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ISSPP
Congress 2022

*International Society
for the Study of Pleura
and Peritoneum*



Regional Treatment Strategies for Peritoneal Metastasis in Gastric Cancer

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Advancing Innovative Therapies for Cancers That Invade the Peritoneum and the Pleura

Disclosures

- I do not have any relevant financial relationships.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

STATE LAW:

The California legislature has passed Assembly Bill (AB) 1195, which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed AB 241, which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

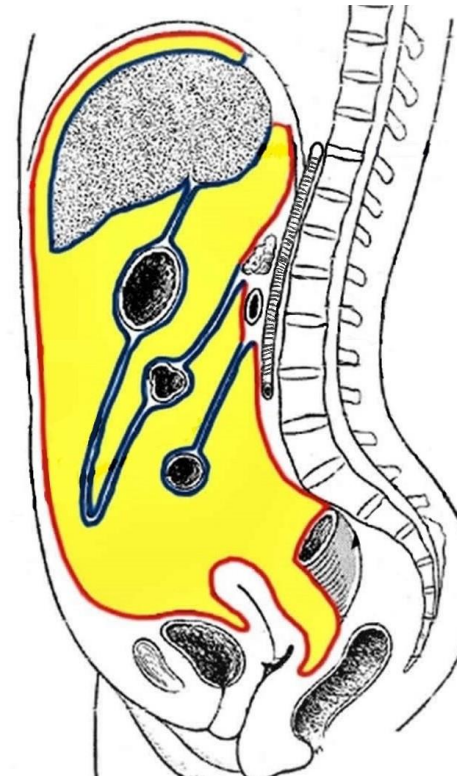
The following CLC & IB components will be addressed in this presentation:

- Races & selection.

Gastric Cancer Peritoneal metastasis (GCPM)


- Peritoneum is the most common site of metastasis from many cancers including gastric cancer
- Distressing Symptoms:
 - Ascites
 - Intestinal obstruction
 - Hydronephrosis
- Resistant to current treatment with median survival ~7 months

