# Activiteitenverslag 2023-2024

**CONTENTS**



## COLOFON


BOARD DCCG:

Prof.dr. J.H.W. de Wilt, Surgical Oncology, chairman
Prof.dr. M. Koopman, Medical Oncology, secretary
Dr. K. Horsthuis, treasurer, Radiology
Dr. M. Noe, Pathology
Dr. M. Berbee, Radiotherapy
Dr. S. Bajwa-ten Broeke, Clinical Genetics
Dr. L.M.G. Moons, Gastroenterologist & Hepatologist
Dr. G.R. Vink, Program Manager PLCRC
Dr. J.W.A. Burger, working group chairman
Prof.dr. C. Verhoef, working group chairman
Prof.dr. H.M.W. Verheul, working group chairman
Dr. R.J.A. Fijneman, working group chairman
Dr. J.W.B. de Groot, delegate DICA

# Voorwoord

Beste leden van de DCCG,

In het begin van het jaar 2024 zijn er weer twee grote trials, de COLLISION trial en de STAR-TREC fase III trial, gestopt omdat de inclusie is bereikt. Het is goed om te constateren dat dergelijke grote trials die 'practice changing' zullen zijn, worden geïnitieerd door Principal Investigators uit Nederlandse centra. Zo zullen op de ASCO van dit jaar ook de resultaten van de ORCHESTRA trial worden gepresenteerd, waar veel belangstelling voor is en mogelijk het beleid voor colorectale metastatische ziekte gaat veranderen. Allemaal voorbeelden van een succesvolle en goede samenwerking tussen de Nederlandse centra. Maar ook de gedegen voorbereiding van de studies tijdens besprekingen in de werkgroepen en plenair van de DCCG zullen hierbij zeker ook een rol hebben gespeeld. Het is mooi om te zien dat we als klein land internationaal steeds relevante studies verrichten.

In mei is er weer een DCCG wetenschapsmiddag, waar hopelijk de voorbereidingen weer worden getroffen voor internationaal belangrijke studies. Daarnaast zijn er verschillende congressen gepland voor het komend jaar, zoals het 3e T1 CRC congres in Utrecht en zal er vanuit de DCCG voor het eerst op 14 en 15 november een masterclass-jaarcongres worden georganiseerd in Rotterdam. Op 14 november kunnen multidisciplinaire teams uit het land zich aanmelden voor een dag bijscholing in het Erasmus MC. De dag erna zal op 15 november een DCCG dag worden georganiseerd waarbij door elke werkgroep een update zal worden gegeven van de huidige ontwikkelingen en studies. De gedachte is dat dit jaarlijks terugkerende dagen worden waarbij iedere keer een andere groep de twee dagen organiseert.

Hopelijk zal dit een succesvol congres worden waarbij we multidisciplinair als colorectaal onderzoekers elkaar kunnen ontmoeten en stimuleren voor nieuwe studies, zodat we de zorg voor patiënten steeds weer beter kunnen maken.

Met vriendelijke groet,

Hans de Wilt

# Aankondiging DCCG bijeenkomsten 2024

DCCG wetenschapsmiddag 2024

Maandag 13 mei 2024, locatie Vredenburg19 te Utrecht, van 12.30-17.00 uur. Opgeven kan via schnater.dccg@gmail.com.

Maandag 4 november 2024, locatie Vredenburg19 te Utrecht, van 12.30-17.00 uur.

5D congres

Het 6e multidisciplinair Gastro-intestinaal Oncologie Congres wordt gehouden op 18 en 19 juni 2024 in Heerlickheijd van Ermelo

Vergaderingen T1 CRC werkgroep

11 juni (fysiek)
24 september (digitaal)
10 december (fysiek)

3e T1 CRC Symposium Zorg op Maat

5 september 2024,
08.30-18.00 uur
Mereveld, Utrecht


Masterclass DCCG

14 en 15 november Rotterdam, meer info volgt nog.

## Corporate Support

DCCG corporate activities are funded with corporate sponsorship. The corporate sponsors provide general support and have no influence on activities or policy of the DCCG.

DCCG is pleased to acknowledge the corporate support of:

Silver corporate sponsor

## Secretariat

Monique Schnater
Zuiderkruis 160
3902 XD Veenendaal, The Netherlands
Tel: 06-22435712
E: info@dccg.nl/ schnater.dccg@gmail.com
W: www.dccg.nl

This newsletter can be downloaded from the DCCG website.

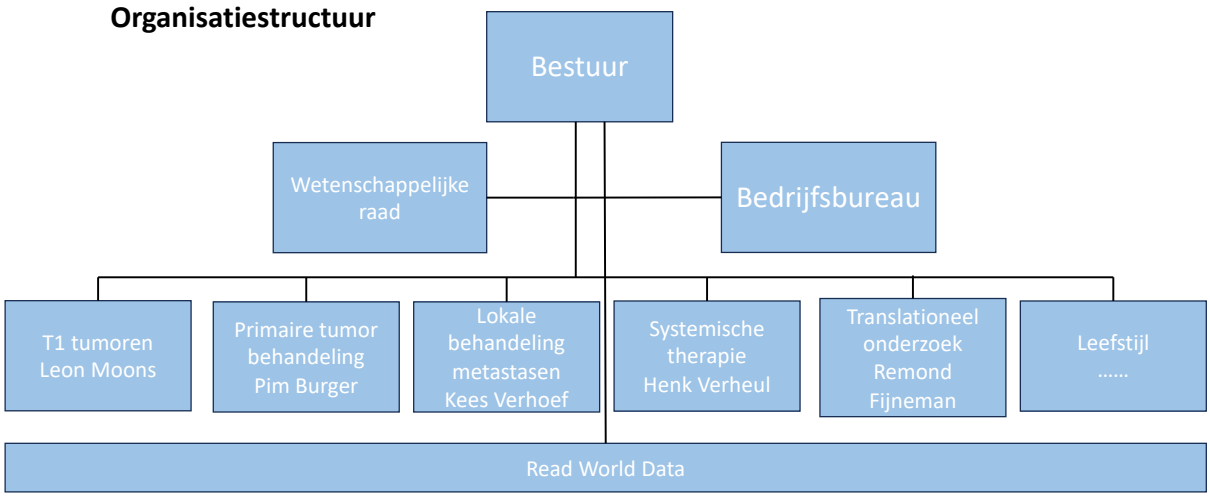
# Algemeen

## Doelstelling en organisatie

Afgeleid van de Statuten:
"*Het bevorderen in nationaal verband van klinisch wetenschappelijk onderzoek om daardoor de kwaliteit van de diagnostiek en de behandeling van het colorectaal carcinoom, te verbeteren*".

Ter verbreding van de statuten scharen we ook het *dunne darm carcinoom en anus carcinoom* tot ons aandachtsveld.

