PROTOCOL


XII
International
WATCH
&
WAIT
IX
III
Database
Rectal cancer
VI

PROTOCOL TITLE 'International Watch & Wait database'

Short title	**IWWD**
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Clinical Research Center (main contact for questions)	Department of surgery Leiden University Medical Center Albinusdreef 2, Postbus 9600 2300 RC Leiden, The Netherlands iwwd@lumc.nl *W.M. Meershoek-Klein Kranenbarg, MSc* Head of the Clinical Research Center w.m.meershoek-klein_kranenbarg@lumc.nl *A.G.H. Roodvoets, MSc* Senior data manager IWWD a.g.h.roodvoets@lumc.nl
Project leaders/steering committee	*G.L. Beets, MD, PhD* Department of Surgery Netherlands Cancer Institute Plesmanlaan 121 1066 CX Amsterdam, The Netherlands g.beets@nki.nl *N. Figueiredo, MD, PhD* Department of Colorectal Surgery Hospital Lusíadas Lisboa Rua Abílio Mendes, 1500-473 Lisboa, Portugal nunolfigueiredo@gmail.com *A. Habr-Gama, MD, PhD* Instituto Angelita e Joaquim Gama R. Manuel da Nóbrega, 1564 - Ibirapuera, São Paulo - SP, 04001-005, Brazil gamange@uol.com.br

	R.O. Perez, MD, PhD Instituto Angelita e Joaquim Gama R. Manuel da Nóbrega, 1564 - Ibirapuera, São Paulo - SP, 04001-005, Brazil rodrigo.operez@gmail.com *C.J.H. van de Velde, MD, PhD* Department of Surgery Leiden University Medical Center Albinusdreef 2, Postbus 9600 2300 RC Leiden, The Netherlands c.j.h.van_de_velde@lumc.nl
Coordinating investigators	*K.C.M.J. Peeters, MD,PhD* Department of Surgery Leiden University Medical Center Albinusdreef 2, Postbus 9600 2300 RC Leiden, The Netherlands k.c.m.j.peeters@lumc.nl *R.R. Bahadoer, MD* PhD student, Department of Surgery Leiden University Medical Center Albinusdreef 2, Postbus 9600 2300 RC Leiden, The Netherlands r.r.bahadoer@lumc.nl
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PROTOCOL SIGNATURE SHEET

Name	**Signature + date**
Legal representative: Leiden University Medical Center Department of surgery Albinusdreef 2, Postbus 9600 2300 RC Leiden, The Netherlands ***Head of Department:*** Prof. R.A.E.M. Tollenaar R.A.E.M.Tollenaar@lumc.nl	
Principal Investigator: Prof. C.J.H. van de Velde Department of Surgery Leiden University Medical Center Albinusdreef 2, Postbus 9600 2300 RC Leiden, The Netherlands c.j.h.van_de_velde@lumc.nl	 28-06-2021
Site Investigator: Name Center City Country	

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SUMMARY

Rationale: The strategy of watch and wait (W&W) in patients with rectal cancer who achieve a complete clinical response (cCR) after neoadjuvant therapy is new and offers an opportunity for patients to avoid rectal resection. However, evidence is based on small-to-moderate sized series from specialist centres.

Objective: The International Watch & Wait Database (IWWD) aims to describe the oncological and functional outcomes, risk factors for local regrowth and distant metastases. The ultimate goal is to improve quality of evidence to support, refine and increase organ-preserving treatment of rectal cancer after induction treatment.

Study design: International multicentre retrospective and prospective cohort study. Data registered during regular care (available in the EPR (Electronic Patient Record) will be collected retrospectively to complete the database. All consecutive patients from 2014 onwards who meet the inclusion criteria can be included. Definition of clinical complete response, timing for the assessment of response, specific treatment regimens used and exact surveillance protocols are at the discretion of each participating institution.

Study population: All patients with rectal cancer, in whom a total mesorectal excision was omitted after neoadjuvant therapy, are eligible to be included in the IWWD.

