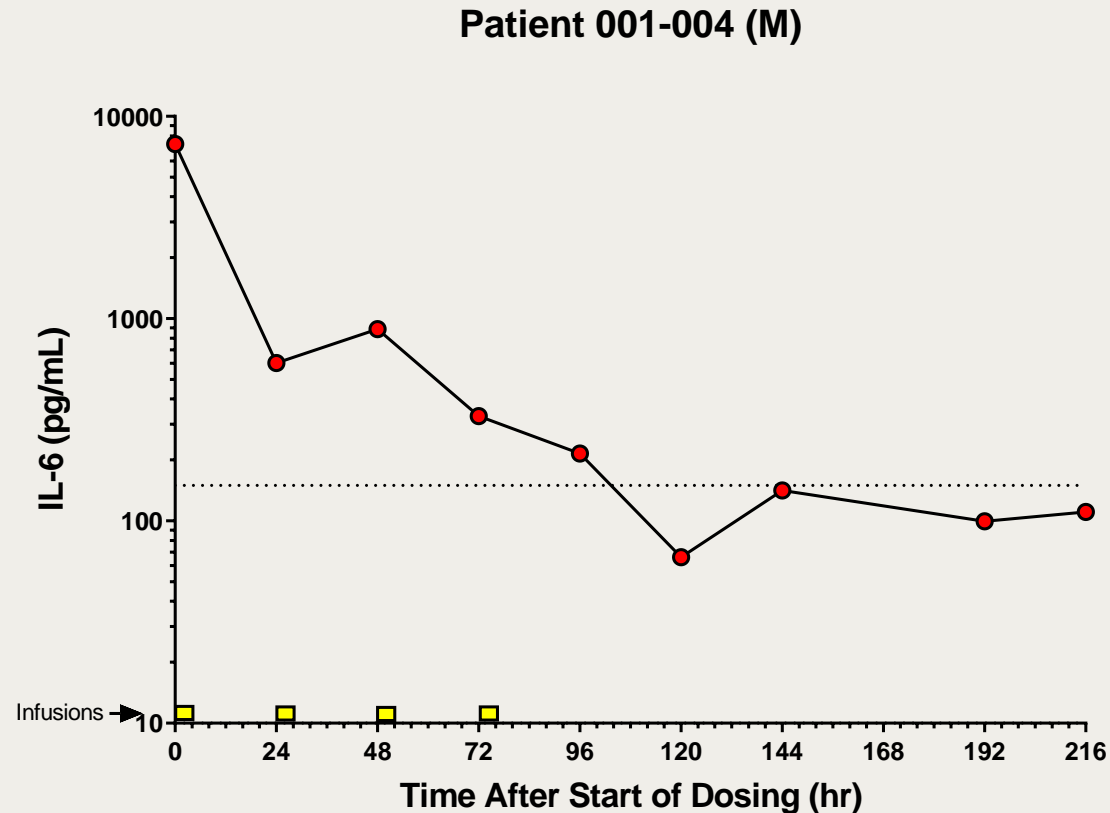


## Developing Novel Therapies for Acute Inflammatory and Immunologic Diseases

Acute Pancreatitis Clinical Expert Event  
September 21, 2023

## Individual Case of a Critically Ill Patient with AP








- Critically ill patient presented with respiratory failure and acute pancreatitis in the ED.
- Randomized to receive high dose of Auxora
- IL-6 >7296 pg/mL at study entry, 66 at 120 hrs
- Managed with high flow oxygen and intermittent bi-pap; no invasive mechanical ventilation
- Discharged home on room air day 8 eating a solid food diet

## Forward-Looking Statements

This presentation contains forward-looking statements which include, but are not limited to, statements regarding CalciMedica's business strategy and clinical development plans; the design and potential benefits of CalciMedica's product candidates; CalciMedica's ongoing and planned clinical trials; and the timing for CalciMedica's receipt and announcement of data from its clinical trials. These forward-looking statements are subject to the safe harbor provisions under the Private Securities Litigation Reform Act of 1995. CalciMedica's expectations and beliefs regarding these matters may not materialize. Actual outcomes and results may differ materially from those contemplated by these forward-looking statements as a result of uncertainties, risks, and changes in circumstances, including but not limited to risks and uncertainties related to: the impact of fluctuations in global financial markets on CalciMedica's business and the actions it may take in response thereto; CalciMedica's ability to execute its plans and strategies; the ability to obtain and maintain regulatory approval for CalciMedica's product candidates; results from clinical trials may not be indicative of results that may be observed in the future; potential safety and other complications from CalciMedica's product candidates; economic, business, competitive, and/or regulatory factors affecting the business of CalciMedica generally; CalciMedica's ability to protect its intellectual property position; and the impact of government laws and regulations. Additional risks and uncertainties that could cause actual outcomes and results to differ materially from those contemplated by the forward-looking statements are included under the caption "Risk Factors" in CalciMedica's most recently filed periodic report, and subsequent periodic reports filed by CalciMedica, under the Securities Exchange Act of 1934, as amended, from time to time and available at [www.sec.gov](http://www.sec.gov). These documents can be accessed on CalciMedica's web page at [calcimedica.com](http://calcimedica.com).

These forward-looking statements are based on information available to, and expectations of, CalciMedica of the date of this presentation. CalciMedica disclaims any obligation to update these forward-looking statements, except as may be required by law.

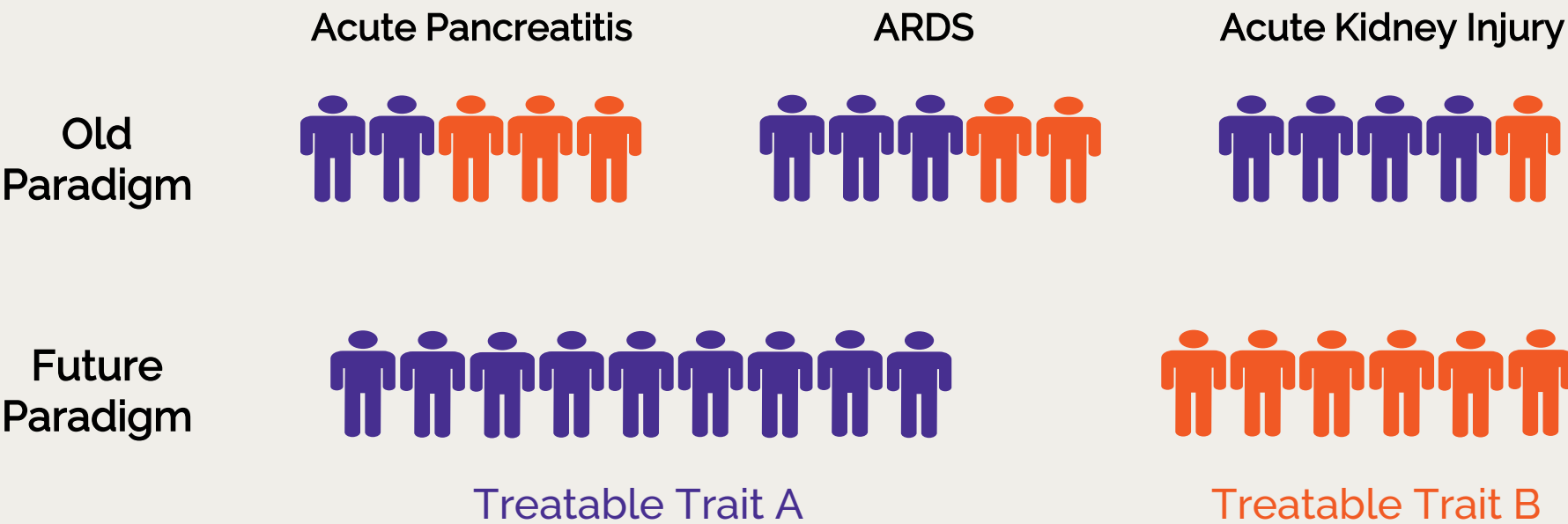
# Investment Highlights

	<b>Differentiated Technology</b>	Proprietary technology targeting CRAC <sup>1</sup> channel inhibition to develop novel therapies for life-threatening inflammatory diseases with high unmet need		
	<b>Compelling Proof-of-Concept Data</b>	AuxoraTM has been studied in multiple Phase 2 trials, demonstrating positive and consistent clinical results and favorable safety profile		
	<b>Substantial Market Opportunity</b>	~100K target patient population in acute pancreatitis represents a potential \$1B+ U.S. market opportunity with no approved therapies		
	<b>Next Clinical Milestones</b>	Acute Pancreatitis <sup>2</sup> Phase 2b Data 1H24	Asparaginase-Induced Pancreatic Toxicity <sup>3</sup> Phase 1/2 Data 2H23	Acute Kidney Injury <sup>4</sup> Phase 2 1H24 (pending funding)
	<b>Strong IP</b>	Composition of matter (2036), formulation (2038), and methods of use (2036-2041+) worldwide patent protection		

# Differentiated Pipeline

Program <sup>1,2</sup>	Indication	Phase of Development				Anticipated Milestones
		Preclinical	Phase 1	Phase 2	Phase 3	
Pancreas						
Auxora	Acute Pancreatitis	<div></div>	<div></div>	<div></div>	<div></div>	CARPO Phase 2b trial ongoing; Data in 1H24
Auxora	Aparaginase-Induced Pancreatic Toxicity	<div></div>	<div></div>	<div></div>	<div></div>	CRSPA Phase 1/2 trial ongoing; Trial expansion underway
CM6336	Chronic Pancreatitis (Oral)	<div></div>	<div></div>	<div></div>	<div></div>	Submit IND in 2024 (pending funding)
Kidney						
Auxora	Acute Kidney Injury	<div></div>	<div></div>	<div></div>	<div></div>	Submit IND 2H23 Phase 2 trial in 1H24 (pending funding)
Lung						
Auxora	ARDS - Ventilated COVID-19 Patients	<div></div>	<div></div>	<div></div>	<div></div>	Data expected 2H23 Will inform the development plan for ARDS

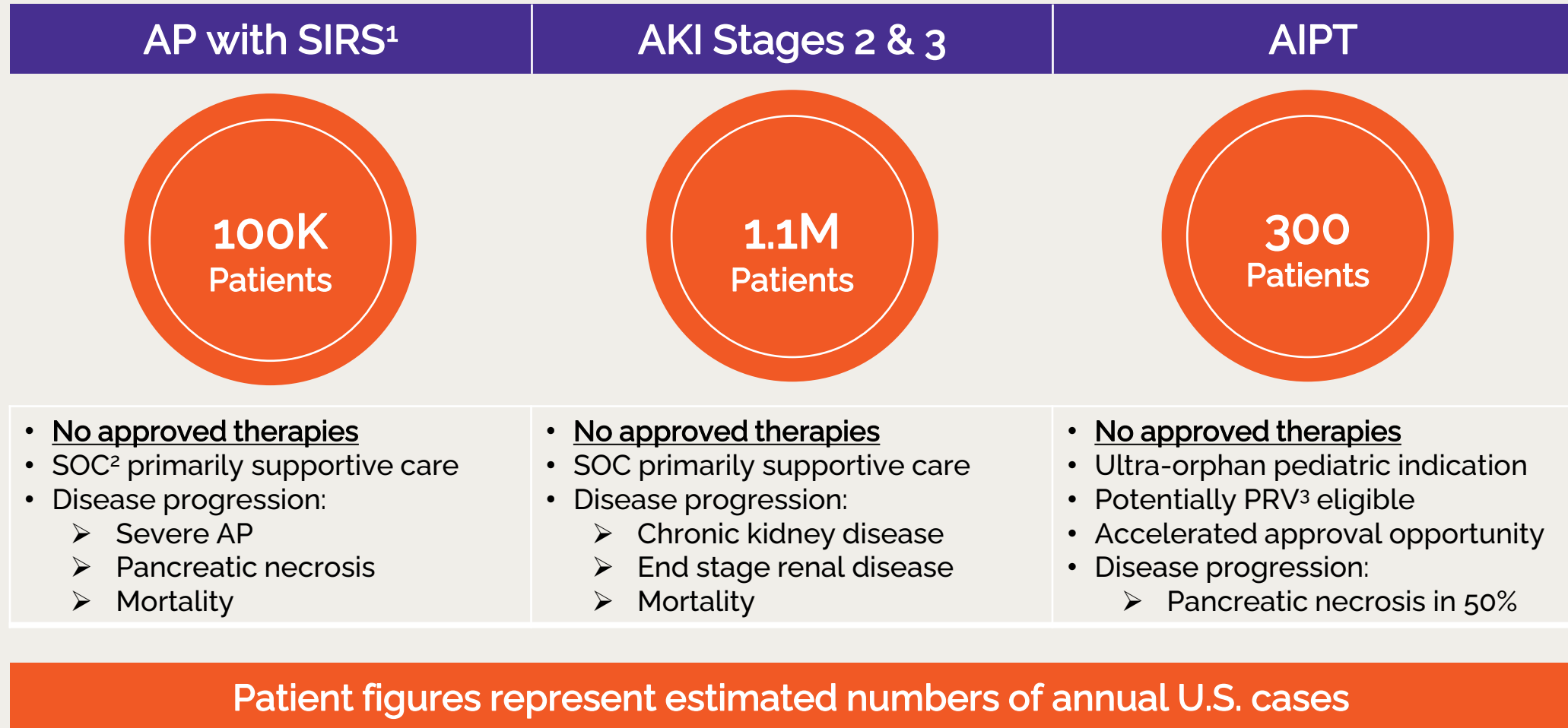
# Acute Inflammation: Underlying Cause Across Many Diseases



Auxora has demonstrated positive clinical results in all 3 of these large, underserved patient populations

1) Sources: Reddy, Kiran, Carolyn S. Calfee, and Danny F. McAuley. "Acute respiratory distress syndrome subphenotypes beyond the syndrome: a step toward treatable traits?." American Journal of Respiratory and Critical Care Medicine 203.12 (2021): 1449-1451.

# Large U.S. Market Opportunity in Acute Inflammatory Diseases



1) **SIRS**: Systemic Inflammatory Response Syndrome; 2) **SOC**: Standard of Care; 3) **PRV**: Priority Review Voucher;  
4) Sources: Primary Market Research, KOLs, Healthcare Cost and Utilization Project, Pancreatitis Foundation



## Anticipated Milestones

AP	Phase 2b Data Expected in 1H24 Phase 3 Initiation Expected in 2025
AIPT	Initial First Cohort Data Release Expected in 4Q23 Trial Expansion Underway
AKI	IND filing Expected in 2H23 Phase 2 Clinical Trial Initiation 1H24 (pending funding)
ARDS	Phase 2 Data in Ventilated COVID Patients Publication Expected in 2H23 Will inform the development plan for ARDS
Cash Runway	Current Cash Runway into 2H24

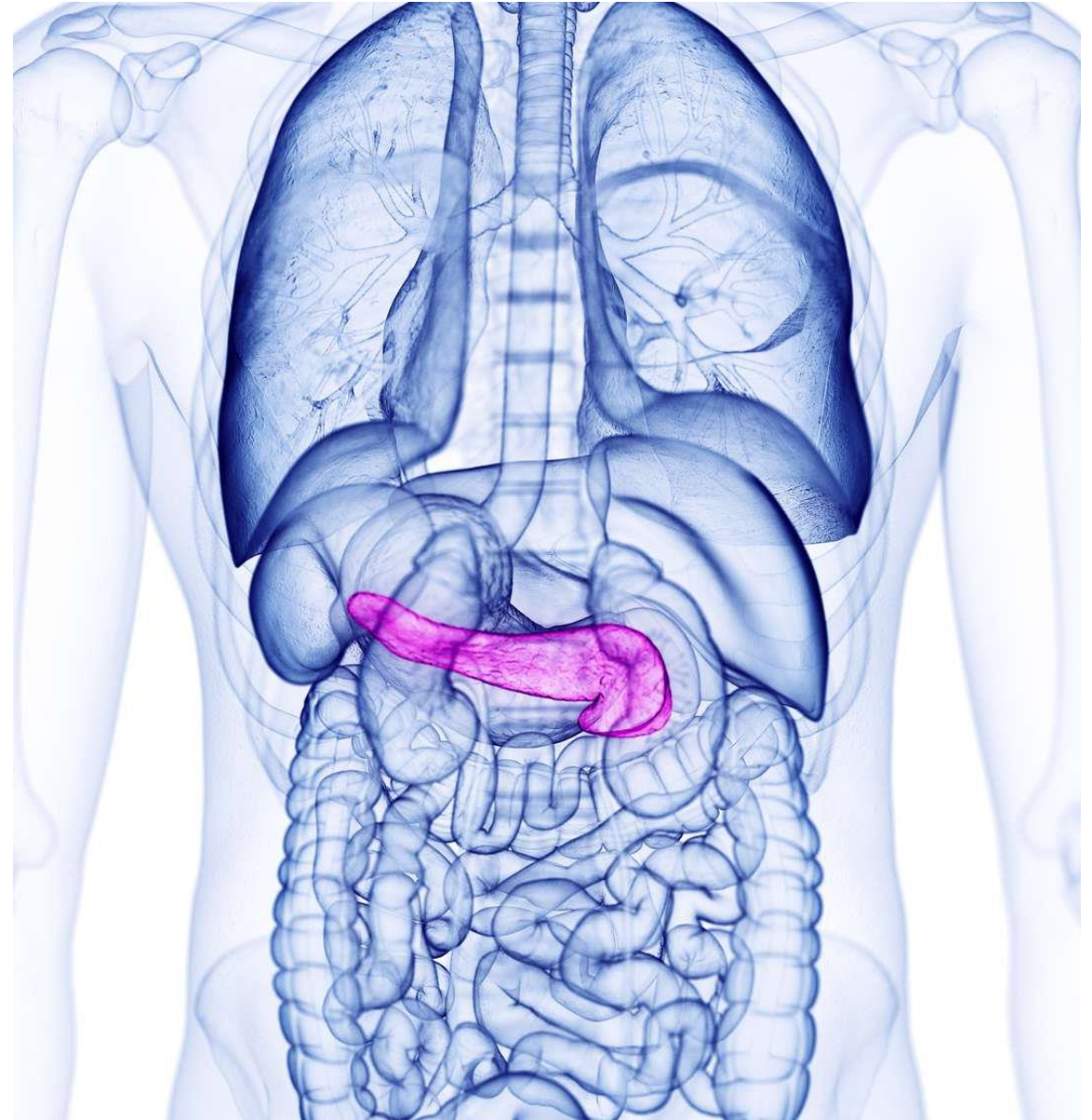


# Acute Pancreatitis

Joseph Miller, MD, MS  
Clinical Associate Professor  
Henry Ford Health | Michigan State University  
Department of Emergency Medicine