Structuur van de Stichting DCCG in organogram:




Aan de doelstellingen van de DCCG wordt op 2 manieren invulling gegeven:
- het initiëren, organiseren en uitvoeren van klinische studies en
- het organiseren van kennis verrijkende multidisciplinaire bijeenkomsten

**Soorten multidisciplinaire bijeenkomsten**
- Tweejaarlijks 5D congres
- 2x per jaar DCCG-participanten vergadering/wetenschapsdag

**Soorten studies:**
DCCG kent twee soorten studies:
- sponsored studies
- endorsed studies

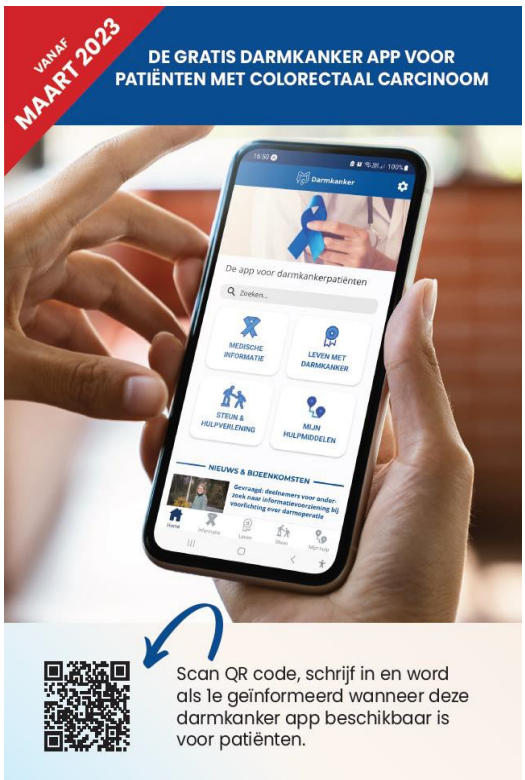
De sponsored studies zijn studies die DCCG heeft geïnitieerd en waarvoor zij sponsorverantwoordelijkheden draagt. Dit betekent dat zij volledig verantwoordelijk is voor het uitvoeren van een dergelijke studie inclusief de financiële verantwoordelijkheid.
Bij de endorsed studies ligt de verantwoordelijkheid voor de uitvoer van de studie bij de organisatie die verrichter is (en dus niet bij de DCCG).

De endorsed studies zijn studies waarbij het initiatief door een onderzoeker/principal investigator in een ziekenhuis genomen is en waarbij de DCCG geen verrichter is. Vanwege samenhang en kennisdeling wordt aan deze studies wel de DCCG-naam verbonden doordat het DCCG-netwerk en publiciteit faciliteiten kunnen worden benut.

Op de wetenschapsdagen wordt een plenaire terugkoppeling gegeven van de nieuwe en lopende studies.

Het beleid van DCCG is gericht op het ondersteunen (endorsen) van klinische studies. Voor dit endorsement kan de DCCG een bijdrage vragen aan de verrichter van de studie. Dit betreft een bijdrage aan de DCCG-infrastructuur.

De DCCG is verrichter van de cohortstudie “Prospectief Landelijk CRC cohort (PLCRC). De governance tussen DCCG en PLCRC is vastgelegd in een governance document. Positieve adviezen van de wetenschappelijke raad van PLCRC voor substudies worden ter accordering voorgelegd aan het DCCG-bestuur. Het projectvoorstel wordt hiertoe ter aanvullende informatie meegestuurd.




De DCCG werkt samen met partners om patiënten te ondersteunen in hun behandeltraject van patiënten.

# Overzicht activiteiten en resultaten van de werkgroepen en studies

## Translationeel

**Using organoids to model metastasis and radio-resistance in colorectal cancer**

Patient-derived organoids (PDOs) are being used in many research areas. In (colorectal) cancer research perhaps the most well-known application is their use in developing personalized medicine strategies. In 2 new papers we show that organoids can also be used to study spontaneous distant metastasis formation in mice. Orthotopic implantation of PDOs into the mouse caecum yields experimental primary tumors that spontaneously metastasize to distant sites. In Kucukkose et al[1] we show that metastatic organotropism (i.e. the pattern of spontaneous distant metastasis formation) is a characteristic that is inherent to each specific PDO.

We employed PDO metastasis models with liver-only, lung-only and liver-and-lung metastases to study liver versus lung metastasis formation The conclusion of this study is that fundamentally distinct processes drive lung and liver metastasis formation, with different evolutionary bottlenecks, seeding entities, anatomical routing, and sub-clonal composition. Lung metastases originated from tumor cell clusters entering the lymphatic vasculature in the primary tumor, while liver metastases originate form single tumor cells entering the blood vasculature. This study highlights the need for developing organ site-specific metastasis prediction, prevention, and treatment strategies.

In a second study by Wijler et al[2], we employed mouse colorectal cancer tumor-derived organoids to study primary metastatic spread (i.e. from the caecum) versus secondary spread (i.e. from the liver). This study showed that secondary spread to distant sites (lungs, peritoneal cavity) was significantly more efficient from liver tumors than from caecum tumors and this was associated with the formation of hotspots of macrophage-surrounded vitronectin-positive blood vessels, specifically in liver tumors. Thus, 'onward spread' from liver metastases plays a major role in multi-organ metastasis, potentially through liver-specific vascular hotspots.

In a third study by Andel et al[3], we employed we employed organoids derived from rectal cancer patients to study radiation resistance in vitro. By comparing single-cell whole-genome karyotypes between unirradiated and irradiated PDOs we show that irradiation causes three patterns of sub-clonal evolution: (1) persistence (2) extinction, and (3) expansion. Organoids in which sub-clonal shifts occurred (i.e., expansion or extinction) became more resistant to re-irradiation. Resistance was associated with reduced chromosomal instability, an association that was confirmed in 529 human cancer cell lines. These data suggest that resistance to irradiation is inherently present and associated with reduced chromosomal instability.

**References**


1. Kucukkose, E., Laoukili, J., Gorelick, A.N., Degner, S., Lacle, M.M., van den Bent, L., Peters, N.A., Verheem, A., Hung, W.T., Frenkel, N.C., et al. (2023). Lymphatic Invasion of Plakoglobin-Dependent Tumor Cell Clusters Drives Formation of Polyclonal Lung Metastases in Colon Cancer. Gastroenterology *165*, 429-444 e415. 10.1053/j.gastro.2023.02.047.

2. Wijler, L.A., Viergever, B.J., Strating, E., van Schelven, S.J., Poghosyan, S., Frenkel, N.C., Te Rietmole, H., Verheem, A., Raats, D.A.E., Borel Rinkes, I.H.M., et al. (2024). Onward Spread from Liver Metastases Is a Major Cause of Multi-Organ Metastasis in a Mouse Model of Metastatic Colon Cancer. Cancers (Basel) *16*. 10.3390/cancers16051073.

3. Andel, D., Viergever, B.J., Peters, N.A., Elisabeth Raats, D.A., Schenning-van Schelven, S.J., Willem Intven, M.P., Zandvliet, M., Hagendoorn, J., Max Borel Rinkes, I.H., and Kranenburg, O. (2024). Pre-existing subclones determine radioresistance in rectal cancer organoids. Cell reports *43*, 113735. 10.1016/j.celrep.2024.113735.

# CAIRO7

**Radioembolization with 166Ho-microspheres in elderly and/or fragile patients with previously untreated unresectable liver-only metastases of colorectal cancer, a randomised phase 2 study.**

**Planned total accrual:** 220 patients

**Primary endpoint:** PFS

**Secondary endpoints:** safety, overall survival, quality of life, cost-effectiveness

**Principal investigators**

Prof. dr. Kees Punt, Julius Center, UMC Utrecht

Prof.dr. Marnix Lam, Imaging Division, UMC Utrecht

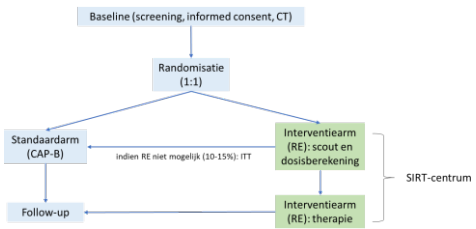
Dr. G.M. Bol, Medical Oncology, UMC Utrecht

**Monitoring and data management**

Trial office Imaging Division UMC Utrecht

E: CAIRO7@umcutrecht.nl

**Study design**




**Study Objective:**

To demonstrate at least comparable efficacy of radioembolization in terms of PFS compared to standard systemic treatment.