Main study parameters/endpoints: To establish an International Watch & Wait database to collate all available retrospective and prospective data in order to provide accurate understanding of the risks and benefits of organ-preserving strategies. The forthcoming information may become the platform for developing best practice guidelines in organ preservation and surveillance.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Current management of rectal cancer usually encompasses multimodality treatment and usually involves rectal resection. In case of good response to neoadjuvant treatment, organ preservation may be an option. In this shared decision-making era, patients' preferences increasingly play a vital role when selecting a treatment option. Organ preservation might be in de patients' interest as it may improve quality of life. The practice of organ preservation requires a careful balance between risks and benefits. It is in the interest of future rectal cancer patients to provide clinical evidence on organ preservation strategies. Through the IWWD consortium and its global collaborative effort, we intend to build up the case for organ preservation in rectal cancer.

1 INTRODUCTION AND RATIONALE

For decades, surgery with total mesorectal excision has been considered the primary treatment of rectal cancer. As local recurrence rates were considerably high, the use of radiation (with or without chemotherapy) was used to improve local disease control, with studies showing that it was better tolerated and more efficient when used in a neoadjuvant setting rather than adjuvant.[1-4] In addition, the use of preoperative chemoradiation also resulted in significant response of the primary tumour, sometimes resulting in complete disappearance of the cancer – pathological complete response (pCR).[5,6] Patients with a pCR have a favourable oncological outcome with very low risk for local or systemic recurrences.[6] Additionally in these patients the value of the role of subsequent radical surgery can be questioned, as it is associated with considerable postoperative morbidity, mortality, sexual and urinary dysfunction, faecal incontinence and the need for temporary and definitive stomas.[7,8,9-14] A group in Brazil led by prof. Angelita Habr-Gama began to assess tumour response after chemoradiation prior to definitive radical surgery, in order to identify patients with a clinical complete response (cCR) who were offered a strict surveillance strategy known as the Watch and Wait strategy instead of major surgery.[7,15] After an initial period of scepticism by the oncological and surgical community, the favourable oncological and functional outcomes observed by the Brazilian group were followed by similar observations by others.[16-19]

However, several limitations of the available data contributed to the lack of widespread uptake of W&W for the management of rectal cancer after the achievement of a cCR. First, consistent high-quality MR imaging from baseline and assessment of tumour response among patients included in the early studies was often lacking.[20] Second, there was significant heterogeneity in treatment strategies in regards to chemoradiation regimens and methods of assessment of tumour response.[21] Third, attempts to standardize the clinical and endoscopic criteria for a cCR became only available in 2010.[15] Also, significant heterogeneity in surveillance schedules was present across different centres. Finally, considering only a minority of patients treated with nCRT will achieve a cCR, individual reported series include a limited number of patients that were, frequently underpowered to substantiate meaningful conclusions regarding oncological safety of the W&W strategy.

While the limitations listed above provide sufficient reasons for the establishment of an international registry of patients treated by this new approach after the achievement of a cCR after (chemo)radiation, additional clinical questions became relevant during the implementation of the W&W into clinical practice. Initially, the W&W approach had a substantial ‘opportunistic’ element, considering a W&W approach only for a very good response after neoadjuvant therapy that had been given for a high-risk tumour without the explicit goal of organ preservation. This is currently also referred to as ‘secondary’ organ preservation. More recently, patients with less advanced tumours with a lower risk for local recurrence are

considered for 'neoadjuvant' treatment with the explicit goal of achieving a cCR and avoiding TME, currently also labelled as 'primary' organ preservation.[22] This "intentional" W&W strategy has been considered among patients with early-stage disease (cT2N0) and may represent a subset of patients with distinct, perhaps more favourable, oncological outcomes after the achievement of a cCR and W&W.