Parietal & Visceral peritoneum

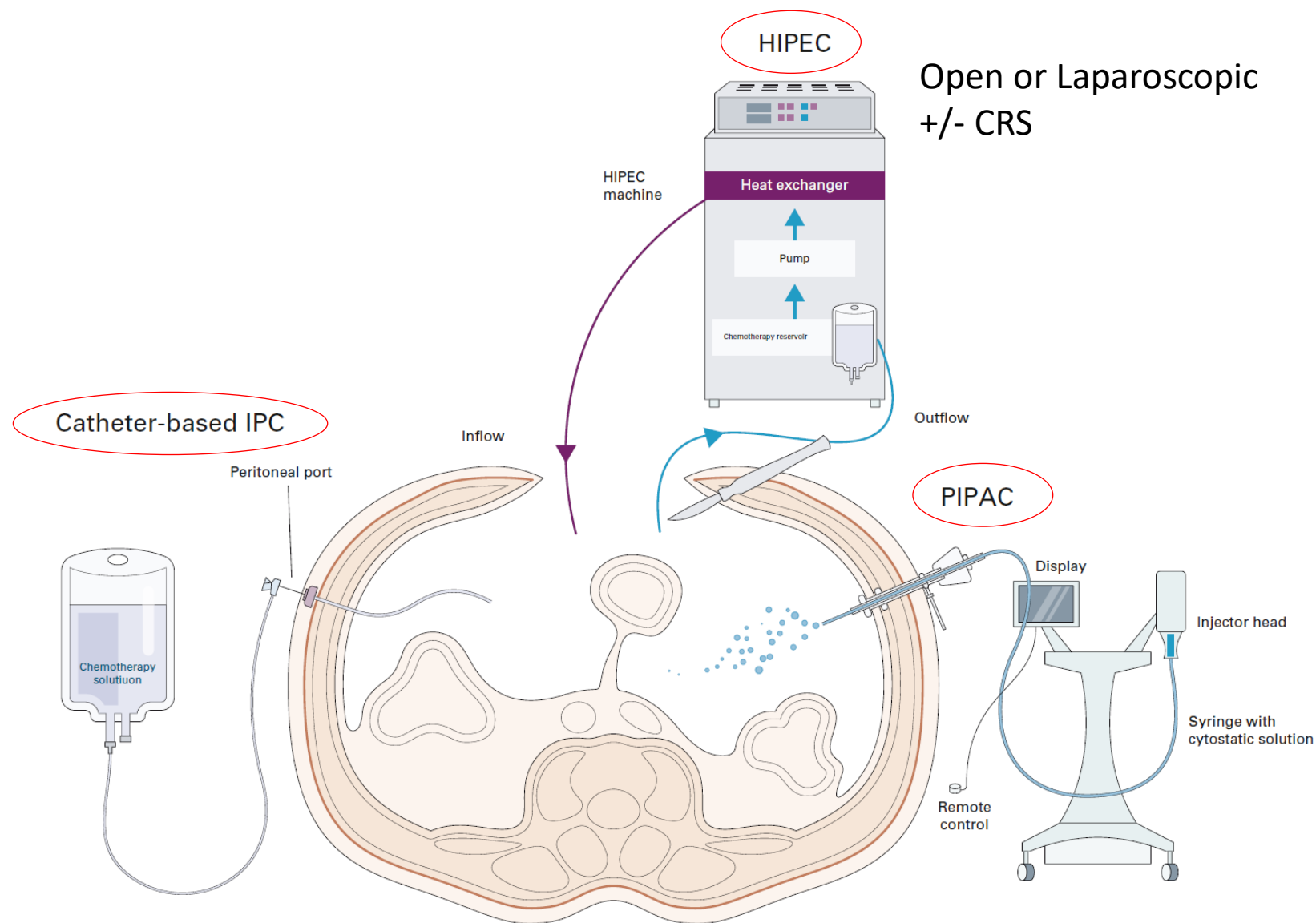


Malignant ascites

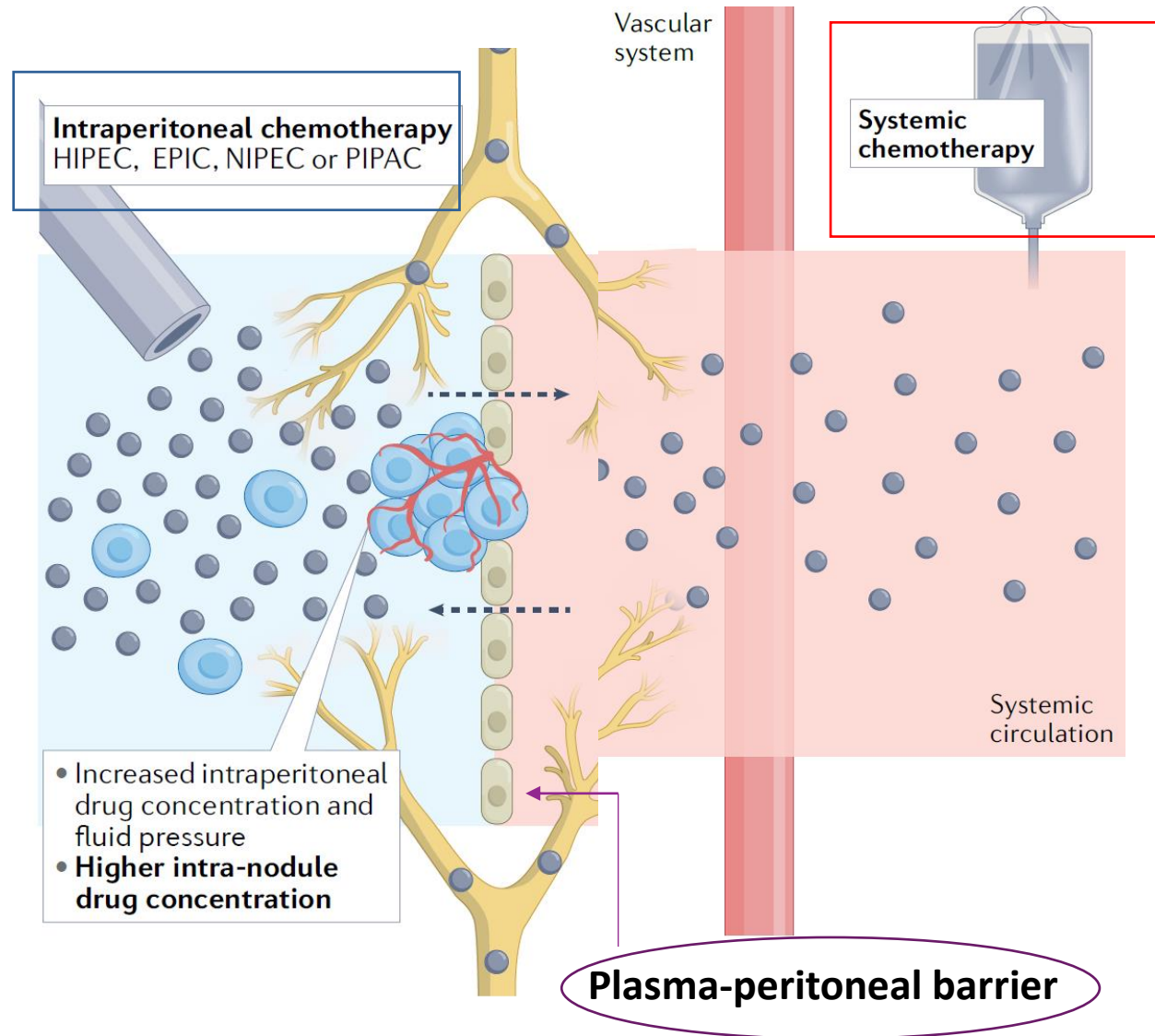
Current treatment options for GCPM

1. Systemic chemotherapy
 2. Hyperthermic intraperitoneal chemotherapy (HIPEC) with cytoreductive surgery (CRS)
 3. Laparoscopic HIPEC
 4. Catheter-based intraperitoneal chemotherapy (IPC)
 5. Pressurized intraperitoneal aerosol chemotherapy (PIPAC)
- 
- Regional chemotherapy**

Regional (Intraperitoneal) chemotherapy strategies for GCPM



Rational for IP chemotherapy: *Plasma-peritoneal barrier*



Pharmacokinetic advantages of IP chemotherapy:

- Higher drug exposure
- Lesser systemic side effects

Modified from Kepenekian et al.,
Nat Rev Clin Oncol 2022

Hyperthermic intraperitoneal chemotherapy (HIPEC) and Cytoreduction surgery (CRS)

Pro:

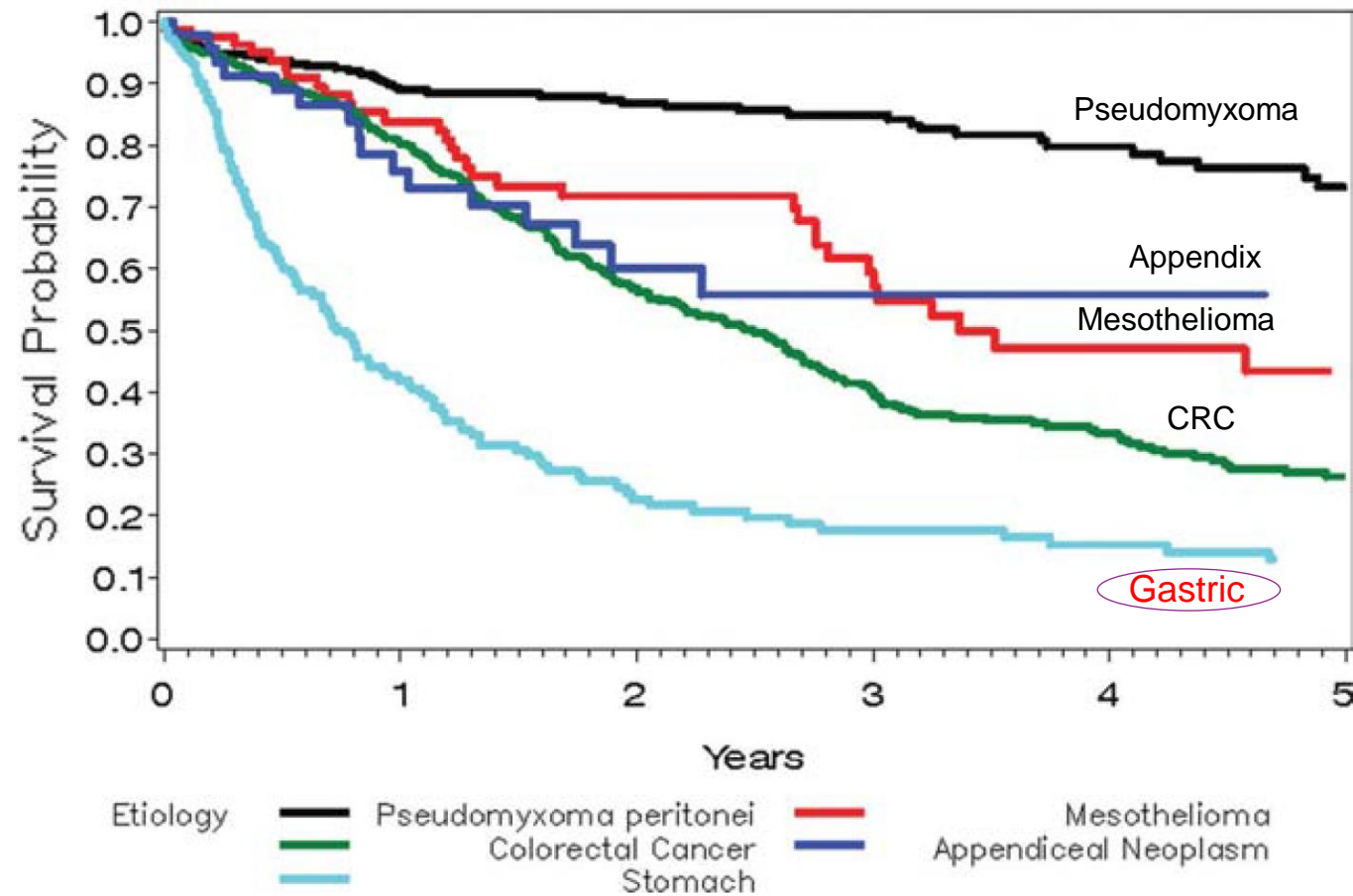
- CRS: R/O macroscopic disease
HIPEC: R/O microscopic disease

