PIPAC FOR GASTRIC CANCER PERITONEAL CARCINOMATOSIS

Yanghee Woo, MD FACS
Co-Chair Medical Advisor of Hope for Stomach Cancer
Gastric Cancer Work Group / Peritoneal Surface Malignancies
Associate Professor of Surgery
City of Hope, Duarte CA, USA
Acknowledgement

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DoD E01 Award W81XWH-19-1-0225 (PI, 2019-2021) & Clinical Trials Internal Funding Prioritization Committee Support

“Discovery of Immune Biomarkers That Predict Response to a Novel Chimeric Immuno-Oncolytic Virus Encoding Anti-PD-L1 in Gastric Cancer Peritoneal Carcinomatosis”

Stand Up 2 Cancer Gastric Cancer Interception Grant (Site PI, 2020-2023)

“Early Detection of Diffuse and Intestinal Gastric Cancer”

Department of Surgery Start Up (PI, 2015-2020)

“Molecular Staging of Gastric Cancer” and “Preclinical studies in evaluation of the safety and efficacy of oncolytic viruses in GI cancers”
My Goal, our goal

- To eliminate deaths due to stomach cancer

- To bring the best of science and technology to improve quality of life and long-term survival for patients with stomach cancer peritoneal carcinomatosis

- Invite all of us to work together to reach this goal
Teaming up to cure stomach cancer

- It takes vision, dedication and a team of collaborators to find a cure for stomach cancer
No Life Should Be Lost to Stomach Cancer
Adversely Impacts Young Adults

Disparate and Alarming Impact of Gastrointestinal Cancers in Young Adult Patients

- The average age of stomach cancer patient in U.S. is 68 years old
- But young (< 40 yo) GC patients are more likely to have more aggressive and treatment resistant tumors
- More than 40% of stomach cancer patients 18-40 yo present with Stage IV cancer
- More likely to present with peritoneal metastases at the time of initial stomach cancer diagnosis: 32.1% vs. 14.1%
Peritoneal Carcinomatosis

- The peritoneum is the most common site of recurrence or metastatic presentation of stomach cancer.
- Tumors in the peritoneum are called peritoneal carcinomatosis and associated with myriad of complications:
  - Accumulation of malignant ascites
  - Development of bowel obstruction
  - Pain, malnutrition and cachexia
- Standard of care is systemic chemotherapy, +/- Herceptin, immunotherapy
- Role of surgery is limited
- Not good enough and unacceptable

<table>
<thead>
<tr>
<th>Primary</th>
<th>Syn</th>
<th>Met</th>
<th>Autopsy</th>
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<tbody>
<tr>
<td>GC</td>
<td>15%</td>
<td>&gt;50%</td>
<td>60%</td>
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Intraoperative image during diagnostic laparoscopy in patient with stomach cancer and peritoneal carcinomatosis.
Progress Against Stage IV Stomach Cancer

- We are entering a new world of cancer treatment
- Historical poor outcomes can be overcome

Survival in Months compared to Best Supportive Care (4 months)

- **5-FU Alone**
  - 7.0 mo

- **Docetaxel + Cisplatin + 5-FU**
  - 9.2 mo
  - 10.5 mo
  - 10.7 mo

- **5-FU + Oxaliplatin (FLO)**
  - 11.2 mo

- **Epirubicin + Oxaliplatin Capecitabine (EOX)**
  - 13.8 mo

- **Trastuzumab + CDDP+5FU or Capitabine**
  - 10.5 mo

- **Capecitabine + Cisplatin (XP)**
  - 11.2 mo

- **FOLFOX**
  - 17.4 mo

- **5-FU + Oxaliplatin (FLO)**
  - 10.8 mo

- **Epirubicin + Oxaliplatin Capecitabine (EOX)**
  - 12.3 mo

- **Trastuzumab + CDDP+5FU or Capitabine**
  - 12.5 mo

- **2017-2018 Pembrolizomab MSI-H or dMMR/PD-L1 +**
  - Pembro Chemo Combo
    - CPS > 1: 10.6 vs 11.1 vs 12.5 mo
    - CPS ≥ 10: 17.4 vs 10.8 vs 12.3 mo
Barriers To Treatment of Peritoneal Carcinomatosis

- PC poses distinct therapeutic challenges
  - Diffuse nature of PC makes complete surgical resection ineffective, if not harmful
  - Tumor protective blood-peritoneal barrier and an immunosuppressive environment that prevent effective drug delivery and promote drug resistance
  - Disease often not measurable → Patients do not qualify for clinical trials
  - Thus, little is known about the effects of established drugs or novel therapies in PC patients
Regional Therapy for Peritoneal Carcinomatosis

IP
Intraperitoneal Chemotherapy

HIPEC
Heated IP Chemotherapy

PIPAC
Pressurized Aerosolized IP Chemo
PIPAC for Gastric Cancer Peritoneal Carcinomatosis

• What is PIPAC?
  – Pressurized IntraPeritoneal Aerosolized Chemotherapy
  – A laparoscopic approach of delivering chemotherapy (or other anti-cancer agents) to destroy cancer cells in the peritoneum
  – Uses a high-pressure drug delivery system CapnoPen that is NOT YET FDA approved in U.S.