Concerns related to oncological outcomes of the W&W strategy include the management of patients with local regrowth. These patients may be at risk for both, local regrowth and development of distant metastases.[23,24] Partially due to the limited number of patients with local regrowth in each of the reported series of W&W, it is still unknown whether patients who develop local regrowth would have been associated with improved oncological outcomes if surgery (TME) had been performed upfront in comparison to salvage TME.[25]

In addition, robust functional outcomes and quality of life after W&W in comparison to upfront TME (with or without RT) should be an integral part of the decision management process but are generally lacking in the literature. [26]

Finally, predictive models and molecular biology studies are expected to provide additional information regarding the optimal selection of patients for W&W, avoiding unnecessary radiation (and its consequences to anorectal function and wound healing) of early-stage disease patients unlikely to achieve a cCR. [27]

In this setting, the development of an international registry may provide the ideal setting to investigate and understand critical issues and relevant clinical questions related to this novel W&W treatment strategy. By providing a significant number of patients and reflecting "real-world" data, this registry may allow the formulation of new clinically relevant hypothesis to be tested within the IWWD database itself or even in prospective studies. These studies may definitely contribute to the understanding of the oncological outcomes of W&W, its associated risk-factors to the development of local regrowth or distant metastases, subgroup of patients likely to have successful oncological and functional outcomes and potentially, ultimately serving as an ideal network for future prospective collaborative studies.

Finally, continued analysis of the data gathered by the consortium may allow for adjustments and standardization of practice across multiple contributing and even non-contributing centres. The first analysis of the IWWD provided interesting information in regards to the overall oncological outcomes of W&W. However, it also pointed out to the significant heterogeneity of the data and potential pitfalls with the approach.[21] These findings led to the establishment of a task-force to reach consensus within the contributing centres using Delphi methodology in an attempt to standardize definitions and homogenize practice. In addition, it led to the exploratory analysis of conditional survival among these patients in an attempt to substantiate

the need for continued intensified surveillance over time. Therefore, even though initial data has been already reported, subsequent publications may provide additional insights and crucial new information to the management of these patients with cCR managed by W&W. More information can be found on the IWWD webpage on https://cast-cancer.eu.

2 OBJECTIVES

Primary Objective: To establish an International Watch & Wait database to collect all available retrospective and prospective data in order to provide accurate understanding of the risks, potential benefits and functional/oncological outcomes of Watch and Wait after the achievement of a clinical complete response.

Secondary Objective(s): The prospective information may become the platform for developing best practice guidelines in organ preservation and surveillance.

3 DEFINITIONS

Assessment of response: methods and studies used for the assessment of response after completion of neoadjuvant therapy. The exact methods/studies and criteria/interpretation used are entirely at the discretion of the participating centres.

Clinical complete response: Absence of evidence of residual disease when assessed by clinical, endoscopic and radiological studies. The identification and diagnosis of a cCR are at the discretion of the participating centre. Clinical and endoscopic findings should include previously described criteria and at least one radiological assessment, preferably MRI, confirming the absence of residual disease within the rectal wall and mesorectal/internal iliac nodes.[15,28]

Clinical near-complete response: Patients that do not fulfil the clinical (endoscopic or radiological) criteria of a cCR but present a substantial response to treatment may be considered as near-complete responders. These patients have been offered deferral of surgery or a subsequent reassessment of response in a 6–8-week time interval. While the identification of such patients is also at the discretion of the participating centres, near-complete responses should only be considered for superficial and small (≤2cm) residual lesions/irregularities showing also excellent response on radiological imaging (low signal intensity area). Only patients with ongoing response – reflected by evidence of significant further response/regression in between subsequent reassessments – and eventually achieve all criteria for a cCR are to be included in the W&W database after initial achievement of a near-complete response.[29,30]

Distant metastases: clinical/radiological or pathological evidence of recurrent adenocarcinoma outside of the rectal wall, mesorectum or lateral pelvic nodes after the achievement of cCR

Local regrowth: reappearance, clinically or radiologically, or overt adenocarcinoma, biopsy-confirmed if possible, in the mucosa or deeper layers of the rectal wall, or in mesorectal/lateral nodes after the achievement of clinical complete response.

Neoadjuvant treatment: radiotherapy, chemoradiotherapy, chemotherapy - or a combination - intended to induce tumour reduction. For the sake of uniformity, it will be used both for primary and secondary organ preservation, regardless of the intent and whether or not it is actually followed by surgery.