Con

- Invasive, single treatment
- Result depends:
 - *Cancer type: Less effective for GC*
 - *Disease burden*

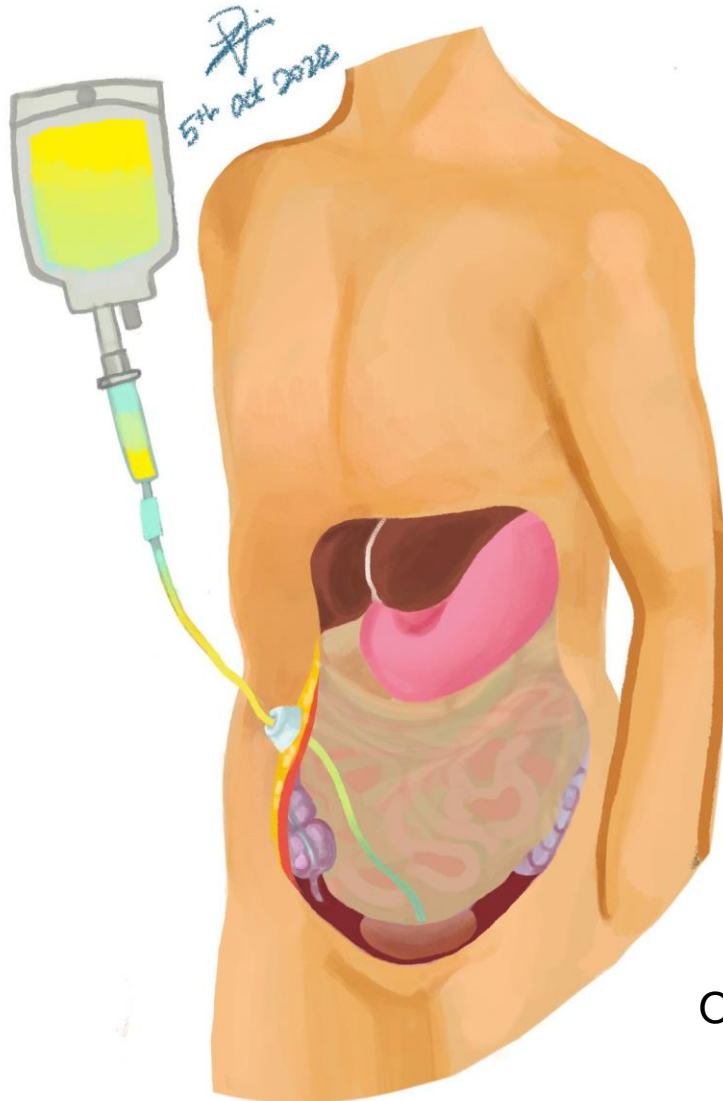


Survival outcomes after HIPEC (n=1290)

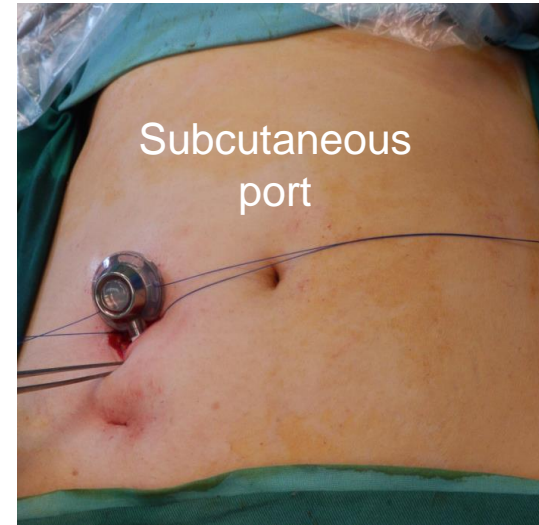


Glehen O et al., Cancer 2009

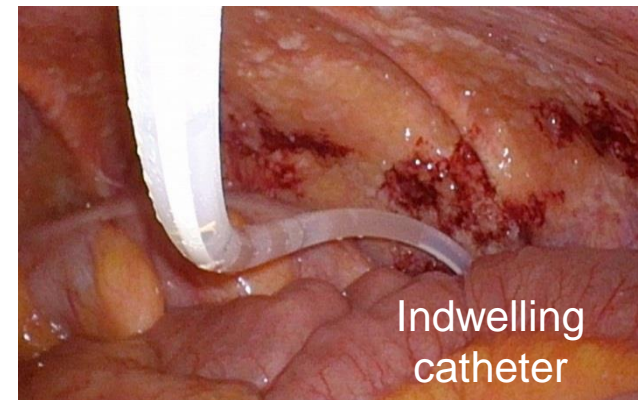
Catheter-based IP Chemotherapy



Outpatient treatment



Chemotherapy solution



Indwelling catheter

NUH IP Chemotherapy protocol

		Each Cycle (3 weekly)		
XELOX	PO Capecitabine	Week 1	Week 2	Week 3 Rest
	IV Oxaliplatin	● Day 1 only		
	IP paclitaxel	● Day 1	● Day 8	

Advantages of catheter-based IP chemotherapy

- Outpatient treatment
- Minimal risk and S/E from surgery and chemotherapy
- Repeated dosing

Intraperitoneal chemotherapy for gastric cancer with peritoneal disease: experience from Singapore and Japan

Koji Kono^{1,2,3} · Wei-Peng Yong⁴ · Hirokazu Okayama¹ · Asim Shabbir² · Tomoyuki Momma¹ · Shinji Ohki¹ · Seiichi Takenoshita¹ · Jimmy So²

2016 SSAT PLENARY PRESENTATION



Gastric Cancer 2017




Conversion Surgery Post-Intraperitoneal Paclitaxel and Systemic Chemotherapy for Gastric Cancer Carcinomatosis Peritonei. Are We Ready?

