Multimodal treatment of mCRC

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Consultant Hepatobiliary Surgeon
Survival for patients with liver limited metastatic colorectal cancer is improving.
Impact of a multi-modal approach: some background facts
Background fact 1: Pathological response to chemotherapy predicts survival

Blazer et al, JCO 2008
Background fact 2: Response to chemotherapy in 1st line setting predicts resectability of liver disease

*Jones et al, EJC 2013*
**Background fact 3:**
Chemotherapy response rates in Phase II/III trials in 1st line mCRC

- **FOLFIRI + Erbitux**
  - 57% vs 40%

- **FOLFOXIRI**
  - 60% vs 34%

- **FOLFOX + DEBIRI**
  - Ox-CT + Erbitux
  - 59% vs 50%

- **IFL + bev**
  - 43% vs 35%

- **FOLFIRI**
  - 40–56%

- **FOLFOX**
  - 45–54%

- **FLOX**
  - 46%

- **Capecitabine**
  - 19–25%

- **5FU**
  - 15%

- **IFL**
  - 31–39%

- **KRAS wt**

**References:**
Background fact 4: Best chance of conversion is in first line of treatment

Highest conversion rates achieved in first line:

- 15%-40% converted after 1\textsuperscript{st} line
- 5% converted after 2\textsuperscript{nd} line
- <1% converted after 3\textsuperscript{rd} line
- <0.1% converted after 4\textsuperscript{th} line

LiverMet Survey
4313 patients

However, preoperative chemotherapy brings problems

<table>
<thead>
<tr>
<th></th>
<th>FOLFOX &amp; Surgery</th>
<th>Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-operative complications</td>
<td>40/159 (25%)</td>
<td>27/170 (16%)</td>
</tr>
<tr>
<td>30 day post-operative mortality</td>
<td>1/159 (1%)</td>
<td>2/170 (1%)</td>
</tr>
</tbody>
</table>

Nordlinger et al, Lancet Oncol 2013
Systemic chemotherapy causes hepatotoxicity

- Steatohepatitis (Irinotecan)
- SOS (Oxaliplatin)

Normal
Number of cycles of chemotherapy affects complications

Background fact 5:
Liver surgery works

115,000 colorectal cancer patients first diagnosed 1998–2004

Morris, BJS 2010
Background fact 6: Patients converted to resection enjoy long-term survival benefit.

![Graph showing survival rates for resectability](LiverMetSurvey 2013)
Defining resectability of liver metastases
Stage IV case
Stage IV case
Stage IV case
Variation in resection rates across UK

Network

Percentage of patients receiving a liver resection within three years of resection of their colorectal primary

Missing patients?

Liverpool

Variation between specialist and non-specialist assessment

Jones et al BJS 2012
Relative risks for prognostic factors assessed and post-surgical survival

So all are RELATIVE contraindications, NONE are absolute contraindications

54 prospective studies of >100 hepatectomies for CRLM 1999-2010

<table>
<thead>
<tr>
<th>Prognostic Factor</th>
<th>Number of studies</th>
<th>mRR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade (poorly differentiated primary)</td>
<td>7</td>
<td>1.88 (1.32-2.67)</td>
</tr>
<tr>
<td>Node-positive primary</td>
<td>20</td>
<td>1.59 (1.46-1.73)</td>
</tr>
<tr>
<td>CEA level &gt; 100</td>
<td>9</td>
<td>1.92 (1.14-3.22)</td>
</tr>
<tr>
<td>&gt;1 liver metastases</td>
<td>36</td>
<td>1.57 (1.39-1.78)</td>
</tr>
<tr>
<td>Liver tumour &gt;3 cm in diameter</td>
<td>20</td>
<td>1.52 (1.28-1.80)</td>
</tr>
<tr>
<td>Extra-hepatic disease</td>
<td>13</td>
<td>1.88 (1.50-2.37)</td>
</tr>
<tr>
<td>Positive resection margin</td>
<td>20</td>
<td>2.02 (1.65-2.48)</td>
</tr>
</tbody>
</table>

mRR, meta relative risk; CEA, carcinoembryonic antigen

List of quality statements

**Statement 1.** People with suspected colorectal cancer without major comorbidity are offered diagnostic colonoscopy.

**Statement 2.** People with colon cancer are offered contrast-enhanced computed tomography (CT) of the chest, abdomen and pelvis to determine the stage of the disease.