Prolonged observation: adding an additional observation period and assessment when after neoadjuvant therapy a good response, but not a cCR is seen on the first assessment. The goal is to observe whether a cCR develops, after which the patient can be followed in a W&W strategy

Watch & Wait: a strict surveillance program after achieving a cCR

4 STUDY DESIGN

International multicentre retrospective and prospective cohort study. Data registered during regular care (available in the EPR (Electronic Patient Record) will be collected to complete the database. All consecutive patients from 2014 meeting the inclusion criteria will be included.

4.1 Inclusion

The inclusion preferably takes place shortly after a (near) clinical complete response is diagnosed at assessment of tumour response after neoadjuvant treatment, and the patient has agreed/opted to refrain from immediate surgery.

4.2 Informed consent

Informed consent is required to include patients in this registration.

5 STUDY POPULATION

5.1 Population

All patients meeting the inclusion criteria in one of the participating hospitals are candidates to participate in this cohort study. Important is that the decision to refrain from immediate TME surgery has already been made.

5.2 Inclusion criteria

a. Patients who achieve a clinical complete response (using clinical, endoscopic and radiological studies) after neoadjuvant therapy at assessment of tumour response or after a local excision (ypT0Nx) after neoadjuvant therapy and undergo a surveillance program with no immediate surgery.
b. Patients with a locally clinical complete response (conform point 5.2.a) and M1 disease, which will be registered under a separate category.
c. Patients with a clinical near-complete response to neoadjuvant therapy in whom it is decided to defer surgery and prolong the observation period and to perform re-assessment. Patients who subsequently achieve a clinical complete response within 24 weeks after the last radiotherapy fraction are considered to follow a W&W strategy.
d. Patients who have not achieved a cCR after neoadjuvant treatment as a result of residual disease but nevertheless have received organ-preserving treatment consisting of strict surveillance. These patients may be included in the registry under a different (near-complete) category.

5.3 Exclusion criteria

- Patients below the age of 18.
- Patients without neoadjuvant treatment.
- Mentally incompetent patients or patients not able to understand the provided information.

5.4 Inability to comply with the surveillance programme. Sample size calculation

To investigate the risks and benefits of organ-preserving strategies, a large number of patients is required. This database is designed to continuously include new patients and will provide an ongoing source of patients who received organ-preserving treatment for multiple studies. Sample size calculation will depend on specific studies and does not apply to the main observational cohort.

6 METHODS

6.1 Main study parameter/endpoint

Oncological outcomes of the W&W strategy (local regrowth's, local recurrences (after radical resection) and distant metastases). Cancer-specific free survival; Local regrowth-free survival and distant-metastases-free survival

6.2 Secondary study parameters/endpoints

- Functional outcomes
- Quality of life
- Overall Survival
- Comparison of W&W strategies between different centres
- Recommended follow-up schedule
- Recommended methods for follow-up

6.3 Participation in the IWWD

International societies, cooperative groups or individual centres with an appropriate patient volume interested in the IWWD project can participate. New participating centres will be pre-evaluated by the steering committee to ensure participation of only W&W-dedicated centres, in order to protect data quality. Local ethical procedures have to be followed, and a Data Sharing Agreement has to be signed. After approval of all documents by the IWWD executive board, the Clinical Research Center in Leiden (iwwd@lumc.nl) will give access to the IWWD database. If, according to internal regulation, applicable to the participating centre, a data transfer agreement will be signed. Participating centres are expected to include a minimum of 5 new patients annually. In addition, the follow-up of the patients must be updated at least twice a year (before the data locks on April 1st and October 1st).

6.4 Study procedures

Patients can only participate in this database if given written informed consent for participation in this observational cohort study. The observational data will be collected for a follow-up period of at least five years. from medical charts by local data managers/researchers and will not require additional time and efforts of patients or health care professionals. This observational cohort study does not involve (clinical) interventions or treatment. Data of individual patients will pseudo-anonymously (coded) with a unique study registration number on a secured server. Personal data that identify the patient will be encrypted and can only be decrypted by the local study team members. Centrally only pseudonymized data can be retrieved.