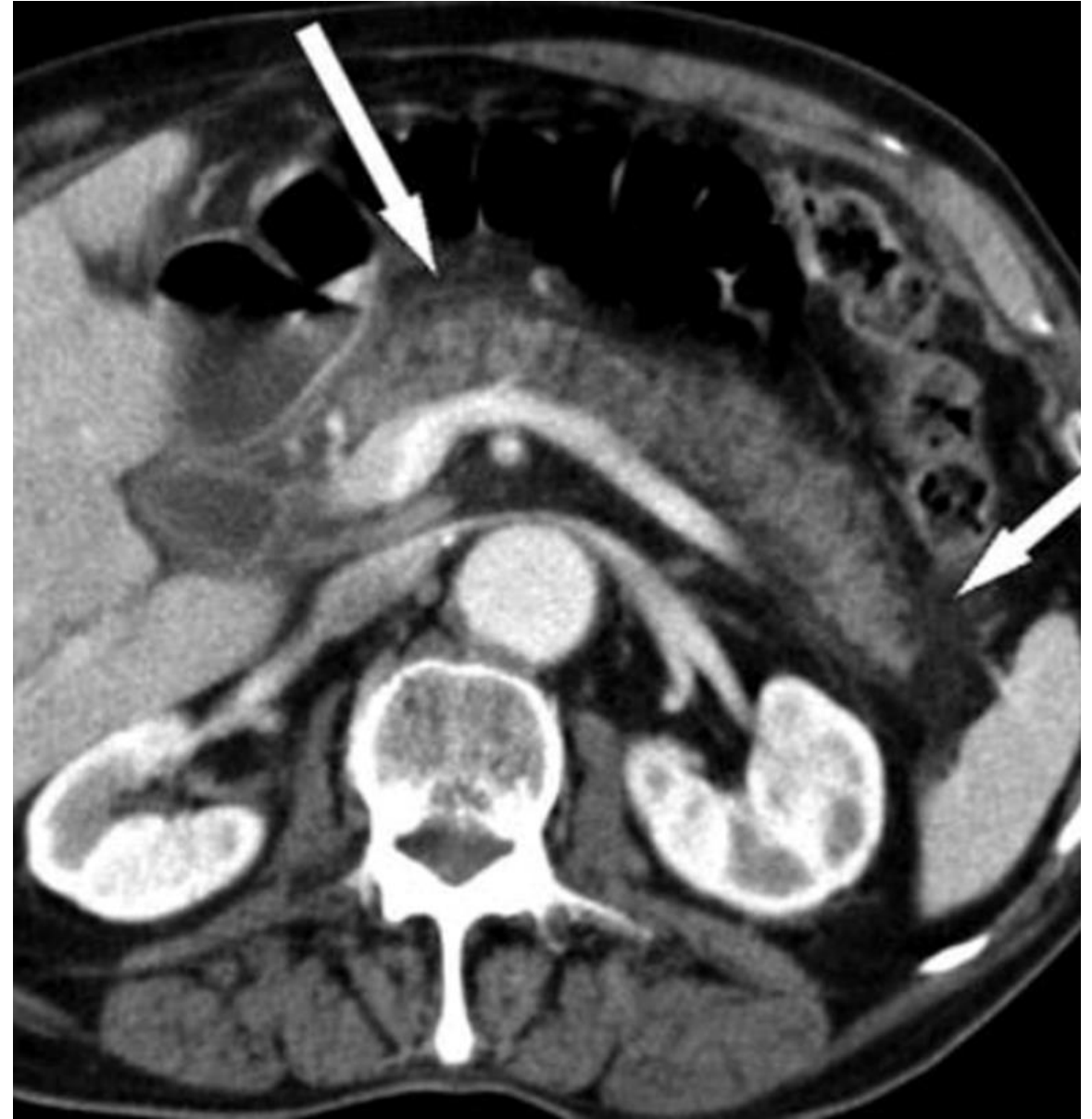
# Acute Pancreatitis

- Definition:
  - Acute inflammation of the pancreas
- Clinical Presentation:
  - Patients have constant abdominal pain
  - Pain may radiate to back
  - Pain aggravated by eating, drinking, lying down
  - Associated symptoms may include nausea, vomiting, low to moderate grade fever



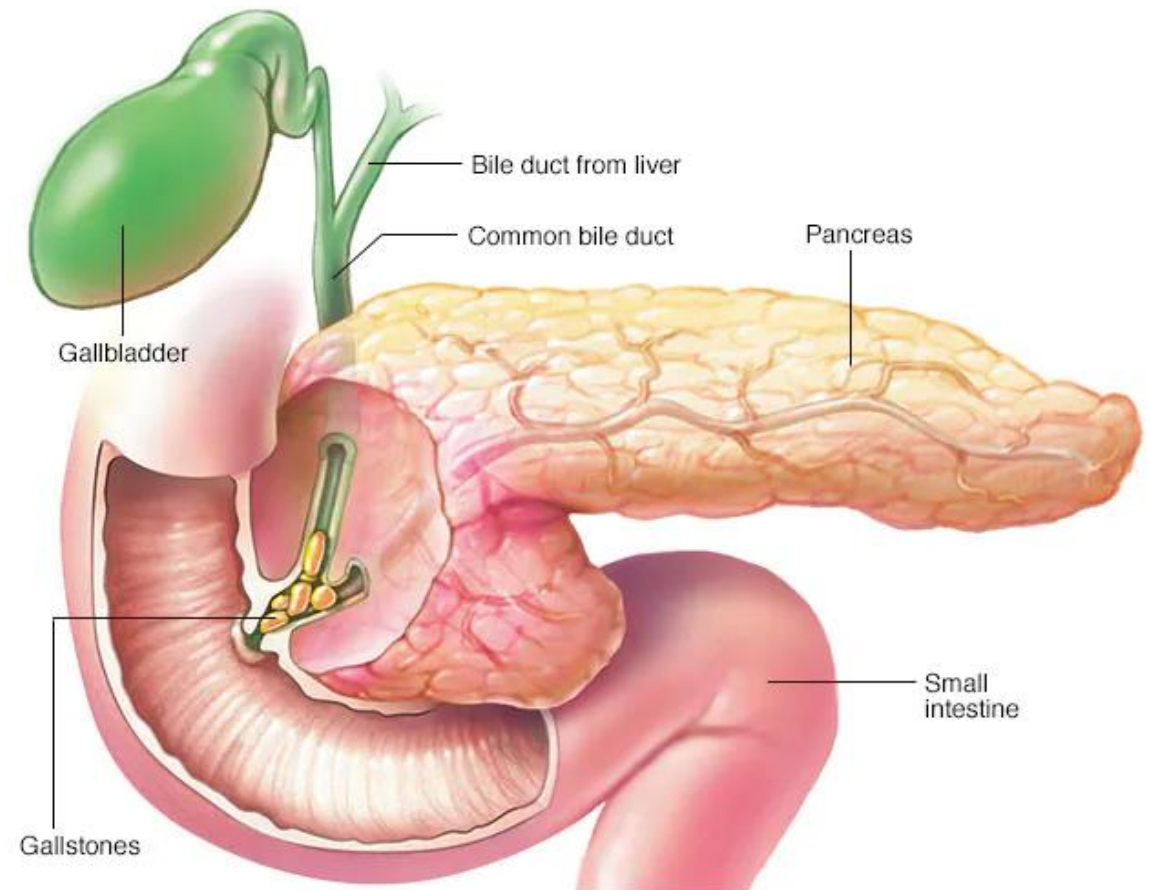
# Diagnosis

- Presence of at least 2 of the 3 following criteria:
  - Abdominal pain suggestive of acute pancreatitis
  - Serum amylase or lipase  $>3\times$  upper limit of normal
  - CT or MRI findings consistent with acute pancreatitis



# Etiology

- Etiology
  - Gallstones 40%
  - Alcohol 30%
  - Hypertriglyceridemia 5%
  - Others include: hypercalcemia, trauma, iatrogenic, medications

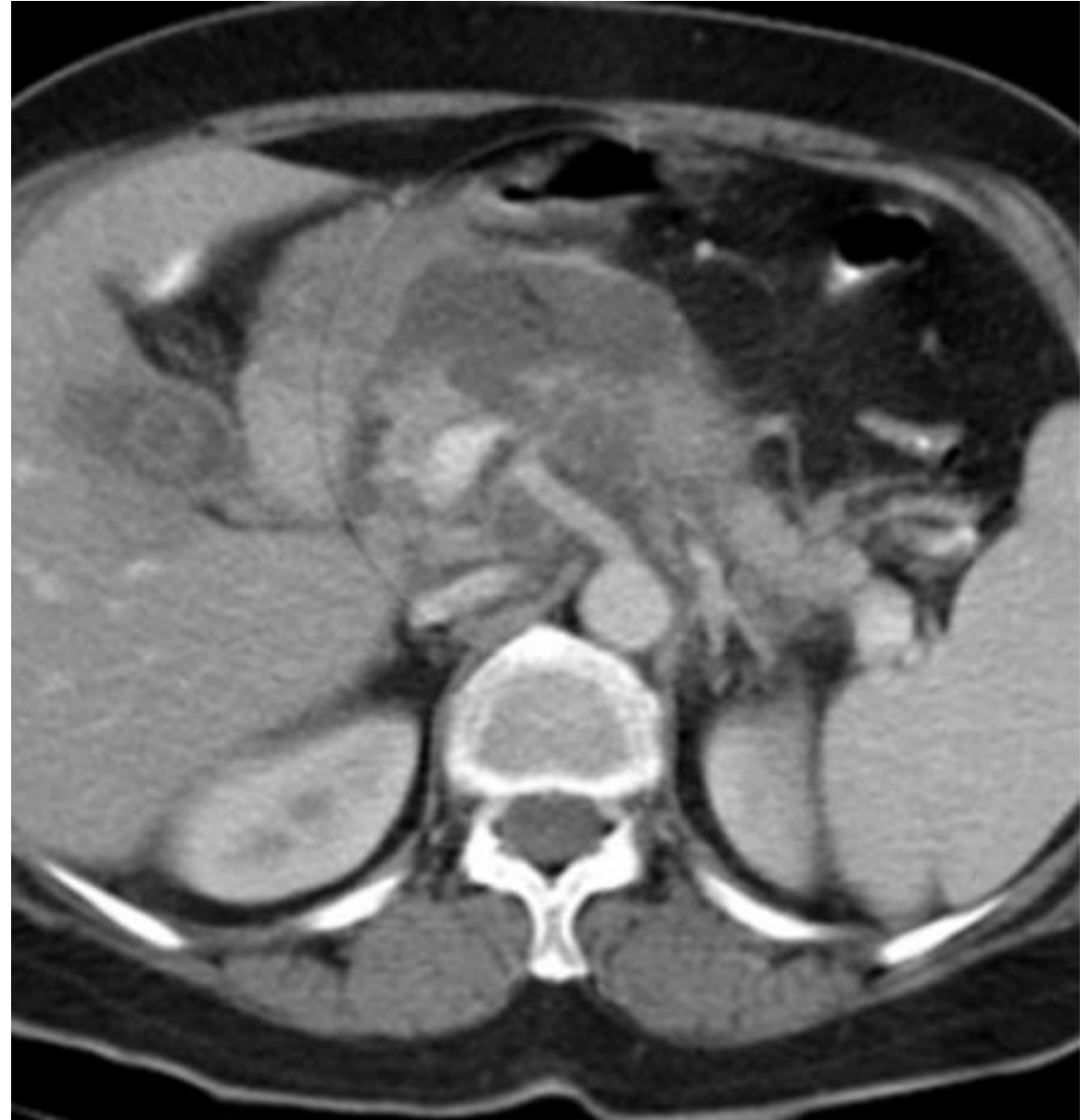


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# Prognosis

- 80% develop mild disease (no complications) or moderately severe disease (develop a local complication such as a fluid collection around the pancreas or necrosis of the pancreas)
- 20% develop severe disease-development of organ failure, usually the lung
- Mortality 20% in patients who develop severe disease!

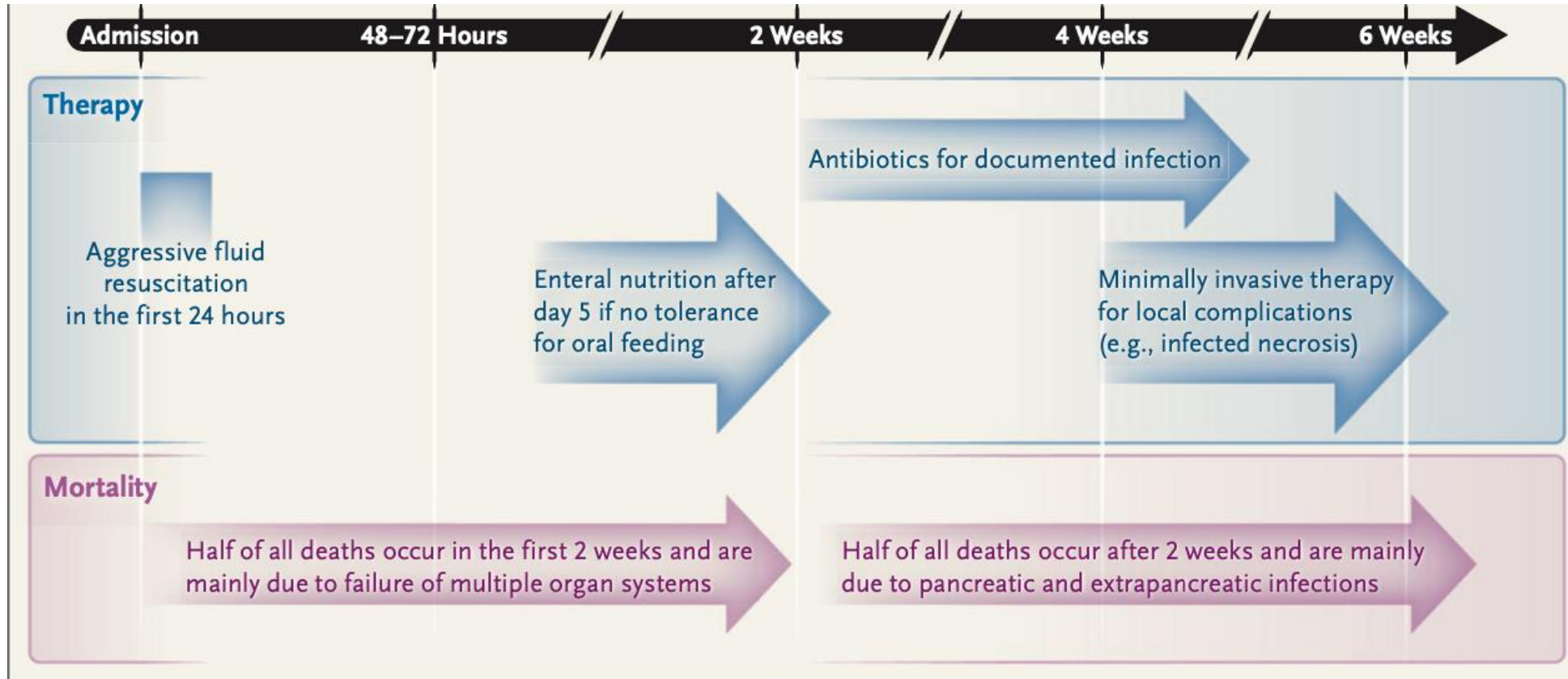


# Goals in the ED

- Rapid Diagnosis of Acute Pancreatitis
  - Straightforward with current diagnostic criteria
- Identification of Patients at Risk of Developing Severe Disease
  - Presence of Systemic Inflammatory Syndrome
  - Presence of Hypoxemia
  - Age >60 years + SpO2 <96% + SIRS had almost 42 times the odds of death
- Triage to Appropriate Hospital Unit
  - Hospitalist
  - Surgeon
  - Intensivist



# Current Management: Limited



**\*Those at Risk for Severe Disease Treated No Differently Than Those at Risk for Mild Disease**



# Economic Burden

- 288,220 annual number of hospitalizations in 2018 in US with AP as principal diagnosis
- 15.4% readmission rate within 30 days
- Aggregate cost 3 billion dollars

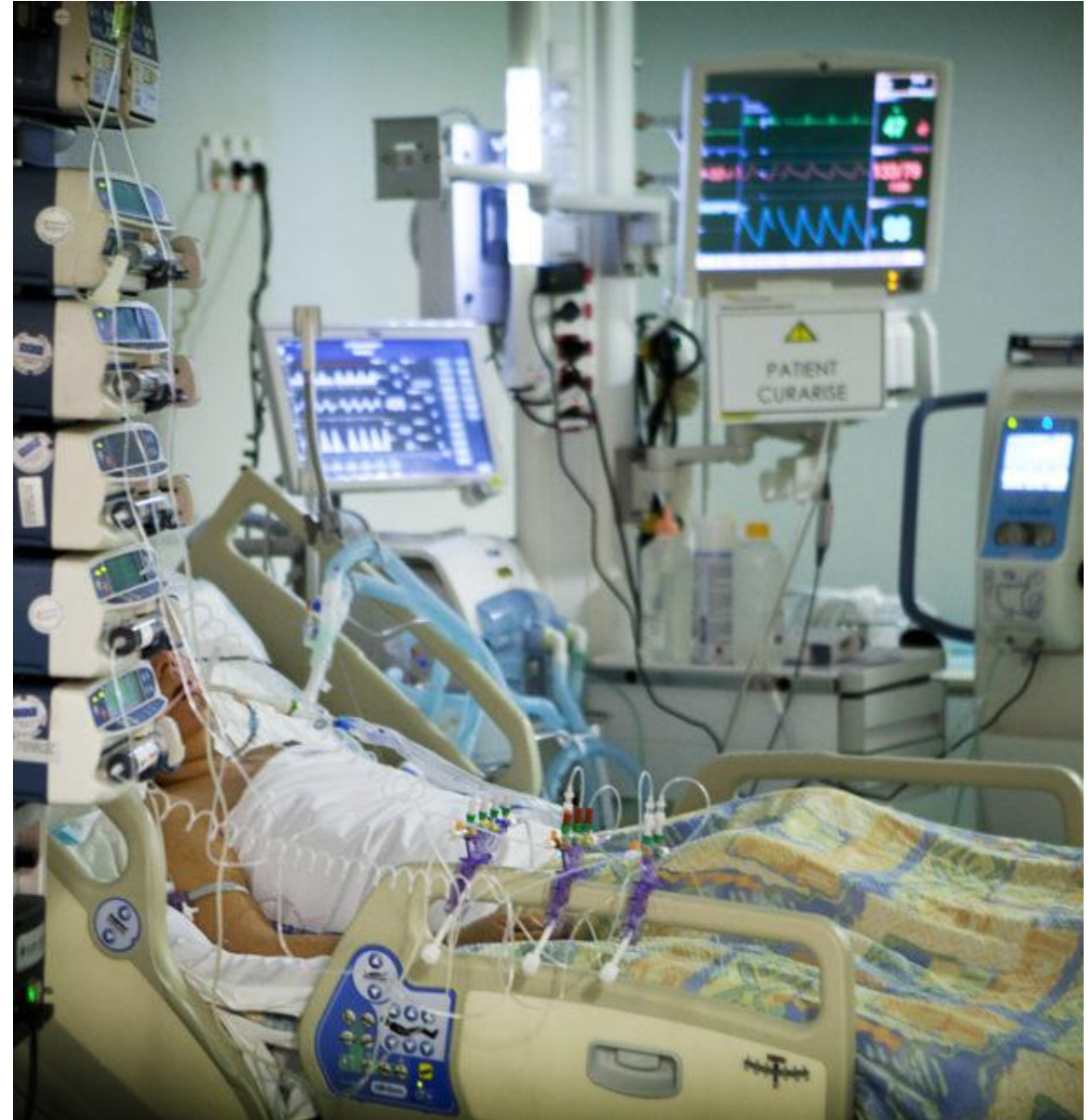


# Patient Story



# AP Patient

- 68 year-old female with gallstone pancreatitis
- Admitted to hospital and soon sent to ICU
- Placed on ventilator for lung injury
- Delirium
- Pneumonia
- Infected pancreatic pseudocysts
- Gastrointestinal bleeding
- Became dialysis dependent
- Hospital stay = 90 days