Dexter Yak Seng Chan¹ · Nicholas Li-Xun Syn^{2,3} · Rachel Yap² · Janelle Niam Sin Phua¹ · Thomas I. Peng Soh² · Cheng Ean Chee² · Min En Nga⁴ · Asim Shabbir¹ · Jimmy Bok Yan So¹ · Wei Peng Yong²

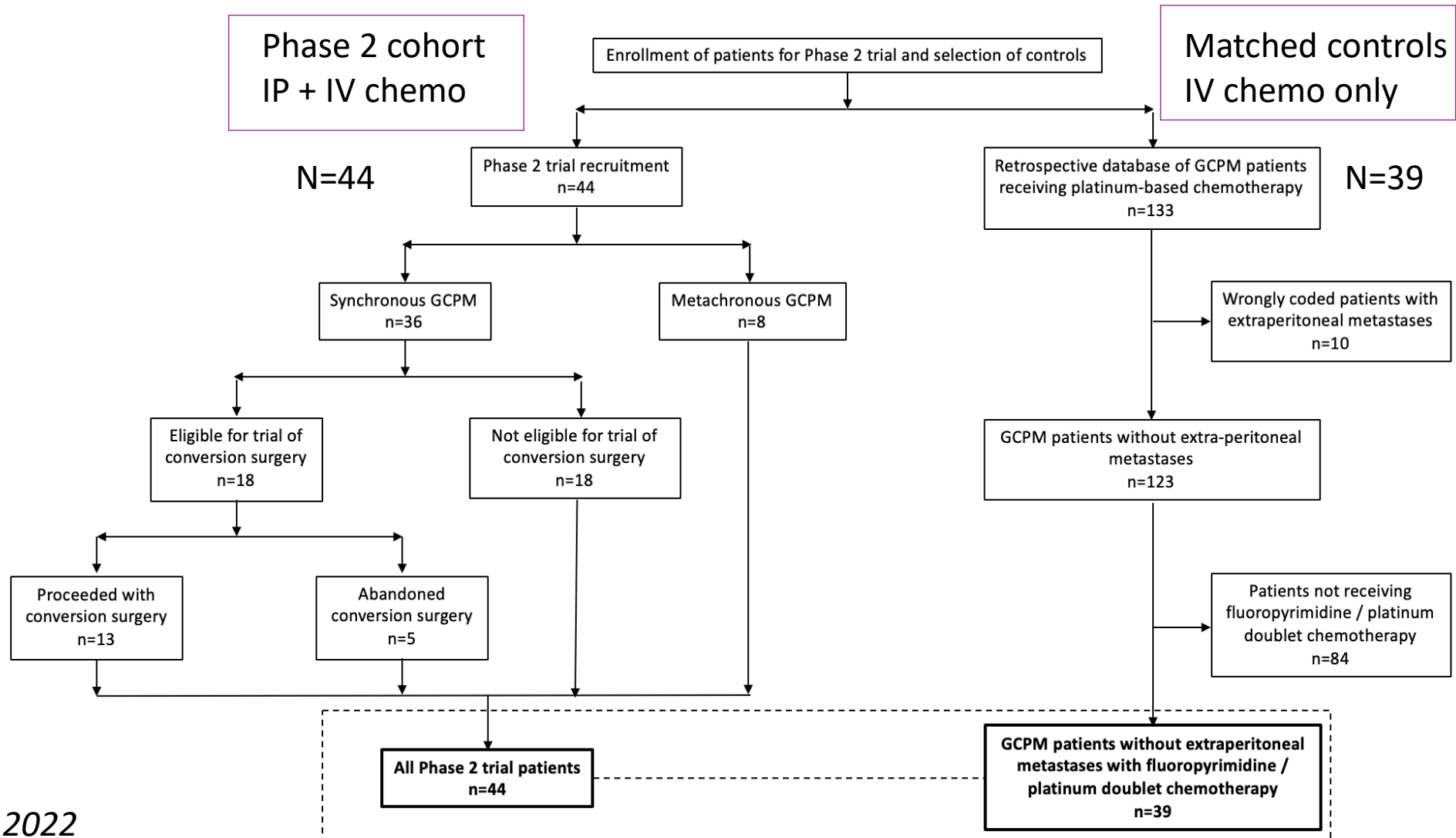
J Gastrointest Surg 2017

Outcomes of a Phase II Study of Intraperitoneal Paclitaxel plus Systemic Capecitabine and Oxaliplatin (XELOX) for Gastric Cancer with Peritoneal Metastases

