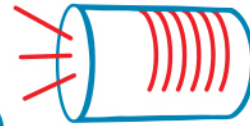


**La pianificazione di
uno studio clinico:
gli elementi
essenziali di un
protocollo**

Giuseppe Penno

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Sperimentale
Università di Pisa

Listen,
Think
and
Plan



Metodologia
degli studi clinici
in diabetologia

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Dichiarazione esplicita di trasparenza delle fonti di finanziamento
e dei rapporti con soggetti portatori di interessi commerciali

Il sottoscritto Dr. Giuseppe Penno

in qualità di

Moderatore

Relatore

ai sensi dell'art. 3.3 sul Conflitto di Interessi, art. 17 del Reg. Applicativo dell'Accordo
Stato-Regioni del 5 novembre 2009,

dichiara

che negli ultimi due anni ha avuto i seguenti rapporti anche di finanziamento con soggetti
portatori di interessi commerciali in campo sanitario:

***Astrazeneca, Boehringer Ingelheim, Eli-Lilly,
Janssen, Merck Sharp & Dohme,
Novo Nordisk, Takeda***

Bologna, 20-21 marzo 2018

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Embarking on a Research Project

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WHAT IS A PROTOCOL ?

- A research proposal (protocol) is a **detailed description** of a study designed to investigate a problem.
- A (clinical vs. non-clinical) research is conducted according to a protocol, i.e., an **action plan**.
- The **primer** of a study protocol is an **idea** that address a (clinical vs. non-clinical) need.
- The protocol (the **DNA of the project**) serves as a guide for conducting the study.
- The plan illustrates what will be made in the study and how it will be carried out. It should be **complete, robust, credible** and **doable**.
- Format may vary, but the **basic principles and key components remain the same**.

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A BRIGHT IDEA: essential but not sufficient





KEY POINTS OF A RESEARCH PROPOSAL



Quale NON è punto essenziale (Key Point) di un protocollo di ricerca (Research Proposal)

A.	Raccogliere le informazioni esistenti nel settore della ricerca.	B.	Formulare l'ipotesi e descrivere gli obiettivi.
C.	Descrivere/ipotizzare i possibili risultati.	D.	Definire una timetable.



KEY POINTS OF A RESEARCH PROPOSAL

- To raise **the research question** and to clarify its relevance (justify for the need of the project, clarify why the study is important).
- **To collect existing knowledge** and discuss the effort of other researchers who worked on the topic (literature search).
- To clearly **formulate the hypothesis and the objectives**.
- To state **where** and **when** the study will take place (the setting, the sites, the timing).
- To address **ethical** considerations.
- To describe **the design** of the study and **the methodology** required for solving the question and achieving the objectives.
- To discuss the **limitations** in achieving the objectives.
- Propose **time table** and budget.



KEY POINTS OF A RESEARCH PROPOSAL



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Components of a Research Protocol

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WRITING THE PROTOCOL - Components

- **Title** of the study
- Administrative details (contact details, signatures, ...)
- **Project summary**
- **The format:**
 - **Introduction**, background, literature review (references)
 - **Study goals and objectives**
 - **Methodology:** study design, study population, follow-up ...
 - **Work plan** (project management), timeline, milestones, data management and statistical analysis
- Strength and limitations of the study
- Issues for **ethical review and approvals** (safety considerations)
- **Significance** of the study (expected outcomes)
- **Dissemination** of results and publication policy
- **Budget proposal**
- **Appendixes**



Title of the Study

- Concise, accurate, descriptive, **informative**, relevant, and **attractive**
- **Acronym**
- The title should ... :
 - ... highlight the main objective in a plain manner
 - ... convey the idea and the research area
 - ... convey the main purpose
 - ... state, eventually, functional relationships
 - ... mention the target population
- ... carry the **maximum information in a few words** (12-15)

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Title of the Study - Acronym

Renal Insufficiency And Cardiovascular Events (RIACE)

This study is ongoing

Sponsor:

Diabetic Nephropathy Study Group

Collaborator:

Italian Society of Diabetology

Information provided by (Responsible Party):

Giuseppe Pugliese, Diabetic Nephropathy Study Group

ClinicalTrials.gov Identifier:

NCT00715481

First received: July 10, 2008

Last updated: February 9, 2015

Last verified: February 2015

[History of Changes](#)



ClinicalTrials.gov

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Project Summary/Protocol Synopsis

- Concise, descriptive, informative, relevant, and **attractive**.
- The summary should ... :
 - ... sum up all **the essentials** of the protocol
 - ... include ...
 - ... the **main research question**
 - ... the **rationale** of the study
 - ... the **hypothesis** and the **objectives**
 - ... the **methods** (shortly the design, the procedures)
 - ... **stand on its own**, and not refer the reader to points in the full project description.
- Remember ... :
 - ... the abstract and summary are **prepared the last**, but **read the first**

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Embarking on a Research Project



Components of a Research Protocol



The format of the protocol: introduction, hypothesis, objectives, variables, ...

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The traditional format: Introduction

- The introduction should ... :
 - ... provide the **background** information
 - ... update published research in the field
 - ... establish a **framework for the research** (the context)
- The introduction is also necessary for the investigators ... :
 - ... to familiarize with the existing knowledge
 - ... to find out **whether or not others** have explored the same problem
 - ... ensures that the study is not “re-investing the wheel”
 - ... describe links to other projects
- The literature selected should be pertinent and relevant
- **Against this background, it will be presented the rationale** of the new study and why it is worth doing (**why this study**)

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The traditional format: Hypothesis

- The hypothesis is a statement **based on sound scientific theory** that recognizes the **predicted correlation** between two or additional variables.
- A hypothesis represents a declarative statement of the **relationship between two or more variables**.
- A hypothesis can be defined as a tentative prediction or explanation of the **relationship between two or more variables**.
- A research hypothesis poses a relationship between two or more variables but **phrases this relationship as a question**.



