Gastrointestinal (GI) Cancers Overview

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Anatomic Sites of Malignancy

- Esophagus
- Stomach
- Colon/Rectum
- Anus
- Pancreas
- Liver
Gastrointestinal Tract

2008 Estimated US Cancer Deaths*

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung &amp; bronchus</td>
<td>31%</td>
<td>26%</td>
</tr>
<tr>
<td>Prostate</td>
<td>10%</td>
<td>15%</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>8%</td>
<td>9%</td>
</tr>
<tr>
<td>Pancreas</td>
<td>6%</td>
<td>6%</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Leukemia</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Esophagus</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>All other sites</td>
<td>24%</td>
<td>25%</td>
</tr>
</tbody>
</table>

ONS=Other nervous system.
Source: American Cancer Society, 2008.
Cancer Death Rates* Among Men, US, 1930-2004

Cancer Death Rates* Among Women, US, 1930-2004

*Age-adjusted to the 2000 US standard population.
Esophageal Cancer

- 16,470 New Cases (5th GI), 14,280 Deaths
- Rising USA Mortality
- Squamous Cell CA
  - 10% Proximal, 60% Middle, 30% Distal
  - Risk - Tob 10x, Tob + ETOH 100x
- Adeno CA (1980 15%, 2003 60%)
  - Distal Esophagus/ GE Junction
  - Risk – Barrett’s Esoph, GERD (30-40x)
- Staging: CT, EUS, PET

Gastric Cancer

- USA Cancer Death Rate 13th (2nd in world)
- Death Rate & Incidence declining since 1900
- Associated with diet, tobacco, food preparation
- Adeno CA 95%
- Staging: CT, EUS, PET, Laparoscopy
Colon Anatomy

Transverse colon

Ascending colon

Descending colon

Colon Carcinogenesis and the Effects of Chemopreventive Agents

Aspirin and other NSAIIDs
Polarae Calcium

Normal epithelium

Hyperplastic epithelium
Aberrant crypt foci

COX-2 overexpression

Apc mutation

Small adenoma

Large adenoma

Colon carcinoma

Estrogen
Aspirin and other NSAIIDs

Colorectal Cancer

- 49,960 Deaths 2008 (2\textsuperscript{nd} CA for male plus female and falling)
- 149,000 New Cases 2008 (4\textsuperscript{th} most common male plus female)
- Adeno CA 95% of tumors
- Related to diet, hereditary, inflammatory bowel disease
- Staging: Colonoscopy, CT, CXR, PET (EUS/MRI – Rectal)

Colon Adenocarcinoma

![Colon Adenocarcinoma Image]
A 67-year-old woman presented with a three-month history of abdominal pain, weight loss, and rectal bleeding.


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**Anal Cancer**

- 5070 Annual Cases, 680 deaths
- 1-2% of all Bowel CA
- 80% Squamous, 15% Adeno CA
- Female 2/3 Cases
- Associated Human Papilloma Virus, AIDS
- Staging: Colonoscopy, CT Scan
Pancreas Cancer

- 37,680 New cases 2008 (10th)
- 34,290 Deaths 2008 (4th & rising)
- 5% of all CA Mortality
- Five year survival <5%
- Related Tobacco (30%), Diabetes, Chronic Pancreatitis, Hereditary (5-8%)
- Staging: CT, ERCP, EUS
Liver Cancer

- Worldwide most common CA
- Annual 21,300 US cases (18,400 deaths)
- Hepatocellular CA
- Associated Cirrhosis, Hep B and C, ETOH, Hemochromatosis
- Staging: CT Scan, MRI, Angiography, Bone Scan

Hepatocellular Cancer
Metastases

- **Bowel and Gastric**
  - First nodal and liver
  - Second lung, bone, brain
  - Rectal exception – lung possible first before liver
- **Anal** – inguinal nodal
- **Esophagus** – nodal, lung, liver, bone
- **Liver** – lung, bone, intraperitoneal
Diagnostic Studies

- Physical exam/performance status
- Chest x-rays, CTs, ultrasound, MRI
- Radionuclide scans (bone scan, PET)
- Laboratory studies
- Endoscopic biopsies and ultrasound (EUS)
- Needle biopsies
- Laparoscopy reports
- Operative notes/pathology reports

Endoscopic Ultrasound
Staging

• Use AJCC Cancer Staging Manual Sixth Edition 2002 (your best friend)
• Stage I-IV
• TNM system
  – T (Primary Tumor) size, local invasion
  – N (Nodal Metastases) regional nodal involvement
  – M (Distant Metastases)