**Statement 3.** People with rectal cancer are offered contrast-enhanced computed tomography (CT) of the chest, abdomen and pelvis to determine the stage of the disease, and pelvic magnetic resonance imaging (MRI) to assess the risk of local recurrence.

**Statement 4.** People with rectal cancer are offered a preoperative treatment strategy appropriate to their risk of local disease recurrence.

**Statement 5.** People with locally excised, pathologically confirmed stage I colorectal cancer whose tumour had involved resection margins (less than 1 mm) are offered further surgery or active monitoring.

**Statement 6.** People with a contrast-enhanced computed tomography (CT) of the chest, abdomen and pelvis suggesting liver metastatic colorectal cancer have their scans reviewed by the hepatobiliary multidisciplinary team to decide whether further imaging is needed to confirm suitability for surgery.

**Statement 7.** People with locally advanced or metastatic colorectal cancer whose disease progresses after first-line systemic anticancer therapy are offered second-line systemic anticancer therapy if they are able to tolerate it.

**Statement 8.** People free from disease after treatment for colorectal cancer are offered regular
List of quality statements

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# Principals of liver surgery

What you take out | What you leave behind
---|---
2000
- Metachronous presentation
- Confined to 1 lobe
- Less than 4 metastases
- No metastases larger than 5 cm
- 1 cm negative resection margin
- 10% patients eligible for resection

2016
- Adequate liver remnant
- Confined to the liver
- Resectable with adequate margins
- Preservation of functional liver anatomy

20% patients eligible for resection at presentation
Parenchymal sparing surgery – planning for the future

Right Hepatectomy

Multiple metastasectomy

Left Hepatectomy
Anatomical Versus Nonanatomical Resection of Colorectal Liver Metastases: Is There a Difference in Surgical and Oncological Outcome?

Zarina S. Lalmahomed · Ninos Ayez · Anne E. M. van der Pool · Joanne Verheij · Jan N. M. Ijzermans · Cornelia Verhoeef

No difference in DFS or OS between AR and NAR.
Which liver operation?
Two stage hepatectomy

- **Two stage hepatectomy:** local resection of metastases in future remnant liver (FRL)
- **Portal vein embolisation/ligation**
- **Four weeks later:** Right hepatectomy
Increasing resectability:
Portal vein embolisation

4 weeks later

? Radioembolization

4 weeks later
Survival following two stage hepatectomy

But 25% of patients never complete 2nd stage!
Associated Liver Partition and Portal vein ligation for Staged hepatectomy

- First presented in 2011 (accidental finding)
- Indicated in patients with very low future liver remnant volumes
- Published world experience is very limited <250 cases
ALPPS – rapid increase in FLR volume

- Large multicentre French Series
- N = 62 (in 9 centres)

Very rapid increase in FLR volume

Truant S, et al. EJSO 2015 Epub
ALPPS – morbidity and mortality?

- Large multicentre French Series
- N = 62 (in 9 centres)