The traditional format: Objectives



Gli obiettivi di uno studio devono essere

A.	Realistici, ma ambiziosi.	B.	Ragionevoli in termini di fattibilità e numerosità.
C.	Molteplici e articolati.	D.	Suscettibili di modificazione nel corso dello studio.



The traditional format: Objectives

- These are the **goals to be achieved** by conducting the research
- The objectives should be ... :
 - ... **explicitly** stated
 - ... **consistent** with the study questions/hypothesis
 - ... **logical** and coherent, feasible and realistic
 - ... **relevant** and time based
- The objective (goals) are to be distinguished in ... :
 - ... **primary objective** one(s)
 - ... **secondary objective** one(s)
 - ... **safety objective** one(s)
 - ... **exploratory objective** one(s)
- They should be stated in **action verbs**, i.e. “to determine, to compare, to verify, to assess, to describe”
- **For each objective, an outcome measure** should be defined
- It is advisable **to resist the temptation to put too many objectives (2 to 5 best)** or over-ambitious objectives that cannot be reasonably achieved
- Too many objectives often lead to inaccurate and poorly defined results



The traditional format: Objectives



Gli obiettivi di uno studio devono essere

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C.	Molteplici e articolati.	D.	Suscettibili di modificazione nel corso dello studio.



The traditional format: Variables

- Identify the **key variables** of the study (and the methods of measurement)
- For types of variables
 - **Dependent variables** (outcome, endpoint)
 - **Independent variables** (cause, predisposing factor, risk factor, determinant, antecedent) = variables that are manipulated or treated (one or more) in order to see the effects on the dependent variables (one or more)
 - **Confounding or intervening variables** = variables that may exert a confounding role in the relationship between the independent variables and the dependent outcome
 - **Background variables** = mandatory variables such as sex, age, ethnic origin, but also education, social status,



Embarking on a Research Project



Components of a Research Protocol



The format of the protocol: introduction, hypothesis, objectives, variables, ...



The format of the protocol: methodology, study design, sample size, ...

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The traditional format: methodology

- This is the plan to tackle the research problems.
- It should contain sufficient information to determine whether the methodology is sound.
- It explains the study design and procedures and techniques used to achieve the proposed objectives.
- Possibly, a good proposal should contain sufficient details for another qualified researcher to implement the study.
- In details: “where”, “who”, “how”

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The traditional format: Study Design



Quale è la principale decisione che deve prendere il ricercatore

A.	Definire l'obiettivo primario.	B.	Definire le procedure di reclutamento.
C.	Scegliere il disegno dello studio.	D.	Definire le dimensioni del campione.



The traditional format: study design

- The **selection of the research strategy** is the core of research design and is probably the most important decision the investigator has to take
- The choice of the strategy is in relation to the study objectives.
- Pilot data or trial runs may be appropriate.

Purpose	Study Design
To determine frequency and burden of a disease	• Cross-sectional survey (prevalence) • Cohort study, longitudinal (incidence)
To identify the risk factors	• Cohort study • Case-control study
To determine prognosis of a disease	• Cohort study
To determine efficacy, effectiveness, safety of a (new) treatment	• Randomized Controlled Trials (RCT) • Non-Randomized Controlled Trials (Observational Designs) • Community intervention



The traditional format: Study Design



Quale è la principale decisione che deve prendere il ricercatore

A.	Definire l'obiettivo primario.	B.	Definire le procedure di reclutamento.
C.	Scegliere il disegno dello studio.	D.	Definire le dimensioni del campione.



The traditional format: study population/subjects

- Why this **population**, why these **individuals**.
- The choice is in relation to the study objectives.

Point	Note
Sampling procedure	• To ensure representativeness and reliability
Criteria for eligibility: inclusion or selection	
Criteria for no eligibility: exclusion	
Criteria for discontinuation	
Allocation of subjects to study arms	• Randomization,
Control group	• Essential in epidemiological studies, in drug trials, in research on effects of intervention programmes,
Sample size	• A smaller than needed sample size might preclude sound scientific improvement



EURODIAB IDDM Complications Study

1. To define the geographical catchment area
- To stratify all eligible individuals into the 14 sex-age-duration of diabetes groups as below:

Age-Duration Structure of the Sample							
Sex		Males			Females		
Age at examination (years)		15-	30-	45-	15-	30-	45-
Duration of diabetes (years)	1-7	n	n	--	n	n	--
	8-14	n	n	--	n	n	--
	≥15	n	n	n	n	n	n

- Use random number tables to select 12 patients for each group with the aim of including 10 patients for each cell (2 acting as reserves)



EURODIAB IDDM Complications Study

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Age at examination (years)		15-	30-	45-	15-	30-	45-
Duration of diabetes (years)	1-7	12 ← 10	12 ← 10	--	12 ← 10	12 ← 10	--
	8-14	12 ← 10	12 ← 10	--	12 ← 10	12 ← 10	--
	≥15	12 ← 10	12 ← 10	12 ← 10	12 ← 10	12 ← 10	12 ← 10

- Use random number tables to select 12 patients for each group with the aim of including 10 patients for each cell (2 acting as reserves)



Inclusion & Exclusion criteria

3.1 Inclusion criteria

Patients should meet all inclusion criteria at the time of randomization. If at the time of enrolment (Visit 1) or start of lead-in (Visit 2) it is known that the patient will not meet criteria after a successful lead-in period, they should not be entered into single-blind placebo lead-in.