• What is role of PIPAC in the treatment of stomach cancer patients in the U.S.?
  – In its INVESTIVATIONAL PHASE
  – Currently undergoing Phase I clinical trial
Phase I Trial In U.S. – PIPAC Device Registry

- To evaluate the safety of the PIPAC device and the method of intraperitoneal delivery of combination chemotherapies by PIPAC

  - Indications:
    - Patients with PC from stomach, ovarian, colon and appendiceal cancers
    - High burden of peritoneal disease
    - Progressed on systemic therapy

- Laparoscopic procedure
- Short hospital stay ~24 hr
- Repeat 3 times

Cisplatin
Doxorubicin

Peritoneal Carcinomatosis Index (PCI) Score: 0 to 39
Minimally Invasive and Short Operative Time

Extra-abdominal view

Intra-abdominal view

OR Setup

Extra-abdominal view
Phase I PIPAC Trial: Experimental Design

Experimental Design Schema

Safety and efficacy of pressurized intraperitoneal aerosolized chemotherapy (PIPAC) in ovarian, colorectal, and gastric cancer patients with peritoneal carcinomatosis (PC)

- Phase I pilot study (single-arm) = 21 evaluable participants

18 weeks

Registration

- < 6 weeks prior to therapy

Protocol Therapy

- PIPAC
  - 3 treatments given 6 weeks apart
  - Tumor response
  - Post-operative surgical complications

Follow-up

- 6 weeks
- Every 12 weeks
- 1 year

- Tumor response
- Time to progression (PD also monitored at any time during study)
- Progression-free survival

AE monitoring (primary)

21 weeks

City of Hope
Evidence for PIPAC from International Experts

- 42 Clinical Trials
- Over 800 total patients
- ~200 stomach cancer
- Safe and feasible
- 79% stable disease or decreased ascites
- 10-20 months survival
- May prolong survival
- On-going trials in Europe and Singapore

Phase I Device Registry trial open at COH (T. Dellinger, PI)
Role for Regional Therapy for Stomach Cancer

All GC patients with advanced stage disease should be cared for by a multidisciplinary team with a patient–tailored tumor-specific strategy

### High Risk
- PCI Score = 0

**Intent:** Curative / Preventative of PC

**Approach:**
- Tumor-directed Neoadj therapy
- Radical Surgery
- Laparoscopic IP, HIPEC or PIPAC

### Minimal Disease
- PCI Score < 6

**Intent:** Convert to Curative

**Approach:**
- Tumor-directed Neoadj therapy
- Restaging Lap
- Radical Surgery?
- IP, HIPEC or PIPAC

### Moderate Disease
- PCI Score 6-12

**Intent:** Improve QoL
- Curative

**Approach:**
- Tumor-directed systemic therapy
- Restaging Lap
- HIPEC, PIPAC?
- Restage
- Consider Surgery?

### High Burden of Disease
- PCI Score > 12

**Intent:**
- Improve QoL

**Approach:**
- Tumor-directed systemic therapy
- Restaging Lap
- PIPAC
  - PIPAC
  - PIPAC
- Improve QoL and Survival
Summary

• Every patient with stomach cancer peritoneal carcinomatosis should be evaluated by a multidisciplinary team for potential regional treatment option

• Treatment strategies should be evidence based but we can always think outside the box and beyond standard of care

• Patient-tailored, tumor specific treatment strategy should be developed
  – Systemic therapy (chemotherapy +/- immunotherapy or targeted therapy)
  – Regional therapy with IP, HIPEC, or PIPAC should be considered on clinical trial or on an individualized patient bases

• PIPAC is INVESTIGATIONAL and undergoing safety evaluation in the United States

• Phase II PIPAC trial for patients with stomach cancer PC is planned at COH

• Many promising new therapies are under preclinical testing and clinical trials
Future of Novel GC PC Therapies

Translation of new drugs / strategies

• Numerous novel agents for cancer are under investigation
• Direct these novel discoveries for stomach cancer patient treatment
• Evaluate these novel agents for stomach cancer peritoneal carcinomatosis in preclinical setting (our laboratories)
• Conduct clinical trials for stomach cancer patients
• Development of better treatment strategies

Improve Stomach Cancer Outcome

Awareness
Advocacy
Funding

Plan: Bring best of science and technology to cure stomach cancer patients

Regional Therapy  Immunotherapy  Oncolytic Viruses  CAR-T Therapy  Liquid biopsy
Thank you for your dedication and advocacy!

PATIENTS & ADVOCATES

STOMACH CANCER FOUNDATION

Eugene and Catherine Ohr Foundation
Mark Allen Ober

DONORS

Eugene and Catherine Ohr Foundation
Mark Allen Ober

MENTORS

Drs. Yuman Fong, Larry Kwak, Benjamin Paz, Mark Hardy, MD and Woo Jin Hyung, MD

FONG-WARNER-HAHN-WOO LAB

GASTRIC CANCER WORKGROUP

J Chao, J Lin, Y Chen, L. Melstrom, B. Paz, S Yoon, G Idos, M J Sullivan, S Buga, M Raoof

PSM WORKGROUP

COH/TGEN CO-INVESTIGATORS

D Von Hoff, H Han, YC Yuan, H Li, M Li, S Priceman, S Forman, C Behrendt, SC Cha

COH Core Facilities

Flow Cytometry
Small Animal and Small Animal Imaging
Pathology, Biostatistics, Integrated Genomics

STAND U2C GC TEAM

J Chao (COH), S. Klemper, A Chan (MGH), S Yoon (MSKCC), S. Rhyuem (UPenn), D Catenacci (U Chicago), H. Lee (Samsung)

Stomach Cancer Task Force

JH Hwang (Stanford U), H Koh (Harvard U), R. Huang (Stanford U), etc

G6+ INTERNATIONAL GC TEAM

WJ Hyung, TI Son, YM Kim (S. Korea)
Y. Hu, G. Li, K Yang (China)
K. Obama, T. Nishigori (Japan)
N. Okabe, T. Kinoshita (Japan)
A. Guner (Turkey)
J Deciderio, A Marano (Italy), A Navaar (Chile)
A. Takasashi (Mexico)
And Growing...

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