CHEMO RADIATION
IN
CARCINOMA PANCREAS

Dr. R. Kapoor,
Additional Professor,
Department of Radiotherapy,
Regional Cancer Center, PGIMER, Chandigarh.
**INTRODUCTION**

- Pancreatic cancer is one of the most lethal cancers, as indicated by a mortality incidence ratio of 98%.
- Fourth leading cause of death from cancer
- Aggressive biology of the tumor and the lack of early disease specific signs and symptoms, only a small minority of patients present with potentially resectable disease at the time of diagnosis
- Periampullary cancers /Pancreatic head malignancies constitutes 70-80%.
- Surgery is the only curative treatment option
## Patterns of Failure After Surgical Resection

<table>
<thead>
<tr>
<th>Study</th>
<th>Surgical Resection (N)</th>
<th>Local Recurrence (%)</th>
<th>Distant Metastasis (%)</th>
<th>2 yr &amp; 5 yr survival (%)</th>
<th>Median survival (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tepper et al (MGH)</td>
<td>45</td>
<td>50</td>
<td>15</td>
<td>-</td>
<td>11.5</td>
</tr>
<tr>
<td>Griffin et al</td>
<td>36</td>
<td>73</td>
<td>42-peritoneum 62-liver</td>
<td>32 &amp; 17</td>
<td>-</td>
</tr>
<tr>
<td>Foo et al (Mayo Clinic)</td>
<td>29</td>
<td>59</td>
<td>38</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Kayahara et al</td>
<td>45</td>
<td>80 LN- 47</td>
<td>53-peritoneum 66-liver</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Willett et al</td>
<td>41</td>
<td>53</td>
<td>-</td>
<td>47 &amp; 38</td>
<td>-</td>
</tr>
</tbody>
</table>
PATTERNS OF FAILURE AFTER SX RESECTION

- Local recurrence – 80%
- Distant mets – 75%
- Hepatic mets – 66%
- Peritoneal dissemination – 53%
- LN relapse – 47%

- Actuarial 5-year survival - 21%; median survival of 15.5 mo
- With negative surgical margins - 5-year survival of 26%
- With positive surgical margins - 5-year survival of 8%.
RISK FACTORS FOR RECURRENCE

- Site – Body or Tail vs Head
- Size – >3cm
- Positive margins
- Residual disease
- Positive nodal status
- Grade – poorly diff.
ADJUVANT T/T AFTER CURATIVE RESECTION

- **Rationale** – to prevent local recurrence & distant mets

- **Options**
  - RT
  - CCT
  - CCRT
**WHY CHEMO RADIATION?**

**RESULTS OF POST-OP ADJUVANT RT ONLY**

<table>
<thead>
<tr>
<th>Study</th>
<th>SURGERY f/b PORT (N)</th>
<th>Local Recurrence (%)</th>
<th>Distant Metastasis (%)</th>
<th>2 yr LC (%)</th>
<th>5 yr survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foo et al (Mayo Clinic)</td>
<td>19 (S) 10 (Sx f/b RT) 45-50 Gy</td>
<td>80% 7%</td>
<td>Liver – 43% Peritoneum-61%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Willett et al</td>
<td>29 (S) 12 (Sx f/b RT)</td>
<td>-</td>
<td>-</td>
<td>50%</td>
<td>8% 23% (NS)</td>
</tr>
<tr>
<td>Bosset et al</td>
<td>14 (S) 14 (Sx f/b RT) 54 Gy</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>23 mths (MS)</td>
</tr>
</tbody>
</table>
**ADJUVANT CCT & CRT**

**CCT**
- Goal – to improve overall survival
- Regimens used – 5-FU infusion/ FAM/ FAP/ Gem/Capcitabine

**CCRT**
- Goal: To improve local control & overall survival
- Types: Adjuvant and Neoadjuvant
- 5-FU based / Gemcitabine based
ADJUVANT CHEMOTHERAPY TRIALS IN RESECTABLE DISEASE
5 FU BASED INITIAL TRIALS