**Table 2**

<table>
<thead>
<tr>
<th></th>
<th>Cumulative data</th>
<th>Stage1 (N = 62)</th>
<th>Stage2 (N = 59)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intraperative data</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of resected segment</td>
<td>5.2 ± 0.9</td>
<td>0.9 ± 0.8</td>
<td>4.3 ± 0.7</td>
</tr>
<tr>
<td>Resection of tumours located on the future RL</td>
<td>41 (66.1%)</td>
<td>41 (66.1%)</td>
<td>0</td>
</tr>
<tr>
<td>Operative time (min)</td>
<td>492 ± 163.4</td>
<td>302.5 ± 92.5</td>
<td>185.8 ± 108.4</td>
</tr>
<tr>
<td>Venous reconstruction</td>
<td>14 (22.6%)</td>
<td>14 (22.6%)</td>
<td>0</td>
</tr>
<tr>
<td>Hepaticojejunostomy</td>
<td>6 (9.7%)</td>
<td>3 (4.8%)</td>
<td>3 (5.1%)</td>
</tr>
<tr>
<td>Digestive procedure</td>
<td>6 (9.7%)</td>
<td>2 (3.2%)</td>
<td>4 (6.8%)</td>
</tr>
<tr>
<td>Operative time (min)</td>
<td>492 ± 163.4</td>
<td>302.5 ± 92.5</td>
<td>185.8 ± 108.4</td>
</tr>
<tr>
<td>Blood loss (ml)</td>
<td>795.1 ± 642</td>
<td>494 ± 418.8</td>
<td>304.5 ± 431.9</td>
</tr>
<tr>
<td>Intraoperative transfusion</td>
<td>18 (29%)</td>
<td>6 (9.7%)</td>
<td>12 (20.3%)</td>
</tr>
<tr>
<td><strong>Postoperative course</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-month mortality</td>
<td>8 (12.9%)</td>
<td>1 (1.6%)</td>
<td>7 (11.9%)</td>
</tr>
<tr>
<td>3-month morbidity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>50 (80.6%)</td>
<td>36 (58%)</td>
<td>42 (71.2%)</td>
</tr>
<tr>
<td>Major (grades 3–4)</td>
<td>25 (40.3%)</td>
<td>14 (22.6%)</td>
<td>19 (32.2%)</td>
</tr>
<tr>
<td><strong>Type of complication</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ascites and/or pleural effusion</td>
<td>22 (35.5%)</td>
<td>8 (12.9%)</td>
<td>18 (30.5%)</td>
</tr>
<tr>
<td>Wound healing impairment</td>
<td>11 (17.7%)</td>
<td>2 (3.2%)</td>
<td>10 (16.9%)</td>
</tr>
<tr>
<td>Biliary fistula</td>
<td>25 (40.3%)</td>
<td>19 (30.6%)</td>
<td>16 (27.1%)</td>
</tr>
<tr>
<td>Sepsis/infection</td>
<td>17 (27.4%)</td>
<td>11 (17.7%)</td>
<td>11 (18.6%)</td>
</tr>
<tr>
<td>Portal vein thrombosis</td>
<td>2 (3.2%)</td>
<td>1 (1.6%)</td>
<td>1 (1.7%)</td>
</tr>
<tr>
<td>Acute kidney failure</td>
<td>12 (19.3%)</td>
<td>11 (17.7%)</td>
<td>6 (10.2%)</td>
</tr>
<tr>
<td>Cardiac/pulmonary complication (except for pleural effusion)</td>
<td>13 (21%)</td>
<td>11 (17.7%)</td>
<td>6 (10.2%)</td>
</tr>
<tr>
<td>Hepatic encephalopathy</td>
<td>4 (6.5%)</td>
<td>0</td>
<td>4 (6.8%)</td>
</tr>
<tr>
<td>Acute PHLF (50–50 criteria)</td>
<td>16 (25.8%)</td>
<td>3 (4.8%)</td>
<td>15 (25.4%)</td>
</tr>
<tr>
<td>Maximal Clavien grade</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>8 (12.9%)</td>
<td>4 (6.5%)</td>
<td>9 (15.3%)</td>
</tr>
<tr>
<td>II</td>
<td>17 (27.4%)</td>
<td>18 (29%)</td>
<td>14 (23.7%)</td>
</tr>
<tr>
<td>III</td>
<td>15 (24.2%)</td>
<td>9 (14.5%)</td>
<td>11 (18.6%)</td>
</tr>
<tr>
<td>IV</td>
<td>10 (16.1%)</td>
<td>5 (8%)</td>
<td>8 (13.6%)</td>
</tr>
</tbody>
</table>

Continuous variables are expressed as the mean ± standard deviation; Results are given by patient for categorical data. RL: remnant liver; PHLF: post-hepatectomy liver failure.