For inclusion in the study, patients should fulfil the following criteria:

- Provision of informed consent prior to any study specific procedures.
- Female or male aged ≥ 18 years and < 75 years.
- History of T2DM for more than 12 months.
- Inadequate glycemic control, defined as HbA1c $\geq 7.0\%$ and $\leq 11\%$ measured at Screening. Note that HbA1c will be rechecked at Visit 4, and must then be ≥ 7.0 and $\leq 10.5\%$ (value from blood sample obtained at Visit 3) for patient to be randomized.
- Stable anti-diabetic treatment regimen, defined as stable diet and exercise therapy alone or in combination with any or both of the two following alternatives:
 - A regimen of any approved oral anti-diabetic medication (except SGLT2-inhibitors) where no dose-changes have occurred during 12 weeks before randomization
 - Long acting or intermediate acting insulin and/or insulin permitted as long as the dose is stable during last 12 weeks before randomization (changes $\pm 10\%$ are allowed (in relation to number of units of insulin at randomization). For example, if the patient is taking 50 units/day of insulin at randomization, the total daily doses in the past 12 weeks should not have exceeded 55 units, or been less than 45 units. However, occasional exceptions (one day/week) during this time period are permitted.
- Renal impairment: CKD 3a
 - eGFR* 40 – 65 mL/minute/1.73 m² at Visit 2 (value from blood sample obtained at Visit 1) to enter the lead-in period.
 - eGFR* 45 – 59 mL/minute/1.73 m² at Visit 4 (average value calculated from the eGFR values at Visit 2 and Visit 3) for randomization.
- Body mass index (BMI) between 18 and 40 kg/m², inclusive.

*according to the re-expressed abbreviated (four-variable) MDRD Study equation, using central laboratory measurements of serum creatinine(sCr). [eGFR (mL/min/1.73m²) = 175 x (standardized sCr)^{-1.154} x (Age)^{-0.203} x (0.742 if female) x (1.212 if Black)] [Note: sCr reported in mg/dL]

3.2 Exclusion criteria

Patients should not enter the study if any of the following exclusion criteria are fulfilled:

Sex and Reproductive Status

- Women of childbearing potential (WOCBP) who are unwilling or unable to use an acceptable method of contraception.
- Women who are pregnant or breastfeeding.
- Women with a history of gynaecological malignancy.

Central Laboratory

- Aspartate Aminotransferase (AST) $> 5 \times$ ULN (ULN = 37 U/L or > 37 U/L)
- Alanine Aminotransferase (ALT) $> 5 \times$ ULN (ULN = 37 U/L or > 37 U/L)
- Total Bilirubin $> 3 \times$ ULN (ULN = 1.2 mg/dL or > 1.2 mg/dL)

Medical History and Concomitant Medication

CV/Vascular diseases:

- Severe uncontrolled hypertension (systolic blood pressure > 180 mmHg at any visit up to Visit 1).

Any of the following CV/Vascular diseases/conditions:

- Myocardial infarction.
- Cardiac surgery or revascularization.
- Unstable angina.
- Unstable heart failure.
- HF New York Heart Association Class III or IV.
- Transient ischemic attack or stroke.

Renal Diseases:

- History of any biopsy or imaging verifying intercurrent kidney disease (such as glomerular nephritis or sign of renal artery stenosis) other than diabetic nephropathy or diabetic nephropathy with nephrosclerosis.
- History of renal transplant.
- Hemodialysis, ultrafiltration therapy, or peritoneal dialysis.

Hepatic Diseases:

- Significant hepatic disease, including, but not limited to, cirrhosis, alcoholic liver disease, and/or severe hepatic insufficiency.
- Documented history of hepatotoxicity with any medication.
- Documented history of severe hepatobiliary disease.

Hematological and Oncological Diseases/Conditions:

- History of hemoglobinopathy, or chronic or recurrent bleeding disorders.
- Donation of blood or blood products to a blood bank; bi participation in a clinical study requiring withdrawal of the 6 weeks prior to signing the consent at visit 1.
- Malignancy within 5 years of the enrolment visit (with basal cell or treated squamous cell carcinoma).
- Known immunocompromised status, including but not limited to HIV, or who are positive for hepatitis virus (HIV).
- History of unexplained microscopic or gross hematuria at visit 2.

Allergies and Adverse Drug Reactions:

- Known allergies or contraindications to the contents of the study medication. The tablets contain lactose and may cause discomfort in patients with lactose intolerance.

Prohibited Treatments and/or Therapies:

- Participation in another clinical study with an IP during the last 30 days prior to signing the consent at visit 1.