- Initial trials (1960s and 1970s) → as a single agent RR – 28%
- Recent trials of 5-FU bolus iv → no activity
- Bolus 5-FU + leucovorin daily for 5 days → no objective response
- Prolonged infusion 5-FU or capecitabine → modest activity
- Infusional 5-FU and mitomycin C vs infusional 5-FU alone.
  - RR – 17.6% vs only 8.4%
  - Median survival - 6.5 mo vs. 5.1 mo ; P = 0.34
- Older 5-FU combinations – FAM, SMF
  - Initial results in phase II trials were encouraging, but none of them demonstrated any significant survival advantage over single agent 5-FU in larger randomized trials.
## Adjuvant Chemotherapy With Gemcitabine vs Observation in Patients Undergoing Curative-Intent Resection of Pancreatic Cancer: A Randomized Controlled Trial

**CONCLUSION:** Postoperative gemcitabine significantly delayed the development of recurrent disease in both R0 (13.1 vs 7.3 mths; p <0.001) and R1 (15.8 vs 5.5 mths; p<0.001) resections compared with observation alone.

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>SCHEDULE</th>
<th>5 yr LC (%)</th>
<th>DFS mo</th>
<th>OS mo</th>
<th>DFS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CONKO-001</td>
<td>368 (R0 - 80% R1-20% )</td>
<td>6 cycles gemcitabine (1,000 mg/m² IV over 30 min) on day 1, 8, and 15 every 4 wks</td>
<td>8%</td>
<td>6.9</td>
<td>20.2</td>
<td>5.5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>26%</td>
<td>13.9</td>
<td>22.1</td>
<td>16.5%   (P&lt;.001)</td>
</tr>
</tbody>
</table>

**CONKO - 001**

**CONCLUSION:** Postoperative gemcitabine significantly delayed the development of recurrent disease in both R0 (13.1 vs 7.3 mths; p <0.001) and R1 (15.8 vs 5.5 mths; p<0.001) resections compared with observation alone.
**ESPAC-3/NCIC-PA2**

**BACKGROUND:** Adjuvant 5-FU/LCV (ESPAC-1 trial) and GEM (CONKO-001 trial) shown improved survival for patients with resected pancreatic cancer compared to no chemotherapy.

**AIM:** To compare 5FU/LCV vs GEM

---

**Resected Pancreatic adenocarcinoma**

- **5 FU/LCV**
  - N= 330
  - 5 FU: 425mg/m2 IV bolus d1-d5
  - LCV: 20mg/m2 IV bolus
  - 4wkly *6 cycles

- **GEMCITABINE**
  - N= 330
  - G: 1000 mg/m2
  - D 1,8,15
  - 4 wkly *6 cycles

- **OBSERVATION**
  - N= 330

---

**Stratification:** 515 patients in each arm
- R0 (65%)
- R1 (35%)
- Grade (25% poorly diff)
- LN + (71%)

---

### RESULTS:

<table>
<thead>
<tr>
<th></th>
<th>5 FU/LCV</th>
<th>GEMCITABINE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TOXICITY:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Diarrhea</td>
<td>13%</td>
<td>2%</td>
</tr>
<tr>
<td>• Stomatitis</td>
<td>10%</td>
<td>0%</td>
</tr>
<tr>
<td>• T/t related hospitalizations</td>
<td>10%</td>
<td>3.5%</td>
</tr>
<tr>
<td>• Thrombocytopenia</td>
<td>less</td>
<td>More</td>
</tr>
<tr>
<td><strong>OVERALL SURVIVAL</strong></td>
<td>23 mths</td>
<td>23.6 mths</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>(p = 0.39)ns</em></td>
</tr>
</tbody>
</table>

Grade, stage, nodal status, resection margins are important prognostic factors

### CONCLUSION:

- **No difference between the two regimens:**
  - equal OS
  - Gemcitabine not superior to 5FU/LCV
- Safety, compliance, adverse events better with Gemcitabine
- No significant difference in the effect of treatment across subgroups according to R status
- Important study as there has been tendency to reject 5 FU/LCV in pancreatic cancer and now it is back on stage.