Truant S, et al. EJSO 2015 Epub
Associated Liver Partition and Portal vein ligation for Staged hepatectomy

- First presented in 2011 (accidental finding)
- Indicated in patients with very low future liver remnant volumes
- Published world experience is very limited <250 cases
- Concerns over high morbidity & mortality
- No published long term survival outcomes
- RCT planned in mCRC of two-stage resection vs ALPPS
Extended resection criteria

Feasible to resect up to 75% of the adult liver based on anatomical principles
Advanced resection techniques

- **Inflow** – Tumours involving bile ducts; bilateral portal vein and hepatic arterial involvement

- **Outflow** – Tumours involving hepato-caval confluence

- **Multivisceral resections**
Advanced resection techniques

• **Inflow** – Tumours involving bile ducts; bilateral portal vein and hepatic arterial involvement

• **Outflow** – Tumours involving hepato-caval confluence

• **Multivisceral resections**
Advanced resection techniques
Advanced resection techniques
Segments II/III ducts

Reconstruction of PV
Advanced resection techniques
Advanced resection techniques

- **Inflow** – Tumours involving bile ducts; bilateral portal vein and hepatic arterial involvement

- **Outflow** – Tumours involving hepato-caval

- **Multivisceral resections**
Liver and IVC resection – avoiding V-V bypass

Less than 30° IVC involvement – Primary repair

Cases 1, 3, 4, 6, 9, 10, 12, 14-24, 26
Liver and IVC resection – avoiding V-V bypass

Up to 270° IVC involvement – Bovine pericardial patch

Cases 2, 5, 7 & 8
Caval replacement with Bovine pericardial patch
Liver and IVC resection

Greater than $270^0$ IVC involvement – Dacron tube graft

Case 11, 13 & 25
Advanced resection techniques

• **Inflow** – Tumours involving bile ducts; bilateral portal vein and hepatic arterial involvement

• **Outflow** – Tumours involving hepato-caval confluence

• **Multivisceral resections**
Multi-visceral resections: Synchronous disease

Synchronous disease

Colonic tumour/liver operable – synchronous resection

Liver disease – operable or borderline?

Site of primary – rectum vs colon? Is the primary symptomatic?

Colonic tumour operable/liver borderline operable – synchronous resection, but consider de-functioning

Rectal tumour/liver operable – synchronous resection

Rectal tumour/liver borderline operable – chemotherapy; radiotherapy then staged “liver first” resection
What factors to consider when planning surgery

Prognostic factors
- Size of tumour
- Vascular invasion
- Nodal status

Patient co-morbidity/unit outcomes
- Medical risk of resection in YOUR unit
- Remaining functional liver tissue
- Invaded structures/segments

Resectability
Prognostic factors

- Size of tumour
- Vascular invasion
- Nodal status

Resectability

- Remaining functional liver tissue
- Invaded structures/segments
Loco-regional treatments
Loco-regional treatments

- Hepatic infusion chemotherapy
- Stereotactic ablative body radiotherapy (SABR)
- Chemo-embolisation
- Radio-embolisation
- Ablation
- Nanoknife
- Chemo-saturation (DELCATH)
Hepatic infusion chemotherapy (HIA)

- Infusion of chemotherapy into hepatic artery via pump
- Meta-analysis of 10 RCT’s including 1277 patients showed no improvement in OS compared to chemo (HR 0.9; P=0.24)
- On going work examining combination HIA with systemic chemotherapy – no published RCT’s
- Cochran review showed no benefit in the adjuvant setting

Mocellin S, JCO 2007
Nelson R, Freels S. Cochrane Database Syst Rev 2006;CD003770
Stereotactic ablative body radiotherapy (SABR)