6.5 Withdrawal of individual subjects

Subjects can leave the study at any time for any reason if they wish to do so without any consequences. When desired, all clinical data in the database is deleted.

6.6 Subjects lost to follow-up

Data from patients lost to follow-up will be censored to the last date data was collected by data managers.

7 SAFETY REPORTING

Due to the observational nature of this registration, safety reporting is not applicable.

8 STATISTICAL ANALYSIS

The STROBE guidelines will be used for reporting of the results. Depending on the sub-study, various statistical methods will be used to analyse different outcome measures. Other methods of statistical analyses than mentioned in this protocol may be utilized in different studies within the project.

9 ETHICAL CONSIDERATIONS

9.1 Regulation statement

This registration study will be conducted according to the principles of the Declaration of Helsinki (64th WMA General Assembly, Fortaleza, Brazil, October 2013 and in accordance with the Medical Treatment Contracts Act (WGBO), the General Data Protection Regulation, the Good Clinical Practice (GCP) guidelines and this study protocol. Participating centres can ask their local ethical committees for approval if needed according to local ethical protocols.

9.2 Recruitment and consent

All patients diagnosed with rectal cancer, refraining from surgery after neoadjuvant treatment, who meet the inclusion criteria, will be asked to participate in this study by their treating physician. Patients are free to choose whether or not they want to participate, and their decision will not affect further treatment. No major exclusion criteria will be applied in order to establish a population-based real-world cohort. The treating physician, local investigator or research nurse who will inform the patients will perform the actual inclusion eventually supported by the central study team of the IWWD.

Only after written informed consent for the prospective observational data collection, the patient will be included. This includes providing pseudonymized information to other parties (collaborators of the IWWD).

9.3 Informed consent

All patients asked to join the registration are already familiar with their rectal cancer diagnosis (and a watch-and-wait strategy). Only after their diagnosis and treatment strategy is disclosed, and they have had the option to discuss it with their physician/ family/ friends, patients are separately asked to join the IWWD.

Informed consent can be signed directly after information on the project is provided or after a decision period. Patients are well informed that participation is voluntary and that they may withdraw at any point during the study.

9.4 Benefits and risks assessment, group relatedness

The decision to refrain from immediate surgery has already been made. Any direct benefit or risk related to W&W outside the realm of IWWD. The IWWD is purely observational. The development of an organ-preserving treatment for rectal cancer after achieving a clinical complete response after neoadjuvant treatment is still ongoing. At this moment, it is unclear how to follow patients through time, how often and what staging modalities should be used. To optimize this treatment, predictive and prognostic markers are necessary. Patients will not experience direct benefit from participation in the registration. By participating, patients will contribute to the evidence on the development of organ preservation treatment for rectal cancer. Risks associated by participating in this observational cohort study are negligible since it does not involve interventions.

9.5 Incentives

The participants of this cohort will not receive any compensation/incentive.

10 DATA HANDLING AND PUBLICATION

10.1 Database system and management

The Clinical Research Center of the Department of Surgery (Leiden University Medical Center) is in charge of central data management and is responsible for the data processing.

The Clinical Research Center, founded in 1987, facilitates patient-related research and coordinates national and international multicentre studies, particularly in the field of oncology. In 2011, the Dutch Cancer Society recognized the Clinical Research Center and therefore granted permission to coordinate data management of clinical trials funded by the DCS.

Since 2007, the Clinical Research Center uses the ProMISe data management system to store data in a highly secured and encrypted research data server (https://www.msbi.nl/promise/) in close collaboration with the department Advanced Data Management (ADM), also based in Leiden University Medical Center, Leiden. Since March 2017, the department and system are ISO27001 certified. ProMISe meets the requirements for data-safety and privacy set by international law. Due to this certification, the ProMISe system facilitates the availability, integrity and confidentiality of data.