**Main inclusion criterium:**

Elderly/fragile patients with previously untreated unresectable metastatic colorectal cancer limited to the liver, who according to their treating medical oncologist are candidates for systemic treatment with capecitabine plus anti-VEGF antibody.

**Study logistics:**

Radioembolization will be performed in one of the participating radioembolization centers. Patients randomized to radioembolization outside these centers will be referred to the nearest radioembolization center. Follow-up of patients randomized to radioembolization and treatment/follow-up of patients randomized to the control arm will be performed in local participating centers.

**Participating centers:**

Radioembolization centers: UMC Utrecht, NKI/AvL, LUMC, UMCG, ErasmusMC, RadboudUMC, MaastrichtUMC, Isala Klinieken.

A total of 42 hospitals have already agreed to participate. For participation please contact CAIRO7@umcutrecht.nl

**Financial support:** The CAIRO7 study is supported by Zorginstituut Nederland, program Veelbelovende Zorg, project 80-86200-98-20014

**Current status**

The first patients have been randomized and started treatment.

The following centers are open for inclusion:

- Albert Schweitzer Zkh (Dordrecht)
- Alrijne Zorggroep (Leiden)
- Amphia Ziekenhuis (Breda)
- Amsterdam UMC
- Antonius Zorggroep (Sneek)
- Bravis Ziekenhuis (Roosendaal)
- Catharina Ziekenhuis (Eindhoven)
- Franciscus Gasthuis & Vlietland (Schiedam)
- Gelre Ziekenhuizen (Apeldoorn)
- Groene Hart Ziekenhuis (Gouda)
- Haaglanden MC (Den Haag)
- Ikazia Ziekenhuis (Rotterdam)
- Laurentius Ziekenhuis (Roermond)
- LUMC (Leiden)
- Maxima MC (Veldhoven)
- MC Leeuwarden
- Meander MC (Amersfoort)
- NKI-AvL (Amsterdam)
- Nij Smellinghe Ziekenhuis (Drachten)
- NoordWest Ziekenhuisgroep (Alkmaar)
- Radboud UMC (Nijmegen)
- Reinier de Graaf Ziekenhuis (Delft)
- Rijnstate Ziekenhuis (Arnhem)
- RIVAS Beatrix Ziekenhuis (Gorinchem)
- Rode Kruis Ziekenhuis (Beverwijk)
- Spaarne Gasthuis (Hoofddorp)
- St. Antonius Ziekenhuis (Nieuwegein)
- Tergooi MC (Hilversum)
- Tjongerschans Ziekenhuis (Heerenveen)
- VieCuri MC (Limburg)
- Wilhelmina Ziekenhuis (Assen)
- UMC Utrecht
- Zaans MC (Zaandam)
- ZorgSaam Ziekenhuis (Zeeuws-Vlaanderen)

# COLLISION

**Colorectal liver metastases: surgery versus thermal ablation – a phase III, single-blind, multicenter, non-inferiority, prospective randomized controlled trial**

*"To prove non-inferiority of thermal ablation compared to surgical resection in patients with at least one resectable and ablatable colorectal liver metastasis (CRLM) of ≤3cm and no extrahepatic disease."*

**Randomized patients:** 300

**Planned patient accrual:** 618

**Primary endpoint:** overall survival.

**Principal investigators**
Martijn Meijerink, MD, PhD, dept. Interventional Radiology, Amsterdam UMC, location VUmc
Petrousjka van den Tol, MD, PhD, dept. Surgical Oncology, Amsterdam UMC, location VUmc

**Study coordinators**
Robbert Puijk, MD, dept. Interventional Radiology, Amsterdam UMC, location VUmc
E: r.puijk@amsterdamumc.nl

Susan van der Lei, MD, dept. Interventional Radiology, Amsterdam UMC, location VUmc
E: s.vanderlei@amsterdamumc.nl
P: 020 444 3047

**Data management**
Clinical Research Bureau Amsterdam UMC, location VUmc. Ires Joore and Janine Stolwijk.

**Website:** *www.dccg.nl/trial/collision*

**Most important inclusion criteria**

- At least ≥1 *resectable* and *ablatable* CRLM (≤3cm) (= target lesion);
- Maximum of 10 CRLM;
- Additional resections for unablatable CRLM and/or ablations for unresectable CRLM are allowed.

**Most important exclusion criteria**

- Extrahepatic disease;
- Insufficient future liver remnant;
- Prior focal liver treatment.

# Study update

The COLLISION study was prematurely terminated for having proven predetermined stopping rules following a second preplanned interim analysis.

We would like to thank all participating centers for their contribution.

**Participating centers:**

The following fourteen centers are currently recruiting patients:
Amsterdam UMC, location VUmc;
Maastricht UMC, Maastricht;
Ziekenhuis Gelderse Vallei, Ede;
Leids UMC, Leiden;
Radboud UMC, Nijmegen.
MC Leeuwarden, Leeuwarden;
Isala, Zwolle;
Maxima MC, Veldhoven;
Deventer Ziekenhuis;
UMC Groningen;
Ospedale San Raffaele, Milan, Italy
Jeroen Bosch Ziekenhuis, 's Hertogenbosch
UMC Utrecht.
Universitair Ziekenhuis Antwerpen

# COLLISION RELAPSE

**Recurrent colorectal liver metastases: upfront local treatment versus neoadjuvant systemic therapy followed by local treatment - a phase III prospective randomized controlled trial**

*"To demonstrate superiority of neoadjuvant systemic therapy followed by repeat local treatment as compared to upfront repeat local treatment in patients with at least one locally treatable recurrent CRLM in the absence of extrahepatic disease*

**Planned total accrual:** 360 patients

**Start of study:** April 24, 2023

**Principal investigators**

Dr. Kathelijn S. Versteeg, dept. of Medical Oncology, AUMC

Prof. dr. Martijn R. Meijerink, dept. of Interventional Radiology, AUMC

Dr. Rutger-Jan Swijnenburg, dept. of Surgery, AUMC

**Study coordinators**

Madelon Dijkstra BSc, PhD Candidate dept. of Interventional Radiology, AUMC

E: m.dijkstra3@amsterdamumc.nl

Drs. Hannah H. Schulz, PhD Candidate dept. of Interventional Radiology, AUMC

E: h.h.schulz@amsterdamumc.nl

Drs. Babette I. Kuiper, PhD Candidate dept. of Surgery, AUMC

E: b.i.kuiper@amsterdamumc.nl

**Primary endpoint:** overall survival

**Secondary endpoints:** distant and local progression-free survival, morbidity, mortality and toxicity, length of hospital stay, quality of life and cost-effectiveness.

