Treatment With Reltecimod Significantly Reduces Inflammation in Mouse Model of Acute Pancreatitis

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BACKGROUND

- Injury to pancreatic exocrine cells initiates both local and systemic inflammation.
- Systemic inflammation contributes significantly to distant organ injury.
- Acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) are common complications.
- Therapeutic interventions, which can dampen systemic inflammatory response and protect distant organs are required.
- Reltecimod is a rationally designed synthetic decapeptide acting as CD28 co-stimulatory receptor antagonist.

AIM

This study was designed to evaluate the efficacy of reltecimod in caerulein-induced acute pancreatitis (AP).

METHODS

- Caerulein-induced AP (CER-AP) was triggered by hourly injections of Caerulein (50 µg/kg, i.p. x12) in BALB/c mice.
- In treatment group reltecimod (AB) (5mg/kg or 10mg/kg) was administered i.v. at initiation of injury concomitantly with first caerulein injection. In double dose (5+5mg or 10+5mg/kg) group, second dose was administered at 3h. Control group was administered saline only.
- Animals were euthanized 12 hours after last caerulein injection.
- Severity of pancreatitis was evaluated using pancreatic and lung histology. Neutrophil sequestration was determined by measuring tissue myeloperoxidase (MPO) activity.

RESULTS

A. There was no significant effect of treatment on plasma amylase or lipase activity in CER-AP

B. Pancreatic MPO is significantly decreased in response to treatment at 23 hours.

C. Pancreatic inflammation is significantly decreased in response to treatment.

D. There was significant reduction in sequestered inflammatory cells (coronin 1A positive) in response to treatment.

E. Lung histology (H&E) and inflammation significantly improved in CER-AP in response to treatment.

CONCLUSION

- Reltecimod treatment resulted in substantial reduction of inflammation in caerulein-induced acute pancreatitis.
- This promising anti-inflammatory drug should be investigated further in more preclinical models of AP.

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