# Advances in Acute Pancreatitis

---

**Georgios Papachristou, MD PhD**

**Professor and Chief**

**Division of Gastroenterology, Hepatology, and Nutrition**

# Case presentation

- **HPI**

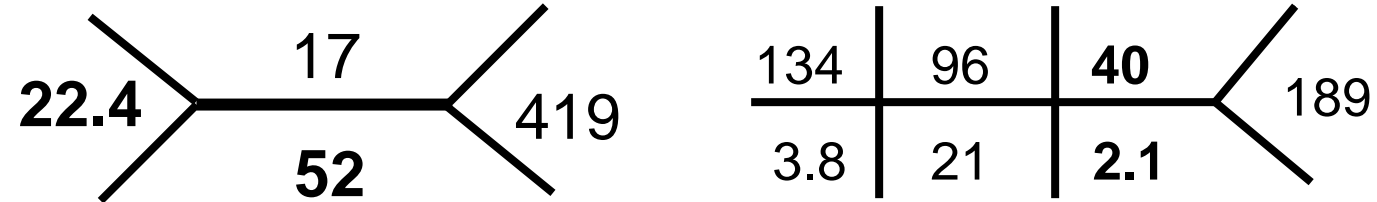
- 58 yo M with acute onset of severe upper abdominal pain radiating to back x 3 hours
- Nausea and vomiting

- **Exam**

- VS: T 38.5, HR 117, RR 24, BP 84/43, BMI 43
- Moderate distress
- Abdomen: obese, +BS, soft, tender with no guarding

# Case presentation

- Labs



**What is the Diagnosis?**

**Acute Pancreatitis**

ALT 790

Triglycerides 153

AST 624

LDH 755

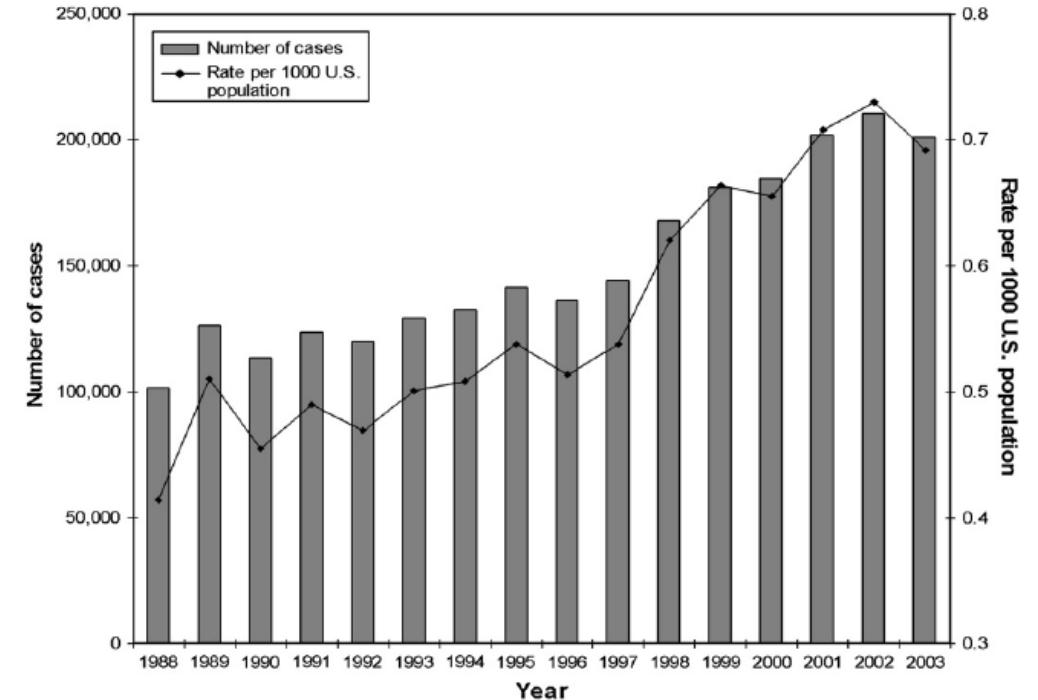
AP 167

Ca 8.8 with nl Alb

# Epidemiology & Burden of AP

Common and costly disease

- ~300k hospitalizations/year
- Annual cost ~3 billion dollars in US
- **Incidence increasing worldwide**
  - Awareness
  - Overdiagnosis
  - Obesity epidemic: gallstones

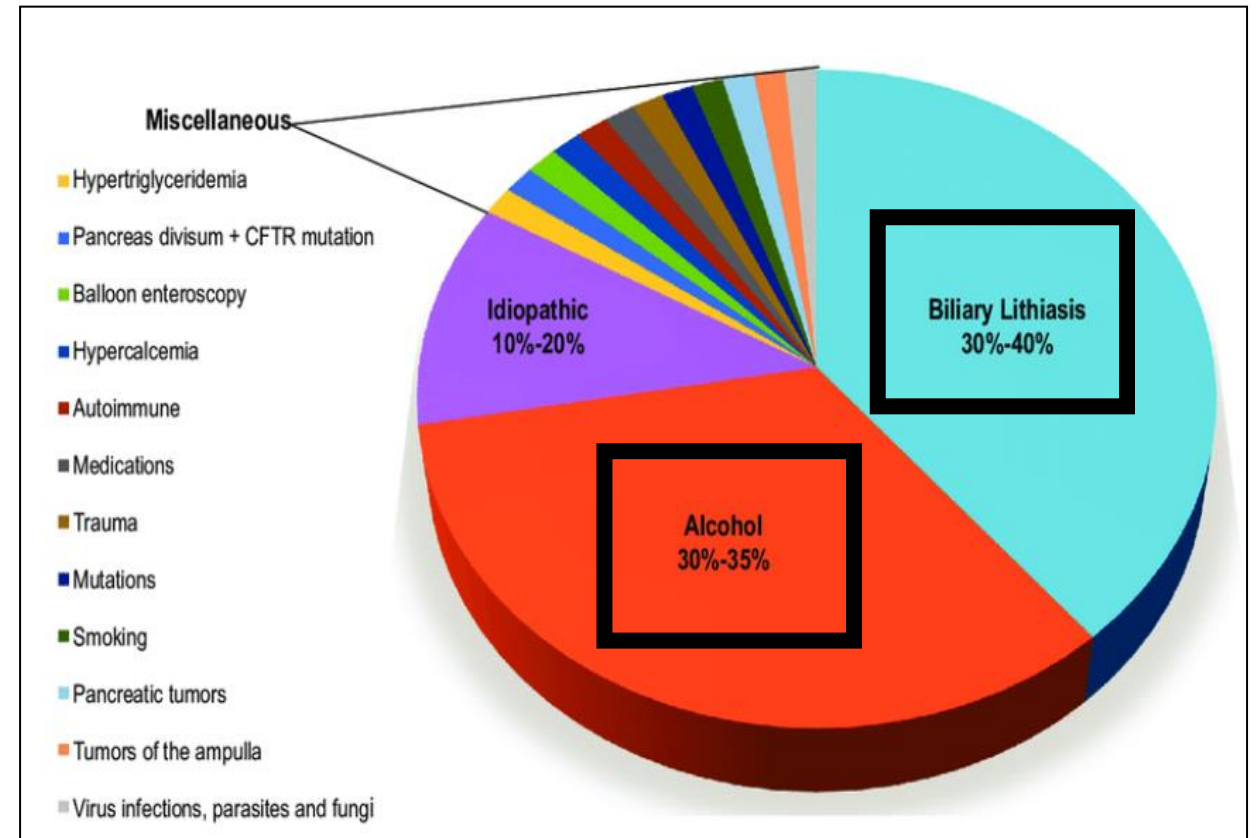




# AP: Diagnosis and Etiology



- **$\geq 2$  of 3 Criteria**
  - Typical upper abdominal pain
  - Amylase/lipase  $>3\times$  ULN
  - Imaging findings



Diaz et al, Rev Col Gastroenterol, 2015  
Otero, Edit Panam Form e Impresos, 2016

# Dynamic Process

- Rapid progression
- Early assessment is key
- Important to assess which patients will progress to severe disease
- Start supportive therapy immediately



# Definition of Severity

## 1. Severe (5-10%)

Persistent Organ failure (>48 hrs) of  $\geq 1$  of the following:

- a. Shock - Systolic BP <90 mm Hg
- b. Pulmonary - PaO<sub>2</sub> < 60 mm Hg
- c. Renal – Creatinine >2 mg/dL, after rehydration

## 2. Moderately Severe (5-10%)

Local Complications: pancreatic necrosis, fluid collections

Exacerbation of chronic comorbidities

Transient organ failure (<48 hrs)

## 3. Mild (80-85%)

# Morbidity & Mortality of AP

## Short-term complications (within 2 weeks)

- Driven by systemic inflammatory response to pancreatic injury
- Majority of deaths occur due to multi-system organ failure

## Long-term complications (>2 weeks)

- Mostly driven by infected necrotic pancreatic collections
- Thought to occur from seeding via bloodstream or translocation of gut microorganisms

# **Risk Stratification**

Back to our patient

# Prediction of SAP: Ranson's Criteria

## ➤ On admission

- Age over 55
- WBC > 16K
- Glucose > 200 mg/dl
- LDH over 350 IU/DL
- ALT over 250 IU/dl

Yes

Yes

No

Yes

Yes

## ➤ First 48 hours

- Hct decreases over 10%
- BUN rise over 5 mg/dl
- Serum calcium below 8 mg/dl
- Arterial PO<sub>2</sub> below 60 mmHg
- Base deficit over 4 mEq/L
- Fluid sequestration > 6 liters

?

?

?

?

?

?

Signs:	0-2	3-4	5-6	7-8
% Died	0.9	16	40	100
% ICU	3.7	40	93	100



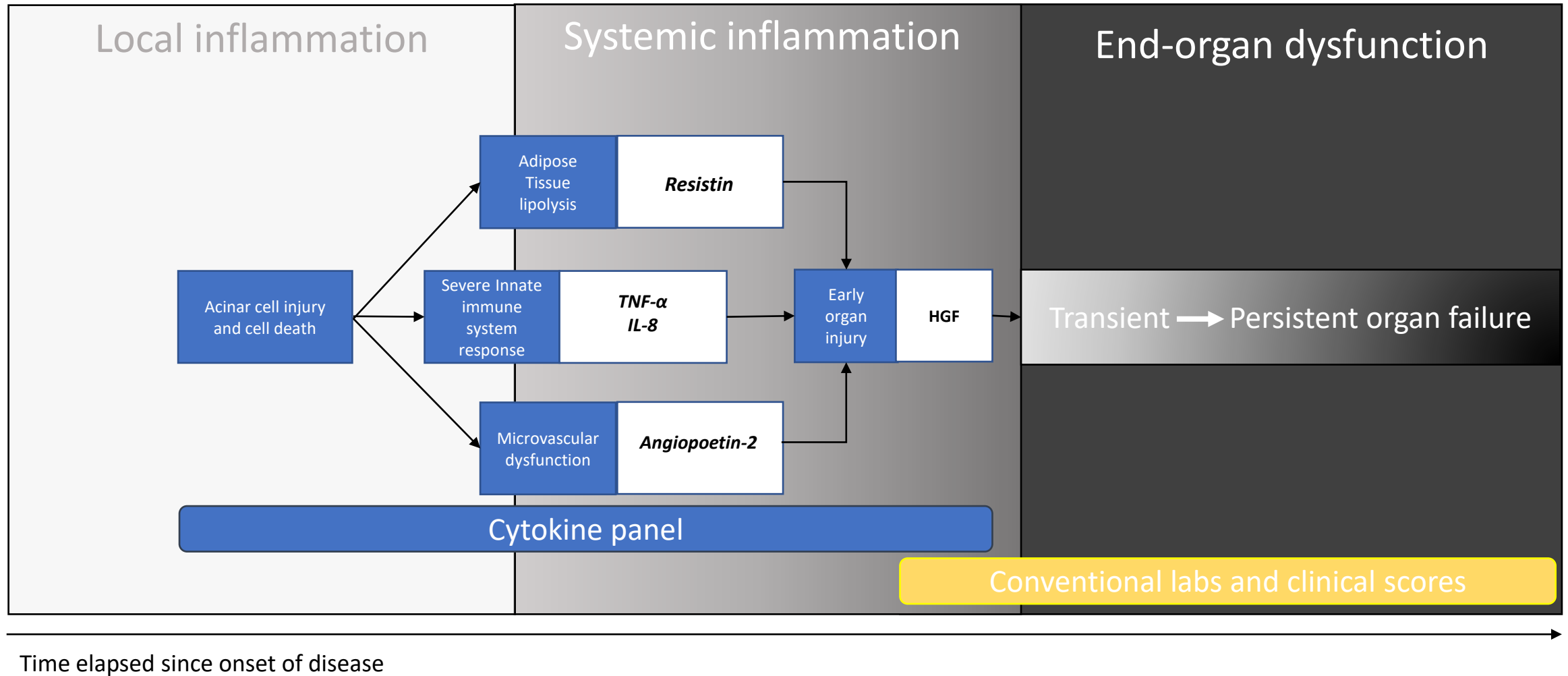
# Plethora of Prognostic Scores

Score	Cut-off	Sensitivity	Specificity	PPV	NPV	AUC	Complete data <sup>a</sup>
APACHE-II	7	0.84 ( $\pm 0.11$ )	0.71 ( $\pm 0.06$ )	0.49 ( $\pm 0.11$ )	0.93 ( $\pm 0.08$ )	0.77 ( $\pm 0.07$ )	96%
BISAP	2	0.61 ( $\pm 0.20$ )	0.84 ( $\pm 0.04$ )	0.54 ( $\pm 0.10$ )	0.87 ( $\pm 0.10$ )	0.72 ( $\pm 0.10$ )	100%
Glasgow	2	0.85 ( $\pm 0.08$ )	0.83 ( $\pm 0.07$ )	0.61 ( $\pm 0.06$ )	0.95 ( $\pm 0.05$ )	<b>0.84</b> ( $\pm 0.06$ )	98%
HAPS	1	0.70 ( $\pm 0.11$ )	0.53 ( $\pm 0.21$ )	0.32 ( $\pm 0.11$ )	0.85 ( $\pm 0.13$ )	0.62 ( $\pm 0.06$ )	99%
JSS	2	0.59 ( $\pm 0.13$ )	0.92 ( $\pm 0.05$ )	0.70 ( $\pm 0.16$ )	0.88 ( $\pm 0.07$ )	0.76 ( $\pm 0.07$ )	95%
Panc 3	1	0.76 ( $\pm 0.15$ )	0.52 ( $\pm 0.05$ )	0.34 ( $\pm 0.11$ )	0.87 ( $\pm 0.11$ )	0.64 ( $\pm 0.06$ )	99%
POP	9	0.57 ( $\pm 0.15$ )	0.76 ( $\pm 0.06$ )	0.43 ( $\pm 0.16$ )	0.85 ( $\pm 0.08$ )	0.67 ( $\pm 0.09$ )	99%
Ranson	2	0.66 ( $\pm 0.09$ )	0.78 ( $\pm 0.10$ )	0.49 ( $\pm 0.17$ )	0.88 ( $\pm 0.08$ )	0.72 ( $\pm 0.06$ )	98%
SIRS	2	0.70 ( $\pm 0.18$ )	0.71 ( $\pm 0.04$ )	0.43 ( $\pm 0.10$ )	0.88 ( $\pm 0.11$ )	0.70 ( $\pm 0.10$ )	98%
BUN	23	0.56 ( $\pm 0.10$ )	0.86 ( $\pm 0.05$ )	0.57 ( $\pm 0.14$ )	0.86 ( $\pm 0.05$ )	0.71 ( $\pm 0.03$ )	98%
Creatinine	1	0.77 ( $\pm 0.09$ )	0.59 ( $\pm 0.04$ )	0.38 ( $\pm 0.08$ )	0.89 ( $\pm 0.04$ )	0.68 ( $\pm 0.06$ )	98%
Validation cohort							
APACHE-II	7	0.97 ( $\pm 0.08$ )	0.44 ( $\pm 0.06$ )	0.14 ( $\pm 0.04$ )	0.99 ( $\pm 0.02$ )	0.71 ( $\pm 0.05$ )	100%
BISAP	2	0.62 ( $\pm 0.20$ )	0.76 ( $\pm 0.04$ )	0.20 ( $\pm 0.06$ )	0.96 ( $\pm 0.04$ )	0.69 ( $\pm 0.11$ )	100%
Glasgow	2	0.65 ( $\pm 0.24$ )	0.82 ( $\pm 0.05$ )	0.22 ( $\pm 0.08$ )	0.97 ( $\pm 0.02$ )	<b>0.74</b> ( $\pm 0.10$ )	91%
HAPS	1	0.73 ( $\pm 0.26$ )	0.58 ( $\pm 0.09$ )	0.12 ( $\pm 0.06$ )	0.97 ( $\pm 0.02$ )	0.66 ( $\pm 0.09$ )	92%
JSS	2	0.42 ( $\pm 0.19$ )	0.89 ( $\pm 0.05$ )	0.23 ( $\pm 0.18$ )	0.95 ( $\pm 0.01$ )	0.66 ( $\pm 0.11$ )	91%
Panc 3	1	0.62 ( $\pm 0.31$ )	0.52 ( $\pm 0.05$ )	0.11 ( $\pm 0.05$ )	0.94 ( $\pm 0.04$ )	0.57 ( $\pm 0.16$ )	100%
POP	9	0.46 ( $\pm 0.31$ )	0.81 ( $\pm 0.04$ )	0.16 ( $\pm 0.12$ )	0.95 ( $\pm 0.02$ )	0.64 ( $\pm 0.16$ )	90%
Ranson	2	0.46 ( $\pm 0.28$ )	0.80 ( $\pm 0.03$ )	0.16 ( $\pm 0.11$ )	0.95 ( $\pm 0.02$ )	0.63 ( $\pm 0.15$ )	91%
SIRS	2	0.69 ( $\pm 0.16$ )	0.58 ( $\pm 0.04$ )	0.11 ( $\pm 0.03$ )	0.96 ( $\pm 0.03$ )	0.64 ( $\pm 0.01$ )	93%
BUN	23	0.65 ( $\pm 0.26$ )	0.81 ( $\pm 0.04$ )	0.21 ( $\pm 0.09$ )	0.97 ( $\pm 0.03$ )	0.73 ( $\pm 0.13$ )	96%
Creatinine	1	0.77 ( $\pm 0.20$ )	0.63 ( $\pm 0.07$ )	0.14 ( $\pm 0.12$ )	0.97 ( $\pm 0.02$ )	0.70 ( $\pm 0.11$ )	98%