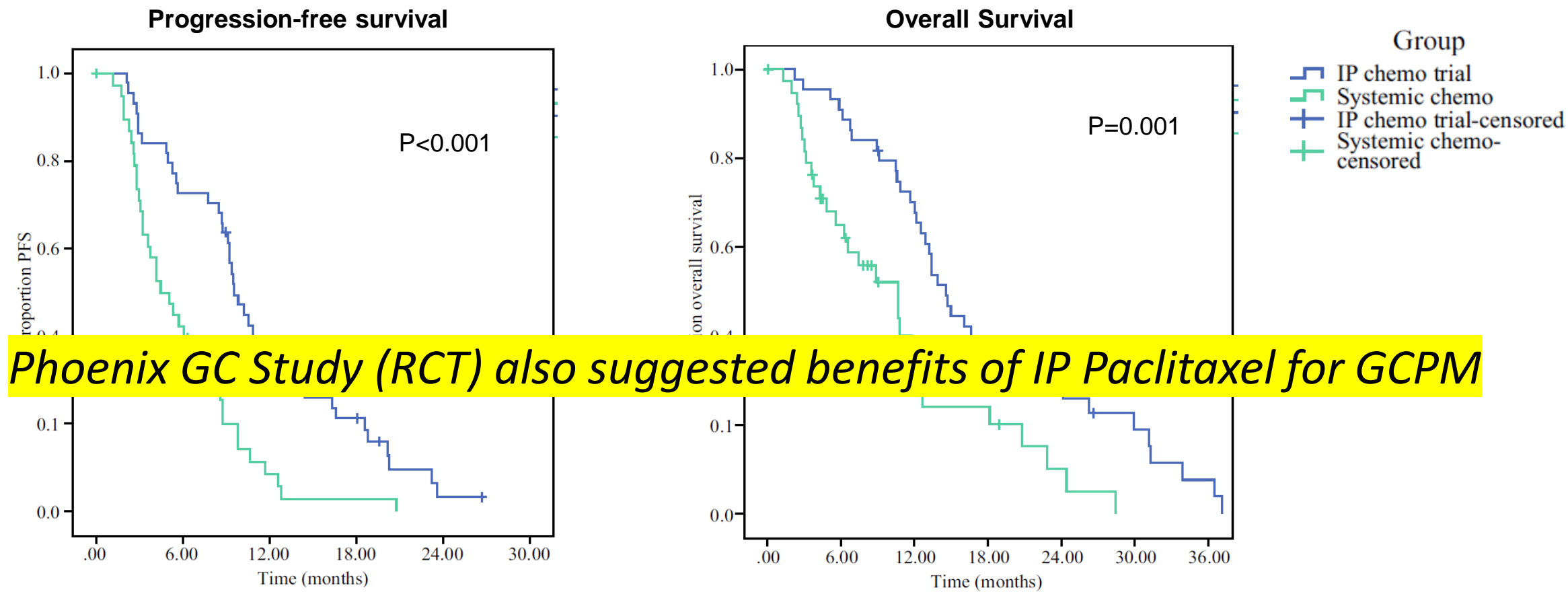
Ann Surg Oncol 2022

Daryl K. A. Chia, FRCS¹, Raghav Sundar, MRCP^{2,3,4}, Guowei Kim, FRCS¹, Jia Jun Ang, MRCS¹, Jeffrey H. Y. Lum, FRCPATH⁵, Min En Nga, FRCPATH⁵, Giap Hean Goh, FRCPATH⁵, Ju Ee Seet, FRCPATH⁵, Cheng Ean Chee, MRCP², Hon Lyn Tan, MRCP², Jingshan Ho, MRCP², Natalie Y. L. Ngoi, MRCP², Matilda X. W. Lee, MRCP², Vaishnavi Muthu, MRCP², Gloria H. J. Chan, MRCP², Angela S. L. Pang, MRCP², Yvonne L. E. Ang, MRCP², Joan R. E. Choo, MRCP², Joline S. J. Lim, MRCP², Jun Liang Teh, FRCS⁶, Aung Lwin, FRCS⁶, Yuen Soon, FRCS⁶, Asim Shabbir, FRCS^{1,3,7}, Jimmy B. Y. So, FRCS^{1,3,7} , and Wei Peng Yong, MRCP^{2,8}

IP Paclitaxel + XELOX phase 2 study



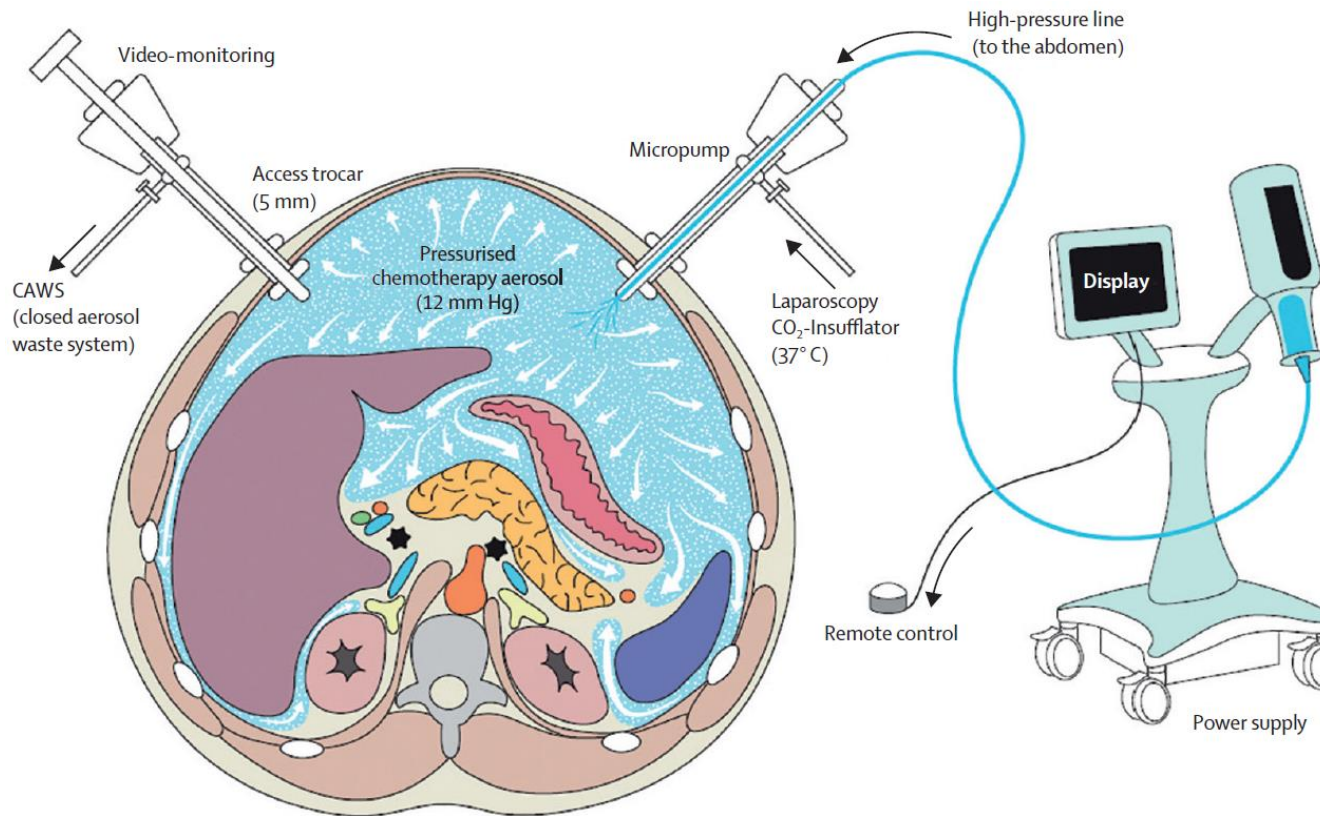
Results:



	IP + IV	IV alone
Median survival (mos)	9.5	4.4
1 Yr PFS (%)	35.4%	8.5%

	IP + IV	IV alone
Median survival (mos)	14.6	10.6
1 Yr OS (%)	68%	32%

PIPAC (Pressurized intraperitoneal aerosol chemotherapy)



Advantages

- Better distribution
- Deeper penetration
- Less systemic toxicity
- Allow repeated applications and assessment of response

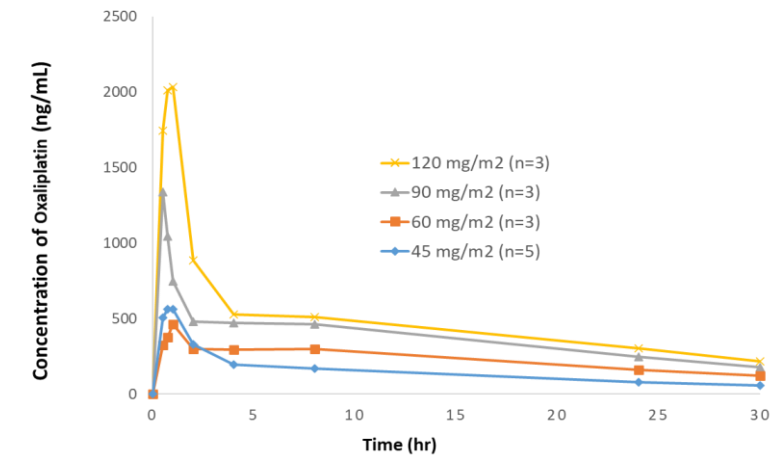
PIPAC-OX: A Phase I Study of Oxaliplatin-Based Pressurized Intraperitoneal Aerosol Chemotherapy in Patients with Peritoneal Metastases **AC**