CHEMORADIATION TRIALS
IN ADJUVANT SETTINGS
IN RESECTABLE DISEASE
**Rationale:**

- To increase local control by radiation
- To decrease chances of metastasis by concurrent use of chemotherapy
- To increase overall survival
### ADJUVANT CHEMORADIATION STUDIES:

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Schedule</th>
<th>MS</th>
<th>2 YR (%)</th>
<th>5 YR (%)</th>
<th>LR (%)</th>
<th>DM (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GITSG (1985)</td>
<td>22</td>
<td>O</td>
<td>11</td>
<td>15</td>
<td>5</td>
<td>33</td>
<td>52 (LIVER) 40 (LIVER)</td>
</tr>
<tr>
<td></td>
<td>21</td>
<td>40 Split + 5 FU Bolus</td>
<td>20</td>
<td>42</td>
<td>19</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>GITSG (1987)</td>
<td>30</td>
<td>40 Split + 5 FU Bolus</td>
<td>18</td>
<td>43</td>
<td>-</td>
<td>55</td>
<td>45 (LIVER)</td>
</tr>
</tbody>
</table>

**CONCLUSION:** Adjuvant chemoradiation beneficial but

Dose of RT & 5 FU alone inadequate. T/t compliance poor

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Schedule</th>
<th>MS</th>
<th>2 YR (%)</th>
<th>5 YR (%)</th>
<th>LR (%)</th>
<th>DM (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EORTC (1999)</td>
<td>54</td>
<td>O</td>
<td>12.6</td>
<td>23</td>
<td>10</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>40 Split + 5 FU CI</td>
<td>17.1</td>
<td>37</td>
<td>20</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**CONCLUSION:** No benefit of chemoradiation in terms of survival

Critized being underpowered
<table>
<thead>
<tr>
<th>N</th>
<th>SCHEDULE</th>
<th>MS mo</th>
<th>2 YR (%)</th>
<th>5 YR (%)</th>
<th>LR (%)</th>
<th>DM (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>69</td>
<td>40 Sp + 5 FU Bo 40 Sp + 5 FU Bo 5 FU- LCV 5 FU Bo(425 mg/m²) - LCV(20 mg/m²) *5 days</td>
<td>16.9</td>
<td>30</td>
<td>8</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>73</td>
<td></td>
<td>13.9</td>
<td>40</td>
<td>21</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>72</td>
<td></td>
<td>19.9</td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>75</td>
<td></td>
<td>21.6 (P=.009)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**CONCLUSION:**

- Survival benefit with adjuvant 5 FU –LCV chemotherapy but not with chemoradiation.
- Critized for having no radiation quality control in chemoradiation arm
### Phase III Trials in Adjuvant Settings in Resectable Disease

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Schedule</th>
<th>MS mo</th>
<th>2 YR (%)</th>
<th>5 YR (%)</th>
<th>LR (%)</th>
<th>DM (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Whitting Gan et al</strong></td>
<td>33</td>
<td>O</td>
<td>15</td>
<td>35</td>
<td>-</td>
<td>85</td>
<td>23 (Liver) 23 (PS) 42 (Liver) 21 (PS)</td>
</tr>
<tr>
<td></td>
<td>19</td>
<td>45 - 48.6 + 5 FU Bolus</td>
<td>15</td>
<td>30</td>
<td>-</td>
<td>55</td>
<td></td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>45-48.6 + 5 FU CI</td>
<td>16</td>
<td>43</td>
<td>-</td>
<td>25</td>
<td>25 (Liver) 15 (PS)</td>
</tr>
<tr>
<td><strong>YeoH et al John Hopkins</strong></td>
<td>53</td>
<td>O</td>
<td>14</td>
<td>30</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>&gt;45 + 5 FU Bo / CI</td>
<td>20 (p=.003)</td>
<td>40</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Picozzi et al Virginia</strong></td>
<td>53</td>
<td>45-54 + 5 FU + Cisp +IFN</td>
<td>46</td>
<td>53</td>
<td>45</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**Conclusion:** Adjuvant CRT with adequate RT doses and 5 FU CI, have shown benefit in patients.
RTOG 9704

Resected pancreatic cancer (n =538)

**GEMCITABINE ARM**
- **SCHEDULE:**
  - G: 3 wks
  - 5 FU with RT (50.4Gy/28 #)
  - G: 12 wks

**5 FU ARM**
- **SCHEDULE:**
  - 5 FU infusion 3 wks
  - 5 FU with RT (50.4Gy/28 #)
  - 5 FU infusion 12 wks

**CONCLUSION:** For pancreatic head tumors ONLY;

- Median survival - 20.5 mths
  - 16.9 mths
- 3 yr survival - 31%
  - 22%

*The addition of gemcitabine to adjuvant 5 FU based CRT was associated with a survival benefit, although this improvement was not statistically significant.*
CONTRIBUTION OF ADVANCED RADIOTherapy TECHniques IN CHEMORADIATION
RT PLANNING