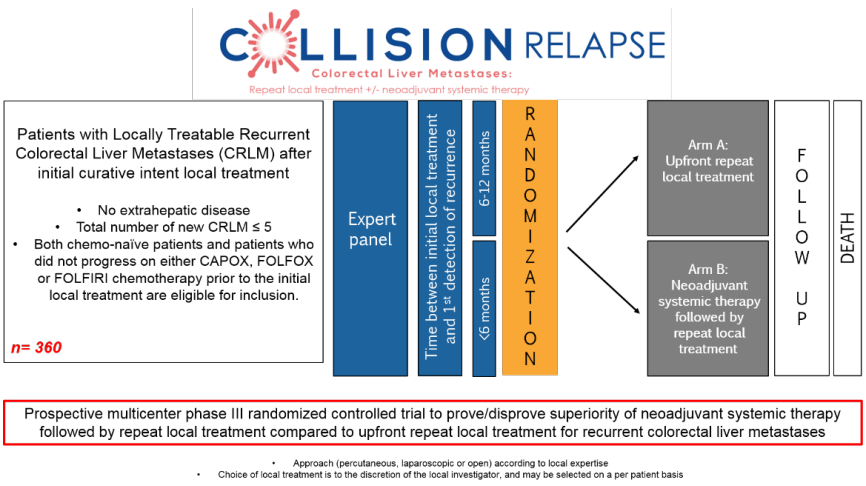
**Main inclusion criteria**

Patients with a maximum of 5 recurrent new locally treatable CRLM within 12 months after initial curative intent local treatment of CRLM, no extrahepatic disease, and a good performance status (ECOG 0-2) are considered eligible. Both chemo-naïve patients and patients who did not progress on either oxaliplatin or irinotecan chemotherapy prior to the initial local treatment are eligible for inclusion.

# Current status

Currently open for inclusion.
Participating centers: AUMC, NWZ, LUMC, Maxima Medisch Centrum.

We would like to thank all participating centers in advance. Anyone who is interested in COLLISION RELAPSE or who would like to participate can contact the study coordinators



# COLLISION XL

**Unresectable colorectal liver metastases: stereotactic body radiotherapy vs microwave ablation – a phase II, multicenter, randomized controlled trial for CRLM 3-5 cm**

*"To compare the efficacy of MWA to the efficacy of SBRT in patients with at least 1 CRLM 3-5 cm suitable for both MWA as SBRT."*

**Randomized patients:** 14

**Planned patient accrual:** 68

**Primary endpoint:** local tumour progression free survival at 1 year

**Principal investigators**
Martijn Meijerink, MD, PhD, dept. Interventional Radiology, Amsterdam UMC, location VUmc

Peter van Rossum, MD, PhD, dept. Radiation Oncology, Amsterdam UMC, location VUmc

**Study coordinator**

Susan van der Lei, MD, dept. Interventional Radiology, Amsterdam UMC, location VUmc

E:s.vanderlei@amsterdamumc.nl

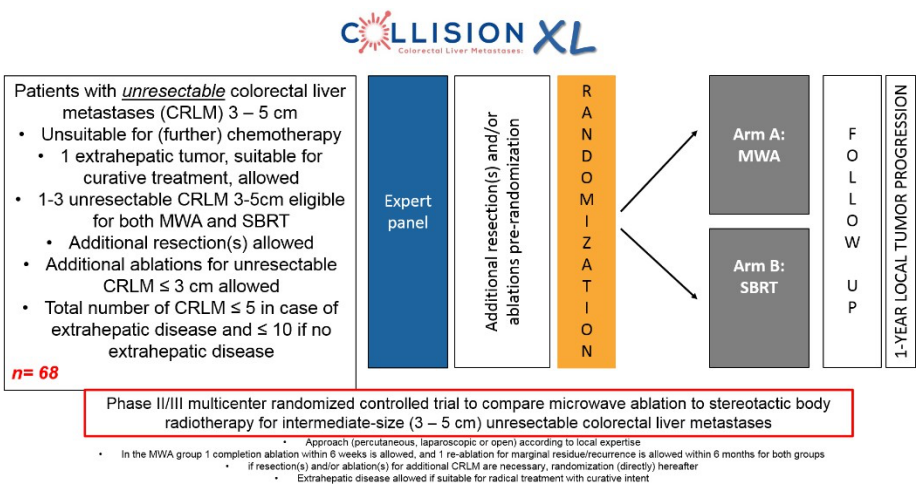
P: 020 444 3047

**Participating centers:**

- Amsterdam UMC, location VUmc;
- Ziekenhuis Gelderse Vallei, Ede;
- UMCG, Groningen
- Medisch Centrum Leeuwarden

**Current status:**

COLLISION-XL is open for inclusion. New inclusions are very welcome. We would like to thank all participating centers! Anyone who is interested in COLLISION-XL or who would like to participate can contact the study coordinators.



# DOSAGE

A multicenter randomized phase III trial of upfront DOSe-reduced Chemotherapy for Advanced Colorectal Cancer in Older patients

**Planned total accrual**: 587 patients

**Planned start of study**: Summer 2024

**Study Objective:** To investigate whether upfront dose-reduced chemotherapy is non-inferior to full-dose chemotherapy in older patients (≥70 years) with metastatic colorectal cancer, stratified for expected risk of toxicity.

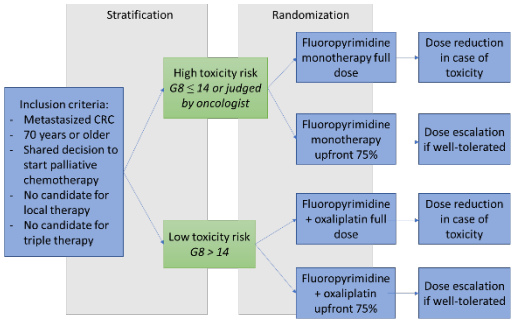
**Primary endpoint**: PFS

**Secondary endpoints:** Grade ≥3 toxicity, number of treatment cycles, dose reductions during treatment, cumulative received dose, hospital admissions, QoL and physical functioning, OS and cost-effectiveness

**Most important inclusion criteria:** Patients aged 70 years or older with metastatic colorectal cancer, who are candidates for systemic treatment according to their treating medical oncologist.

**Most important exclusion criteria:** Prior palliative chemotherapy or prior adjuvant chemotherapy in the year before inclusion, DPD deficiency, candidates for triple therapy or local therapy.

**Study design:** Before treatment initiation, patients undergo geriatric screening by a Geriatric-8 (G8) and are classified as "low risk of toxicity" or "high risk of toxicity". Patients classified as "low risk" will be 1:1 randomized between combination treatment in full-dose or with an upfront 25% reduction. Patients classified as "high risk" will be 1:1 randomized between monotherapy with a fluoropyrimidine in full-dose or upfront 25% reduction




**Participating centers:**
A total of 36 Dutch hospitals have already agreed to participate. For participation, please contact DOSAGE@lumc.nl

**Principal investigator:**
Prof.dr. Johanneke Portielje, Department of Medical Oncology, LUMC
E: DOSAGE@lumc.nl

**Monitoring and data management:**
Clinical Research Center, LUMC

**Study coordinator:**
drs. Joosje Baltussen, Department of Medical Oncology, LUMC
E: J.C.Baltussen@lumc.nl
E: DOSAGE@lumc.nl

**Current status:**
The DOSAGE study has received external funding and we have submitted the study to the CTR for approval. It is expected that the first patient can be included in June 2024.

# IMARI

**IMARI***: Multi-Interventional program for prevention and early Management of Anastomotic leakage after total mesorectal excision in Rectal cancer patients, the IMARI-trial*

All relevant information can also be found on www.imari-trial.nl or requested from the trial coordinator.