Guowei Kim^{1,2,3}, Hon Lyn Tan^{2,4}, Raghav Sundar^{2,4,5}, Bettina Lieske^{1,2,3}, Cheng Ean Chee^{2,4}, Jingshan Ho⁴, Asim Shabbir^{1,2,3}, Maria V. Babak^{6,7}, Wee Han Ang^{6,8}, Boon Cher Goh^{2,4,9}, Wei Peng Yong^{4,9}, Lingzhi Wang^{2,9}, and Jimmy B.Y. So^{1,2,3}



GW Kim

- GI primary, received ≥ 1 line chemotherapy
- 2 PIPAC, 6 weeks apart
- **N=16, no major morbidity**
- **MTD of PIPAC Oxaliplatin = 120 mg/m² (RP2D)**



- Linear pharmacokinetics
- Significantly lower (> 10 fold) systemic drug concentration in PIPAC than IV



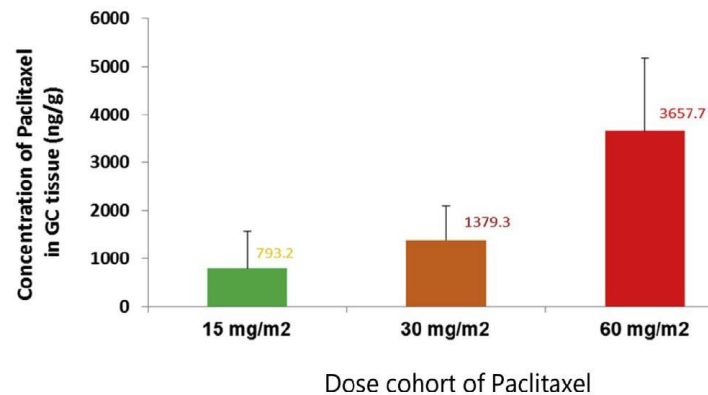
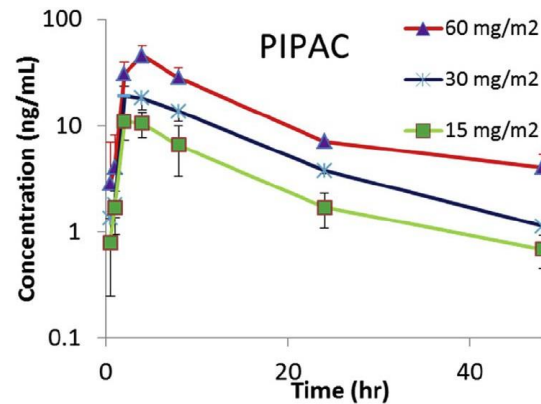
HL Tan

Safety, pharmacokinetics and tissue penetration of PIPAC paclitaxel in a swine model

Study Protocol Overview

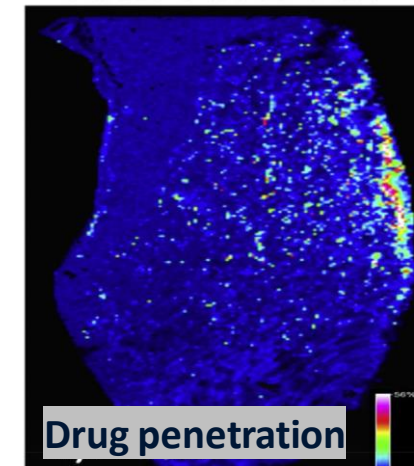


Phase 1 study with PIPAC paclitaxel will start in 2022



Linear pharmacokinetics

After PIPAC-PTX





Ongoing study

PIPAC + Immunotherapy (PIANO trial)

PIPAC oxaliplatin with systemic nivolumab for GCPM

Study sites

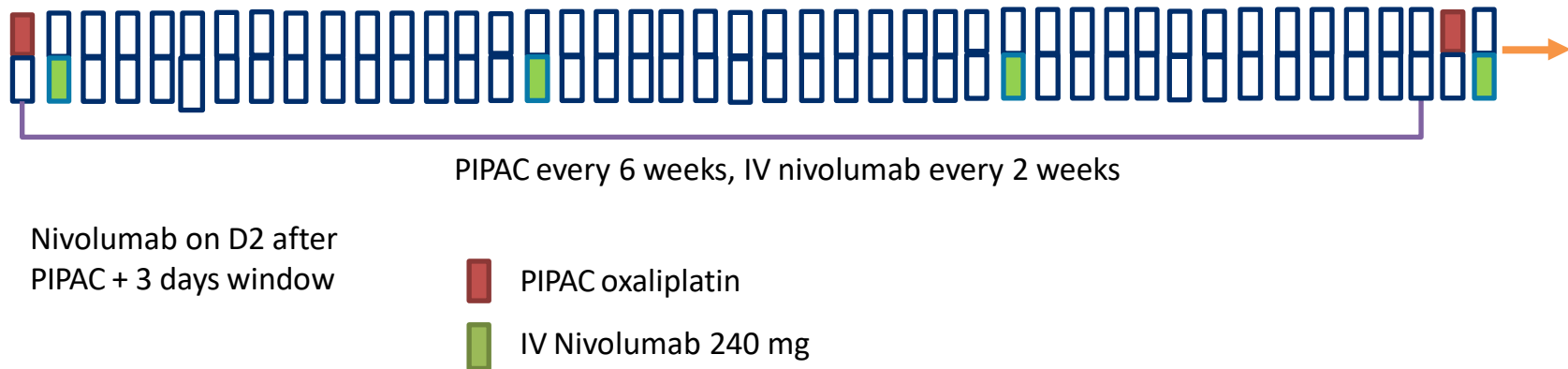
 National University Hospital
National Cancer Centre