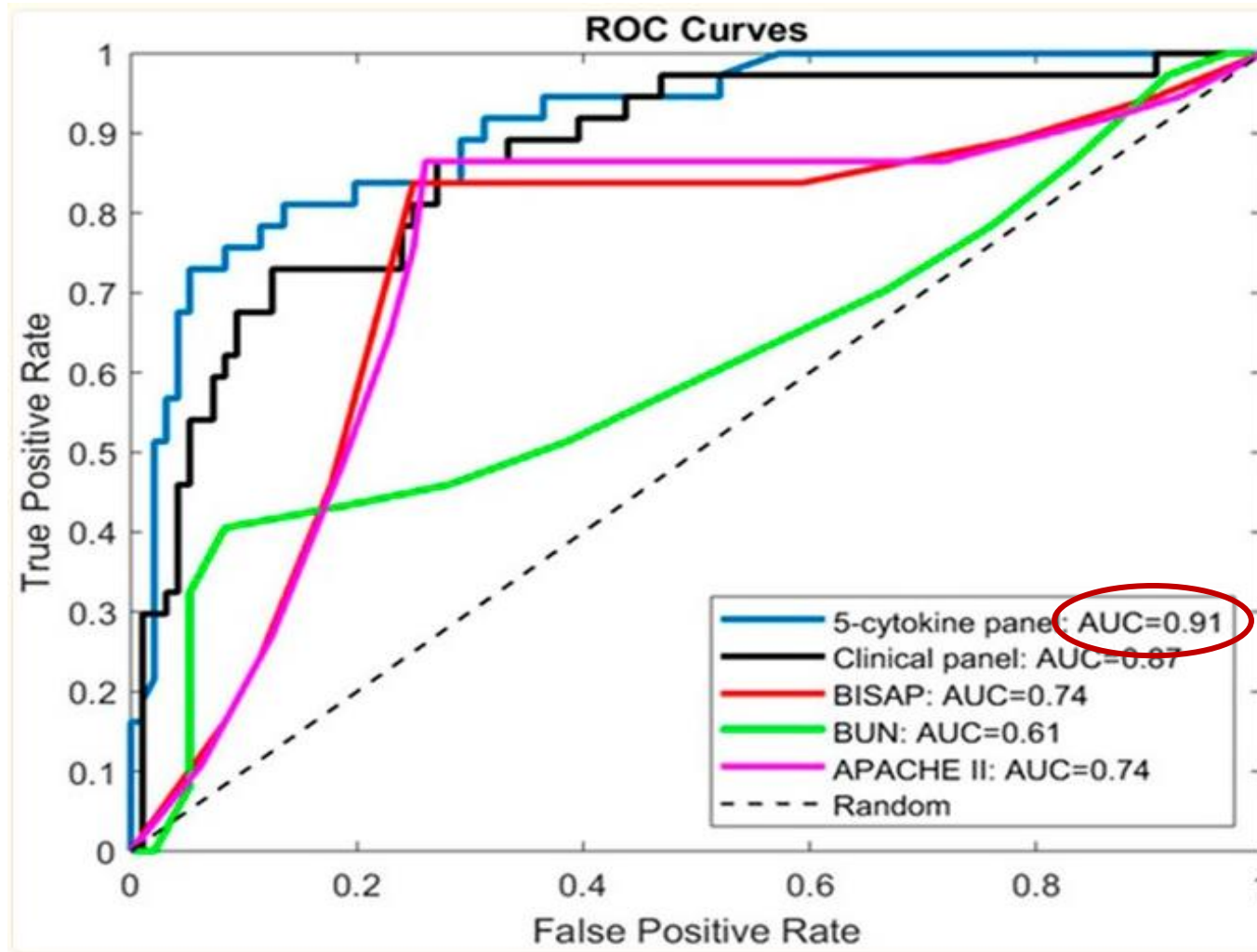
Existing scores have only modest predictive accuracy of  $\leq 0.75$



# Conceptual Model for Prediction of Severe AP



# Multi-cytokine panel's AUC



# MoSAIC Study

- NIH-funded, observational, multi-center study focusing on early events in AP
- Collaboration between Immunologists & Pancreatologists
- Aim 1: Validate the novel multi-cytokine panel for early prediction of SAP
- Aim 2: Identify circulating immune cells that correspond with early cytokine signatures & characterize the immune pathways driving SAP development

# MoSAIC Study

## CLINICAL

- ~200 AP subjects within 36 hrs
- 4 enrolling sites
  - OSU, UPMC, UIC & USC
- A well-phenotyped data registry and a robust biorepository

## IMMUNOLOGIC

- Early & Serial Blood Samples (enrollment, D2 and D7)
- Cytokine measurement (OLINK)
- Mass Cytometry for Immune Cell Shifts (CyTOF)
- Whole blood RNAseq for Transcriptional Signatures

# Back to AP Management: Supportive Care

- No AP-specific Pharmacologic Therapy available
- Early Fluid Resuscitation
- Pain Control
- Nutritional Support
- Correction of Primary Insult
  - Consider early ERCP
  - Cease Alcohol use
  - Correct Triglyceride or Calcium levels
- Prevention of Future Attacks

# Fluid Resuscitation

## WATERFAL trial

Table 3. Safety Outcomes.\*

Outcome	Aggressive Fluid Resuscitation (N=122)	Moderate Fluid Resuscitation (N=127)	Relative Risk (95% CI)	Adjusted Relative Risk (95% CI)	P Value
Fluid overload†					
Moderate-to-severe fluid overload‡	13 (10.7)	7 (5.5)	1.93 (0.80–4.68)	1.34 (0.54–3.36)	0.53
Symptoms of fluid overload§					
Signs of fluid overload¶					
Peripheral edema					
Pulmonary rales					
Increased jugular venous pressure, hepatojugular reflux, or both	3 (4.1)	3 (2.4)	1.74 (0.42–7.10)	1.33 (0.33–7.11)	0.58
Evidence of fluid overload on hemodynamic testing or imaging	13 (10.7)	7 (5.5)	1.93 (0.80–4.68)	1.34 (0.54–3.36)	0.53
Evidence of heart failure on echocardiogram	0	1 (0.8)	0.35 (0.01–8.43)§	NA	0.32
Radiographic evidence of pulmonary congestion	13 (10.7)	7 (5.5)	1.93 (0.80–4.68)	1.34 (0.54–3.36)	0.53
Invasive cardiac catheterization	1 (0.8)	2 (1.6)	0.52 (0.05–5.67)	0.50 (0.05–5.51)	0.56

Aggressive Fluid Resuscitation does not prevent Moderately Severe/Severe AP (22% vs. 17%), but results in significant Fluid Overload (21% vs. 6%, p=0.004)

### Aggressive or Moderate Fluid Resuscitation in Acute Pancreatitis

E. de-Madaria, J.L. Buxbaum, P. Maisonneuve, A. García García de Paredes, P. Zapater, L. Guilabert, A. Vaillo-Rocamora, M.Á. Rodríguez-Gandía, J. Donate-Ortega, E.E. Lozada-Hernández, A.J.R. Collazo Moreno, A. Lira-Aguilar, L.P. Llovet, R. Mehta, R. Tandel, P. Navarro, A.M. Sánchez-Pardo, C. Sánchez-Marin, M. Cobreros, I. Fernández-Cabrera, F. Casals-Seoane, D. Casas Deza, E. Lauret-Braña, E. Martí-Marqués, L.M. Camacho-Montaño, M. Ubieta, M. Casuza, and F. Bolado, for the ERICA Consortium\*

# Fluid Resuscitation

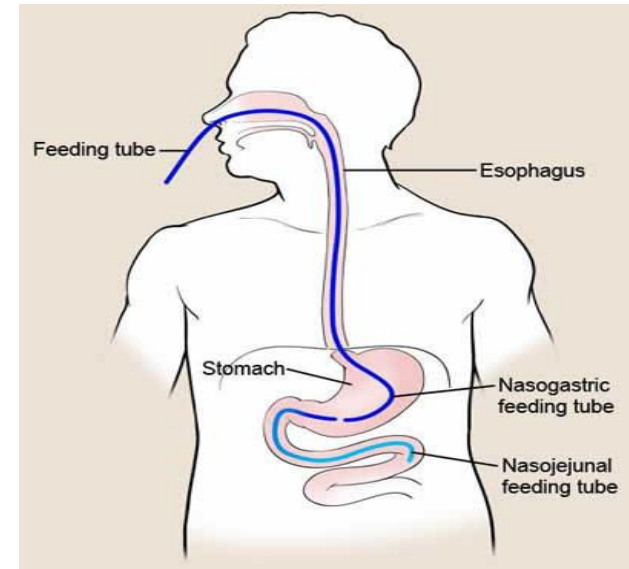
- Inadequate Hydration → Hypotension, Renal Dysfunction, Damage to Pancreatic Microcirculation
- Cornerstone of Therapy
  - 1 L bolus, followed by 150 cc/hr of IVF for 48hr
  - **Lactated Ringers** preferred: decreases Pancreatic Acidosis, Trypsin Activity, & the Inflammatory Response (**WATERLAND** trial underway)
- Adequacy assessed by improvement in vitals, urine output, correction of hemoconcentration (BUN, Cr, Hct)





# Nutritional Support (NS)

- In mild AP, attempt oral feeding within 24h
- NS required in AP pts predicted to remain fasting for >72h (Severe AP, large PNec)
- ~30% of pts in tertiary centers receive NS
- Enteral feeding (NG or NJ) preferred to TPN



**Table 3**  
Effect of enteral nutrition compared with parenteral nutrition on clinical outcomes

	Infection	Organ Failure	LOS	SIRS	Mortality
McClave et al, <sup>15</sup> 2006	++	++	+	NR	None
Al-Omran et al, <sup>13</sup> 2010	NR	NR	+	None	++
Blaser et al, <sup>3</sup> 2017	++	NR	NR	None	NR
Petrov et al, <sup>4</sup> 2008	++	None	NR	NR	++

McClave et al, JPEN 2006  
 Crockett et al, 2018  
 Machicado et al, Pancreas, 2018  
 Roberts et al, Gastro Clin N Am, 2019

# Specific AP-Modifying Therapies

- Molecular targets
- Historical perspectives
  - Clinical trial successes and failures

There is great interest in developing therapeutics for AP,  
currently no specific disease-modifying therapies

Environmental, Metabolic, or  
Mechanical Insult

Acinar & Pancreatic  
Ductal cell injury

Recruitment of  
Neutrophils/  
Cellular Mediators  
of Inflammation

Local Release of  
Pro-inflammatory  
Cytokines

Release of Trypsin,  
Activated Proteases

Auto-Digestion

Local Inflammation

**Anti-Secretory Agents**

*Octreotide*

**Protease Inhibitors**

*Gabexate*

**Ca<sup>2+</sup> Channel Inhibitors**

*Auxora*

**Anti-inflammatory**

*Indomethacin*

Successful  
Compensatory  
Mechanisms

Interstitial  
Pancreatitis

Systemic Release of  
Pro-Inflammatory Cytokines  
Acute Phase Proteins  
Proteo and Lipolytic Enzymes  
Platelet Activating Factor  
Oxygen Free Radicals

**Immuno-modulating**

*Lexipafant, Infliximab*

**Anti-Oxidant Agents**

*N-acetyl-cysteine*

Pancreatic  
Necrosis

Systemic  
Inflammatory  
Syndrome

Infected  
Pancreatic  
Necrosis

Vascular Leak Syndrome  
Hypovolemia  
Remote Organ Injury  
Bacterial Translocation

**Antibiotics**

*Imipenem*

Organ Failure,  
Sepsis, Shock

**Sites of Action of  
Pharmacological Agents during  
the Natural History  
of Severe AP**

# Historical Randomized Trials

**TABLE 2.** Randomized Trials on Medical Treatment for Severe AP

Reference	n	Level of Evidence	Design	Treatment	Dosage	Application	Need for surgery	Sepsis	MOF	Mortality
Buchler et al <sup>19</sup>	115	I	db	Gabexate	53 mg/kg per day	Cont inf	25/115 <sup>§</sup> (22%)	—	—	18/115 (16%)
	108			Placebo			23/108 <sup>§</sup> (21%)	—	—	16/108 (15%)
Chen et al <sup>22</sup>	26	II	rand	Gabexate	100 mg/hr	Cont inf	7/27 (25.9%)*	—	—	2/26 (7.7%)*
	26			Control			13/26 (50%)	—	—	8/26 (30.8%)
Johnson et al <sup>27</sup>	148	I	db	Lexipafant	100 mg/day	Cont inf	—	4/148 (3%)*	85/148 (57%)	14/148 (10%)
	138			Placebo			—	13/138 (9%)	80/138 (58%)	21/136 (15%)
McKay et al <sup>28</sup>	26	I	rand	Lexipafant	100 mg/day	Cont inf	—	—	2/11 <sup>†</sup> (18.2%)	3/26 (11.5%)
	24			Placebo			—	—	5/15 <sup>†</sup> (33.3%)	6/24 (25%)
Uhl et al <sup>31</sup>	98	I	db	Octreotide	100 µg	3 × 1 sc	13/98 (13%)	4/98 (4.1%)	—	15/98 (15%)
	101			Octreotide	200 µg	3 × 1 sc	14/101 (14%)	5/101 (5%)	—	12/101 (12%)
	103			Placebo			19/103 (18%)	4/103 (3.9%)	—	16/103 (16%)
Paran et al <sup>35</sup>	25	II	rand	Octreotide	100 µg	3 × 1 sc	—	6/25 (24%)*	2/25 (8%) <sup>‡</sup>	2/25 (8%)*
	25			Control			—	19/25 (76%)	3/25 (12%) <sup>‡</sup>	8/25 (32%)
Planas et al <sup>34</sup>	24	II	rand	Octreotide	3.5 µg/kg per hour	Cont inf	9/24 (37.5%)	21/24 (87.5%)	—	9/24 (38%)
	22			Control			14/22 (63.3%)	20/22 (90.9%)	—	7/22 (32%)
McKay et al <sup>32</sup>	28	II	db	Octreotide	40 µg/hr	Cont inf	—	—	3/28 (10.7%)	5/28 (17.9%)
	30			Placebo			—	—	4/30 (13.3%)	6/30 (20%)

\*Significant in original publication.

<sup>†</sup>New MOF after treatment start (total: 17/26 (65.4%) vs. 14/24 (58.3%); improvement of MOF: 9/15 (60%) vs. 5/9 (55.5%).

<sup>‡</sup>Only renal failure reported.

<sup>§</sup>Indication for surgery not defined.

MOF indicates multiorgan failure; db, randomized double-blind trial; rand, randomized trial; cont inf, continuous infusion; sc, subcutaneous injection.

## Gabexate Mesilate in Human Acute Pancreatitis

MARKUS BÜCHLER,\* PETER MALFERTHEINER,\* WALDEMAR UHL,\* JÜRGEN SCHÖLMEIERICH,<sup>§</sup>  
FRITZ STÖCKMANN,<sup>||</sup> GUIDO ADLER,<sup>†</sup> WILHELM GAUS,<sup>#</sup> KLAUS ROLLE,<sup>\*\*</sup> HANS G. BEGER,\*  
and the GERMAN PANCREATITIS STUDY GROUP<sup>‡‡</sup>

- 293 pts from 29 hospitals randomly assigned **Gabexate mesilate i.v.** 4 g/day for 7 days vs. placebo

**Table 1.** Inclusion Criteria

Obligatory criteria
First symptoms of acute pancreatitis $\leq 168$ hours until enrollment of patients
Threefold enzyme elevations of total amylase or lipase within 96 hours after onset of acute pancreatitis
Upper abdominal pain
Written informed consent of the patient
Facultative criteria (4 had to be fulfilled)
Upper abdominal guarding
Subileus/ileus
Arterial $pO_2 < 65$ mm Hg
Shock: pulse rate $\geq 100$ /min; systolic RR $\leq 80$ mm Hg for longer >10 minutes
Anuria
Leukocyte count $\geq 12$ G/L
Blood glucose (fasting) $\geq 8.4$ mmol/L (this criterion was excluded in case of pre-existing diabetes mellitus)
Characteristic findings of moderate to severe acute pancreatitis by ultrasound and/or CT scan
Hypocalcemia $\leq 2.0$ mmol/L
Serum creatinine $> 240$ $\mu$ mol/L

**Table 8.** Number and Type of Newly Developed Complications

	Placebo (n = 108)	GM (n = 115)
Shock	9	7
Sepsis	18	17
Pulmonary failure	15	18
Renal failure	10	11
Peritonitis	6	5
Hemorrhage	2	2
Ileus/subileus	6	3
Hypocalcemia	24	26
Clotting disorders	4	7
Jaundice <sup>a</sup>	10	19
Hyperglycemia	10	15
Encephalopathy	2	2
Metabolic acidosis	23	28
Death	16 (15%)	18 (16%)
Pancreatitis-related operations	23 (21%)	25 (22%)

- No statistical difference in either mortality or AP complications between placebo and gabexate groups

# A randomised, double blind, multicentre trial of octreotide in moderate to severe acute pancreatitis

W Uhl, M W Büchler, P Malfertheiner, H G Beger, G Adler, W Gaus, and the German Pancreatitis Study Group

- 302 patients from 32 hospitals randomly assigned to:
  - group P (n=103) received placebo
  - O1(n=98) & O2(n=101) received 100 & 200mcg **Octreotide sc** TID for 7 d.