**Summary:** Multicenter prospective clinical effectiveness trial, whereby current local practice (control cohort) will be subsequently compared to the results of a multi-interventional program (intervention cohort) in patients undergoing total mesorectal excision (TME) for rectal cancer. This program includes:

1. Mechanical bowel preparation with oral antibiotics
2. Tailored full splenic flexure mobilization
3. Intraoperative fluorescence using ICG
4. Routine CRP-measurement at day three postoperatively, CT-scan with rectal contrast on indication
5. EVAC with early transanal closure of the anastomotic defect

**Microbiome:** Microbiome analysis will be conducted to investigate changes in rectal microbiome environment and correlation to AL.

**Primary endpoint:** Anastomotic integrity at 1 year postoperative on CT-scan

**Secondary endpoints include:** AL during follow-up, QoL, protocol compliance, changes in rectal microbiome, FA details and other postoperative outcomes.

**Trial coordinator:**

Drs. K. (Kiedo) Wienholts

Amsterdam UMC, location AMC

E: k.r.wienholts@amsterdamumc.nl

Tel: 020-5666626

**Principle investigators:**

Prof. dr. P.J. Tanis

E*: p.tanis@erasmusmc.nl*

Dr. R. Hompes

E: *r.hompes@amsterdamumc.nl*

**In-/exclusion criteria:**

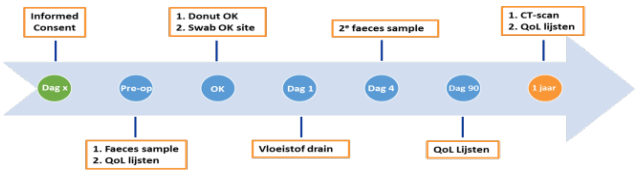
*Inclusion criteria*

Primary rectal cancer, or regrowth in a watch and wait protocol, or completion/salvage surgery after local excision;

*Exclusion criteria*

No colo-rectal/anal anastomosis; Local recurrent rectal cancer; Extended or multi-visceral excision; Synchronous colonic resections

**Details follow-up control-cohort:**




# Study progress

**Current accrual:**

- 244 control cohort = completed
- **147 intervention cohort**

Planned accrual control cohort: 244

Planned accrual intervention cohort: 244

**Participating centers**:

*Central and local approval obtained:*

1. Amsterdam UMC
2. Flevoziekenhuis
3. Ziekenhuis Groep Twente
4. Isala Ziekenhuis
5. Jeroen Bosch Ziekenhuis
6. Meander Medisch Centrum
7. OLVG
8. Radboud UMC
9. Spaarne Gasthuis
10. Zuyderland Medisch Centrum
11. Maastricht UMC+
12. Catharina Ziekenhuis
13. Laurentius Ziekenhuis Roermond
14. St. Antonius Ziekenhuis Nieuwegein

# LaNoReC

Lateral Nodal Recurrence in Rectal Cancer: a multi-center prospective study to evaluate lateral local recurrence rate after standardized treatment of the multidisciplinary team and lateral lymph node dissection.

**Study design:** Multi-center, prospective observational study

**Patient target group:** Patients with rectal cancer with one or more lateral nodes with a short-axis of ≥7mm or ≥5mm with one or more malignant features (i.e. round shape, irregular margins, heterogeneity, loss of fatty hilum).

**Inclusion criteria:** Adult (>18 years), with primary rectal cancer and lateral lymph nodes in the internal iliac or obturator compartment between 5.0-6.9mm with at least one malignant feature or ≥7.0mm

**Exclusion criteria:** Presence of synchronous distant metastasis, previous malignancy affecting oncological outcomes, family adenomatous polyposis, pregnancy.

**Methods:** Observational study with a sample size based on the main arm for patients with lateral lymph nodes ≥7.0mm who undergo nerve-sparing minimally-invasive LLND. Registration arm for patients with intermediate lateral lymph nodes (5.0-6.9) or patients who do not undergo nerve-sparing minimally-invasive LLND.

**Study objective:** To decrease the LLR rate by dedicated training of the multidisciplinary team and selective LLND with nerve-sparing techniques. The quality of life of patients will also be evaluated.

**Primary outcome:** Lateral local recurrence free survival after 3 years.

**Secondary outcome:** Morbidity, disease free survival, overall survival and quality of life.

## Study progress

**Current status**: Actively recruiting patients.

**Accrual status**: 17/200 patients included in main arm. Registration arm: 6 patients.

**Open in**: Alrijne Ziekenhuis, Amphia Ziekenhuis, Amsterdam UMC, Antonius Ziekenhuis, Bravis Ziekenhuis Canisius-Wilhelmina Ziekenhuis, Deventer Ziekenhuis, Dijklander Ziekenhuis, Erasmus MC, Franciscus Gasthuis & Vlietland, Haaglanden Medisch Centrum, Haga Ziekenhuis, LUMC, Instituut Verbeeten, Isala Kliniek, Maastro, MUMC+, Meander MC, MC Leeuwarden, Noord West Ziekenhuis, OLVG, Radboud UMC, Radiotherapie Groep, Radiotherapie Instituut Friesland, Reinier de Graaf Gasthuis, Rijnstate, Royal Adelaide Hospital, Spaarne Gasthuis, St Antonius Ziekenhuis, Zuyderland Ziekenhuis

**Principal investigators:**
Dr. M. (Miranda) Kusters
Prof. dr. P.J. (Pieter) Tanis
Prof. dr. C.A.M. (Corrie) Marijnen

**Study coordinator:**
Drs. E.G.M. (Eline) van Geffen, MD
Department of Surgery,
Amsterdam University Medical Center
T. 0031 6 - 33177458
E. Lanorec@amsterdamumc.nl

# Mend-it

De MEND-IT studie is een multi-center, single-arm, fase II studie waarbij we het effect onderzoeken van het toevoegen van FOLFOXIRI als inductiechemotherapie aan de neoadjuvante behandeling van lokaal gevorderd rectum carcinoom met specifieke hoog risico factoren. Deze specifieke hoog risico factoren omvatten:

- Invasie van de mesorectale fascie
- Extramurale veneuze invasie graad IV
- Bilaterale extromesorectale lymfeklieren ≥ 7mm
- Tumordeposities

Deze kenmerken zijn geassocieerd met een hogere kans op lokaal recidief en afstandsmetastasen. Indien één van bovenstaande benoemde hoog risico kenmerken aanwezig is op de MRI-scan, kan een patiënt geïncludeerd worden in de MEND-IT studie. Alle geïncludeerde patiënten ontvangen FOLFOXIRI als inductiechemotherapie, gevolgd door chemoradiotherapie en operatie (of watch and wait bij een complete respons).

**Totaal benodigde inclusies:** 128
**Inclusies momenteel**: 83

**Top 3 includerende centra:**

Catharina Ziekenhuis: 28

Isala Klinieken: 24

Erasmus Medisch Centrum: 17

**Project leider**

Dr. J.W.A. Burger, Chirurgische Oncologie, Catharina Ziekenhuis Eindhoven
pim.burger@catharinaziekenhuis.nl

**Trial coördinatoren**

Drs. Evi Banken, Medische Oncologie, Catharina Ziekenhuis

Drs. Davy Creemers, Chirurgie, Catharina Ziekenhuis
Contact: mend-it@catharinaziekenhuis.nl

# Study update

We zijn de afgelopen tijd bezig geweest de MEND-IT studie te openen in meerdere centra in Nederland. Op korte termijn is het gelukt om de studie te openen in 7 extra ziekenhuizen, waardoor de studie nu open is in 14 verschillende ziekenhuizen en 2 radiotherapeutische instituten in Nederland. Het voornemen is om binnenkort ook te openen in het Leids Universitair Medisch Centrum. Momenteel zitten we op ongeveer twee derde van de inclusies en daar zijn we erg tevreden mee. Met het openen van deze extra centra, is de verwachting dat we het totaal benodigde inclusies snel gaan behalen. We zijn daarom actief bezig na te denken over een vervolg op de MEND-IT studie.

