The future of cancer therapy

CONCEPT OVERVIEW

• The definition of resectability of colorectal liver metastasis (CRLM) has broadened because of better systemic therapy and diagnostic modalities.
• Different surgical techniques are now possible depending on:
  - Future remnant liver volume
  - Possibility to achieve R0 resection
• However, prospective and high quality data are lacking to determine the impact on survival of these techniques.

CURRENT TREATMENT FOR COLORECTAL LIVER METASTASIS

<table>
<thead>
<tr>
<th>Upfront resectable</th>
<th>Borderline resectable</th>
<th>Unresectable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goal: Definitive cure</td>
<td>Goal: Increase resectability</td>
<td>Goal: Palliative; attempt to increase resectability</td>
</tr>
<tr>
<td>Options: Palliative therapy +/- Neoadjuvant therapy</td>
<td>Options: Conversion therapy then Surgery or Combined Ablation &amp; Resection (CARE)</td>
<td>Options: Palliative therapy +/- Surgery or CARE</td>
</tr>
</tbody>
</table>

KEY QUESTIONS TO BE ANSWERED

1. Which surgical treatment strategy leads to best over-all survival?
2. Do multiple complex surgeries improve patient outcomes?
3. What is the impact of different treatment combinations to over-all survival?
4. Can we benchmark quality of liver metastasis surgery?
5. Can innovative research methodologies generate high quality data in surgical research?

IMPACT OF CLIMB

• CLIMB will benchmark the quality liver metastasis surgery in Europe through high quality, real-life data about different treatment strategies with complex CRLM.
• This is the first project between EORTC and the European Society of Surgical Oncology (ESSO) that will initiate more prospective surgical clinical research within and beyond Europe.

OBJECTIVES

• To benchmark quality of liver metastasis surgery in Europe by documenting morbidity and mortality rates from different surgical strategies for unresectable, borderline resectable or initially unresectable CRLM.
• To determine long-term outcomes of patients who undergo different treatment strategies (different combinations of systemic treatment vs. multiple surgeries).

STUDY ENDPOINTS

• Rate of Post-operative complications graded according to the Clavien and Dindo Classification of Surgical complications at 30 and 90 days
  * Sample size: at least 100 post-operative patients must be registered in the study within 1 year
  * Duration of follow-up: until 2 years from initial registration
• Over-all survival, progression free survival and recurrence rate based on the different treatment strategies (chemo and surgery)
• Proposal for Quality parameters for complex liver metastasis surgery

DESCRIPTION OF PATIENT POPULATION

• Histologically proven colorectal adenocarcinoma with liver metastasis.
• With unresectable, borderline or initially unresectable liver metastasis assessed by a multi-disciplinary tumor board (MDT) before surgery.
• With a possibility to undergo a surgical procedure after systemic treatment.
• Age > 18 years
• Absence of other active malignancy and other exclusion criteria
• Written informed consent according to ICH/GCP regulations.

TRIAL DESIGN AND INTEGRATED QA PROGRAM

• Prospective observational clinical research
• Patients are registered only after MDT.
• MDT must include at least a liver surgeon, oncologist and radiologist.
• Data to be collected include:
  * MDT evaluation and plan
  * Surgery, post-operative complications
  * Pathology evaluation and Follow-up
• Site monitoring will be performed for quality assurance.

16 PARTICIPATING CENTERS FOR SPECIALIZED LIVER SURGERY

<table>
<thead>
<tr>
<th>Country</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>Rudolf Foundation Salzburg University Hospital</td>
</tr>
<tr>
<td>Belgium</td>
<td>Ghent University Hospital</td>
</tr>
<tr>
<td>Denmark</td>
<td>Aarhus University Hospital</td>
</tr>
<tr>
<td>France</td>
<td>Institute Bergonié Centre Leon Berard</td>
</tr>
<tr>
<td>Germany</td>
<td>Universitätsklinikum Carl Gustav Carus</td>
</tr>
<tr>
<td>Italy</td>
<td>Policlinico Universitario Gemelli Instituto Europeo di Oncologia</td>
</tr>
<tr>
<td>Norway</td>
<td>Oslo University Hospital</td>
</tr>
<tr>
<td>Spain</td>
<td>Hospital Universitario de Fuenlabrada</td>
</tr>
<tr>
<td>Sweden</td>
<td>Danderyd / Karolinska University Hospital</td>
</tr>
<tr>
<td>Switzerland</td>
<td>Hôpitaux Universitaires de Genève</td>
</tr>
<tr>
<td>The Netherlands</td>
<td>The Netherlands Cancer Institute Leiden University Medical Center</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>Aintree University Hospital</td>
</tr>
</tbody>
</table>

STUDY STATUS

• CLIMB is now open in 6 centers and is actively recruiting patients.
• All sites are expected to be open by second semester of 2015.
• High quality MDT have been confirmed among the participating sites through initial site visits.

CORRESPONDENCE

Study coordinator: Serge Evrard
Co-coordinator: Graeme Poston
Clinical research fellow: Carmela Caballero
Contact us at 1409@eortc.be