 Ghent University Hospital

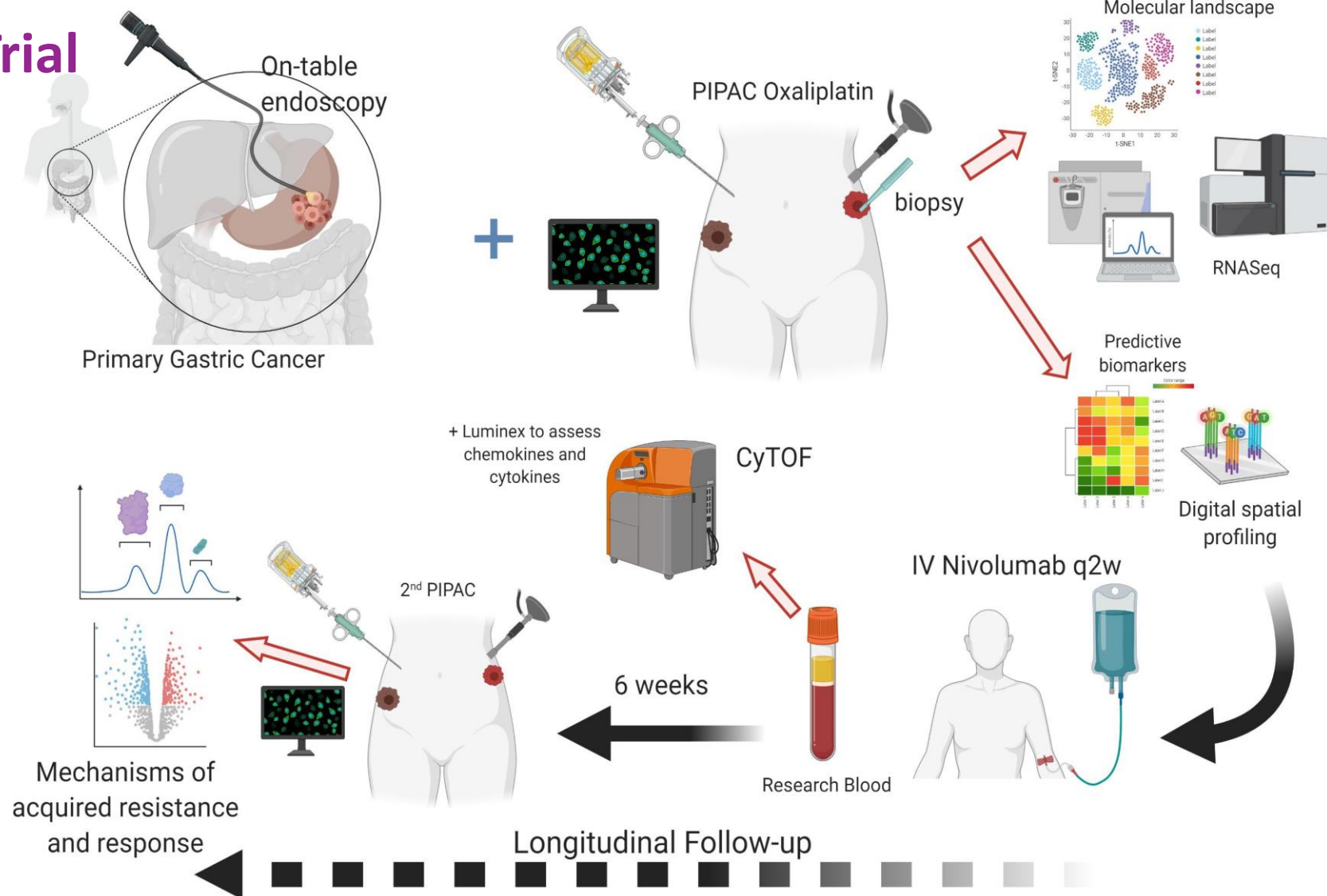
Single arm
Phase 1
First-in-human

Gastric cancer with
peritoneal mets
Progressed on at
least 1 line of
systemic therapy

16/21 patients have been recruited and results will open in 2023



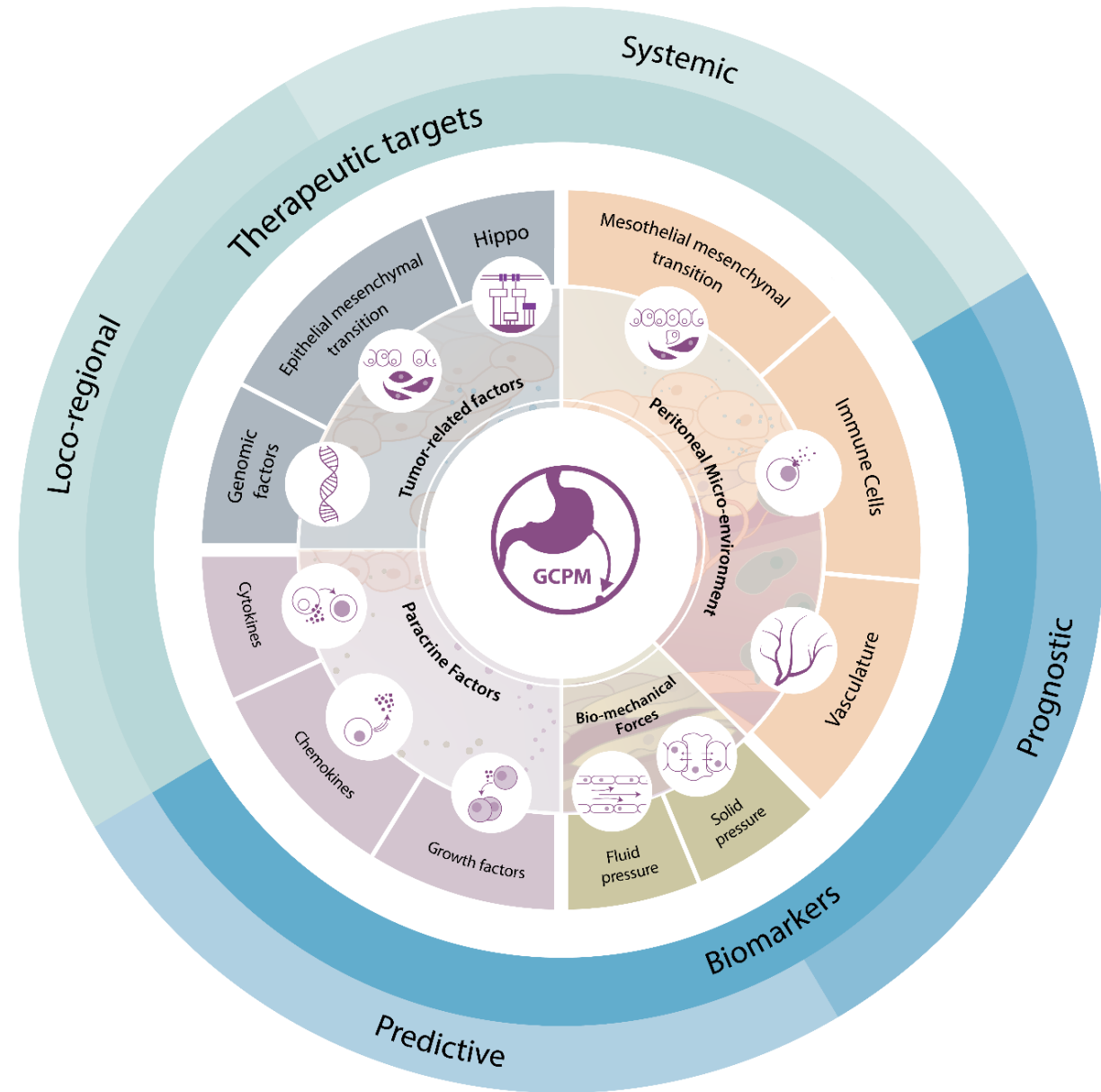
PIANO Trial



Raghav Sandar
MBBS PhD

Integration of Genomic Biology Into Therapeutic Strategies of Gastric Cancer Peritoneal Metastasis

- 11 biologic hallmarks into 4 categories:
 - Tumor-related factors
 - Peritoneal microenvironment
 - Paracrine factors
 - Bio-mechanical forces
- Combination strategies may improve outcomes



Take Home Message

- Intraperitoneal (IP) chemotherapy has superior advantage over systemic chemotherapy due to plasma peritoneal barrier
- Various modalities of IP chemotherapy have been developed recently with promising results
- International collaboration for practice changing studies is needed to bring our discoveries to our patients

