CELAC and European consortium for a personalized medicine approach to Gastric Cancer (LEGACy)

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Western Management strategies have been ineffective to modify the poor prognosis of GC. This proposal will focus on this specific challenge to *improve GC outcomes*, and will seek to gather evidence through international high-quality translational...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Malignant and unspecified neoplasms gastrointestinal NEC
Study type	Observational invasive

Summary

ID

NL-OMON48300

Source
ToetsingOnline

Brief title
LEGACY

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC
- Bacterial infectious disorders

Synonym
Gastric cancer, stomach cancer

Research involving
Human

Sponsors and support

Primary sponsor: Fundación para la investigación del hospital clínico de la comunidad Valenciana

Source(s) of monetary or material Support: Europese unie

Intervention

Keyword: Gastric Cancer, Gastroenterology, Medical research, Oncology

Outcome measures

Primary outcome

The primary aim of the LEGACY project is to improve GC outcomes by applying personalized medicine at the three levels of prevention in EU and CELAC populations participating in this Project based on an *omics integrative epidemiology* conceptual model as a strategy to be extended worldwide.

Secondary outcome

1. Implement a personalized medicine strategy at the first level of prevention: establish coordinated work targeted at the general public based on two pillars: a) improving educational material for the lay population on the risk factors of GC, b) creating a hospital-based registry for H. pylori treated patients including a report on therapeutic resistance, to assist in the update the protocols with effective eradication therapies.

2. Improve early GC detection through a personalized medicine strategy at the second level of prevention: educating the lay population on the signs and symptoms of GC, facilitate access to endoscopy, by implementing specific measures adapted to each centers* characteristics and needs. Furthermore, implement a prospective hospital-based GC registry that will facilitate data collection and analysis on the different causes of GC diagnosis delay, and thus aid in planning health strategies at the second level of intervention.

3. Improve GC treatment approach through the stratification of patients for

personalized medicine therapies. A therapeutic approach to GC based on current histological and image criteria (Tumor Node Metastasis -TNM- stage) is insufficient. Molecular landscape, complex patient history, histopathological features of the tumors (including tissue biomarkers), environmental factors, together with personal microbiome and immune landscape must contribute to the development of new therapies and ultimately patient treatment and care. LEGACy aims to improve the current knowledge on each of these aspects of the disease and treatment and thus deliver high-risk group identification through the design of a cost-effective algorithm.

4. Analyze regional variations in respect to GC among the EU-CELAC populations. Identify regional differences based on behavioral, socioeconomic, educational and belief structure, as well as the healthcare policy backgrounds and the socio-economic strata of each country.

Study description

Background summary

Globally, gastric cancer (GC) is the third leading cause of cancer death in both sexes worldwide (723,000 deaths, 8.8% of the total)1.Despite multiple attempts to improve treatment in recent decades, no strategies have improved prognosis in locally advanced stage III and IVGC. Urgent intervention is therefore needed. The highest estimated mortality rates are in Eastern Asia (24 per 100,000 in men, 9.8 per 100,000 in women), with the lowest in Northern America (2.8 and 1.5, respectively). High mortality rates are also present in both sexes in Central and Eastern Europe, and in Central and South America1. Histologically, GCs can be divided into two types, diffuse and intestinal. Epidemiological and molecular features of GCs can vary widely according to their histological type, location and genetic makeup of the tumour. Tumour location at a proximal site is more common in Europe and CELAC countries (approximately 20%) than in Asia-Pacific, where antral location predominates. Signet-ring cell histology predominates except in Europe, where adenocarcinoma