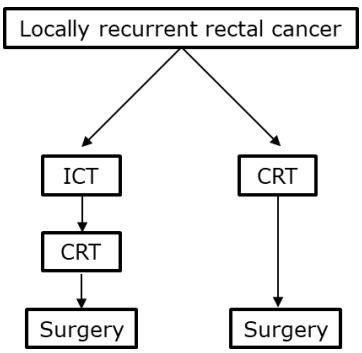
Bij vragen over de studie of over potentiële studiekandidaten kan er altijd contact met ons worden opgenomen telefonisch of via email

# PelvEx II

Per 1 April staat de inclusieteller op 183 deelnemers voor de PelvEx II. Dit betekent dat we officieel voorbij de helft van de inclusies zijn geraakt. We hebben sinds het begin van het nieuwe jaar alweer 15 nieuwe deelnemers mogen includeren in onze studie!

Mocht u een patiënt hebben met een recidief rectumcarcinoom, maar twijfelt u of uw patiënt kan deelnemen aan de PelvEx II? Aarzel niet en stel deze vraag bij uw regionale expert centrum. Mocht u andere vragen hebben dan laat het ons weten via het bekende e-mailadres of neem contact met ons op via het vermelde telefoonnummer. Voor verdere vragen en/of opmerkingen omtrent de studie kunt u ons ook op dezelfde wijze bereiken!

**Primair eindpunt**: R0 resectie ratio




**Totaal benodigde inclusies:** 364

**Inclusies momenteel**: 183 (1 April 2024)

**Top 3 includerende centra in 2024**

1. Catharina Ziekenhuis Eindhoven
2. NKI-AvL
3. Skånes University Hospital (SE)

**Project leider**

Dr. J.W.A. Burger, Chirurgische Oncologie, Catharina Ziekenhuis Eindhoven

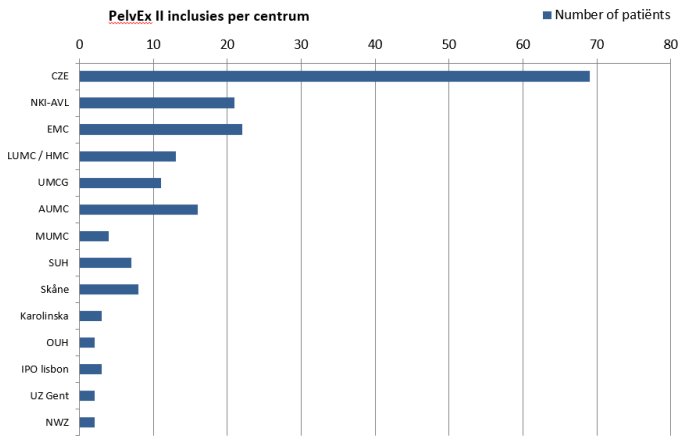
pim.burger@catharinaziekenhuis.nl

**Trial coördinatoren**

Drs. Davy Creemers, Chirurgie, Catharina Ziekenhuis Eindhoven

Drs. Floor Piqeur, Radiotherapie, Catharina Ziekenhuis Eindhoven

pelvex2@catharinaziekenhuis.nl; T: 040-2398858



# PLCRC

**PLCRC, the Prospective Dutch Colorectal Cancer cohort, is a population-based observational cohort study for all Dutch patients diagnosed with small bowel, colorectal and anal cancer. Aim is to establish a continuous source for a large variety of research purposes. Currently more than 25 studies make use of the infrastructure.**

For this project, prospectively collected clinical data are requested from the Netherlands Cancer Registry. Participating patients will also be invited to complete questionnaires on self-reported Health Related Quality of Life (HRQoL) and work ability, and to donate blood and tumor tissue samples for future research purposes. This cohort of lower Gi cancer patients provides an infrastructure for research and can be used for studies, like studies to evaluate the impact of diet and lifestyle on treatment response, or to evaluate new treatment modalities according to the Trials within Cohort design (TwiCs).

**Program manager**
Dr. G.R. Vink
06-15866038
g.vink@iknl.nl

**PLCRC Study team**
06-46919566
info@plcrc.nl
www.plcrc.nl

- **DISTANCE:** Towards patient-led follow-up after curative treatment of stage II and III colorectal cancer.
- **DOLPHIN**: DNA-testing of Liquid biopsies for Patient care close to Home In the Netherlands
- **MEDOCC:** Prospective observational cohort study to evaluate the prognostic relevance of ctDNA in stage II CRC.
- **MEDOCC-CrEATE:** circulating tumor DNA based adjuvant chemotherapy in stage II colon cancer patients
- **OLIPEC**: Cytoreduction, HIPEC and local treatment for patients with colorectal peritoneal and limited liver/lung metastases; a parallel cluster trial.
- **OPTIC**: Organoids to Predict Treatment response In mCRC.
- **ORCA:** Observational study to explore changes in *RAS* mutation status in ctDNA in patients with *RAS*wt non-liver limited mCRC over time (inclusion completed)
- **PROTECT:** Observational study to evaluate the impact of diet and lifestyle on treatment response (inclusion completed).
- **PROTECT+:** Observational study to examine the association of (changes in) body composition and grade II-IV treatment toxicities of adjuvant systemic therapy in patients with stage IIb/III colon cancer (inclusion completed).
- **VANTAGE**: Optimizing minimal invasive surgical techniques for rectal cancer in 'dedicated centers': a prospective observational multicentre study

# Study update

**Number of patients**: In April 2024 the number of 20,000 included patients was reached. There are 63 participating centers. Protocol version 15 was implemented April 2024**.**

Several multicenter substudies are ongoing, including (www.plcrc.nl)

# PLCRC - DOLPHIN

**Monitoring treatment response in patients with metastatic colorectal cancer using cfDNA fragmentomics testing: the DOLPHIN trial**

**Inclusion criteria**:

- Metastatic colorectal carcinoma
- Inclusion in PLCRC + informed consent for additional blood withdrawals
- First-line and before start second-line systemic therapy
  - Immunotherapy
  - Targeted therapy
  - (Induction) Chemotherapy

**Exclusion criteria**:

- Other metastatic malignancies in the past 5 years
- Pregnancy

**Patient accrual**: 242/400

Primary endpoint: The association between ctDNA changes and clinically determined treatment response in mCRC patients.

**Principal investigators**:

Dr. N.F.N. Kok, department of Surgical Oncology, Netherlands Cancer Institute

Dr. R.J.A. Fijneman, department of Pathology, Netherlands Cancer Institute

Dr. .J.M.L. Roodhart, department of Medical Oncology, University Medical Center Utrecht

Dr. G.R. Vink department of Medical Oncology, University Medical Center Utrecht / Netherlands Comprehensive Cancer Organisation (IKNL

Dr. M.J. Lahaye, department of Radiology, Netherlands Cancer Institute

Dr. M.N.G.J.A. Braat, department of Radiology, University Medical Center Utrecht

**Study coordinator**:

D.E. van Steijn, NKI-AVL. T: 020-512-6054

E: d.v.steijn@nki.nl

## Study update

Patient accrual is over halfway. mCRC patients can still be included in PLCRC-DOLPHIN

The following centers are participating in PLCRC-DOLPHIN:

1. Antoni van Leeuwenhoek
2. UMC Utrecht
3. Spaarne Gasthuis
4. OLVG
5. Meander MC
7. Rijnstate
8. Beatrix ziekenhuis
9. Bernhoven
10. Tergooi
11. NWZ

# PUMP-IT RCT

*Hepatic arterial infusion **PUMP** chemotherapy combined with systemic therapy versus systemic therapy alone as **I**nduction **T**herapy for initially unresectable colorectal liver metastases.*

**Objective:** to investigate whether hepatic intra-arterial chemotherapy combined with systemic therapy (HAIP-SYST) prolongs survival in chemo-naive patients with initially unresectable synchronous colorectal liver metastases.