From the year 2022, the data management system ProMISe will be discontinued, therefore the database will be transferred to the CASTOR electronic data capturing system (www.castoredc.com). This online medical research database system is certified to meet international security standards and is compliant with all relevant regulations, amongst which are ICH-GCP, GDPR, HIPAA, FDA 21 CFR part 11, ISO 27001 and ISO 9001. More information and individual security certificates can be found on https://www.castoredc.com/security-statement.

10.2 Case report form (eCRF)

A detailed eCRF in ProMISe (and later in CASTORedc) is provided to the invited centres. The eCRF includes info points with definitions and guidelines that aid in adequate scoring of the listed parameters.

10.3 Data collection and data entering

All patient data will be entered pseudonymously by or under the supervision of the treating physician(s). Up to 2 users per participating centre will receive a ProMISe login username and password. These users can enter data into the database. The Clinical Research Center provides a manual and can help the local teams with any data collection issues if needed.

10.4 Data privacy statement

Pseudonymous study data will be available in the IWWD. The data will not contain identifiable patient parameters in compliance with the General Data Protection Regulation (GDPR - EU 2016/679). Each patient will be coded within PRoMISe (and later CASTORedc) with a unique patient number so that patients in the study are untraceable from the study database. Identifying patient data will be only available to the data-entering centre (local staff of the treating healthcare facility) within ProMISe (later CASTORedc). Participating centres are asked to keep a password coded file (enrolment log file) that can identify individual patients locked away in their practice. This file can be accessed by the local investigators if needed, for example, in case a relevant new research question requires entering of additional data into the database. Data will be stored for a maximum of 15 years after the 5-year follow-up of the last included patient is entered in the database.

10.5 Public disclosure and publication policy

The prospective data collection initiative on an international watch and wait database is an investigator-driven study. This project aims to provide a national and international accessible source of data on W&W in rectal cancer. These data will be available (pseudonymized) for all collaborators of the IWWD. In order to guarantee that the data is only used for scientific, sociological and/or economic relevant research and research

questions are not answered by multiple parties simultaneously, the data from this registration will only be shared after permission of the executive committee (project leaders) of the IWWD. Permission to perform research with (part of) the data or to collect additional blood samples in the context of an observational study will only be granted if a research proposal is submitted and approved by this scientific committee. Rationale, methodology and objectives must be sufficiently elucidated in all research proposals before they can be accepted.

10.6 Acknowledgments and authorship.

10.6.1 Authorship and recognition as 'the IWWD consortium'

On the IWWD website, the logo of participating centres that contributed the last 5 years will be displayed.

Next to the authors that contributed significantly to the establishment of a manuscript, centres that at the time of the data lock - of that particular manuscript - have enrolled an average of 10 patients per year over the last 5 years are eligible to appoint 1 main author. However, feedback from this author is expected on the manuscript before submission to a journal.

Other participating centres, meeting the participation criteria (as mentioned in paragraph 6.3; enrolling a minimum of 5 new eligible patients annually and updating the follow-up of the included patients at least twice a year, before the data locks on April 1st and October 1st) can nominate 2 authors who will be listed as 'the IWWD consortium' in the appendix. This will be re-evaluated for each publication and the choice of Consortium members will be at the discretion of each centre. Participating networks or groups of centres, can nominate more authors with the above criteria applied to the individual centres.

10.6.2 Required acknowledgments

The European Registration of Cancer Care (EURECCA), financed by the European Society of Surgical Oncology ESSO and the Champalimaud Foundation Lisbon should always be acknowledged as the founders of the IWWD (in each presentation and publication).

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Appendix A

Patient information sheet and informed consent

International Watch & Wait database

Patient information

The IWWD is an international project initiated by the Champalimaud Foundation, Lisbon, Portugal, and EURECCA, acronym for European Registry of Cancer Care, based in Leiden, the Netherlands.