Table 1 Inclusion criteria

Necessary criteria
First symptoms of acute pancreatitis not more than 96 hours before enrolment
Serum amylase or lipase increased at least threefold during this period
Spontaneous upper abdominal pain during this period
Written informed consent to participate in the study*
Supporting criteria (fulfilment of at least four required)
Local abdominal resistance
Subileus/ileus
Shock: pulse $\geq 100$ /min and systolic blood pressure $\leq 80$ mm Hg for more than 10 minutes
Arterial $PO_2 < 60$ mm Hg
Leucocyte count $> 12$ g/l
C-reactive protein $> 120$ mg/l
Fasting blood glucose $> 8.4$ mmol/l†
Hypocalcaemia $\leq 2.0$ mmol/l
Serum creatinine $> 240$ $\mu$ mol/l
Characteristic findings of moderate or severe acute pancreatitis on ultrasound or contrast enhanced CT

Table 11 Primary and secondary outcome variables in the valid for efficacy analysis

Outcome variables	Total (n=251)	Treatment groups		
		Placebo (n=90)	O1 (n=78)	O2 (n=83)
Death	27 (11%)	13 (14%)	7 (9%)	7 (8%)
Death $\leq 14$ days	4	1	2	1
Death $> 14/\leq 30$ days	8	3	2	3
Death $> 30$ days	15	9	3	3
Patients with newly developed complications	180 (73%)	61 (68%)	59 (76%)	60 (72%)
Duration of pain (days)*	6 (0-209)	6 (0-209)	6 (0-105)	7 (1-89)
Hospital stay (days)*	21 (5-210)	22 (7-210)	21 (5-105)	20 (7-163)

- An intent to treat analysis revealed no significant differences in
  - mortality (P:16%; O1:15%; O2:12%),
  - rate of newly developed complications, duration of pain, surgical interventions, or LOS



# Double blind, randomised, placebo controlled study of a platelet activating factor antagonist, **lexipafant** in the treatment and prevention of organ failure in predicted severe acute pancreatitis

C D Johnson, A N Kingsnorth, C W Imrie, M J McMahon, J P Neoptolemos, C McKay, S K C Toh, P Skaife, P C Leeder, P Wilson, M Larvin, L D Curtis, for the UK Acute Pancreatitis Study Group

- 290 AP ps randomly assigned placebo vs. **Lexipafant i.v.** 100 mg/24 hrs for 7 days

## Inclusion and exclusion criteria

All of the following were required for inclusion: severe abdominal pain of **<72 hours** duration at initiation of study treatment; serum amylase level >3 times the upper limit of the normal range in the 72 hours before study entry; a clinical picture consistent with acute pancreatitis; and an **APACHE II score<sup>27</sup> >6** in the 24 hours

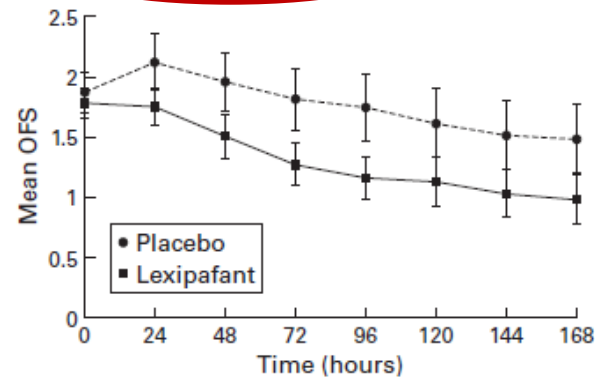


Table 3 Incidence of organ failure, local complications, and deaths in the two groups

Complications	Placebo group	Lexipafant group
Organ failure		
On admission	59 (43%)	67 (45%)
Day 3	46 (33%)	40 (27%)
Day 7	36 (26%)	29 (20%)
Overall	80/138 (58%)	85/148 (57%)
Local complications		
Pseudocyst	19 (14%)	8 (5%) <sup>a</sup>
Necrosis	29 (21%)	23 (16%)
Abscess	6 (4%)	5 (3%)
Overall	41/138 (30%)	30/148 (20%) <sup>b</sup>
Systemic sepsis	13/138 (9%)	4/148 (3%) <sup>c</sup>
Deaths		
All attributable deaths	21/136 (15%)	14/147 (10%)
Attributable deaths in patients treated ≤48 h	17/95 (18%)	8/104 (8%) <sup>d</sup>

- Organ failure scores reduced in Lexipafant group only on D3.
- Lexipafant had no effect on new OF during treatment.
- The high incidence of OF within 72 hrs of symptom onset undermined 1ry hypothesis



# Oral Pentoxifylline RCT

- Design: single-center, double-blind, randomized placebo-controlled trial conducted at Mayo (2015-2017)
- Population: 83 adults with AP within 72h of admission
  - 233 met eligibility criteria, 176 approached, 91 declined: **36% enrolled**
- Intervention: Oral pentoxifylline 400 mg, three times daily, total 9 doses
- Primary Endpoint: Composite Outcome including
  - Death, pancreatic necrosis, persistent organ failure, persistent SIRS, hospital stay >4 days, need for intensive care
- Findings: Pentoxifylline use not associated with any benefit
  - but with longer stay & higher readmission rates

# Rectal Indomethacin RCT

- Design: single-center, parallel-group, double-blind, randomized placebo-controlled trial conducted at UPMC (2015-2019)
- Population: 42 adults with AP +SIRS within 72h of admission
- Intervention: Rectal Indomethacin q8h, total 6 doses
- Primary Endpoint: SIRS score change from baseline to 48h
- Results: Safe when administered over 48 hours
  - however, not superior to placebo in reducing SIRS or clinical progression in a high-risk AP population

# Why did previous RCTs fail?

- **Sample Size**
  - Single center, small trials: Pentoxifylline, Indomethacin
- **Time between Presentation & Enrollment**
  - Gabexate 7d; Octreotide 4d
- **Inaccurate Predictive Tools**
  - 4 supporting criteria, APACHE-II >6, SIRS >1, all comers
- **Primary Endpoints**
  - Composite Outcome, Death, Organ Failure, SIRS change, CRP levels

# Novel Drugs

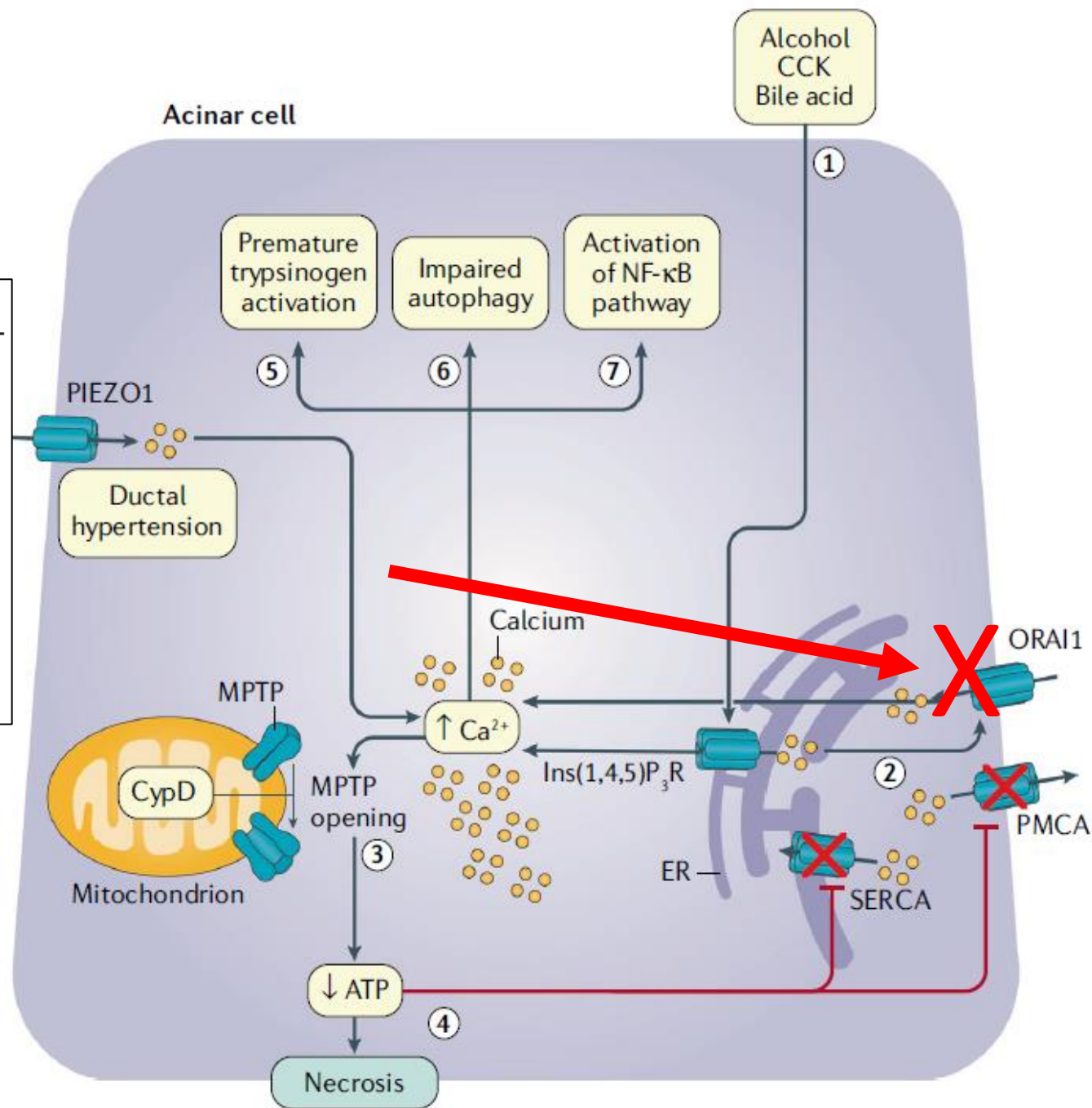
ORIGINAL ARTICLE

OPEN

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

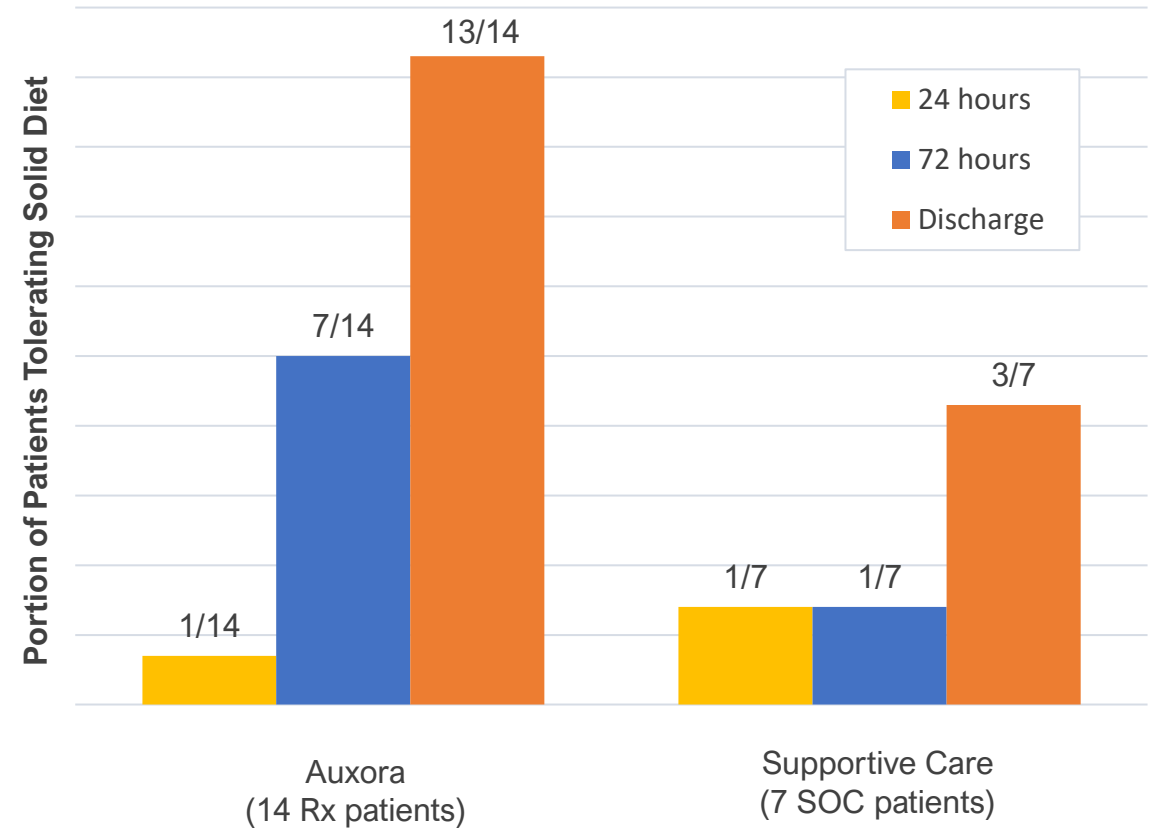
*Clinical Development of a Calcium Release-Activated Calcium Channel Inhibitor*

Charles Bruen, MD,\*† Joseph Miller, MD,‡§ John Wilburn, MD,|| Caleb Mackey, MD,¶# Thomas L. Bollen, MD,\*\* Kenneth Stauderman, PhD,†† and Sudarshan Hebbar, MD††

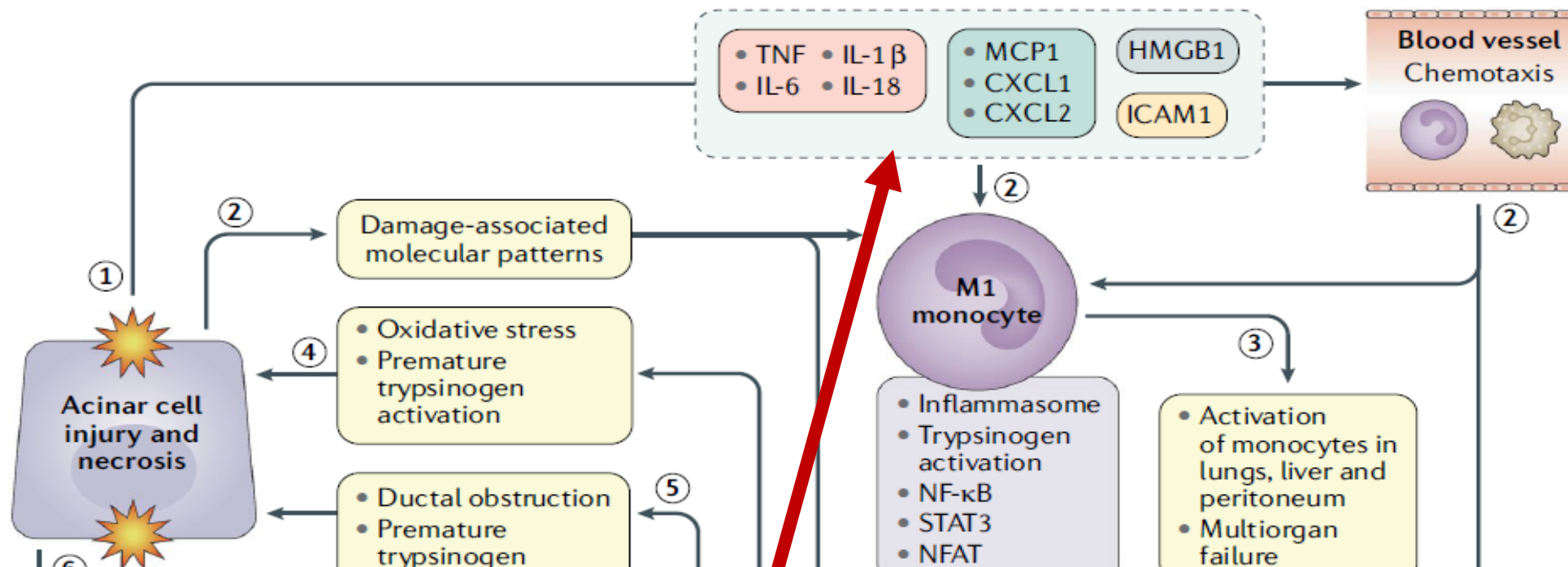


# Auxora Pilot Study

- Phase 2a, open-label, dose-response, multi-center
- 21 subjects with 2:1 randomization
- Inclusion: SIRS + Hypoxemia
- Endpoint: **Solid Food Tolerance**\*
- Auxora-treated pts tolerating solid food
  - Admission: 1/14
  - At 72 hours: 7/14
  - At Discharge: 13/14
- SOC pts tolerating solid food
  - Admission: 1/7
  - At 72 hours: 1/7
  - At Discharge: 3/7



\*eating  $\geq 50\%$  of solid meal without vomiting or increase in pain



## Randomised Treatment of Acute Pancreatitis With Infliximab: Double-blind Multi-centre Trial (RAPID-I) (RAPID-I)

ClinicalTrials.gov Identifier: NCT03684278



The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our [disclaimer](#) for details.

**Recruitment Status** ⓘ : Suspended (COVID-19 Pandemic)

**First Posted** ⓘ : September 25, 2018

**Last Update Posted** ⓘ : November 4, 2020

### Sponsor:

Professor Robert Sutton



Table 2 | Potential therapeutic targets and target pathways in acute pancreatitis

Agent	Target	Target pathway	Status
GSK-7975A	ORAI1	Store-operated calcium entry channel; calcium signalling pathway	Preclinical <sup>20,31</sup>
CM4620	Calcium release-activated calcium channel	Store-operated calcium entry channel; calcium signalling pathway	Phase II <sup>274</sup>
TRO40303	Mitochondrial permeability transition pore	Mitochondrial dysfunction	Preclinical <sup>19</sup>
Disaccharide trehalose	Unknown	Autophagy	Preclinical <sup>33</sup>
HMG-CoA inhibitors	HMG-CoA	Unfolded protein response	Commercially available; clinical trial in progress <sup>97</sup>
Lactated Ringer's solution	G <sub>i</sub> protein-coupled receptor 81	NLRP3 inflammasome pathway; binds free fatty acid	Pilot clinical trial completed <sup>133,138,195</sup>
Pentoxifylline	Synthesis of TNF	Phosphodiesterase; inflammatory response	Pilot clinical trial in progress <sup>144</sup>
Orlistat	Unsaturated free fatty acids	Hydrolysis of triglycerides to free fatty acids; lipotoxicity	Commercially available; no trials conducted
Tocilizumab	IL-6	Inhibition of IL-6 receptor; inflammatory response	Preclinical in acute pancreatitis in progress; successful clinical trials in other diseases <sup>145,147,275</sup>

HMG-CoA, 3-hydroxy-3-methylglutaryl-CoA; NLRP3, LRR- and pyrin domain-containing 3; ORAI1, calcium release-activated calcium channel protein 1.