Acknowledgement

Singapore Peritoneal Oncology Study (SPOS) Group



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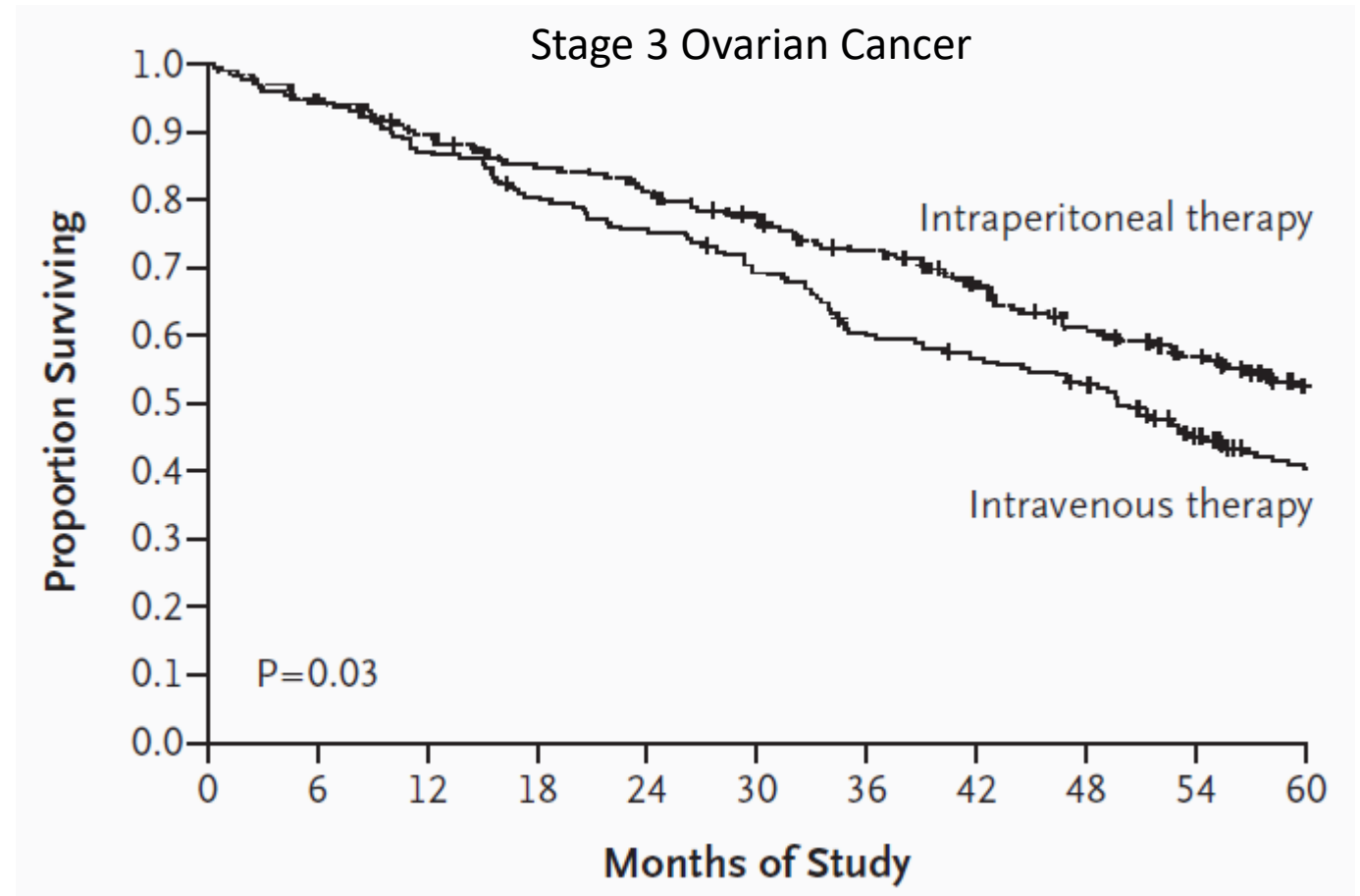
Paclitaxel as Intraperitoneal chemotherapy

1. Large molecular size

- less systemic absorption
- Peritoneal conc. >2000x for IP vs IV

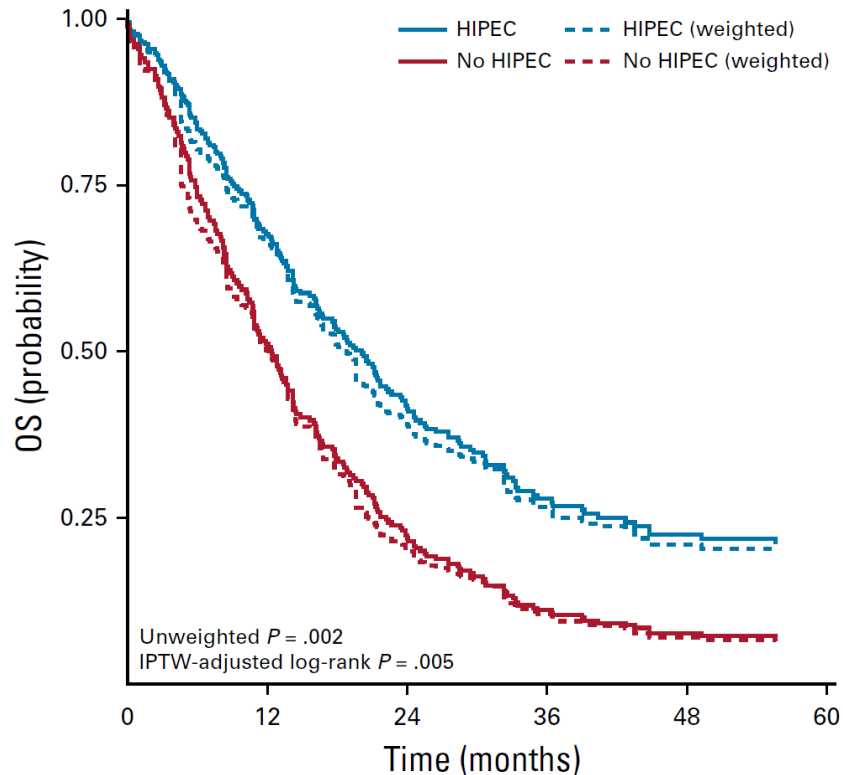
2. Antiproliferative

- Less adhesion
- Allows repeated use



Cytoreductive Surgery With or Without Hyperthermic Intraperitoneal Chemotherapy for Gastric Cancer With Peritoneal Metastases (CYTO-CHIP study): A Propensity Score Analysis

Observational study



- Median OS: 19 vs 12 months
- 5Y OS: 20% vs 6% ($p = 0.005$)
- Major complication rate: 54% vs 55%
- Overall median PCI: 3 (0-25)
- *Observation study, heterogenous populations & treatment regimen*