“Connecting towards impact”

Prospective Dutch CRC cohort
– Providing an infrastructure for scientific research –

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Colorectal cancer

- Most common cause of cancer in The Netherlands with almost 16,000 newly diagnosed patients/yr
50% of patients will never have a recurrence of disease, irrespective of chemotherapy.

20% of patients are being cured because of chemotherapy.

30% of patients will always get a recurrence of disease, irrespective of chemotherapy.

- This means that 80% of patients are exposed to the toxicity and costs of adjuvant chemotherapy without any effect on survival.
- The problem is that we cannot predict who these patients are!
Metastatic colorectal cancer

Systemic treatment in 2005

• Fluoropyrimidines, oxaliplatin, irinotecan

• Response rates:
  - 20-30% partial/complete response
  - 30-40% stable disease
  - 20-30% progressive disease

• No subgroups

• Again, no predictive markers were available
Metastatic colorectal cancer

*Progress and complexity 2016*

**Molecular subgroups**
- Potentially resectable
- Unresectable
- Primary resected
- Primary in situ
- Liver only
- Lung only
- Rectal cancer
- Colon cancer

**Clinical subgroups**
- Fluoropyrimidines
- Irinotecan
- Oxaliplatin
- Bevacizumab
- Anti-EGFR
- Regorafenib
- Afiblercept
- TAS102
- Immunotherapy

**Drugs**
- Monotherapy, combination, triple, quadriple
- Maintenance, observation
- Local treatment: radioembolisation/RFA/RT

**Different treatment strategies**
This raises the obvious question whether the results of clinical trials are applicable to daily practice?
Prospective Dutch CRC cohort

*Validation of study results, is this relevant?*

Outcomes strongly argue against the use of cancer treatments in other patient categories than included in the original trials in which these treatments were investigated.
First conclusions

• Only 5-10% of the patients are included in clinical trials, results from studies are not applicable to general population.

• Colorectal cancer consists of many different subgroups.

• Prospective randomized trials are not feasible for all these different subgroups.

• There is an urgent need for individualized treatment!
Prospective large cohorts

- Clinical factors
- Tumour characteristics
- Information / genes
- Blood
- Imaging
- Patient

PROSPECTIEF LANDELIJK CRC COHORT
PLCRC is a cohort study to facilitate scientific research.

Prospective Data Collection Initiative on Colorectal Cancer
PLCRC
Patient population: Colorectal cancer stage I, II, III, IV

Observational: Collection of data

Interventional: Cohort Multiple Randomized Controlled trial (cmRCT)

Clinical data
Tissue
Blood
PROMs

OPEN ACCESS of all these data

Verkooijen et al. NTVG 2013
www.plcrc.nl
Connecting

Profiles

Prospectief Landelijk CRC cohort
Prospective Dutch CRC cohort

*Impact – current situation*

- To compare:
  - Most successful classical phase 3 study to date: 400 patients per year in 80 Dutch hospitals
  - PLCRC: last year 600 patients in 13 hospitals
  - If we extrapolate this to participation of 80% Dutch hospitals we will have almost 4,000 patients per year in PLCRC
Prospective Dutch CRC cohort

*Impact of outcomes*

- Improve outcome and quality of care of colorectal cancer by:
  - Validation of study results in daily clinical practice
  - Collecting patient reported outcomes
  - Better inside in safety
- Infrastructure to facilitate scientific research:
  - Effect of lifestyle and diet on outcome
  - Cost-effectiveness
  - Quality of life
  - Compare interventions (cmRCT design)
  - Innovation
  - Prognostic and predictive markers: individualized treatment
Prospective Dutch CRC cohort

**Impact of outcomes**

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Prospective Dutch CRC cohort
*Impact – validation of trial results*

- Radioembolisation in salvage setting
- Reimbursed
- Reporting results in daily clinical practice to ZiNL

Adapted from:
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Prospective Dutch CRC cohort

Impact – aims

• Improve outcome and quality of care of colorectal cancer by:
  • Validation of study results
  • Patient reported outcomes
  • Safety
• Infrastructure to facilitate scientific research
  • Quality of life/lifestyle/dietary intake
  • Cost-effectiveness
  • Compare interventions
  • Innovation
  • **Prognostic and predictive markers: individualized treatment**
Prospective Dutch CRC cohort

**Impact – Prognostic and predictive markers: individualized treatment through MEDOCC**

- MEDOCC: molecular early detection of colorectal cancer

- **Aim**: determine prognostic value of ctDNA in stage II colon cancer patients

- **Population**: 850 stage II colon cancer patients
Stage II-III colon cancer

- PLCRC as perfect platform
- Approval of ethical board for collecting blood samples with a maximum of ten times per year during regular blood withdrawals

Follow-up every 6-12 months at surgical department
Prospective Dutch CRC cohort

*Impact – Prognostic and predictive markers: individualized treatment through CONNECTION*

- Improving clinical management of colon cancer through CONNECTION, a nation-wide Colon Cancer Registry and Stratification effort

**PLCRC as perfect infrastructure**

- One of the objectives: the identification and use of molecular subgroups to predict outcome with and without adjuvant chemotherapy in early stage colon cancer
  - Need of registry + biobank

*Guinney et al. Nature 2015*
Prospective Dutch CRC cohort

*Impact – Prognostic and predictive markers: individualized treatment*

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Providing an infrastructure for scientific research

• Connecting
  – multidisciplinary teams
  – basic/translational/clinical researchers
  – Regional/academic hospitals
  – public and private partners

Towards

• Impact
  – Better outcome and quality of life of colorectal cancer patients