Principal Investigators:

- Prof G.L. Beets, Netherlands Cancer Institute, Amsterdam, The Netherlands
- Dr N. Figueiredo, Champalimaud Foundation, Lisboa, Portugal
- Prof C.J.H. van de Velde, Leiden University Medical Center, Leiden, The Netherlands
- Prof A. Habr-Gama, Angelita and Joaquim Gama Institute, São Paulo, Brazil
- Prof J. Gama, Angelita and Joaquim Gama Institute, São Paulo, Brazil
- Dr R.O. Perez, Angelita and Joaquim Gama Institute, São Paulo, Brazil

Purpose of the research

Currently, many different treatment strategies are being used to treat patients with rectal cancer. A selection of patients will undergo primary chemotherapy and/or radiotherapy. Often, this treatment is followed by surgery, usually with a temporary ostomy and in about one third of the patients a permanent colostomy. Besides the standard complications, there is also a considerable risk of temporary or permanent problems with sexual function, bladder function, and the function of the anal sphincter.

Some patients respond very well to the chemo- and/or radiotherapy and there is no sign of tumor after the treatment (complete response). We may consider observation and subsequent surveillance as an alternative to immediate radical surgery among these patients. Currently worldwide this “Watch and Wait” strategy has shown promising results. However, further research of the long-term effects of omitting surgery (Watch and Wait) after complete response is necessary. Participation in long term prospective observational studies will contribute to the understanding of this new treatment option.

Type of Research Intervention

Participating in this International Watch and Wait Database does not influence the treatment. Patient data will be anonymously stored in a secure database.

Participant Selection

Patients with a complete response after 12 weeks of chemotherapy and/or radiotherapy for rectal cancer will be able to participate in this study.

Voluntary Participation

Participation in this observational study is on a voluntary basis, patients should approve having information coded in the database for research questions to be answered.

Procedures

On each visit to the doctor for follow up/surveillance, information about the health status related to the rectal cancer will be entered in the database.

Risks

Since this study only concerns the registration of data, there are no risks involved.

Benefits

Benefits to participate are usually not foreseen at a short notice to the individual patient. The database will deliver a great value of information on a treatment that cannot be studied in a different way due to the nature of the treatment. Especially the long-term effects will show the efficacy and safety of this treatment. If this study proves that a Watch and Wait

treatment is a good and safe alternative option to surgery, this treatment can be offered to all future patients with rectal cancer.

Reimbursements

We will not be able to provide participants any reimbursement for their participation.

Confidentiality

We will not be sharing information about patients to anyone outside of the research team. The information that we collect from this research project will be kept private. Any patient information will be anonymized. The database used is certified, highly secured and is stored in a encrypted server that meets all the requirements for data-safety and privacy set by international law.

Sharing the Results

Sharing of the result will be done annually during a forum and by publications to appear in international scientific journals.

Right to Refuse or Withdraw

Participation is voluntary and includes the right to withdraw.

Appendix B

List of participating centres

Hospital Udaondo
BUENOS AIRES, ARGENTINA
Dr. S. Soledad Iseas
www.hospitaludaondo.org

Instituto Alexander Fleming
BUENOS AIRES, ARGENTINA
Dr.F. Fernando Sanchez Loria
www.alexanderfleming.org

Hospital Italiano de Buenos Aires
BUENOS AIRES, ARGENTINA
Dr.C.A.Carlos Vaccaro
www.hospitalitaliano.org.ar

Flinders Medical Centre
BEDFORD PARK, AUSTRALIA
Dr. S. Sina Vatandoust

University Hospitals Leuven
LEUVEN, BELGIUM
Prof. dr.A.André D'Hoore
www.uzleuven.be

Universidade Federal do Ceará
FORTALEZA, BRASIL
Dr.S.Sthela Murad Regadas
www.ufc.br

Instituto Angelita e Joaquim Gama
SÃO PAULO, BRASIL
Prof. dr.A.Angelita Habr Gama
www.ajgama.com.br

Changhai Hospital
SHANGHAI, CHINA
Dr.W.Wei Zhang
http://chhospital.com.cn/html/

Sun Yat-sen Univercity Cancer Center
GUANGZHOU, CHINA
Dr.P.Peirong Ding
www.english.sysucc.org.cn