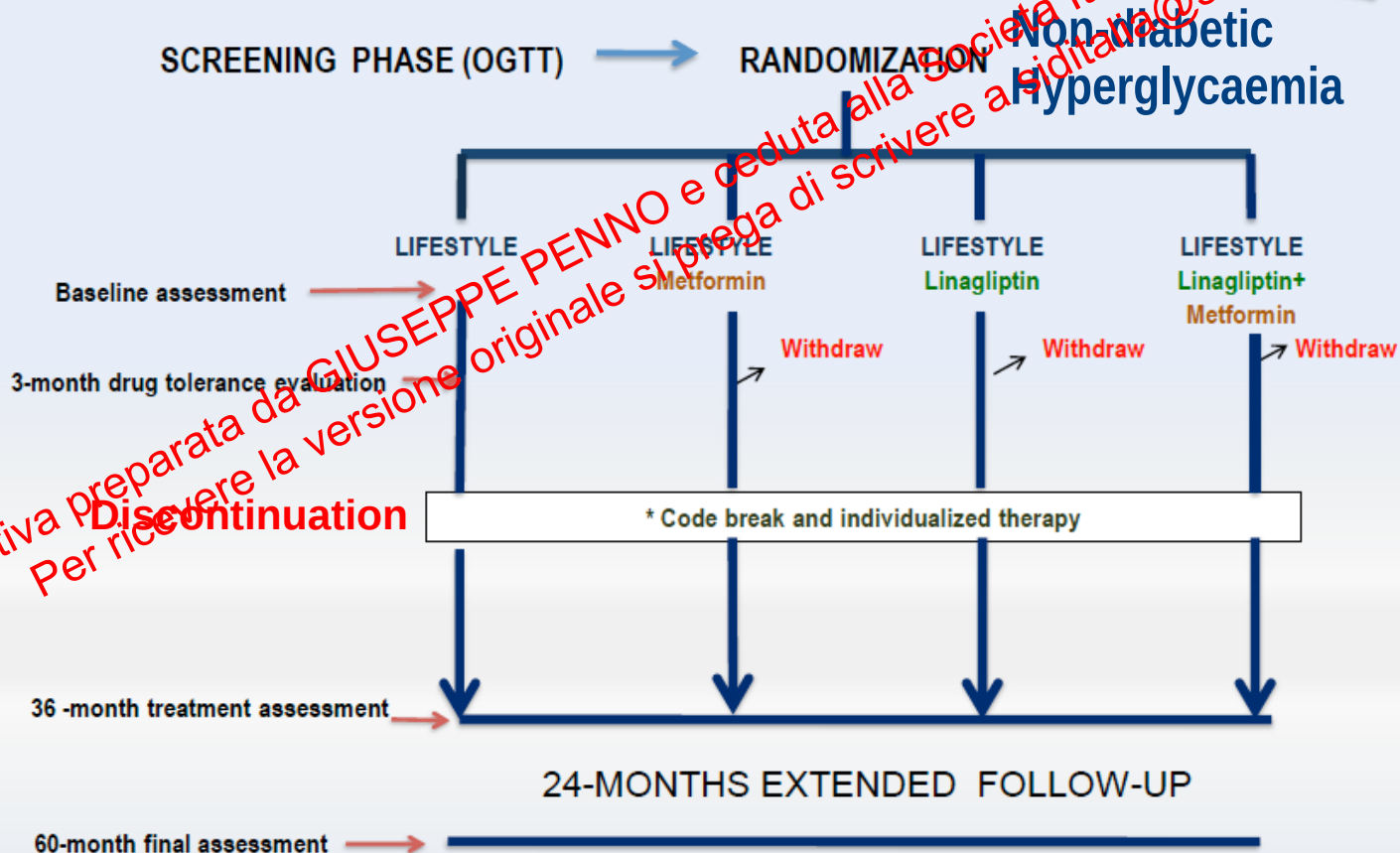
48

Eligibility criteria for this study have been carefully considered to ensure the safety of the study patients and to ensure that the results of the study can be used. It is imperative that patients fully meet all eligibility criteria.



Early Prevention of Diabetes Complications in people with Hyperglycaemia in Europe: Study e-PREDICE

FLOW-CHART DESIGN



* If HbA1c >6.5% or fasting glucose ≥ 7.0 mmol/l or 2hr post-load glucose ≥ 11.1 mmol/l in two consecutive blood samples at any time



The traditional format: intervention(s)

- Full **description of proposed intervention** should be given.
- All activities and actions should be recorded in their order of occurrence.

Intervention/activities	Note
Drug/treatment	• Scientific and brand name • Manufacturing company, city, country • Drug route, dosage, frequency of administration, duration of treatment • Approval of the drug regulatory agency
Apparatus or device	• Name and characteristics • Manufacturing company, city, country
Involved personnel	• Who is responsible • What activities each personnel will perform



The traditional format: data collection/management

- Several details should be provided.

Tools/instruments	Note
Retrospective data	- Medical reports - Laboratory reports
Validated questionnaires/Interview schedules	- Structured - Semi-structured
Specifically designed questionnaires	- Details about preparing, precoding and pretesting - Appended to the proposal
Laboratory tests	- Established tests (literature) - Not established tests (description)
Clinical examinations, screening procedures, techniques	- Established (literature) - Not established (description)
Description of instruments	- Tools used for data collection/extraction - Validity of the procedures employed



The traditional format: data collection/management

- Several details should be provided.

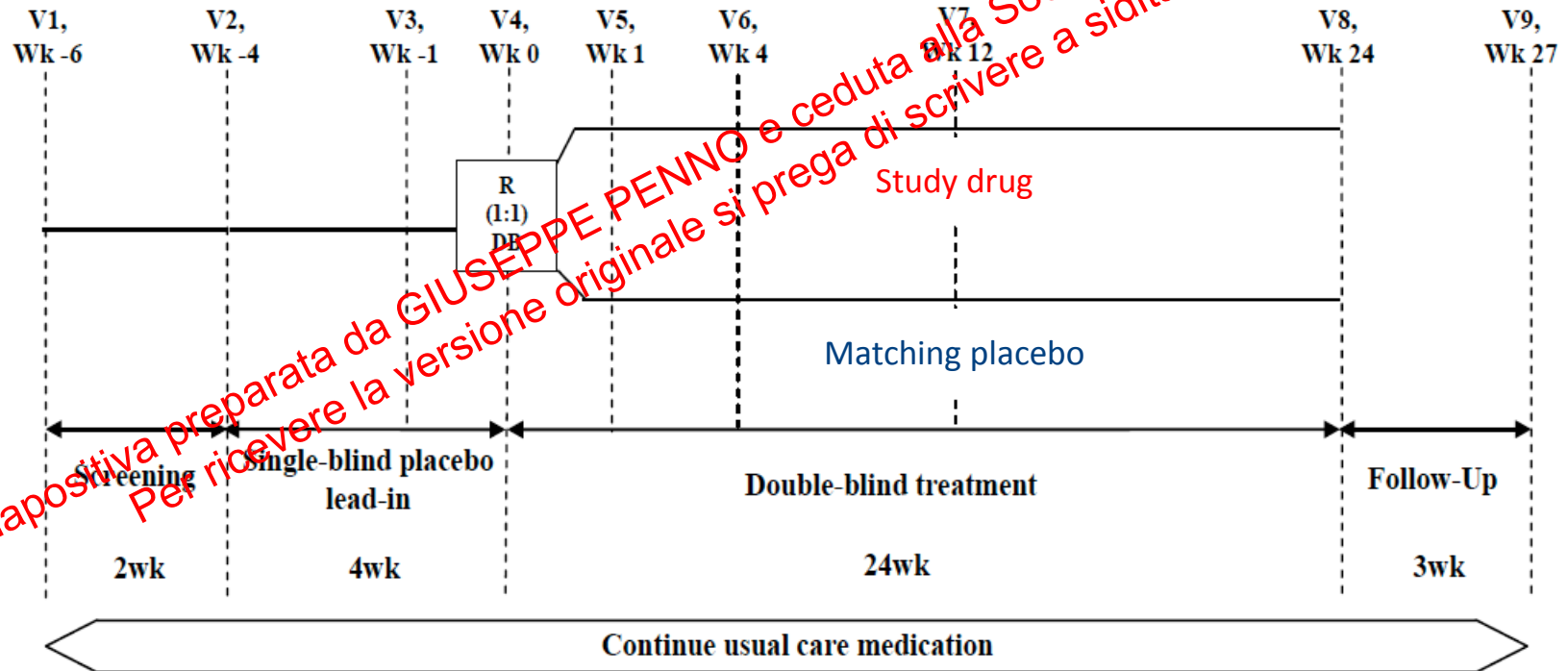
Tools	Note
Data analysis plan	<i>Statistical advice from a statistician</i>
Statistical tests	- Which (name of statistical tests) - Steps
Variables	Dependent, independent, confounders, etc
Software/version	