# CARPO Study

- Phase 2b, Double-Blind, Dose-Ranging, RCT of Auxora (*CRAC Inhibitor*) in AP pts & accompanying SIRS
- **Inclusion Criteria**
  - AP Dx based on RAC
  - SIRS diagnosis based on  $\geq 2$  of 4 criteria
    - Temperature; Heart rate; Respiratory rate; WBC
  - Additionally,  $\geq 1$  of following criteria:
    - Peripancreatic fluid collection or pleural effusion on CECT within 12h
    - Abdominal guarding or rebound tenderness on exam
    - Hematocrit  $\geq 44\%$  for men or  $\geq 40\%$  for women
- All pts receive Screening CECT scan before randomization & at Day 30

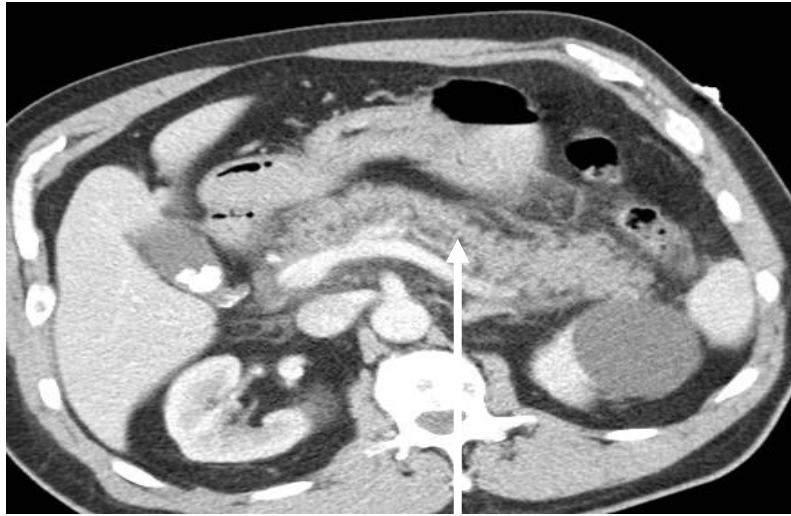
# CARPO Study

- 216 pts to be randomized at ~30 sites
- Pts randomized to Auxora receive 1:1:1 dose levels
  - 2 mg/kg, 1 mg/kg, or 0.5 mg/kg (IV infusion over 4 hrs) every 24 hrs for 3 days
- **Primary Outcome**
  - Time to solid food tolerance
- **Secondary Outcomes**
  - Solid food tolerance at 48, 72, & 96 hrs, and at discharge
  - Time to medically indicated discharge, LOS, & ICU LOS
  - Re-hospitalization for AP by Day 30
  - Change in CTSI score from screening to Day 30 CECT, Development of necrosis
  - Persistence of SIRS  $\geq 48$  hours; Development & duration of OF
  - Mortality by Day 30
  - Change in pain score and opioid use (*patient centered outcome*)

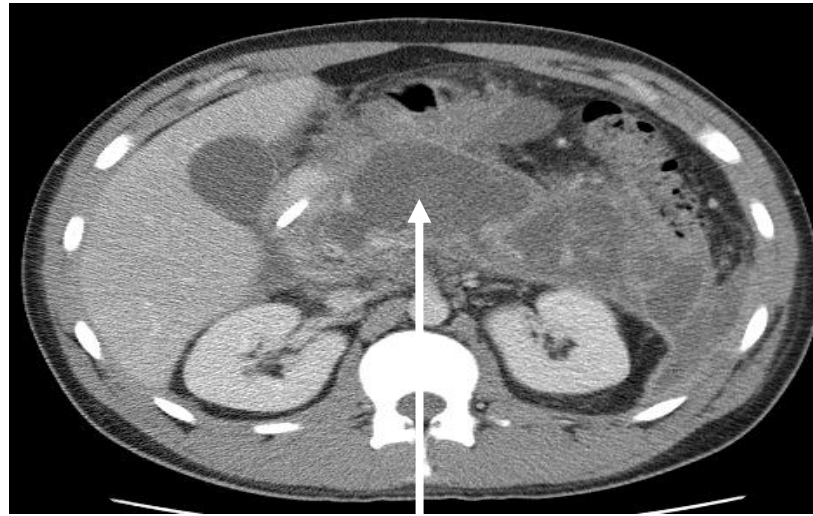
# CARPO Design

- Adequate Sample Size, Double-Blinded
- Unclear Time between presentation & study enrollment
- Predictive tools for Inclusion
  - **Composite Tool:** SIRS + one of: CECT findings, Abdominal exam, or ↑ Hct
  - High-risk population; more difficult to enroll; less generalizable results
- Primary Outcome
  - Meaningful to patients & health care providers; Indirectly associated with LOS
- Intense Protocol
  - Several assessments & blood draws (team fatigue; incomplete data/samples)
- 30 Day f/u with CECT scan
  - Concerns for subject compliance & drop out rates

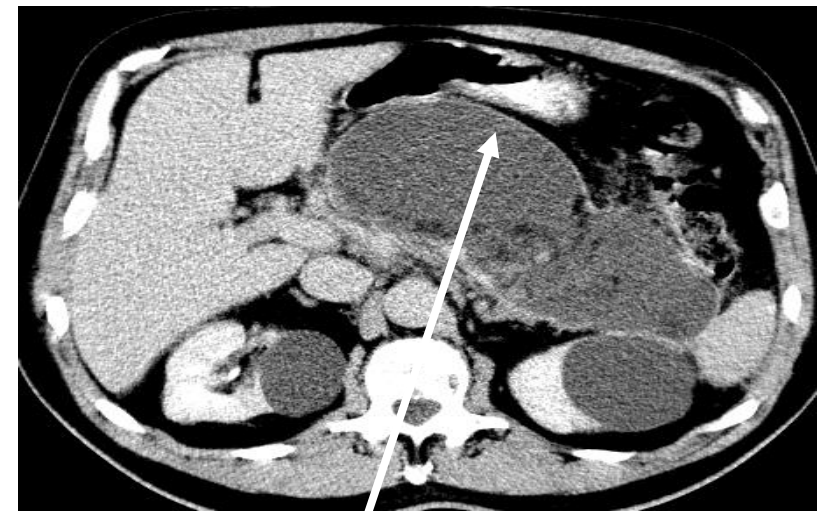
# Pancreatic Necrosis (PNec)



Normally enhancing pancreas



Non-enhancing necrosed pancreas



Capsule

- Approx 10-20% of AP patients at tertiary medical centers develop PNec
  - Infectious complications occur in ~20-30%
  - 2-5 weeks from occurrence of PNec
  - New fevers, worsening abdominal pain, nausea, vomiting, growth of collection
  - Septic complications from infected PNec account for most of late AP deaths

# 2020 AGA Clinical Practice Update

An endoscopic step-up paradigm as the evolving first-line approach to treating patients with Infected Pancreatic Necrosis

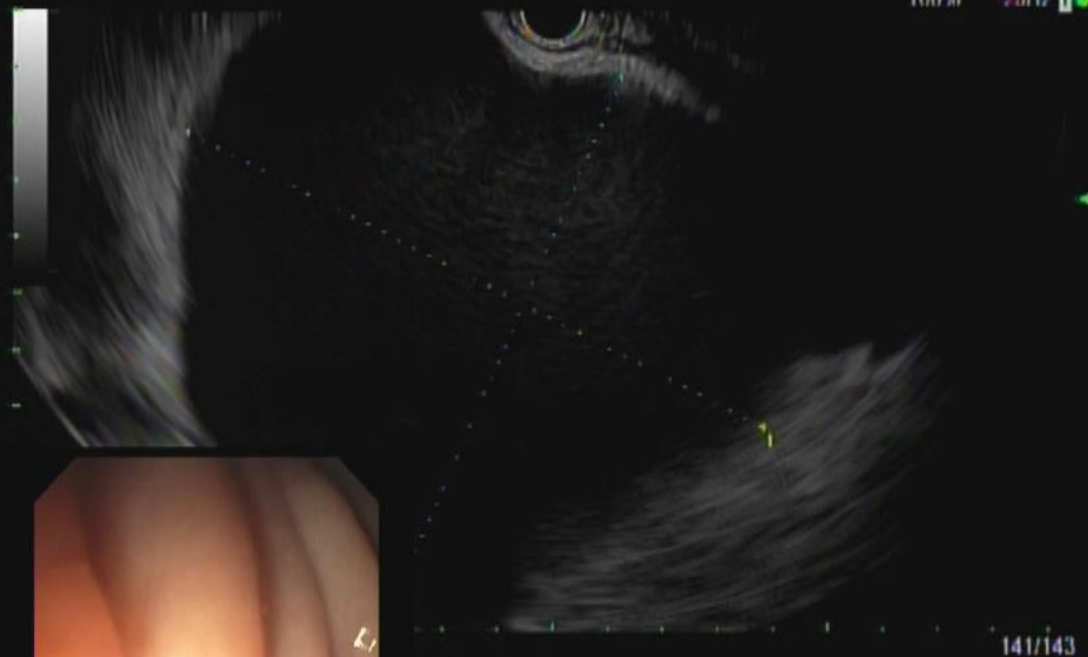
## **Back to our patient**

- Transferred to the ICU
- Developed Respiratory and Renal Failure
- Follow up CT scan showed extensive pancreatic necrosis
- Six weeks later...



# Scope

ALDIKA OSU HOSPITAL No ID 03.11.21 10:40:16



AIP

(x1)

Live Fluoro

03/11/2021 10:11

Default Acq Mode: FL 11H MAG Mode: Normal

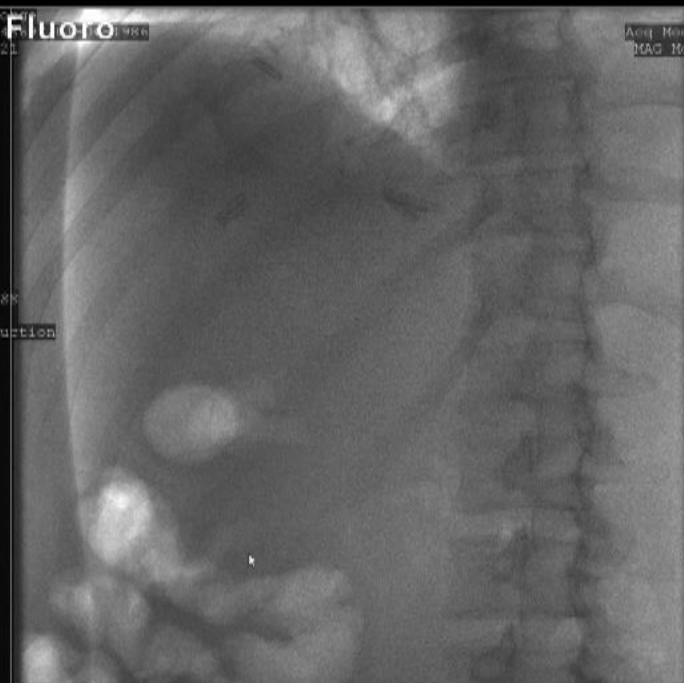
ROI HYDARK Auto ROI HIGH Reduction

LAO 1°

CAU/CRA 1°

72 kV

OSU



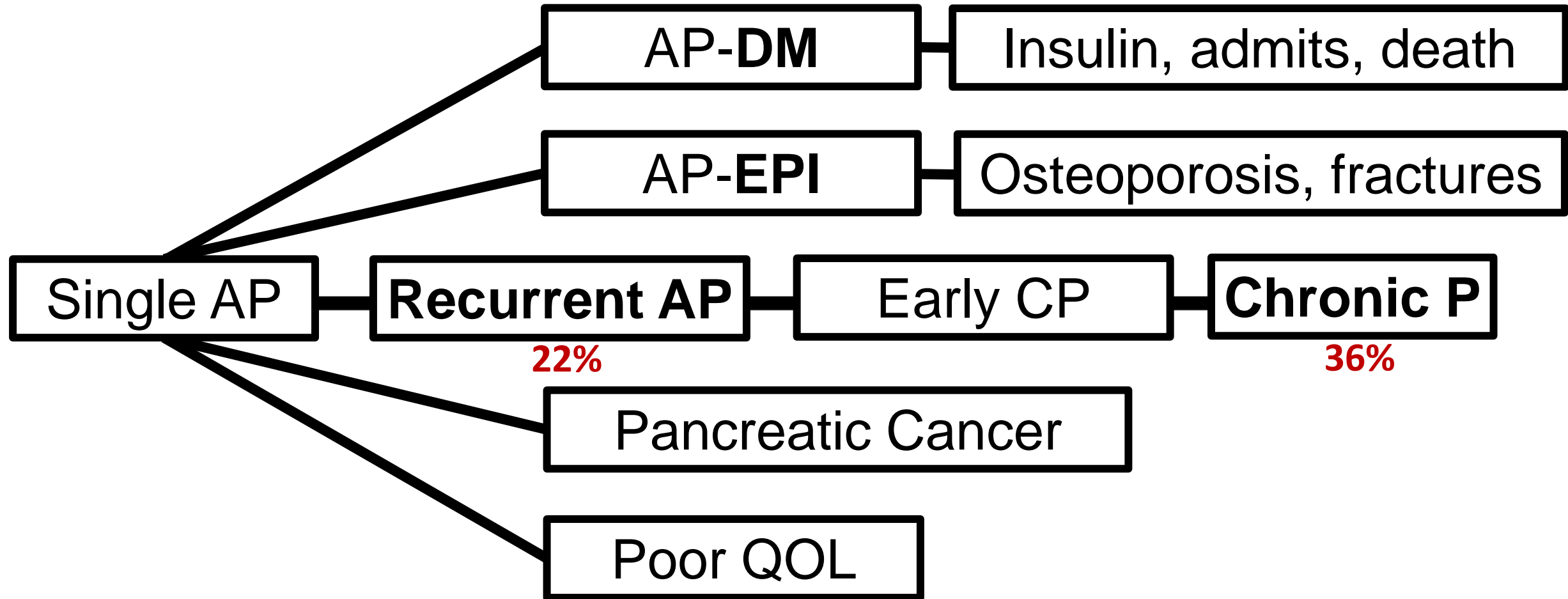
Dose 1 mAs

Acq AM 1 mAs

Fl Time 0.0 min.

R

# Progression & Long-term Sequelae of AP



# PAPPEI Study

## ORIGINAL ARTICLE

### Post–Acute Pancreatitis Pancreatic Exocrine Insufficiency *Rationale and Methodology of a Prospective, Observational, Multicenter Cohort Study*

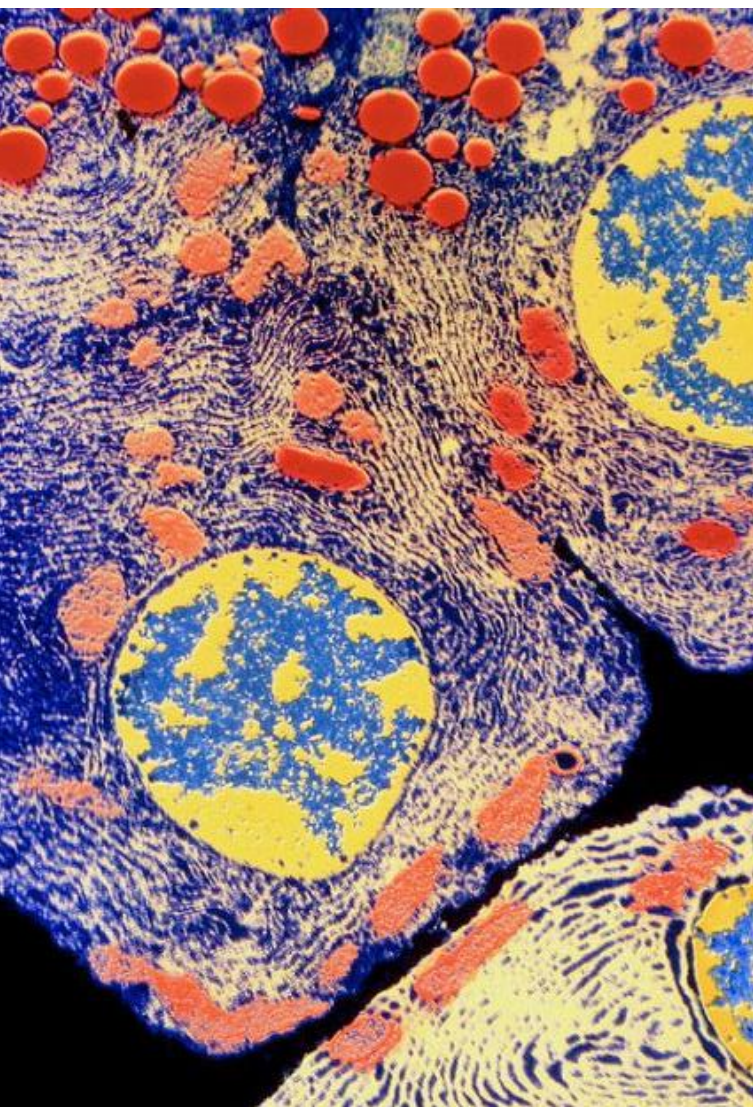
*Pedram Paragomi, MD,\* Anna Evans Phillips, MD, MS,\* Jorge D. Machicado, MD,† Ali Lahooti, BA,‡  
Ayesha Kamal, MD,§ Elham Afghani, MD,§ Ioannis Pothoulakis, MD,||¶ Shari L. Reynolds, MS,\*  
Melanie Mays, MS,\* Darwin L. Conwell, MD, MS,‡ Luis F. Lara, MD,‡  
Vikesh K. Singh, MD, MSc,§ and Georgios I. Papachristou, MD, PhD‡*

- A prospective, observational, & longitudinal AP cohort at OSU, UPMC & JHU
- To estimate the 3- & 12-mo incidence rate of AP-EPI & AP-DM
  - To define risk factors; evaluate impact of EPI on Nutritional Status & QoL
  - ~90 pts completed 12-mo f/u
  - Incidence of AP-DM **10%** & AP-EPI **34%** at 12 months

# DREAM Study

- NIH-U01 funded consortium of 10 sites in the US in 2020
  - Study the Prevalence & Mechanisms of AP-DM