- **Indications**
  - +ve margins
  - Gross residual tumor
  - LN involvement
  - Perineural involvement

- **Goal**
  - Decrease local recurrence

- Should be given in even T1, T2 pts (high chance of local failure)

- **Treatment volume** – tumor bed, peripancreatic ln, PALN

- **Fields** – 4 field or 3D CRT

- **Dose** – 45 to 50 Gy in 1.8 Gy/
RT PLANNING

- **Information reqd**
  - Pre-op CT – location of tumor before resection
  - Post-op CT – persistent/ residual/ metastatic disease
  - Pre-op → barium/ ERCP/ angiography/ USG – findings
  - I/O findings
  - CT based planning
  - Renal contrast – delineation of kidneys
  - Oral contrast – stomach & duodenal C loop
  - Clips (extent of tumor)
**AP/PA fields**

- Sup. – T10/T11
- Inf. – L3/L4
- R. lat – 2-3cm beyond gross disease
  - Head – lat 1/3- medial 2/3 jn of right diaphragm
  - Body & tail – 2-3 cm right to vertebral border
- L. lat –
  - Head - 2-3 cm left to vertebral border
  - Body & tail - lat 1/3- medial 2/3 jn of left diaphragm
LATERAL fields

- Sup. & inf. – same
- Ant. – 1.5-2 cm beyond gross disease as defined on pre-op CT
- Post. – spinal cord is blocked, but at least 1.5-2 cm of ant. Portion of vertebral body is in the field

DOSE CONSTRAINTS

- Lateral field contribution limited to 15-18 Gy (liver & kidney)
- Spinal cord – 45 Gy
**DIFFICULTIES IN PLANNING**

- Radiation field include tumor/tumor bed, peri-pancreatic nodes, para-aortic node.
- This volume is difficult to encompass without involvement of renal parenchyma.
- So, during early period when two dimensional radiotherapy technique was used dose was limited due to large volume of normal tissue to be encompassed.
Stepwise Approach to Contouring

• Delineate ROI’s
  – Portal Vein (PV)
  – Pancreaticojejunostomy (PJ)
  – Celiac Artery (CA)
  – Superior Mesenteric Artery (SMA)
  – Aorta
  – Tumor Bed

• Expansion 1
  – 1.0 cm expansion on PV, PJ, CA, and SMA

• Expansion 2
  – 2.5 to 3.0 cm to the right, 1.0 cm to the left, 2.0 to 2.5 cm anteriorly, 0.2 cm posteriorly on Aorta

• CTV
  – Boolean addition (merging) of Expansion 1 and 2
  – Confirm that CTV encompasses tumor bed and contoured clips

• PTV
  – 0.5 cm expansion on CTV
CONTOURING
Sparing of Liver
Sparing of Kidney
Sparing of Liver & Kidney

IMRT Dose Distributions
3 DCRT planning
19 Gy to 50% of the Right kidney

15 Gy to 50% of the Left kidney
34 Gy to 1/3rd of the intestine

95% of the tumor volume is receiving at least 54 Gy
ADJUVANT CHEMORADIATION TRIALS WITH MODIFIED RADIATION TECHNIQUES
**ESPAC 4:**
- Comparing Gemcitabine (1000 mg/m² D1,8,15 4 Wkly *6 cycles) vs Gemcitabine + Capecitabine (800 mg/m² BD for 21 days 4 wkly)
- Capecitabine (Xeloda alone arm not been taken??)

**RTOG 0848:**
- Comparing Gemcitabine (1000 mg/m² D1,8,15 4 Wkly *6 cycles) vs Gemcitabine + Erlotinib (100 mg/day PO for 6 cycles)
  If no progression: then 2nd randomization to 5FU / Capecitabine based CRT (50.4 Gy/28#)
EORTC 40013:

- Comparing Gemcitabine 4 cycles vs Gemcitabine 2 cycles f/b Gemcitabine wkly concurrent with XRT 50.4 Gy/28#
- PH II results have shown that adjuvant gemcitabine based CRT is feasible, well-tolerated, and not deleterious. And 1st local recurrences are less in CRT arm

ACOSOG:

5-FU (200 mg/m²/d for 5 weeks), weekly cisplatin (30 mg/m²), and S/C interferon- (3 MIU s.c three times a week) combined with XRT 50 Gy f/b 2 cycles of CI 5-FU (200 mg/m²/d) on days 64 to 105 and 120 to 161.
CHEMORADIATION TRIALS
IN NEOADJUVANT SETTINGS
IN UNRESECTABLE DISEASE
**BORDERLINE RESECTABLE TUMORS**

- **Definition**
  - abutting 180 degrees or less (50% or less of the vessel circumference) of the superior mesenteric artery
  - encasing a short segment of the common hepatic artery,
  - causing segmental venous occlusion.