- Ablative treatment of tumour using precisely targeted external beam radiotherapy
- Indicated in patients with ECOG 0-1; maintained liver function and non-tumour liver volume >700mls
<table>
<thead>
<tr>
<th>Author, year, prospective/retrospective</th>
<th>No. of patients/No. of liver metastases</th>
<th>Organ of origin</th>
<th>RT dose</th>
<th>Complications</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blomgren 1995 (65), retrospective</td>
<td>14</td>
<td>1 CRC, 1 anal canal, 1 renal, 1 ovarian</td>
<td>7.7-45 Gy/1-4 fx</td>
<td>Hemorrhagic gastritis (2)</td>
<td>50% response</td>
</tr>
<tr>
<td>Katz et al 2007 retrospective (66)</td>
<td>69/174</td>
<td>20 CRC, 16 breast, 9 pancreas, 5 lung</td>
<td>30-55 Gy/5-15 fx</td>
<td>No grade 3 or 4 toxicities</td>
<td>Infield local control at 10 months: 76%; at 20 months: 57%</td>
</tr>
<tr>
<td>Rusthoven 2009 (67), prospective</td>
<td>47/63</td>
<td>15 CRC, 10 lung, 4 breast, 3 ovarian</td>
<td>36-60 Gy/3 fx</td>
<td>No grade 4 or 5 toxicities</td>
<td>MS 20.5 months</td>
</tr>
<tr>
<td>IY LC 95% Lee 2009 (63), prospective</td>
<td>686</td>
<td>CRC 40 Breast Gastric</td>
<td>27.7-60 Gy/6 fx</td>
<td>gastritis, nausea</td>
<td>1Y local control: 58-95% S 17.6 months</td>
</tr>
<tr>
<td>Chang 2011 (68) retrospective, mult-institutional</td>
<td>65</td>
<td>CRC 102</td>
<td>22-60 Gy</td>
<td>No grade 4 toxicities</td>
<td>1Y LC: 62%</td>
</tr>
<tr>
<td>Mendez Romero 2008 (69) prospective</td>
<td>17/34</td>
<td>37 CRC, 2 lung, 4 breast, 1 carcinoid</td>
<td>5 Gy 5 or 30 Gy × 10 3% duodenal ulcers</td>
<td>Local control at 1 year: 94% and for HCC: 82%</td>
<td></td>
</tr>
<tr>
<td>Goodman 2010 (70), prospective</td>
<td>26/32</td>
<td>6 CRC, 5 IHCC, 2 HCC, 27 other primary lung and other organs also included</td>
<td>18-30 Gy/1 fx</td>
<td>2/31 with duodenal ulcers 2/31</td>
<td>Median survival: 28.6 months</td>
</tr>
<tr>
<td>Hoyer 2006 (71), prospective</td>
<td>64/44</td>
<td>27 other primary lung and other organs also included</td>
<td>45 Gy/3 fractions</td>
<td>1 hepatic failure, 1 colonic perforation</td>
<td>NR for liver metastases</td>
</tr>
</tbody>
</table>

**Stereotactic ablative body radiotherapy (SABR)**

*Nosher et al J Gastrointest Oncol. 2015*
DEBIRI-TACE
*(Drug Eluting Beads with Irinotecan – Transarterial Chemoembolization)*

- PVA microspheres
- Loaded with Irinotecan
- Intra-arterial delivery
- Reduced first pass metabolism
- Reduced off-target side-effects
Patient histopathology

Treated metastasis

Untreated metastasis
Salvage 3\textsuperscript{rd} line DEBIRI for liver dominant colorectal cancer

Failed first line chemotherapy n=74

DEBIRI
Median 2 treatments

FOLFIRI
Median 8 cycles

<table>
<thead>
<tr>
<th></th>
<th>DEBIRI</th>
<th>FOLFIRI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response rate (mRECIST)</td>
<td>69%</td>
<td>20%</td>
<td>NA</td>
</tr>
<tr>
<td>2 year survival</td>
<td>56%</td>
<td>32%</td>
<td>0.006</td>
</tr>
<tr>
<td>Toxicity (GI/neutropenia)</td>
<td>7%</td>
<td>35%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Fiorentini et al, Anticancer Research 2012
Aliberti et al  82 patients treated in 2\textsuperscript{nd} line - 75\% response rate by mRECIST
Median survival 25 months

Martin et al  55 patients treated in first line - 71 \% response by RESICT
Median survival 28.6 months

Ongoing registry of chemo-embolisation sponsored by CIRSE
Pathological Response Rates after Treatment

![Minor response](image1)

![Major response](image2)

![Complete response](image3)

<table>
<thead>
<tr>
<th>Pathological response</th>
<th>% lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>2</td>
</tr>
<tr>
<td>Minor</td>
<td>22</td>
</tr>
<tr>
<td>Major</td>
<td>59</td>
</tr>
<tr>
<td>Complete</td>
<td>17</td>
</tr>
</tbody>
</table>

