What is a Clinical Trial?

Development of a New Drug/New Treatment

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What is a Clinical Trial?

A clinical trial can be started by a pharmaceutical company or by an investigator (typicalley a doctor/professor at a hospital or other institution)

- If the trial is started by an investigator, there is often a collaboration with one or more pharmaceutical companies if drugs are involved in the clinical trial
- Usually clinical trials are international (multiple sites) – meaning that hospitals from several countries are involved in the clinical trial
- A clinical trial can be open or blinded. If it is blinded the patient does not know which drug she is taking (the drug being tested or a comparison drug/placebo) (the doctor can also be blinded).
- A clinical trial is often randomised meaning that the patient is either participating in the arm with the new drug or in the arm with a comparison drug/placebo.

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- In randomised controlled trials, trial participants are randomly assigned to either treatment or control arms. The process of randomly assigning a trial participant to treatment or control arms is called ‘randomisation’. Different tools can be used to randomise (closed envelopes, computer generated sequences, random numbers).

- The clinical trial must be approved by an ethics committe.

- When a patient has accepted to participate in a trial, she is asked to sign an informed consent

- The patient can withdraw from the trial at any time.

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What is a Clinical Trial?

The 3 phases of trials

Phase I – only a small number of patients are included.

- Purpose: establishing safety and the dosage of the drug
- Duration: several months

Phase II – Up to several hundred patients with the disease/condition.

- Duration: several months to 2 years
- Purpose: antitumor activity and side effects, also after multiple cycles in an "idealized" situation

Phase III – 300 to 3,000 people with the disease or condition

- Duration: 1 to 4 years
- Purpose: clinical advantages over standard treatment in daily life (efficacy and side effects)
- **All clinical trials can be found at https://clinicaltrials.gov and European trials at https://engot.esgo.org**

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What is a Clinical Trial?

Outline of the content of a study protocol

Project summary/abstract

General information

- Protocol title, protocol identifying number (if any), and date.
- Name and address of the sponsor/funder etc.
- Name and title of the investigator(s)

Roles and responsibilities

- Name(s) and address(es) of the clinical laboratory(ies) and other medical and/or technical department(s) and/or institutions involved in the research

Rationale & background information

- The Rationale specifies the reasons for conducting the research in light of current knowledge and examines benefits and harms of each intervention.

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Study goals and objectives

- Goals are broad statements of what the proposal hopes to accomplish
- Specific objectives are the scientific questions to be answered by the trial

Study Design

- The scientific integrity of the study and the credibility of the study data depend substantially on the study design and methodology. The design of the study should include information on the type of study, the research population or the sampling frame, and who can take part (e.g. inclusion and exclusion criteria, withdrawal criteria etc.), and the expected duration of the study
- **Inclusion/exclusion criteria**

  Patients characteristics which might affect the results

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Methodology

Safety Considerations

- Safety aspects of the research should always be kept in mind.
- Table with investigations to be performed (also for safety reasons) to be included.

Follow-Up

- The research protocol must give a clear indication of what follow up will be provided to the research participants and for how long.

Data Management and Statistical Analysis: if the quality of the data is not granted and the study is not large enough, the results could be questionable.

Quality Assurance

Expected Outcomes of the Study (Hypothesis)

- The protocol should indicate how the study will contribute to advancement of knowledge, and how the results will be utilized.

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Dissemination of Results and Publication Policy: negative results should be reported

Duration of the Project depends on feasibility

Research ethics approval

Declaration of interest: by investigators and study team

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Appendices

Informed Consent Forms: accessible, complete but not too long, regularly updated with toxicity.

Information for patients: to be approved by Ethics Committee

Samples for biorepertories in ancillary studies

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Placebo

Substance or treatment with no active therapeutic effect. A placebo can be made to resemble an active medication or therapy so that it functions as a control.

Problems in study design with placebo

- Placebo as control when there is a recognized standard treatment of proven efficacy.
- No possibility of cross-over when the tumor doesn't respond to the first therapy.
- Treatment with placebo is burdensome for patients.

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Disease: Ovarian Cancer – what do you know about the disease?

Study protocol: DESKTOP III – surgery and chemotherapy or chemotherapy alone in case of relapse

Randomized controlled phase III study evaluating the impact of secondary cytoreductive surgery in recurrent ovarian cancer

Study protocol: TRINOVA-3: A Phase **3** Randomized, Double-blind, Placebo-controlled, Multicenter Study of Trebananib with Paclitaxel and Carboplatin as First-line Treatment of Subjects with FIGO Stage III-IV Epithelial **Ovarian**, Primary Peritoneal or Fallopian Tube **Cancers**

10 minutes discussion in groups, 5 minutes – result of discussion

ENGOT-ov2/BGOG-ov7/GOG3001/Trinova-3
Trebananib (AMG 386)
in first line ovarian cancer

Stratification: -
AUC 5 or 6
- PDS or IDS
- Resid Tumour,
- IIIa-B vs IIIc-IV

Ovarian, tubal or peritoneal cancer
FIGO stage III-IV (n = 2000)

Randomisation 2:1

Accrual 152/2000

6 courses
Paclitaxel 175 mg/m² q3w
Carboplatin AUC 5 or 6 q3w
Trebananib 15mg/kg qw

6 courses
Paclitaxel 175 mg/m² q3w
Carboplatin AUC 5 or 6 q3w
Placebo qw

Interval debulking allowed after 3 cycles

Interval debulking allowed after 3 cycles

Maintenance Trebananib qw 18 months IV

Maintenance Placebo qw 18 months IV

Primary Endpoint: Progression-free survival

Secondary endpoints: Overall Survival, Quality of Life, Complications,PK