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The traditional format: study plain and timing of procedures

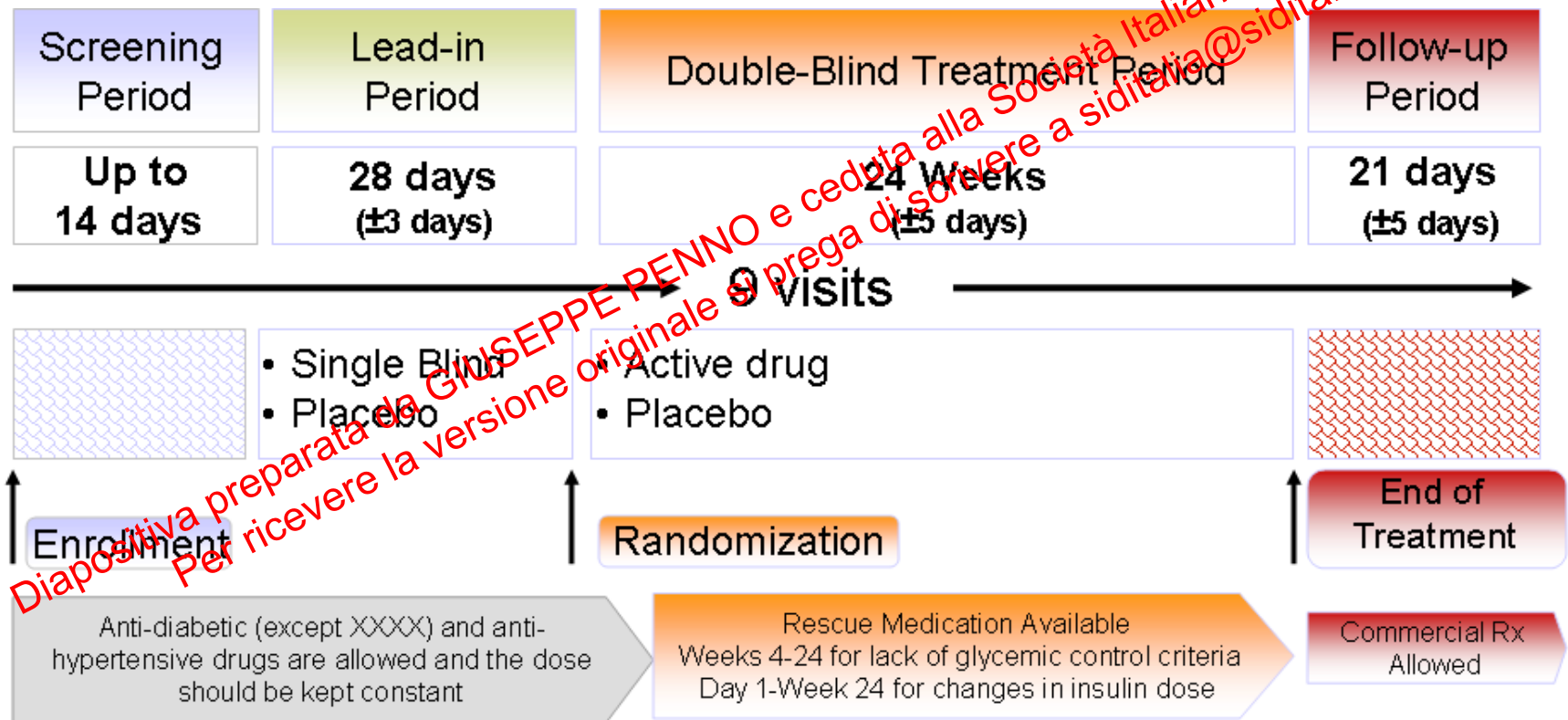
Study flow Chart



R = Randomization, DB = Double-blind, V = Visit, Wk = Week



The traditional format: study plain and timing of procedures





The traditional format: study plain and timing of procedures

Study Period	Screening period	Lead-in period		Treatment period					Follow-up period	For details see Protocol Section						
Visit	Enrolment	Start of lead-in	Lead-in	Random-ization	Treat-ment	Treat-ment	Treat-ment	End of Treatment/Discontinuat-ion/Rescue	Follow-up							
Visit Number (Fasting/Non-fasting)	1 ^a Non-fasting	2 ^b Fasting	3 ^c Fasting	4 ^{c,d} Fasting	5 ^{c,d,e} Non-fasting	6 ^{c,d,e} Fasting	7 ^{c,d,e} Fasting	8 ^{c,d,e} Fasting	9 ^{c,d,e} Fasting							
Week	-6	-4	-1	0	1	4	12	24	27							
Day	-42 to -29	-28	-7	0	7	28	84	168	189							
Visit Window		± 0	± 1	± 1	Study Period	Screening period	Lead-in period		Treatment period					Follow-up period	For details see Protocol Section	
Signed and Dated Informed consent ^f	X				Enrolment	Enrolment	Start of lead-in	Lead-in	Random-ization	Treat-ment	Treat-ment	Treat-ment	End of Treatment/Discontinuat-ion/Rescue	Follow-up		
Inclusion/Exclusion Criteria	X	X		X ⁴	Visit Number (Fasting/Non-fasting)	Study Period	Screening period	Lead-in period		Treatment period					Follow-up period	For details see Protocol Section
Allocation of E-code via IVRS/IWRS	X				Week	Enrolment	Enrolment	Start of lead-in	Lead-in	Random-ization	Treat-ment	Treat-ment	Treat-ment	End of Treatment/Discontinuat-ion/Rescue	Follow-up	
Randomization to study treatment via IVRS/IWRS				X	Day	Visit Number (Fasting/Non-fasting)	1 ^a Non-fasting	2 ^b Fasting	3 ^c Fasting	4 ^{c,d} Fasting	5 ^{c,d,e} Non-fasting	6 ^{c,d,e} Fasting	7 ^{c,d,e} Fasting	8 ^{c,d,e} Fasting	9 ^{c,d,e} Fasting	
Demographics	X				Visit Window	Week	-6	-4	-1	0	1	4	12	24	27	
Medical and Surgical History	X				Waist circumference	Day	-42 to -29	-28	-7	0	7	28	84	168	189	
Brief Physical Examination	X			X	Seated BP and Pulse	Visit Window		± 0	± 1	± 1	± 5	± 5	± 5	± 5	± 5	
Complete Physical Examination		X			Orthostatic BP and Pulse	Day										
Height	X				12-lead ECG ^h	Visit Window										
Weight	X	X	X	X	Hepatitis Screen Panel	Day										
					Blood samples for Safety Laboratory Panel ⁱ	Visit Window										
					Blood samples for HbA1c	Day										
					Blood samples for S-Crea (eGFR calculation)	Visit Window										
					Blood samples for FPG	Day										
					Assess FPG for Rescue	Visit Window										
					Blood samples for Fasting Lipids and Uric acid	Day										
					Blood samples for Serum Metabolism Marker	Visit Window										
					Pregnancy test ^m	Day										
						Review of diaries										
						Dispensation of Study Medication via IVRS/IWRS										
						Return of Study Medication and accountability										
						Adverse event review (AEs and SAEs) ⁿ	X	X	X	X	X	X	X	X	X	
						Hypoglycemic events review		X	X	X	X	X	X	X	X	
						Concomitant medication	X	X	X	X	X	X	X	X	X	

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The traditional format: study plain and timing of procedures