Colon Cancer Staging
Pancreatic Cancer Staging

Prognostic factors

- Staging
  - T (tumor) size, extension
  - N (nodes) location
  - M (metastases)
- Histologic sub-type-adenocarcinomas (except for liver), squamous cell for esophagus and anus
- Sites of metastases
- Prior therapy-surgery, radiation, chemotherapy
Treatment Modalities

- Surgery
- Radiation
- Chemotherapy
- Multimodality
- Targeted Molecules (Avastin, Erbitux)
- Directed Therapy (RFA, Microspheres)
- Palliative Devices (Stents)


The Application of Expandable Metal Stents within the Gastrointestinal Tract
Pancreatic CA Biliary Stent

GI Malignancy Therapy

- Primary – Surgical (except Anal, Esophageal)
- Neoadjuvant – Anal, Esophageal
- Adjuvant – Gastric, Pancreatic, Colorectal
- Locally Advanced – Multimodality
- Metastatic – Systemic, Rarely Surgery
Colon Cancer Resection

Colon CA Surgery
Recent Therapy Advances

- Chemotherapy
  - Oxaliplatin, Irinotecan
  - Combination: FOLFOX, FOLFIRI
- Targeted Small Molecules
  - Avastin, Erbitux, Vectibix (panitumumab)
- Metastatectomy, RFA, Chemoembolization
- Prevention
  - ASA, Celebrex

CALGB GI TRIALS
(What the CRA will have to identify in primary record for the on-study forms)

- Type of surgery
- Tumor size (bowel wall penetration) and nodal status
- Margins of resection (R0, R1)
- Pathologic sub-type & differentiation
- Sites and numbers of metastases
- Number of prior chemotherapies for metastatic disease
Response Assessment

- Complete response
- Partial response
- Stable disease
- Progression/relapse
- RECIST Criteria
- Note: re-biopsy may be necessary to confirm a response, i.e., after CT/RT for anal carcinoma

Follow-up

- Relapse (time to progression, sites of relapse)
- Survival
- Toxicity
- Quality of life
Active CALGB Trials

- **Gastric:** 80101 Adjuvant chemoradiation
- **Colon:** 80405 Metastatic Chemo + Targeted Molecules 1st Line RX*
- **Colon:** 80502 Metastatic 2nd line Irinotecan + AZD2171*
- **Esophageal:** 80302 Neoadjuvant Chemo + Rads
- **Esophageal:** 80403 Chemotherapy for metastatic*
- *Schema to follow

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**CALGB 80405**

Colorectal CA Metastatic

1 Cycle = 8 Weeks

**ARM A**
Bevacizumab 5 mg/kg IV every 2 weeks followed by FOLFOX or FOLFIRI** every 2 weeks.

**ARM B**
Cetuximab 400 mg/m² IV on Day 1 of Cycle 1 only, then 250 mg/m² IV weekly followed by FOLFOX or FOLFIRI** every 2 weeks.

**ARM C**
Cetuximab 400 mg/m² IV on Day 1 of Cycle 1 only, then 250 mg/m² IV weekly followed by Bevacizumab 5 mg/kg IV every 2 weeks, followed by FOLFOX or FOLFIRI** every 2 weeks.

Continue treatment until disease progression or unacceptable toxicity (see Sec. 7.1).
**CALGB 80502**

2nd Line Colon CA Metastatic

Patients must initiate treatment within 14 days of registration.

*One cycle = 21 Days*

- **Irinotecan**
  - 350 mg/m² IV
  - over 90 minutes
  - every 21 days
  - and

- **AZD2171**
  - 30 mg PO daily;
  - taken before food.

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**CALGB 80403**

Esophageal CA Metastatic

Patients must initiate treatment within 14 days after registration/randomization.

*One cycle = 21 days on Arm A and B, One cycle = 14 days on Arm C*

- Arm A: 1 cycle = 21 days
  - ECF-C (Epirubicin, Cisplatin, Continuous Infusion 5-FU, and Cetuximab)

- Arm B: 1 cycle = 21 days
  - IC-C (Irinotecan, Cisplatin and Cetuximab)

- Arm C: 1 cycle = 14 days
  - FOLFOX-C (5-FU, Oxaliplatin, Leucovorin, and Cetuximab)

Patients will receive a minimum of 2 cycles of therapy on Arm A or B, or a minimum of 3 cycles of therapy on Arm C, and will continue treatment until disease progression or unacceptable toxicity.
CALGB
GI Correlative Science Trials

• **15008**: Familial Factors in the Development of Colon CA
• **15075**: Correlative Science Studies in Colon CA