**Primary endpoint**: overall survival.

**Secondary endpoints**: progression free survival (PFS), conversion-to-resection rate, R0/R1 resection rate, liver specific PFS, radiological and pathological response, complications and toxicity, Quality of Life (QoL) and cost-effectiveness

**Study design**

Multicentre, phase III randomised controlled trial.

**Arm A**: Induction treatment with systemic therapy according to standard clinical practice (based on results of the CAIRO5 study).

**Arm B**: Surgical implantation of the hepatic arterial infusion pump (HAIP) with resection of the primary tumour followed by subsequent induction treatment with HAIP-SYST.

# Study update

The study is currently under review by the METC. We plan to open the first centres early summer.

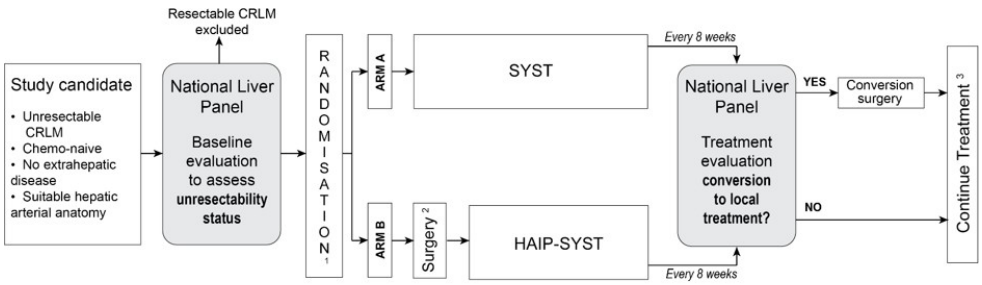
**Planned participating sites|** 20 Dutch liver centres

**Planned start of study|** Q3 2024

**Planned total accrual |** 306


**Principle investigator**
Dr. K.F.D. (Koert) Kuhlmann
k.kuhlmann@nki.nl
Department of Surgical Oncology
Antoni van Leeuwenhoek, Amsterdam

**Study coordinator**
Drs. E.M. (Elisa) ter Kuile
e.t.kuile@nki.nl / pump@nki.nl / 020 512 8104
Department of Surgical Oncology
Antoni van Leeuwenhoek, Amsterdam

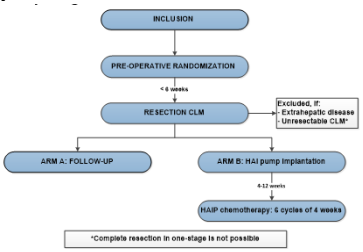

**CRLM** colorectal liver metastases **SYST** systemic therapy **HAIP-SYST** hepatic arterial infusion pump chemotherapy with systemic therapy

[1] Stratification: side primary tumour, *RAS* and *BRAF*$^{V600E}$ mutation status, uresectability status, inclusion centre, preference for doublet or triplet chemotherapy for patients in arm A.
[2] Pump placement and resection primary tumour. Preoperative: CT-angiography of the liver. Postoperative: $^{99m}$Tc-MAA scintigraphy
[3] In case of conversion, the total treatment duration for both arms is 6 months

# PUMP-I trial

A multicenter RCT comparing resection vs resection plus adjuvant hepatic intra-arterial chemotherapy in the liver for patients with resectable colorectal liver metastases and a low clinical risk score.

**Study design**




Inclusion criteria:

- Resectable index CRLM
- Clinical Risk Score (CRS) of 0-2*
- No (history of) extrahepatic metastases
- No previous local treatment in the liver
- No second malignancy < 5 years ago
- No liver-first resections (synchronous primary and liver resections are allowed)

**Important! Only pN+ status scores a CRS point (not cN+). Nodal status is always considered negative (N0) in case of synchronous primary and liver resection.*

**Study coordinators**

L. (Loubna) Outmani, MD

W.F. (Wills) Filipe, MD

Dept. of surgery, Erasmus MC

Mail: l.outmani@erasmusmc.nl

Tel: +31 681 786 093/+31 107 042 125

**Principal investigator**

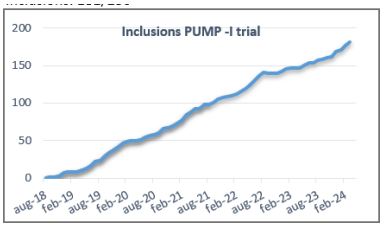
B. (Bas) Groot Koerkamp, MD, PhD, dept. of surgery, Erasmus MC

Mail: b.grootkoerkamp@erasmusmc.nl

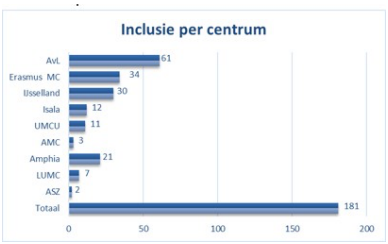
Tel: +31 107 040 234

# Study update (first of April 2024)

Inclusions: 181/230




Inclusions per center:




As of today, we have included 181 of the 230 patients we aim to include. We want to thank everyone for their efforts to fulfill this study. We need your help to complete this study. If you have a candidate for the trial, please do not hesitate to contact the study coordinators or one of the participating centers.

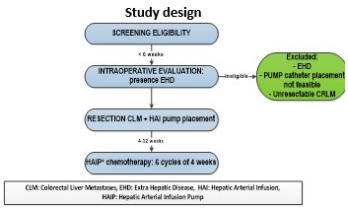
We have noticed our patients find the information video on the homepage of our website helpful in understanding the trial. Please refer them to the website for additional information.

Website URL: www.chemopomp.nl

Website QR code:

# Pump III

A multicenter single arm phase II trial assessing efficacy of resection plus adjuvant hepatic intra- arterial chemotherapy in the liver for patients with recurrent resectable colorectal liver metastases.




Inclusion criteria:

- Recurrent CRLM after metastasectomy
- No (history of) extrahepatic metastases
- No second malignancy < 5 years previously
- No residual CRLM after first local treatment

**Study coordinators**

L. (Loubna) Outmani, MD

W.F. (Wills) Filipe, MD

Dept. of surgery, Erasmus MC

Mail: l.outmani@erasmusmc.nl

Tel: +31 624 809 581 /+31 107 042 125

**Principal investigator**

D.J. (Dirk) Grünhagen, MD, PhD

Dept. of surgery, Erasmus MC

Mail: d.grunhagen@erasmusmc.nl

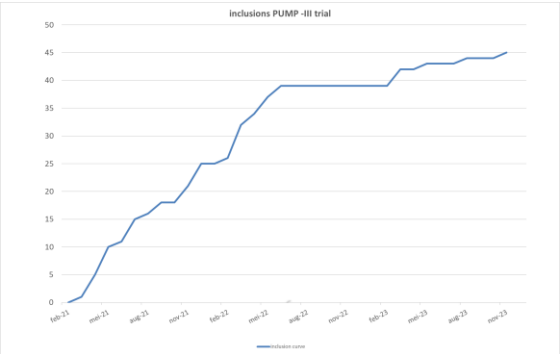
Tel: +31 107 041 902

Website URL: www.chemopomp.nl

Website QR code:

# Study update:

Inclusions: 45/45




In November we included our 45th patient and with that have completed out trial.