- **Goal** → sterilizing tumor at the periphery, where direct contact with arterial structures occurs → curative resection may be possible

- **Treatment strategy** → NA CRT f/b Sx
RATIONALE:

- Chemoradiation for unresectable pancreas was initiated after GITSG study demonstrated a survival advantage over external radiation alone.

- Chemoradiation is based upon the following premises:
  - Some patients may become resectable after chemoradiation which can improve their prognosis (downstaging)
  - The addition of chemotherapy adds to the local control by increasing the radiosensitivity of the tumor.
  - Chemotherapy in addition has the theoretical potential of eliminating systemic micrometastasis.
# NEOADJUVANT CHEMORADIATION STUDIES

<table>
<thead>
<tr>
<th>Series</th>
<th>N</th>
<th>Median Survival</th>
<th>Local Failure</th>
<th>1 yr Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mayo Clinic¹</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RT only (35 – 40 Gy)</td>
<td>32</td>
<td>6.3</td>
<td>NA</td>
<td>6%</td>
</tr>
<tr>
<td>RT + 5 FU</td>
<td>32</td>
<td>10.4</td>
<td>NA</td>
<td>22%</td>
</tr>
<tr>
<td><strong>GITSG²</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RT (60 Gy) alone</td>
<td>25</td>
<td>5.3</td>
<td>24</td>
<td>10%</td>
</tr>
<tr>
<td>RT (40 Gy) + 5FU</td>
<td>83</td>
<td>8.4</td>
<td>26</td>
<td>35%</td>
</tr>
<tr>
<td>RT (60 Gy) + 5FU</td>
<td>86</td>
<td>11.4</td>
<td>27</td>
<td>46%</td>
</tr>
<tr>
<td><strong>GITSG³</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RT (60 Gy) + 5FU</td>
<td>73</td>
<td>8.5</td>
<td>58</td>
<td>33%</td>
</tr>
<tr>
<td>RT (40 Gy) + Adria</td>
<td>70</td>
<td>7.6</td>
<td>51</td>
<td>27%</td>
</tr>
<tr>
<td><strong>GITSG⁴</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RT (54 Gy) + SMF</td>
<td>22</td>
<td>9.7</td>
<td>45</td>
<td>41%</td>
</tr>
<tr>
<td>SMF only</td>
<td>21</td>
<td>7.4</td>
<td>48</td>
<td>19%</td>
</tr>
<tr>
<td><strong>ECOG⁵</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RT(40 Gy) + 5FU</td>
<td>47</td>
<td>8.3</td>
<td>32</td>
<td>26%</td>
</tr>
<tr>
<td>5 FU</td>
<td>44</td>
<td>8.2</td>
<td>32</td>
<td>32%</td>
</tr>
</tbody>
</table>

# GEMCITABINE BASED CCT+RT. (2000)

<table>
<thead>
<tr>
<th>Series</th>
<th>N</th>
<th>Median Survival</th>
<th>Response</th>
<th>Toxicity (Gr III/IV)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Wilkowski et al</strong>¹</td>
<td>57</td>
<td>14.8</td>
<td>CR 12%</td>
<td>54.7% (Hemat)</td>
</tr>
<tr>
<td>RT (45 -50 Gy) Gem 300mg/m² + Cisplatin</td>
<td></td>
<td></td>
<td>PR 57.5%</td>
<td></td>
</tr>
<tr>
<td><strong>Crane et al</strong>²</td>
<td>53</td>
<td>11</td>
<td>NA</td>
<td>24.5% (GI)</td>
</tr>
<tr>
<td>RT 30 – 33 Gy + Gem 250 – 500 mg/m² weekly</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Brunner et al</strong>³</td>
<td>36</td>
<td>14</td>
<td>PR 28.6%</td>
<td>66.7% (Hemat)</td>
</tr>
<tr>
<td>RT 50.4 Gy + Gem 300 – 600 mg/m² weekly</td>
<td></td>
<td></td>
<td>SD 71.4%</td>
<td>19.4% (GI)</td>
</tr>
<tr>
<td><strong>DeLange et al</strong>⁴</td>
<td>24</td>
<td>10</td>
<td>CR 4.2%</td>
<td>37.5% (GI)</td>
</tr>
<tr>
<td>24Gy (3 x 8Gy) + Gem 300 mg/m²</td>
<td></td>
<td></td>
<td>PR 25%</td>
<td></td>
</tr>
</tbody>
</table>
• 215 patients with locally advanced pancreatic cancer