DEBIRI-TACE
Pathological Response Rates after Treatment

- Minor response
- Major response
- Complete response

Blazer et al JCO 2008
Segmental vs Lobar DEBIRI-TACE
Hepatic activation of irinotecan predicts tumour response in patients with colorectal liver metastases treated with DEBIRI: exploratory findings from a phase II study

R. P. Jones · P. Sutton · R. M. D. Greensmith · A. Santoyo-Castelazo · D. F. Carr · R. Jenkins · C. Rowe · J. Hamlett · B. K. Park · M. Terlizzo · E. O’Grady · P. Ghaneh · S. W. Fenwick · H. Z. Malik · G. J. Poston · N. R. Kitteringham

Normal liver tissue needed to activate irinotecan for DEBIRI to be effective

Jones et al, Cancer Chemotherapy Pharmacology 2013
Significant improvement in response rates in Phase II/III trials in 1st line mCRC

- FOLFOX-BEV + DEBIRI
  - FOLFIRI + Erbitux
    - 57% vs 40%
  - FOLFOXIRI
    - 60% vs 34%
  - FOLFOX + Ox-CT + Erbitux
    - 59% vs 50%

- IFL + bev
  - 43% vs 35%

- KRAS wt

- Capecitabine
  - 19–25%

- Fluoropyrimidine
  - 5FU
    - 15%

- Irinotecan
  - IFL
    - 31–39%
  - FOLFIRI
    - 40–56%

- Oxaliplatin
  - FLOX
    - 46%
  - FOLFOX
    - 45–54%

References:
Martin et al ASCO 2013
Radio-embolisation (SIRT)

- PVA or glass microspheres with Yttrium-90
- Intra-arterial delivery
- 3 small RCT’s and 19 case series with mixed results
- Current NICE recommendation supports use in third line palliative treatment
- Results from FOXFIRE global awaited – provisional results from SIRFLOX show improvement in liver but not overall PFS
Ablation

- **RFA** – established with more evidence especially in HCC
- **Microwave** – faster than RFA, larger case series being published
- **HIFU** – novel, potentially less toxic. NICE (IPG 118) in prostate cancer but limited evidence in other tumours
Survival after liver ablation: CLOCC (EORTC 40004)

Overall Survival

Median (95% CI) (Months)
- Systemic: 40.54 (27.50, 47.67)
- RF+Systemic: 45.60 (30.32, 67.75)

8-year OS (95% CI)
- Systemic: 8.9% (3.3, 18.1)
- RF+Systemic: 35.9% (23.8, 48.2)

HR = 0.58, 95% CI (0.38-0.88), P = 0.010 (Log-rank test)

T Reus ASCO 2015
Combining surgery with ablation?
Resection with ablation: the RAID study

- 288 pts. from 4 centres (Bordeaux, Liverpool, Aarhus, MSKCC)
- Mean size largest ablatable lesions 1.5cm
- Median tumour number 5
- Median follow-up 3.17 years

THIS PROCEDURE IS SAFE:
In Liverpool mortality after liver surgery for mCRC is 0.01%

*Evrard et al. ASCO 2013*
Five year overall survival:
Two stage v RAID

**LiverMetSurvey**
Two Stage  versus One Stage

**RAID**
Irreversible Electroporation (IRE)

- Uses electrical pulses to irreversibly destroy cancer cells
- Can be used to deal with tumours involving vessels
- Technician dependent
- Literature contains small case series
Case

37 female

Stage 4 presentation, Ras mutated

T3 NO Sigmoid Ca

Post 6 cycles FOLFOX and bevacizumab.
Irreversible Electroporation

Post IRE CT

Left Hemi-hepatectomy with multiple R side metastasectomies
A paradigm shift in the management of these patients
Novel technologies being incorporated into improving outcomes
Management sequencing tailored to the individual patient

Which when you include the type of systemic therapy regimen, patient fit or not fit for, or declines treatment, gives you 2.4 million permutations of treatment strategy variables!
The impact of multi-modal management

Liverpool

2010 chemotherapy
Median survival >30 months
5 year survival 15%

2010 overall (Surgery + Chemo)
Median survival >40 months
5 year survival 30%

>50%?