Fudan University Shanghai Cancer Center
SHANGHAI, CHINA
Dr.Z. Zhen Zhang
www.shmc.fudan.edu.cn/eng/show/CancerCenter

Vejle Sygehus
VEJLE, DENMARK
Prof. dr.A.Anders Jakobsen
www.sygehuslillebaelt.dk

Centre Antoine-Lacassagne
NICE, FRANCE
Dr.J.P.Jean-Pierre Gerard
www.centreantoinelacassagne.org

Universitätsklinikum Erlangen
ERLANGEN, GERMANY
Prof. dr.K.Klaus Matzel
www.uk-erlangen.de/en

Imam Khomeini Hospital Complex
TEHRAN, IRAN
Dr.A.Amir Keshvari
www.ikhc.tums.ac.ir/en

St. Vincent's University Hospital
DUBLIN, IRELAND
Prof. dr.D.Des Winter
www.stvincents.ie

Universitario A. Gemelli
ROMA, ITALY
Prof. dr.C.Claudio Coco
www.policlinicogemelli.it

Humanitas Research Hospital
ROZZANO, ITALY
Dr.A. Antonio Spinelli
www.humanitas.net

Ospedale di Bressanone
BRESSANONE, ITALY
Dr.J. Josef Wildmann
www.asdaa.it/it/osp-bressanone.asp

Maastricht University Medical Center
MAASTRICHT, NETHERLANDS
Drs.J.Jarno Melenhorst
www.mumc.nl

Netherlands Cancer Institute
AMSTERDAM, NETHERLANDS
Prof.dr.G.L.Geerard Beets
www.nki.nl

Catharina Hospital
EINDHOVEN, NETHERLANDS
Prof.dr.H.J.T.Harm Rutten
www.catharinaziekenhuis.nl

Leiden University Medical Center
LEIDEN, NETHERLANDS
Dr.K.C.M.J.Koen Peeters
www.lumc.nl

European Registration of Cancer Care (EURECCA)
LEIDEN, NETHERLANDS
Prof.dr.C.J.H. Cornelis van de Velde
www.essoweb.org/projects/eurecca-cancer-care/

MSC Memorial Cancer Center
WARSZAWA, POLAND
Prof. dr.K.Krzysztof Bujko
www.pib-nio.pl

IPO Francisco Gentil
LISBOA, PORTUGAL
Dr.R.G.Rita Barroca
www.ipolisboa.min-saude.pt

Centro Clínico Champalimaud
LISBOA, PORTUGAL
Dr. Oriol O. Pares
www.fchampalimaud.org

Hospital Lusíadas Lisboa
LISBOA, PORTUGAL
Dr N.L.Nuno Figueiredo
https://www.lusiadas.pt/hospitais-clinicas/hospital-lusiadas-lisboa

Institutul Regional de Oncologie
IAŞI, ROMANIA
Prof.dr.G.Gabriel Dimofte
www.institutiimedicale.ro/spital/institutul-oncologie-iasi

Russian Cancer Research Centre
MOSCOW, RUSSIA
Dr.Z.Z.Zaman Mamedli
www.ronc.ru

Hospital Ramón y Cajal
MADRID, SPAIN
Dr.F.Fernando López Campos
www.comunidad.madrid/hospital/ramonycajal/

Karolinska University Hospital
STOCKHOLM, SWEDEN
Prof.dr.A.Anna Martling
www.karolinska.se

Boğaziçi Klinik Bilimler Akademisi
ISTANBUL, TURKEY
Dr.H.Handan Tokmak
www.bkba.com.tr

The Christie Clinic
MANCHESTER, UNITED KINGDOM
Prof. dr.A.G. Andrew Renehan
www.christie.nhs.uk

The Cleveland Clinic
CLEVELAND, USA
Dr.S.Steven Wexner
www.my.clevelandclinic.org/florida

University of Minnesota
MINNEAPOLIS, USA
Dr.W.B.Wolfgang Gaertner
www.twin-cities.umn.edu