EORTC 1409-GITCG: CLIMB
A Prospective Colorectal Liver Metastasis Database with an Integrated Quality Assurance Program

A pilot project of EORTC and ESSO
Concept Overview

- The definition of resectability of colorectal liver metastasis (CRLM) has broadened because of better systemic therapy and diagnostic modalities.

- Different treatment combinations are now possible depending on the:
  - 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 different techniques.
Overview of Treatment for Colorectal Liver metastasis

**Upfront resectable**
- **Goal**: Definitive Cure
- **Options**: Surgery +/- Neoadjuvant therapy

**Borderline resectable**
- **Goal**: Increase resectability
- **Options**: Conversion therapy then Surgery or Combined Ablation and Resection (CARE)

**Unresectable**
- **Goal**: Palliative; attempt to increase resectability
- **Options**: Palliative therapy +/- Surgery or CARE
Current surgical techniques for borderline and unresectable tumors

Resection

Ablation
A. Normal anatomy

B. Occlusion of right portal vein
   - Atrophy
   - Hypertrophy

C. Multiple liver tumors

D. Occlusion of right portal vein with tumorectomies in left hemiliver

E. Hypertrophy of the left hemiliver and tumor shrinkage after chemotherapy

F. Right hemihepatectomy

European Society of Surgical Oncology
Key Questions to be answered in CLIMB

1. Which surgical treatment strategy offers less complications and 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 we use observational data to improve surgical research?
Study objectives

Primary objectives

- Evaluate complications from different surgical strategies for complex (unresectable/borderline/initially unresectable) CRLM
- Identify quality parameters to evaluate liver metastasis surgery

Secondary objectives

- Evaluate the long-term outcomes of patients treated with different strategies
- Determine the impact of participating in CLIMB in terms of improvement in complication rates over time
Study endpoints

- **Primary endpoints:**
  1. Rate of Post-operative complications graded according to the Clavien and Dindo Classification of Surgical complications at 30 and 90 days
  2. Proposal for Quality parameters for complex liver metastasis surgery

- **Secondary endpoints:**
  1. Trend in complication rates between first 50 surgeries and second 50 surgeries
  2. Long-term outcomes of all patients in the study
     - Over-all survival
     - Progression-free survival
     - Recurrence rates
Patient population of CLIMB

• Complex liver metastasis from colorectal cancer
  – Difficult to resect upfront but operable)
    • Borderline resectable
    • Unresectable
    • Initially unresectable
    • Recurrent liver mets
    • With limited extra-hepatic metastasis

• Sample size: at least 100 post-operative patients

• Duration of study: 2 years accrual; 2 years follow-up
Inclusion Criteria

- 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 $\geq 18$ years
- Absence of other active malignancy and other exclusion criteria
- Written informed consent according to ICH/GCP regulations
<table>
<thead>
<tr>
<th>Lesions are easily <strong>resectable</strong> up front</th>
<th>Is Conversion Chemotherapy needed?</th>
<th>Eligibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>No</td>
<td>No</td>
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</table>

| Lesions are **unresectable** and a palliative intent is clear (no possible resection even after chemo)  
  - multiple/extensive extra-hepatic mets  
  - Performance status not safe for surgery | Yes (palliative intent) | No |

| Lesions are **borderline** resectable but resection will be difficult or dangerous | Yes (preferred) | Yes |

| Lesions are **unresectable** but a curative option is possible after at least a partial response to conversion chemotherapy | Yes | Yes if the lesions become resectable (both the Liver mets and the extra hepatic lesions) |

| Recurrent lesions  
  - Patient had previous surgeries already  
  - Patient had previous adjuvant treatment already | Possible | Yes |
<table>
<thead>
<tr>
<th>For surgical teams using both resection and ablation</th>
<th>Is Conversion Chemotherapy needed?</th>
<th>Eligibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesions are <strong>resectable</strong> (by resection only) up front</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Lesions are <strong>non-operable</strong> by combined resection and ablation (CARe) and a palliative intent is clear</td>
<td>Yes (palliative intent)</td>
<td>No</td>
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<tr>
<td>Lesions are <strong>operable</strong> by CARe</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Lesions are <strong>borderline resectable</strong> for a CARe procedure</td>
<td>Yes (preferred)</td>
<td>Yes</td>
</tr>
<tr>
<td>Lesions are <strong>non-operable</strong> but a curative intent is possible if the lesions respond to conversion therapy</td>
<td>Yes</td>
<td>Yes (if the both the liver and extra-hepatic lesions become operable)</td>
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<tr>
<td>Recurrent lesions</td>
<td>Possible</td>
<td>Yes</td>
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Study design

Prospective observational cohort study

MDT before surgery

Prospective enrollment

Complications must be documented
Overview of Data Collection

- Diagnosis of unresectable/borderline/initially unresectable CRLM
- CLIMB Registration
- MDT Presentation & treatment planning
- Treatment implemented (Chemo/Surgery +/- ablation)
- Re-evaluation of treatment response/evaluation of complications of surgery/long-term follow-up
16 Participating Centers for Specialized for Liver Surgery

<table>
<thead>
<tr>
<th>Country</th>
<th>Institution</th>
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<tbody>
<tr>
<td>Austria</td>
<td>Rudolf Foundation Salzburg University Hospital</td>
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<tr>
<td>Belgium</td>
<td>Ghent University Hospital</td>
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<td>Denmark</td>
<td>Aarhus University Hospital</td>
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<td>France</td>
<td>Institute Bergonié Centre Leon Berard</td>
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<td>Germany</td>
<td>Universitaetsklinikum Carl Gustav Carus</td>
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<td>Italy</td>
<td>Policlinico Universitario Gemeilli Instituto Europeo di Oncologica</td>
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<td>Norway</td>
<td>Oslo University Hospital</td>
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<td>Spain</td>
<td>Hospital Universitario de Fuenlabrada</td>
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<td>Sweden</td>
<td>Danderyd/Karolinska University Hospital</td>
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<td>The Netherlands</td>
<td>The Netherlands Cancer Institute Leiden University Medical Center</td>
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<tr>
<td>UK</td>
<td>Aintree University Hospital</td>
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Study Status

- CLIMB is now open and is actively recruiting patients.
- All sites are expected to be open by the second semester of 2015.
- High quality MDT have been confirmed among the participating sites through initial site visits.
Expected Impact of CLIMB to Quality Assurance in Surgery

- CLIMB will benchmark the quality liver metastasis surgery using prospective, “real-life” but high quality clinical data.
- CLIMB is the pilot project of EORTC and the European Society of Surgical Oncology (ESSO).
  - This will initiate more prospective surgical clinical research within and beyond Europe.
  - A framework for quality assurance in surgery will be developed.
Correspondence

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Contact us at 1409@eortc.be
The EORTC-ESSO Partnership for Quality Assurance in Surgery