Procedure	Name	Description	Visit 9
			m 36
CRFs	Medical Interview	Patient's personal data and update background information	M
	Physical examination	Height, weight, waist circumference blood pressure (BP)	M
	Drug Accountability Log		M
	Adherence Questionnaire	Includes pills count	M
	Lifestyle	Nutrition questionnaire	M
		physical activity (RPAQ), 3x24h, PA diary	M
		7 X 24 pedometer	O
		workshop records and individual intervention forms	M
	Neuropsychological assessment	Quality of life (5D)	M
		Cognition (MOCA, TMT AB, Digit Span – Forward and Backward)	M
		Extended test series	O
		Anxiety and depression (Hamilton and MINI)	M
		Sleep disorders	M
		Neuropathic symptoms (MNSI_ Scoring Version)	M



The traditional format: study plain and timing of procedures

.....

Local Laboratory Test	Hemogram		M
	Complete OGTT	0, 30, 60, 90 and 120 min glucose	M
	HbA1c		M
	Hepatic profile	AST, ALT, ALP, gamma-GT	M
	Pancreatic profile	Amylase, Lipase	M
	Renal profile	Creatinine, uric acid, MELD-4, CKD-EPI	M
	Lipid profile	Total-Cholesterol, HDL-Cholesterol, Triglycerides, LDL-Cholesterol	M
	Morning urine spot	albuminuria, creatinine, alb/creat ratio,	M
FJD SPAIN	Insulin and C-peptide	0, 30, 60, 90 and 120 min	M
	Biomarkers		M
	Morning urine	albuminuria, creatinine, alb/creat ratio	M
Diagnostic Procedure	EKG		O
	Endo-PAT	Microvascular endothelial index	O
	CCA-IMT (CHS)	Common carotid intima-media thickness	O
	Retinography	Retinal vasculature	M
	SUDOSCAN	Sudomotor index	M
	Sleep and Cardiorespiratory recording	Nocturnal respiratory, blood pressure variation indices	O
M: Mandatory, O: Optional			CA.



Embarking on a Research Project



Components of a Research Protocol



The format of the protocol: introduction, hypothesis, objectives, variables, ...



The format of the protocol: methodology, study design, sample size, ...



Ethical issues

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Issues for Ethical Review and Approvals

- Ethical considerations **apply to all types of health research.**
- Documents **to be appended** to the proposal (where appropriate) before submission to the Ethics Committee:
 - **Statement about Conflict of Interest**
 - **The Informed Consent form:**
 - Subjects' mother tongue
 - Simple language, lay summary
 - To describe, in sequence, what will happen in the course of the study
 - To describe possible benefits and risks
 - To state freedom to withdraw from the study at any time
 - **Ethics checklist:**
 - Accordance with the Declaration of Helsinki
 - Agreement with the Good Clinical Practices (GCP)
 - Answers to the following questions:
 - Is the study adequate to the research question?
 - Is the selection of research subjects justified?
 - Are the intervention justified in terms of risk/benefit?
 - Is confidentiality ensured? (data safety)

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Embarking on a Research Project



Components of a Research Protocol



The format of the protocol: introduction, hypothesis, objectives, variables, ...



The format of the protocol: methodology, study design, sample size, ...



