

1. Any concurrent clinical condition that a study physician believed could potentially pose an unacceptable health risk to the patient while involved in the study, including a cardiovascular Sequential Organ Failure Assessment score of 4 at the time of Screening, or may have limited expected survival to <6 months:
2. Suspected presence of cholangitis, in the judgment of the treating investigator;
3. An Endoscopic Retrograde Cholangio-Pancreatography performed in the previous 7 days;
4. Any malignancy being treated with chemotherapy or immunotherapy;
5. Any autoimmune disease being treated with immunosuppressive medication or immunotherapy;
6. A history of:
   a. Chronic pancreatitis, pancreatic necrosis or necrosectomy, or pancreatic enzyme replacement therapy;
   b. Biopsy proven cirrhosis, portal hypertension, hepatic failure/hepatic encephalopathy;
   c. Known hepatitis B or C, or HIV;
   d. History of organ or hematologic transplant;
   e. Resuscitated cardiac arrest, myocardial infarction, revascularization, cardiovascular accident in the 30 days prior to day 1;
7. Current renal replacement therapy;
8. Current known abuse of cocaine or methamphetamine;
9. Known to be pregnant or are nursing;
10. Participated in another study of an investigational drug or therapeutic medical device in the 30 days prior to day 1;
11. A history of allergy to eggs or known hypersensitivity to any components of Auxora.

Prespecified Endpoints

Computed Tomography Severity Index

The computed tomography severity index (CTSI) score was defined as the sum of the Balthazar score (Supplemental Digital Table 1) and Pancreatic Necrosis score (Supplemental Table 2). The CTSI score was categorized in accordance with Supplemental Table 3.

SUPPLEMENTAL TABLE 1. Definition of Balthazar Score

Grade	CTSI Finding Balthazar	Points Awarded
A	Normal pancreas	0
B	Enlargement of pancreas	1
C	Inflammatory changes in pancreas and peripancreatic fat	2
D	Ill-defined single peripancreatic fluid collection	3
E	≥2 poorly defined peripancreatic fluid collections	4

SUPPLEMENTAL TABLE 2. Definition of Pancreatic Necrosis Score

Pancreatic Necrosis	Points Awarded
None	0
<30%	2
30–50%	4
>50%	6

SUPPLEMENTAL TABLE 3. CTSI Score

Score Awarded	Classification
0–3	Mild acute pancreatitis
4–6	Moderate acute pancreatitis
7–10	Severe acute pancreatitis