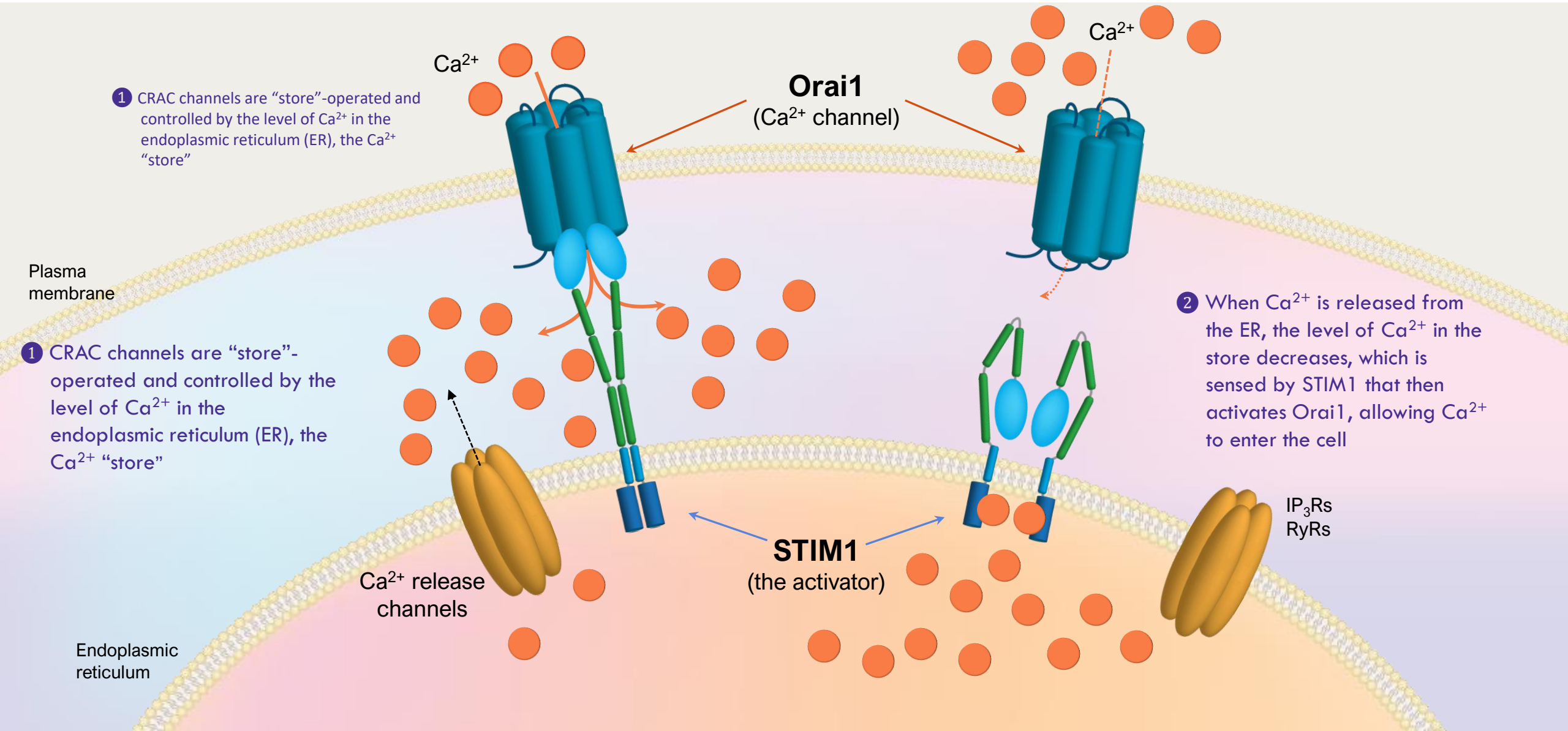


## CRAC Channels, Auxora™ and Clinical Program Overview

Sudarshan Hebbar, M.D.  
CMO, CalciMedica



# CRAC Channels Play Essential Role in Store Operated Calcium Release

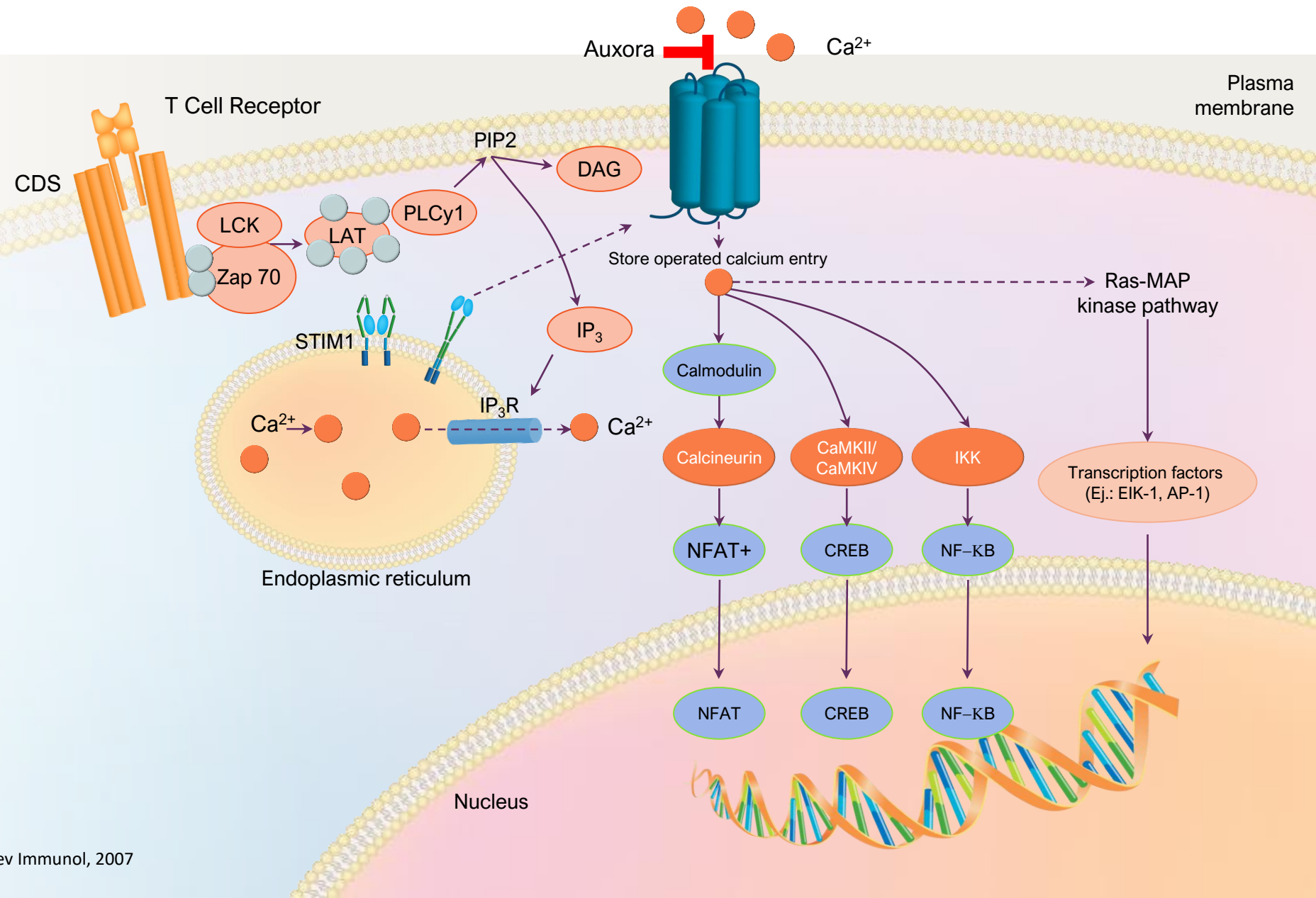




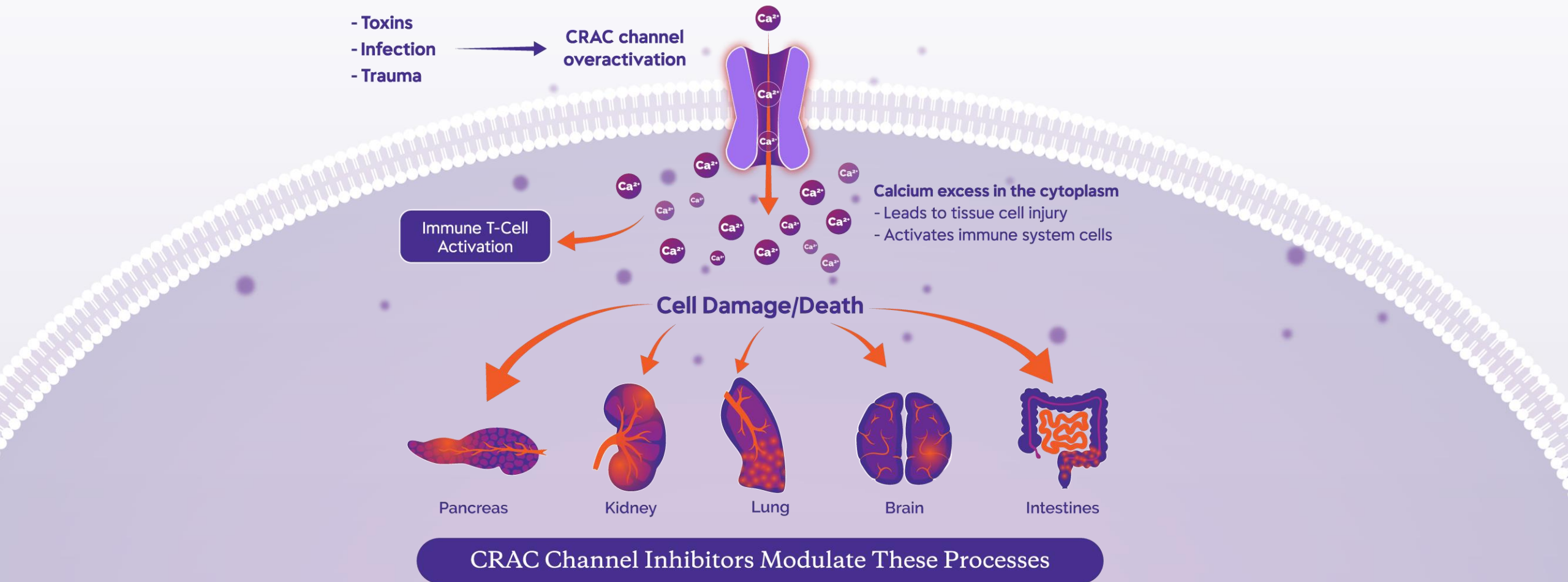
# CRAC Channels Play an Essential Role in Activating T cells

- Antigen binding to the T cell receptor causes  $\text{Ca}^{2+}$  release from the ER through IP<sub>3</sub>R, activating STIM1 and opening CRAC channels
- $\text{Ca}^{2+}$  entering the cell through open CRAC channels activates the calcineurin/NFAT pathway, and other pathways, resulting in cytokine expression and release
- CRAC channel inhibitors modulate the downstream calcium-dependent pathways, most notably the calcineurin/NFAT pathway

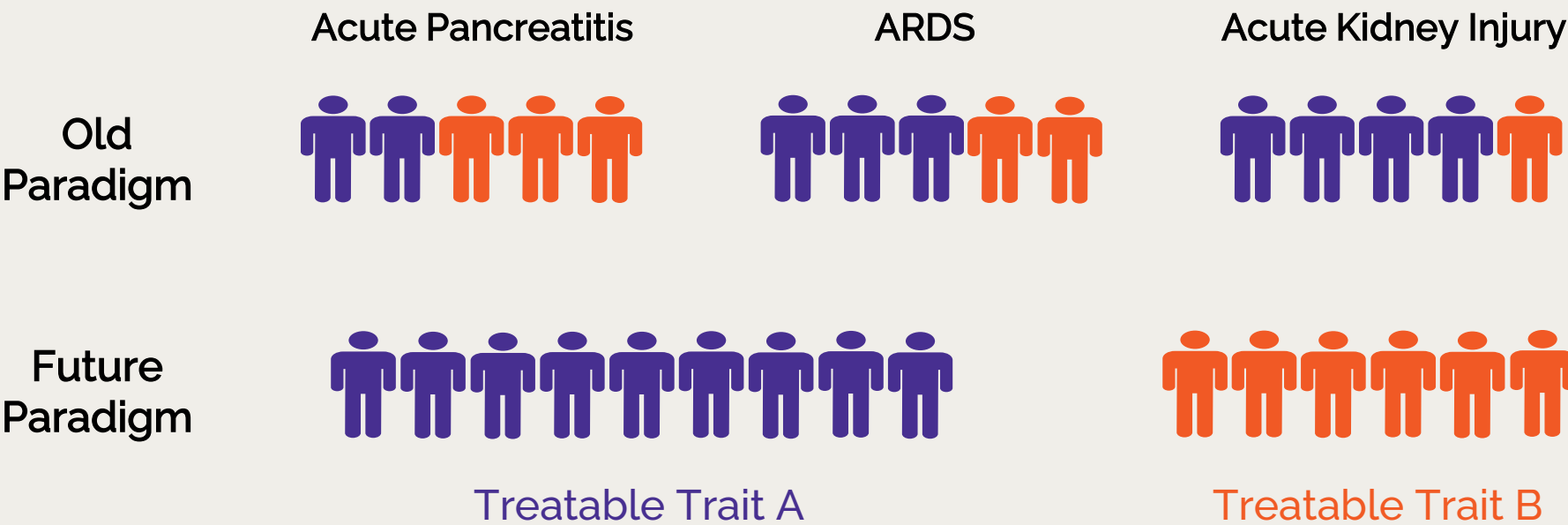
NFAT: Nuclear Factor of Activated T cells



# Overactivation of CRAC Channels: Immune System Activation and Tissue Cell Injury



# Acute Inflammation: Underlying Cause Across Many Diseases

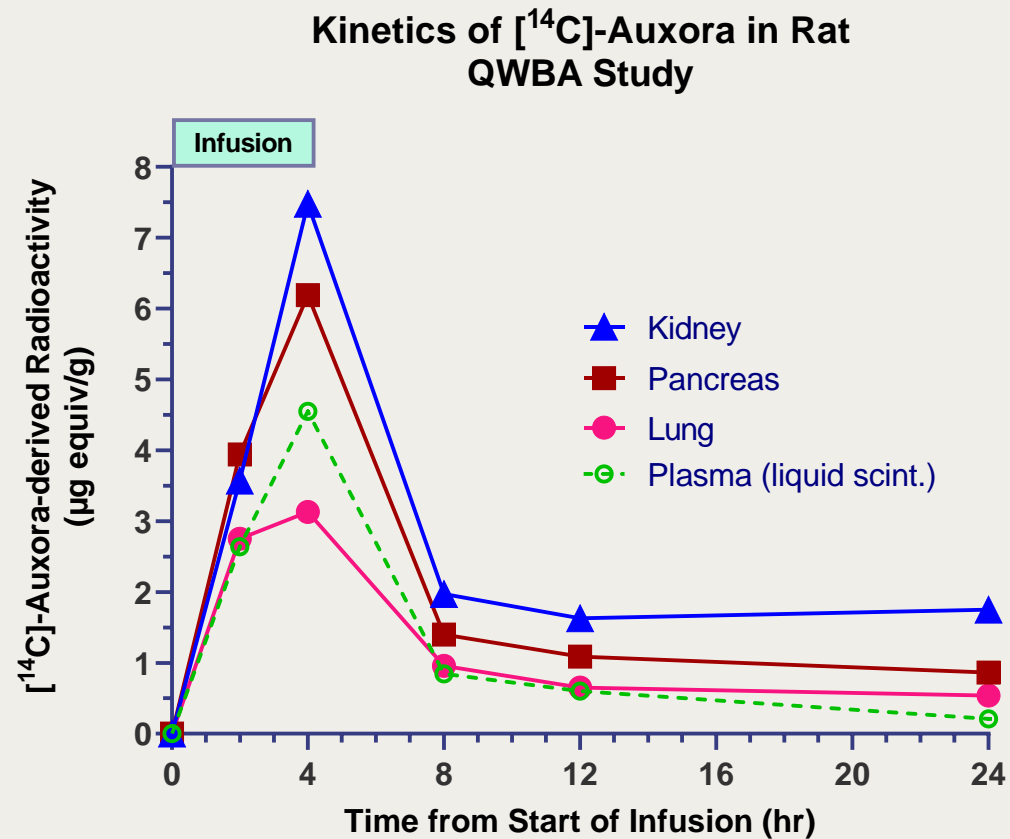


Auxora has demonstrated positive clinical results in all 3 of these large, underserved patient populations

1) Sources: Reddy, Kiran, Carolyn S. Calfee, and Danny F. McAuley. "Acute respiratory distress syndrome subphenotypes beyond the syndrome: a step toward treatable traits?." American Journal of Respiratory and Critical Care Medicine 203.12 (2021): 1449-1451.

# Auxora: IV Lipid Nanoemulsion of Zegocractin

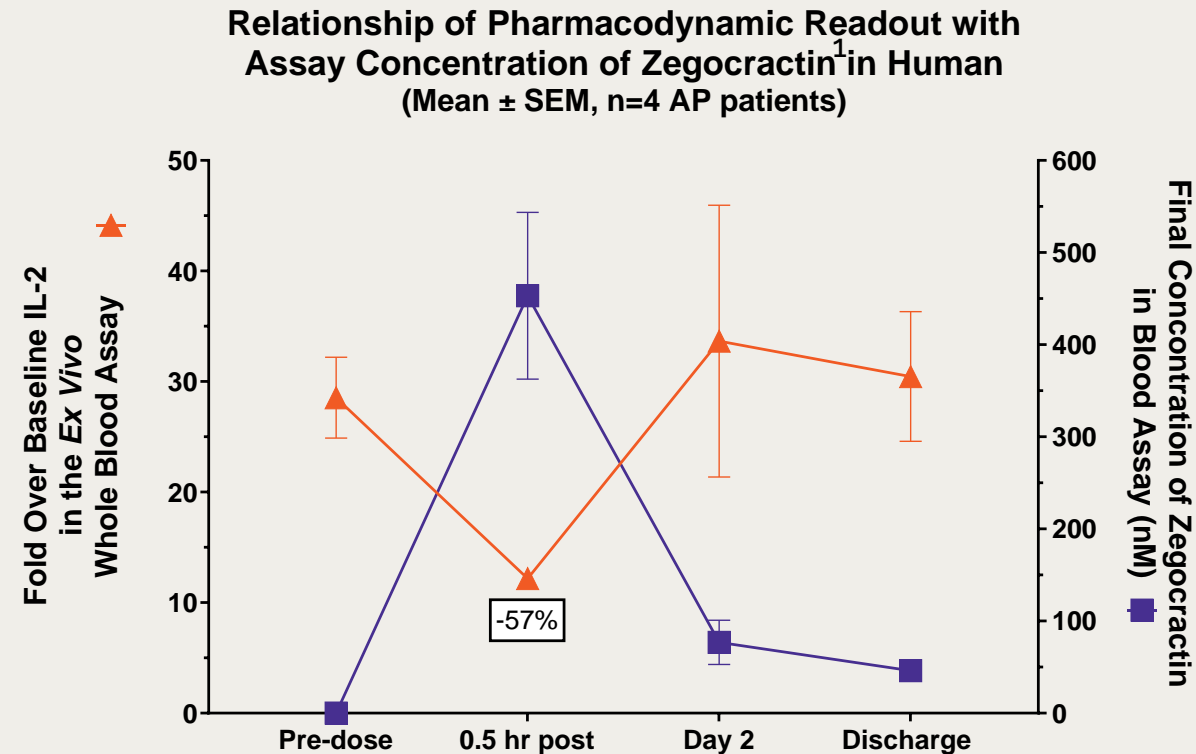
## Rapid Targeting of Inflamed Tissues



- Clearance predominantly via the liver
- No metabolites identified in human plasma
- No inhibitory effect on P450 system
- QWBA = Quantitative whole-body autoradiography

## IV Formulation Provides Ideal Benefits for Acute Inflammation

Rapid onset of immunomodulatory action reaches peak by the end of 4-hour infusion



Recovery within 24-48 hours of dosing may limit the potential for immunosuppression