Thank you to the participating centers, the Netherlands Cancer Institute in Amsterdam and IJsselland Hospital in Rotterdam for all your hard work in treating the patient.

We would also like to thank all referring hospitals for making this high accrual rate possible. Without your efforts we would not have been able to complete this study!

# STAR-TREC II phase 3

END OF STUDY REACHED 27 MARCH 2024

Can we Save the rectum by watchful waiting or TransAnal surgery following (chemo)Radiotherapy versus Total mesorectal excision for early REctal Cancer?

The STAR-TREC is an international, multicentre, open-label, phase 2-3 study with partial randomization after patient preference. Patients with rectal cancer, staged by CT and MRI as ≤cT3b (up to 5mm of extramural spread) N0M0 can be included. For patients treated with organ preserving strategies, clinical response to (chemo)radiotherapy determines the next treatment step.

**Arm A** Standard TME surgery if the patient has no preference or prefers surgery

**Arm B** Patients who prefer organ preservation (OP) will be randomized 1:1 between:

**B1** Chemoradiotherapy (25x2 Gy and capecitabine)

**B2** Short-course radiotherapy (5x5 Gy)

**Primary endpoint**

The proportion of patients with successful organ preservation at 30 months from the start date of (chemo)radiotherapy.

**Principal investigators**

Prof.dr. J.H.W. de Wilt, Department of Surgery, Radboudumc

Prof.dr. C.A.M. Marijnen, Department of Radiation Oncology, AvL/NCI

Dr. F.P. Peters, Department of Radiation Oncology, AvL/NCI

**Study coordinators:**

Drs. Aaya Darai (Radboudumc)

Drs. Max Tanaka (AvL/NCI)

T: 06-34251046 (Radboudumc)

E: star-trec@radboudumc.nl/

Aaya.darai@radboudumc.nl or STARTREC-RT@nki.nl (AvL/NCI)

**Central data management**: Integraal kankercentrum Nederland (IKNL)

Tel: 088 – 234 65 00

Email: trialbureau@iknl.nl

# Study update

**The Netherlands**

The end of March the study was closed, because internationally more than 400 patients were included. In total 180 Dutch patients were included for this study. We want to thank all participating sites for their tremendous efforts.

| Ziekenhuis | Inclusies |
|---|---|
| Catharina Ziekenhuis | 30 |
| Martini Ziekenhuis - UMCG | 24 |
| Radboudumc | 19 |
| ETZ- Verbeeten Instituut | 17 |
| Antoni van Leeuwenhoek | 18 |
| Medisch Centrum Leeuwarden | 15 |
| LUMC | 11 |
| Isala Zwolle | 14 |
| Diakonessenhuis | 9 |
| Laurentius | 7 |
| Spaarne Gasthuis | 7 |
| Deventer | 5 |
| Amphia | 3 |
| VUMC | 1 |

**Follow-up STAR-TREC III – platform study**.

For this new KWF funded study, organ preservation rate is aimed to increase by adding a boost radiotherapy (internal or external) or chemotherapy to 5x5Gy radiotherapy. Centers are now asked for letters of commitment and in summer the inclusion will hopefully start in this platform designed study.

# UNITED

*Uniform Noting for International Application of the Tumor-Stroma Ratio as an Easy Diagnostic Tool*

**Principle investigator:** Dr. W.E. (Wilma) Mesker, dept. of Surgery, LUMC**.** E: w.e.mesker@lumc.nl

**Coordinating investigator:** Drs. M. (Meaghan) Polack, dept. of Surgery, LUMC**.**
E: m.polack@lumc.nl and united@lumc.nl

**Data management:** Clinical Research Center, dept. of Surgery, LUMC**.**
E: clinicalresearchcenter@lumc.nl

**Study design**

The international UNITED study is a prospective, multicenter cohort study, validating the tumor-stroma ratio (TSR) in patients with stage II/III colon carcinoma as independent prognosticator besides the TNM-classification. Participating pathologists, well-trained through an E-learning, scored the TSR using conventional microscopy, and classified the tumor as stroma-high (>50% stroma) or stroma-low (≤50%).

A total of 1,537 patients were included in 27 centers from 12 countries. We are grateful for the inclusions and support of all participating centers, which have made the finalization of the UNITED study possible.

A warm thankyou goes out especially to the support of the DCCG and fruitful collaboration with the PLCRC

## Study update

The UNITED study has been published in the ESMO Open recently, as final validation of the TSR. Disease-free survival was indeed significantly shorter in stroma-high than in stroma-low patients, which effect remained significant in multivariate analysis as independent prognosticator. Moreover, patients with stroma-high tumors appeared to benefit less or not at all from adjuvant chemotherapy.

Currently, new collaborations are being explored for future research, for instance in validating this potential of the TSR in prediction of benefit of therapy

**Websites:**

**https://dccg.nl/trial/united**

**www.watchstroma.com**

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ESMO OPEN SCIENCE FOR OPTIMAL CANCER CARE

**ORIGINAL RESEARCH**

### Results from the UNITED study: a multicenter study validating the prognostic effect of the tumor—stroma ratio in colon cancer

M. Polack[1], M. A. Smit[1], G. W. van Pelt[1], A. G. H. Roodvoets[2], E. Meershoek-Klein Kranenbarg[2], H. Putter[3], H. Gelderblom[4], A. S. L. P. Crobach[5], V. Terpstra[6], G. Petrushevska[7], G. Gašljević[8], S. Kjær-Frifeldt[9], E. M. V. de Cuba[10], N. W. J. Bulkmans[11], G. R. Vink[12,13], R. Al Dieri[14], R. A. E. M. Tollenaar[1], J. H. J. M. van Krieken[15] & W. E. Mesker[1*], the UNITED Collaboration[†]

[1]Department of Surgery, Leiden University Medical Center, Leiden; [2]Clinical Research Center, Department of Surgery, Leiden University Medical Center, Leiden; Departments of [3]Biomedical Data Sciences; [4]Medical Oncology; [5]Pathology, Leiden University Medical Center, Leiden; [6]Department of Pathology, Haaglanden Medical Center, The Hague, The Netherlands; [7]Department of Pathology, Medical Faculty of Ss. Cyril and Methodius University, Skopje, Republic of North Macedonia; [8]Department of Pathology, Onkološki institut—Institute of Oncology, Ljubljana, Slovenia; [9]Department of Pathology, Vejle Sygehus—Sygehus Lillebælt, Vejle, Denmark; [10]PATHAN Laboratories, Rotterdam, The Netherlands; [11]Department of Pathology, Spaarne Gasthuis, Haarlem; [12]Department of Medical Oncology, University Medical Center Utrecht, Utrecht University, Utrecht; [13]Department of Research and Development, Netherlands Comprehensive Cancer Organisation (IKNL), Utrecht, The Netherlands; [14]European Society of Pathology, Brussels, Belgium; [15]Department of Pathology, Radboud University Medical Center, Nijmegen, The Netherlands