is most prevalent2.The reasons behind these differences are multiple and complex and may include genetic susceptibility, strains of the bacterium Helicobacter pylori (H. pylori) and dietary factors. In particular, H. pylori infection plays an important role in GC incidence. Similarly, about 10% of GC patients test positive for infection by the Epstein Barr Virus (EBV)3. Interestingly, EBV is characteristic of South American populations. Several other factors, non-related to infectious agents, including excessive consumption of salty food, the ingestion of poorly preserved, smoked or pickled foods; contamination of food by aflatoxin, nitrates or fungi; pernicious anaemia and smoking are also associated with GC4,5,6.
The implementation of better screenings for high-risk populations in Japan, a country with high incidence of GC, resulted in a dramatic shift in stage at diagnosis along with a reduction in GC-related mortality7. Conversely, Western Countries with more restricted access to screening programs have seen a dramatic increase in GC8,9. Late diagnosis is probably one of the main reasons for the high mortality rates observed in GCs, in fact at least half of GC patients are diagnosed at advanced stages of the disease. On the other hand, most studies and current international databases on late-stage/advanced GC are largely based on Asian populations; in sharp contrast, the tumour biology and genome of European Union (EU)or Community of CELAC and Caribbean State (CELAC)populations remains poorly known. Furthermore, existing database genomic information is poorly integrated with clinical data from patients, due principally to a lack of multi-omics profiling, long turn-around times and the high costs behind bioinformatics analyses. These factors have contributed to the low number of clinical practice guidelines based on current information.
Prevention is a key factor in medicine, especially in cancer. In recent years, the arrival of personalized (or precision) medicine has revolutionized available treatments for cancer patients. Consequently, here we propose a novel concept: *personalized prevention*. From a public health standpoint, prevention can be conducted at three levels: primary, secondary, and for improving outcomes at the advanced stage of disease. Surprisingly, the concept *personalized medicine* has been restricted to this last setting, which relates to improving outcomes of already diagnosed patients in order to avoid cancer progression. However, we speculate that the first two levels of prevention can also benefit from a *personalized* approach, by identifying high-risk populations, working on specific measures based on the specific health situation of each country. To this end, precise risk prediction models need to be constructed. Epidemiologists aim to integrate *omics* data along with crucial information coming from other sources (questionnaires, candidate markers) that has been proved to be relevant in discrimination risk assessment of complex diseases.

Study objective

Western Management strategies have been ineffective to modify the poor prognosis of GC. This proposal will focus on this specific challenge to *improve GC outcomes*, and will seek to gather evidence through international

high-quality translational collaborative research, to tailor GC control with coordinated and consensual measures of intervention at different levels of prevention, each adapted to the different characteristics of the countries participating in this project: CELAC (Mexico, Chile, Argentina and Paraguay) and European cohorts (Spain, Netherlands, Portugal, Belgium and Germany).
In the selection of CELAC countries participating in this multicentre case-control project, we have included countries with a high incidence of GC such as Chile, and others with medium incidence, such as Mexico, Argentina and Paraguay. Currently there are no accurate data regarding GC incidence and characteristics in CELAC countries, so the registries proposed in this project will be of great value to demonstrate as a pilot how the useful strategies proposed will improve GC outcomes.

Study design

Prospective cohort study.

Study burden and risks

It is very likely that patients will not see any health benefits from participating in this study.
Any risks and inconveniences will arise from the gastroscopy. Performing biopsies can cause slight bleeding. Needle puncture collection is not a problem for most people. However, sometimes they can cause bleeding, bruising, discomfort, infections and / or pain at the site of the blood sample. You may also feel dizzy.
For biopsy purposes during the gastroscopy procedure a different gastroscopy may be necessary. This will cause minimal physical discomfort for the patient because the patient is sedated during the procedure.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Subjects >18 years old from IPATIMUP, INCAN, VUMC, PUC, VHIO, IAF, INCLIVA and GENPAT centres.
Has given and signed the IC to participate in this study.
With a gastroscopy indication due to the high diagnostic suspicion of GC as part of the study of the disease and PT-INR/PTT <1.5 x ULN, unless coumarin derivatives are used
Proven H. Pylori infection (only for legacy study 3)

Exclusion criteria

Patients diagnosed with GC from other centres/ countries not participating in this proposal.
Subjects from a different geographic area from the cases
Patients unable to give IC

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial

Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	10-02-2020
Enrollment:	400
Type:	Actual

Ethics review

Approved WMO Date:	19-11-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-09-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL69480.029.19