• NACRT: 52.2 Gy @1.8 Gy/# with concurrent gemcitabine (GEM) at a dose of 300 mg/m$^2$ weekly, followed by adjuvant GEM (1000 mg/m$^2$)

• RESULTS:
  --- Resection rate : 26%
    R0-resection : 39.2%
    R1-resections : 41.2%,
    R 2 resection: 11.8%
  --- Median OS : 22.1 vs 11.9 months in non-resected patients.
  --- In most cases the first site of disease progression was systemic with hepatic (52%) and peritoneal (36%) metastases

• CONCLUSION: Patients with locally advanced pancreatic cancer can undergo secondary resection after gemcitabine-based chemoradiation and has a relative long-term prognosis.
**I.M.R.T. TRIALS**

- Dose escalation
- Reduced dose to liver, kidneys, stomach & small intestine

**Landry et al (2002)**
- Compared normal organ sparing of IMRT vs 3DCRT.
- Dose prescribed was 61.2 Gy to the gross tumor volume (GTV) and 45 Gy to the clinical treatment volume (CTV)
- Significant reduction in dose to small intestine.

- 66 Gy to the gross tumor and 46 Gy to the subclinical disease.
- 14/25 (56%) patients were alive with median follow-up of 20 months (range 3-40 months)
- Actuarial 1-year survival was 26%
- Four (16%) pts → **grade 3** or greater GI toxicity.
- A **single** patient exhibited grade 4 gastrointestinal bleeding immediately after completing the treatment course
OUR EXPERIENCE & RESULTS

Original Article

Role of neoadjuvant concurrent chemoradiation in locally advanced unresectable pancreatic cancer: a feasibility study at tertiary care centre

Rakesh Kapoor, Divya Khosla, Rajesh Gupta, Amit Bahl, Arvind K. Shukla, Suresh C. Sharma
Department of Radiotherapy and Oncology, Regional Cancer Centre, \(^1\)Department of Surgery, Postgraduate Institute of Medical Education and Research, Chandigarh, Haryana and Punjab, India

NEOADJUVANT CHEMORADIOTHERAPY

• N= 15, Locally Advanced Pancreatic cancers
• Neoadjuvant treatment –

**Oral Capecitabine** 1000 mg/m2 daily in three divided doses, 5 days per week, coinciding with radiation therapy administration. Therapy continued for the entire duration of radiation therapy.

**Radiotherapy** : 30 Gy/10 # / 2 weeks
RESULTS : NACRT

- 4 patients underwent surgery
- 5 patients had partial response but were unresectable
- 2 patients had stable disease
- 3 patients had progressive disease
- Toxicity : Grade 1 -2
- Median survival : 15 months for resected & 8.5 months for unresected
- 2 year actuarial overall survival  34.6 months
RESULTS: PERIAMPULLARY CANCERS

Retrospective analysis (2007-2009)
N=40
M:F – 33:7
Whipples surgery followed by post operative radiotherapy 45Gy/25#/5 weeks
Six cycles of adjuvant GEMOX chemotherapy
RESULTS: PERIAMPULLARY CANCERS

- At end of treatment
  - Complete response - 70%
  - Partial Response - 7.5%
  - Progressive Disease - 15%
  - Defaulted for treatment – 2.5%
  - Dead - 5%

At 2 year follow up DFS was 65%
CONCLUSIONS

- Addition of chemotherapy to radiation adds to the survival by 5 – 8 months in adjuvant setting.
- Chemoradiation makes tumors resectable in 10% - 33% of the patients in neoadj settings.
- In the palliative setting chemoradiation improves pain relief by 30% - 40%.
- Either RT / CCT doses needs to be modified when given concomitantly.
- Patient selection is of paramount importance in order to achieve desired results.
- Therefore, the realistic goal of chemoradiation for most patients is to delay local recurrence than to prevent it.