1) Zegocractin is the active pharmaceutical ingredient in Auxora

# Auxora: Demonstrated Biological Activity and Favorable Safety Profile in Multiple Phase 2 Trials

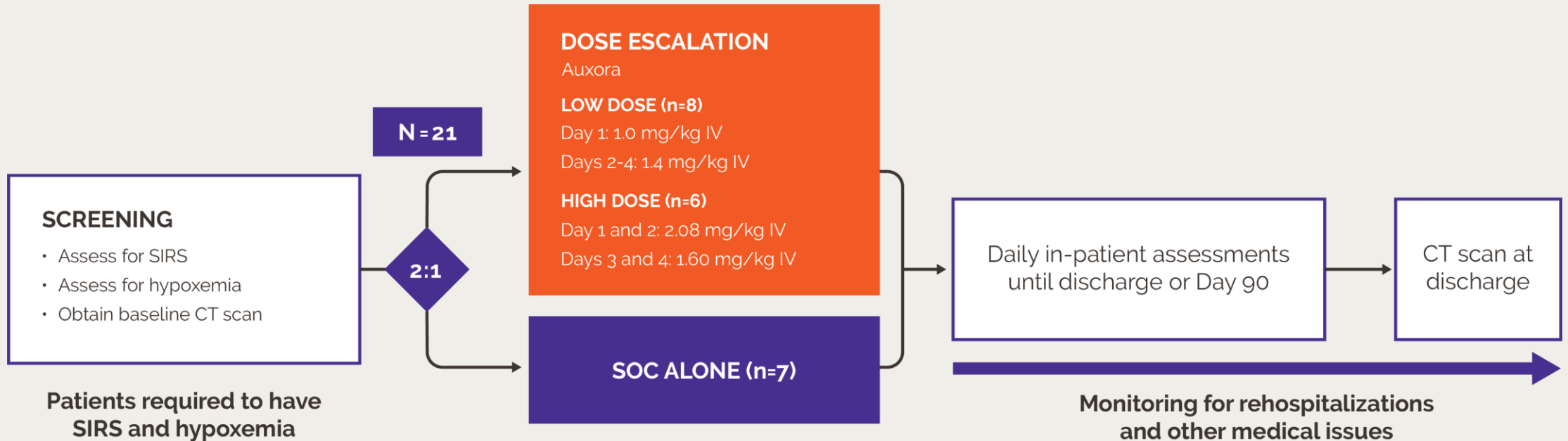
Population	Results
<b>Pancreas</b>	
Asparaginase- Induced Pancreatic Toxicity	<ul style="list-style-type: none"> <li>• Trial ongoing, preliminary results show rapid resolution of pain and food tolerance</li> </ul>
Acute Pancreatitis	<ul style="list-style-type: none"> <li>• Trial ongoing</li> </ul>
Acute Pancreatitis <sup>1</sup>	<ul style="list-style-type: none"> <li>• Target engagement of CRAC channels in peripheral lymphocytes</li> </ul>
Acute Pancreatitis <sup>1</sup> Accompanied by SIRS and Hypoxemia	<ul style="list-style-type: none"> <li>• Rapid increase in patients tolerating solid diet (potential trial pivotal endpoint)</li> <li>• &gt;2-day reduction in hospital stay and 50% reduction SIRS</li> </ul>
<b>Lung</b>	
COVID-19 with Respiratory Failure on LFO <sub>2</sub> <sup>2</sup> and HFNC <sup>3</sup>	<ul style="list-style-type: none"> <li>• 56% statistically significant decrease in mortality at Day 30</li> <li>• 33% reduction in ventilation</li> <li>• &gt;2-day shorter hospital stay</li> <li>• ~40% reduction in reported acute kidney injury</li> </ul>
COVID-19 with Respiratory Failure on IMV <sup>4</sup>	<ul style="list-style-type: none"> <li>• Open-label trial with varying doses showing pharmacodynamic response</li> </ul>

1) Completed Phase 1 trials in healthy volunteers showed no evidence of dose-dependent safety or tolerability findings through 365 days

2) LFO<sub>2</sub>: Low Flow Oxygen; 3) HFNC: High-Flow Nasal Cannula; 4) IMV: Invasive Mechanical Ventilation

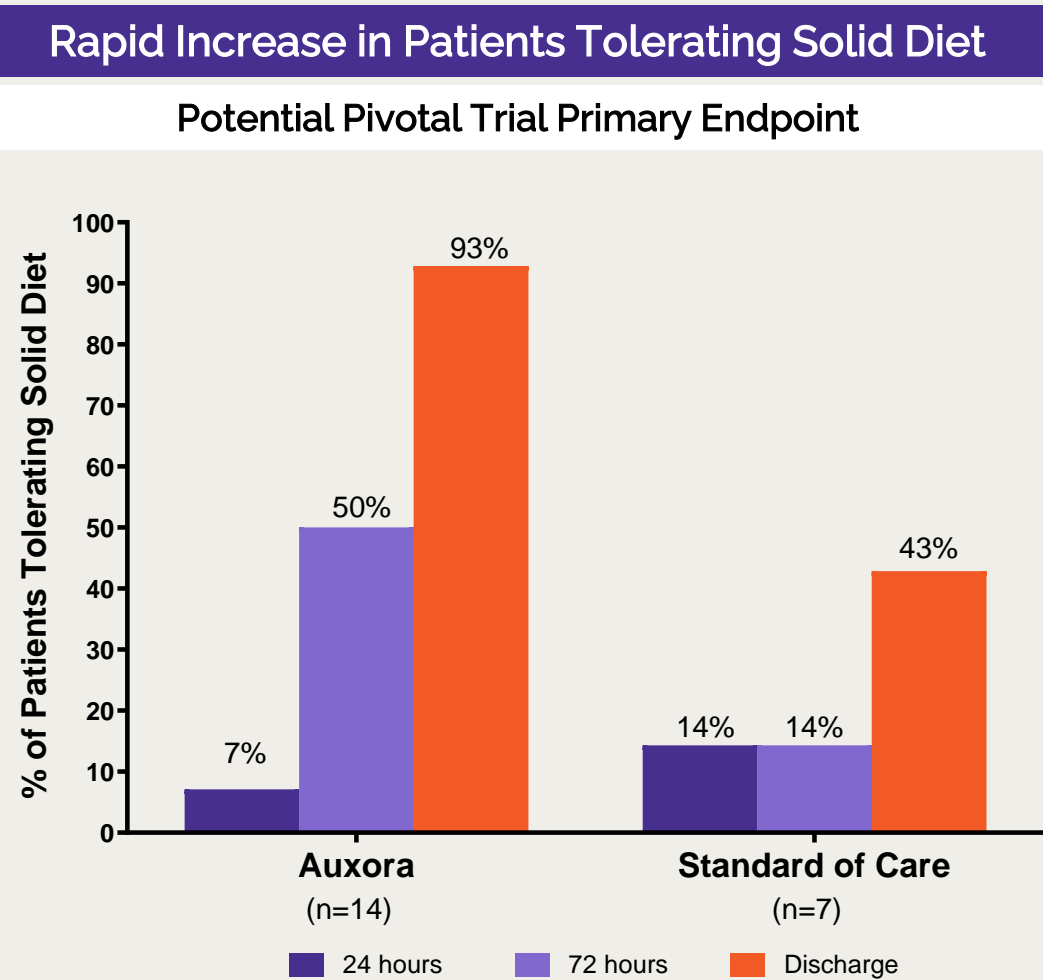
# AP Phase 2a Clinical Trial

Safety, tolerability, and efficacy trial for various doses of Auxora compared to standard of care





# Positive Phase 2a Results on Potential Pivotal Trial Primary Endpoints



>2 Fewer Days Spent in Hospital	
Median Hospital Stay	
SOC patients (n=7)	6.0 days
Auxora-treated patients (n=14)	3.7 days
Only Auxora Patients Improved on CTSI <sup>1</sup> Scores	
Moderate to Severe CTSI <sup>1</sup> Scores	
SOC patients (n=4)	0/4
Auxora-treated patients (n=8)	3/8
50% Reduction in Persistent SIRS	
Patients with Persistent SIRS	
SOC patients (n=7)	5/7
Auxora-treated patients (n=14)	5/14

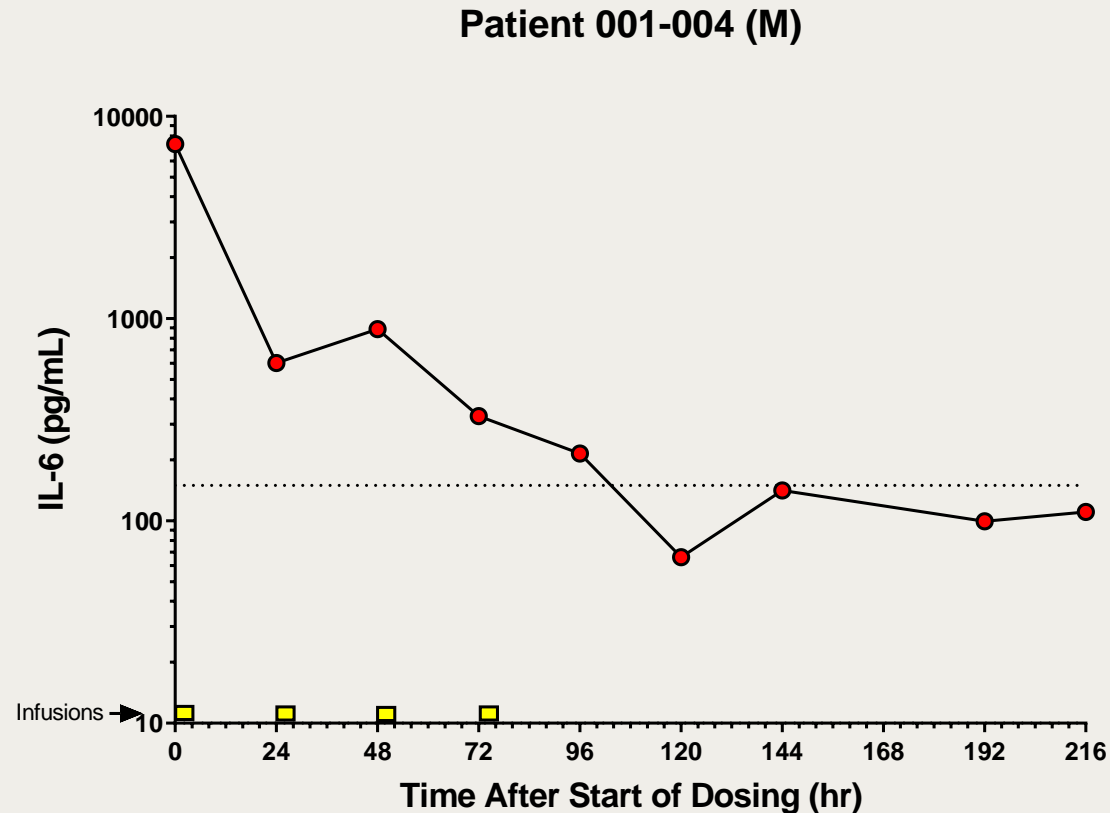
1) CTSI: CT Severity Index

## IL-6 Reduction with Auxora

	Admission IL-6 levels			Discharge IL-6 levels	
	IL-6 $\geq$ 1000 pg/mL	150 pg/mL $\leq$ IL-6 <1000 pg/mL		IL-6 $\geq$ 1000 pg/mL	150 pg/mL $\leq$ IL-6 <1000 pg/mL
201 Standard of Care Alone	0	3		0	2
201 Low Dose Auxora	0	4		0	0
201 High Dose Auxora	2	1		0	1
202 Single Dose Auxora	0	1		0	0

2/3 of patients treated with standard of care continued to have elevated IL-6 levels  
 Only 1/8 patients treated with Auxora continued to have elevated IL-6 levels

## Individual Case of a Critically Ill Patient with AP



- Critically ill patient presented with respiratory failure and acute pancreatitis in the ED.
- Randomized to receive high dose of Auxora
- IL-6 >7296 pg/mL at study entry, 66 at 120 hrs
- Managed with high flow oxygen and intermittent bi-pap; no invasive mechanical ventilation
- Discharged home on room air day 8 eating a solid food diet

## Potential Clinical Benefits of Auxora for Patients with Predicted Severe AP

Current standard of care is limited to supportive therapy

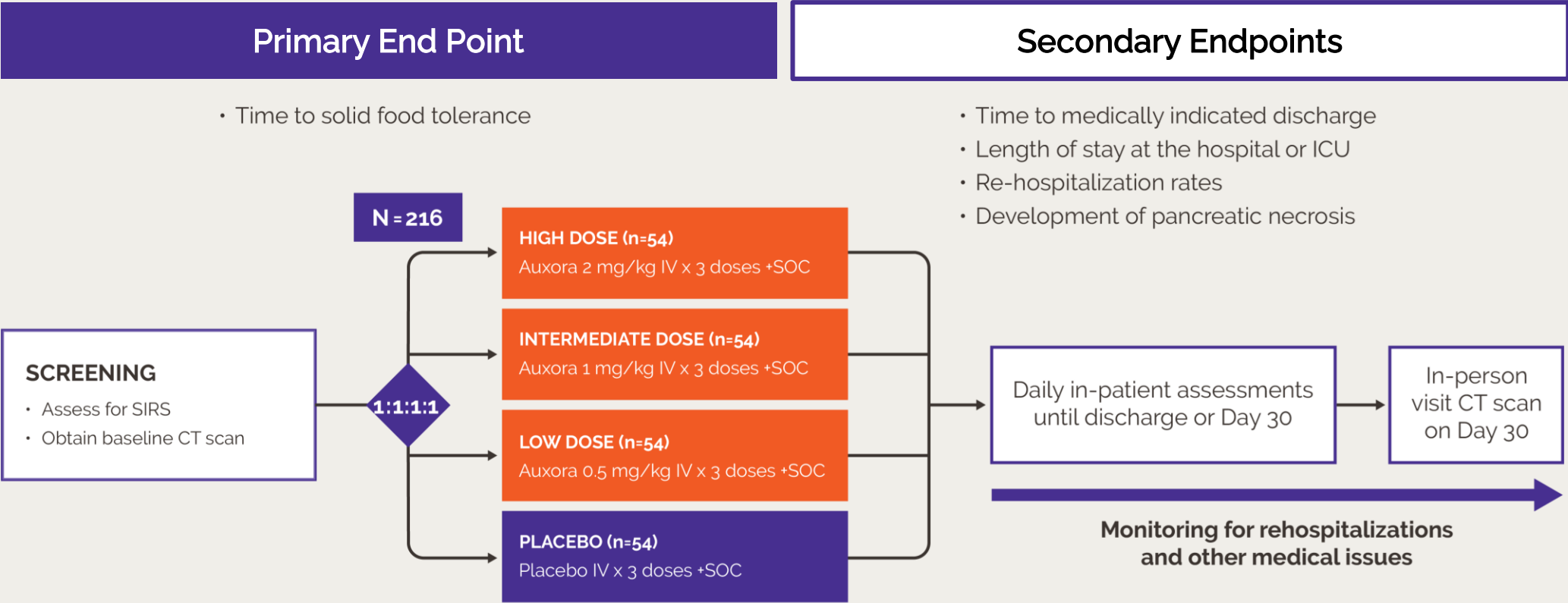
- Fluid resuscitation
- Enteral nutrition for food tolerance
- Antibiotics for infection
- Minimally invasive therapy for local complications

Auxora benefits are expected to drive adoption

- Reduction in organ failure
- Reduction in pancreatic necrosis
- Earlier food tolerance
- Fewer days in hospital or ICU

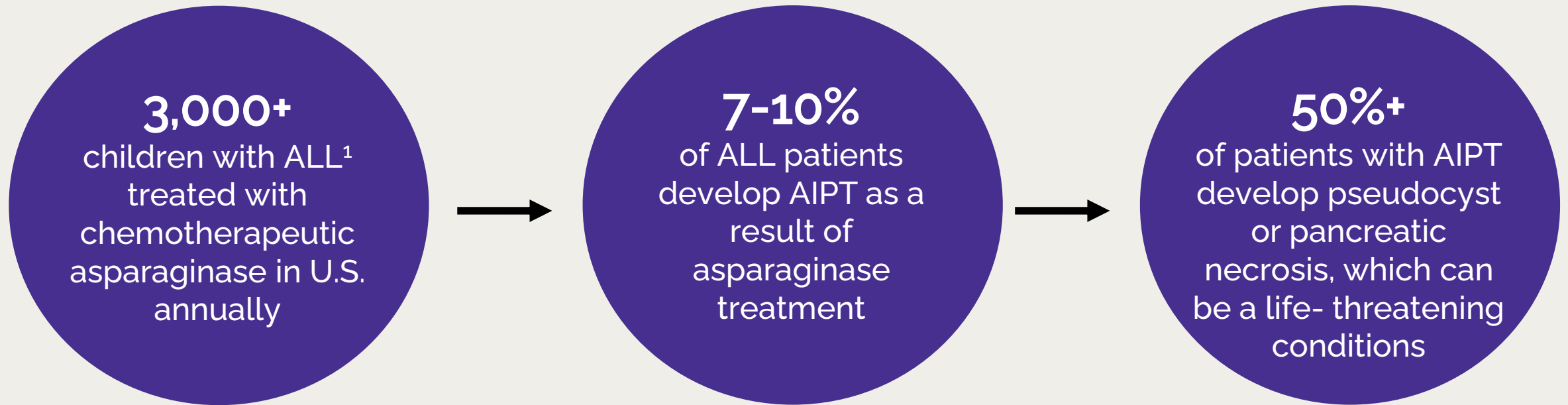
# CARPO Phase 2b Clinical Trial in AP

## Ongoing with Data Expected 1H 2024



Responder analysis planned to validate food tolerance endpoint with FDA

## Potential Clinical Benefits in Asparaginase-Induced Pancreatic Toxicity (AIPT)



**Auxora has potential to rapidly resolve AIPT with improvement in food tolerance and pain while preventing development of further complications such as pancreatic necrosis**

1) **ALL:** Acute Lymphoblastic Leukemia

2) Sources: Liu C, Yang W, Devidas M, et al. Clinical and Genetic Risk Factors for Acute Pancreatitis in Patients With Acute Lymphoblastic Leukemia. J Clin Oncol. 2016. Abaji R, Gagne V, Xu CJ, et al. Whole-exome sequencing identified genetic risk factors for asparaginase-related complications in childhood ALL patients. Oncotarget. 2017;8: 43752-43767. Rank C, Wolthers B, Grell K, et al. Asparaginase-associated pancreatitis in acute lymphoblastic leukemia: results from the NOPHO ALL 2008 treatment of patients 1-45 years of age. J Clin Oncol. 2019 38:145-154.

# Proof-of-Concept Ongoing in AIPT

## Pediatric Patients Had Rapid Resolution of Pain and Food Intolerance

### CRSPA Phase 1/2 Trial in Pediatric AIPT

- Investigator-initiated open-label trial being conducted at St. Jude Children's Research Hospital
- Assess the safety in pediatric patients with ALL who have developed AIPT
- Estimate the efficacy of Auxora to prevent pseudocyst or necrotizing pancreatitis in pediatric patients with AIPT

### Trial Status

- Cohort 1 complete, expanding to additional sites
- Blinded matched historical control comparison underway

### Trial Status

- 8 patients received four daily infusions of Auxora and had rapid resolution of pain and food intolerance
- 1 patient received less than a single infusion of Auxora and developed pancreatic necrosis

Data release planned for 4Q23