Ethical issues



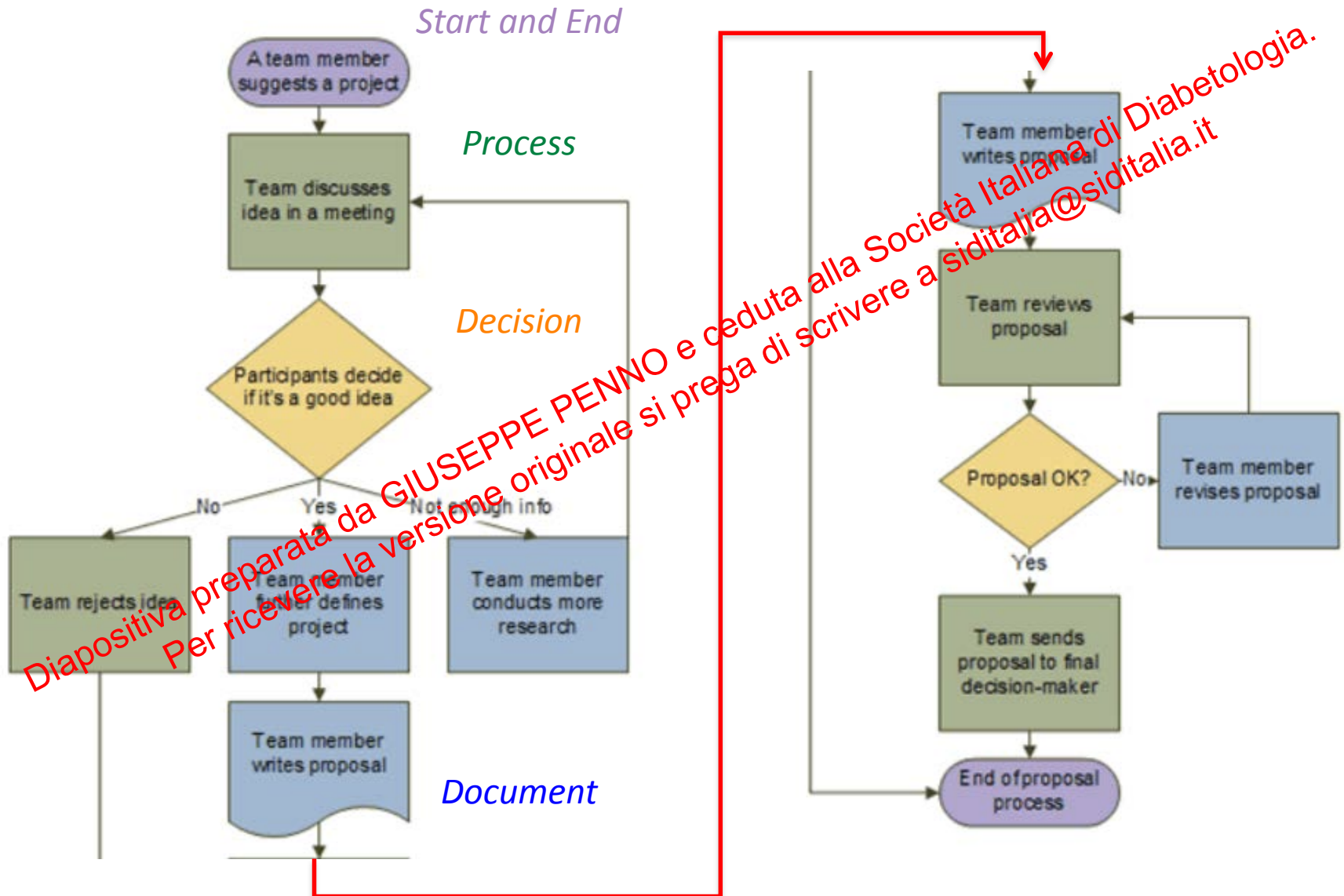
Flowchart & Gantt chart

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Flowcharts

- Flowcharts are diagrams that show the steps in a process.
- Basic flowcharts are easy to create and easy to understand.
- A good flowchart helps to understand the flow of information in the system (the project).
- There are many symbols that can be used in flowcharts to represent different kinds of steps.
- Accurate flowcharts can be created using very few of them.
- Five basic flowchart symbols: **Start and End, Process, Decision, Document, Sub Process** and Connectors.





The traditional format: Gantt chart





AZIENDA OSPEDALIERA UNIVERSITARIA DI PISA

Dipartimento di Medicina Clinica e Sperimentale

U.O. Malattie Metaboliche e Diabetologia

Centro Regionale di Riferimento per il Diabete Mellito in Età Adulta

Direttore Prof. S. Del Prato



Progetto di Ricerca Regione Toscana

- Endothelial injury and repair in diabetes. The development of a non-invasive multimarker index for "vascular competence"

Responsabile: Prof. Stefano Del Prato



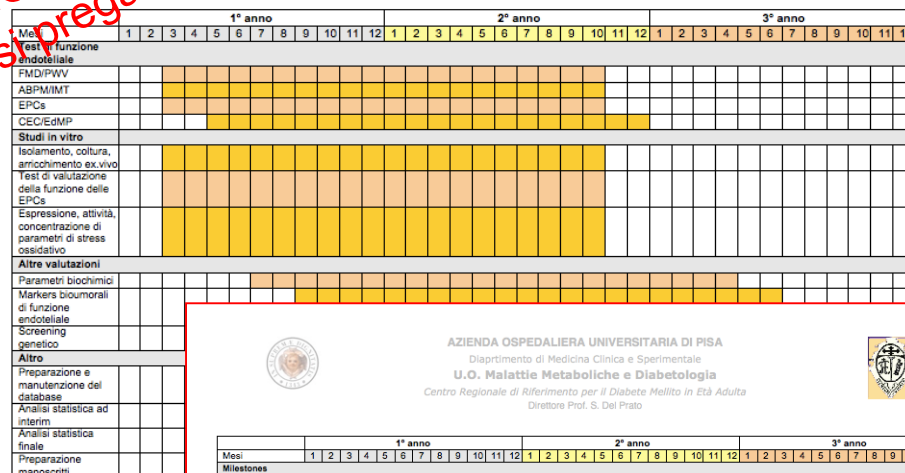
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Gantt chart



Budget proposal

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The budget proposal

Project Type: Ordinary/Progetti ordinari di Ricerca Finalizzata

Proposed total budget (Euro)

Costs	Budget Year 1	Budget Year 2	Budget Year 3	TOTAL BUDGET	Co-Funding	List of costs proposed for funding to the moh
1 Staff salary	138.645,00	138.645,00	138.645,00	415.935,00	415.935,00	
2 Researchers contracts	44.000,00	60.000,00	40.000,00	144.000,00	0,00	144.000,00
3a Equipment (leasing)	0,00	0,00	0,00	0,00	0,00	0,00
3b Supplies	80.000,00	100.000,00	81.505,00	291.505,00	29.085,00	262.420,00
3c Model costs	0,00	0,00	0,00	0,00	0,00	0,00
4 Subcontracts	0,00	0,00	0,00	0,00	0,00	0,00
5 Patient costs	1.250,00	2.500,00	1.250,00	5.000,00	0,00	5.000,00
6 IT services and data bases	0,00	0,00	0,00	0,00	0,00	0,00
7 Travels	0,00	0,00	0,00	0,00	0,00	0,00
8 Publication costs	0,00	0,00	0,00	0,00	0,00	0,00
9 Training and Dissemination	2.000,00	1.000,00	1.000,00	4.000,00	4.000,00	0,00
10 Overheads	12.533,00	12.533,00	12.534,00	37.600,00	0,00	37.600,00
11 Coordination costs	0,00	0,00	0,00	0,00	0,00	0,00
Total	278.428,00	344.678,00	274.934,00	898.040,00	449.020,00	449.020,00

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The budget proposal

Project Type: Ordinary/Progetti ordinari di Ricerca Finalizzata

Proposed budget distribution (Euro)

Costs	Unit 1 Total Budget	Unit 1 costs MOH funding	Unit 2 Total Budget	Unit 2 costs MOH funding	Unit 3 Total Budget	Unit 3 costs MOH funding
1 Staff salary	142.910,00		168.462,00		104.563,00	
2 Researchers contracts	96.000,00	96.000,00	24.000,00	24.000,00	24.000,00	24.000,00
3a Equipment (leasing)	0,00	0,00	0,00	0,00	0,00	0,00
3b Supplies	99.405,00	70.320,00	91.600,00	91.600,00	100.500,00	100.500,00
3c Model costs	0,00	0,00	0,00	0,00	0,00	0,00
4 Subcontracts	0,00	0,00	0,00	0,00	0,00	0,00
5 Patient costs	5.000,00	5.000,00	0,00	0,00	0,00	0,00
6 IT services and data bases	0,00	0,00	0,00	0,00	0,00	0,00
7 Travels	0,00	0,00	0,00	0,00	0,00	0,00
8 Publication costs	0,00	0,00	0,00	0,00	0,00	0,00
9 Training and Dissemination	4.000,00	0,00	0,00	0,00	0,00	0,00
10 Overheads	16.400,00	16.400,00	9.200,00	9.200,00	12.000,00	12.000,00
11 Coordination costs	0,00	0,00				
Total	363.715,00	187.720,00	293.262,00	124.800,00	241.063,00	136.500,00

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Ethical issues



Gantt chart



Budget proposal



Appendixes

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The informed consent





THE INFORMED CONSENT



Quali caratteristiche devono essere estranee al consenso informato

A.	Fornire informazioni circa i benefici e i rischi.	B.	Dichiarare che il farmaco in oggetto è sicuro ed efficace.
C.	Dichiarare che verrà garantita la riservatezza del partecipante.	D.	Contenere un linguaggio persuasivo.

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The informed consent

The Consent process:

**Information
provided**

**Information
understood**

**Decision
made**

**Comprehension
monitored and
maintained**

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The informed consent

In base alle linee guida EMA, le informazioni fornite al futuro partecipante devono spiegare quanto segue:

Lo studio è una ricerca e ha uno scopo.

Le procedure che devono essere seguite per lo studio, incluse tutte quelle invasive.

Le responsabilità del partecipante.

Eventuali aspetti sperimentali dello studio.

Il trattamento/trattamenti dello studio e la probabilità di assegnazione casuale ai trattamenti.

I rischi o gli inconvenienti ragionevolmente prevedibili per il partecipante.

I benefici ragionevolmente prevedibili.

Se non è previsto alcun beneficio clinico per il partecipante, questi dovrebbe esserne informato.

Il compenso o il trattamento disponibile in caso di lesione correlata allo studio.

L'eventuale remunerazione ripartita proporzionalmente prevista per il paziente per la partecipazione allo studio.

Le eventuali spese previste per il paziente per la partecipazione allo studio.

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The informed consent

Inoltre i futuri partecipanti devono sapere che:

La partecipazione allo studio è volontaria e chiunque può rifiutare di parteciparvi o ritirarsi da esso in qualsiasi momento senza alcuna penalizzazione o perdita di benefici a cui avrebbe altrimenti diritto.

Il monitor, gli auditor, i comitati etici e le autorità non hanno accesso direttamente alle cartelle cliniche del paziente per la verifica delle procedure e/o dei dati dello studio senza violare la riservatezza del partecipante.

I documenti che consentono di identificare il partecipante saranno mantenuti riservati e, nella misura consentita dalle leggi o dalle normative vigenti, non saranno resi pubblici.

Se i risultati dello studio saranno pubblicati, l'identità del partecipante resterà riservata.

Il partecipante sarà informato quando saranno disponibili informazioni che possono influenzare la volontà del partecipante di continuare lo studio.

Le circostanze o le ragioni prevedibili per cui la partecipazione allo studio può essere interrotta.

La durata prevista della partecipazione allo studio e il numero approssimativo di partecipanti coinvolti.

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Appendixes

- To be attached at the end of the protocol:
 - Participant information sheets and informed consent forms
 - GP information letters
 - Letters from ethics committees
 - Study questionnaires
 - Case Record Forms (CRFs)
 - Budget details
 - Curriculum Vitae (CV) of the principal investigator and co-investigators and their role in the study

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unite for diabetes

Thank for your
attention!

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