ENGAGe
ESGO | European Network of Gynaecological Cancer Advocacy Groups

12th Patient Advocacy Seminar

March 8 - 9, 2024, Barcelona, Spain

Clinical Trials Educational Workshop

How to read and understand a clinical trial protocol

The Clinical Trials Project

The Clinical Trials project is an ongoing project to get patients and patient advocates involved in clinical trials in order to get the patient perspective into the design of clinical trials.

ENGAGe + ENGOT Clinical Trials project

In charge of the project are:

- **Prof. Jalid Sehouli, Charité Universitätsmedizin, Berlin, Co-chair of ESGO ENGAGe on behalf of ENGOT**
- **Birthe Lemley, patient, EEG member of ESGO ENGAGe, (took initiative to start the project)**
- **Petra Adámková, patient advocate, past Co-chair of ESGO ENGAGe**

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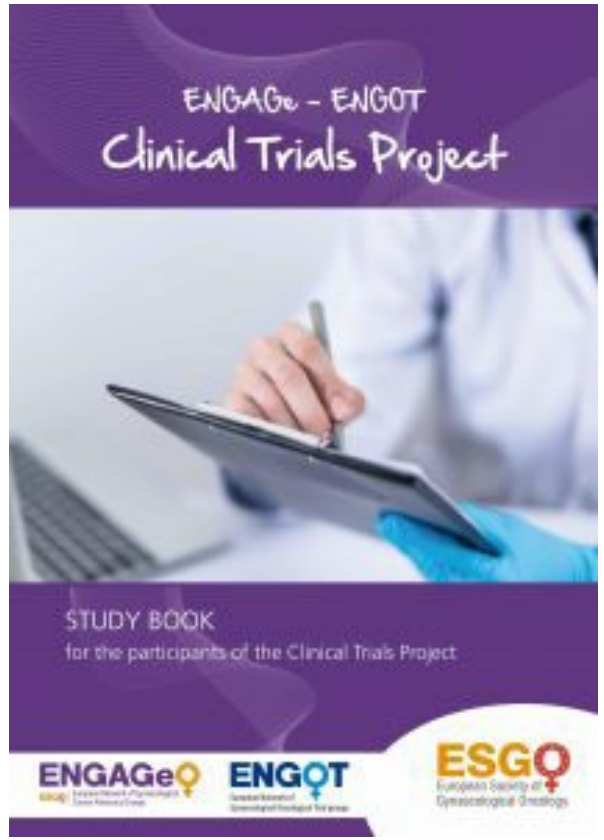
ENGAGe and ENGOT have been developing capacities of **patient experts in clinical trials.**

- ✓ **3 ½ years** of training patient experts
- ✓ **21 members** of patient experts in the clinical trials project
- ✓ **11 webinars** prepared by ENGOT clinicians for ENGAGe participants of the CT project.
- ✓ **1 Face to face meeting** held in Berlin, October 2022.
- ✓ **3 study books** have been produced. The content is summarizing the webinars, which were presented by ENGOT representatives to educate ENGAGe members.



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Clinical Trials Project

STUDY BOOK 2

for the participants of the Clinical Trials Project

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ENGOT European Network of Gynaecological Oncological Trial groups

ESGO European Society of Gynaecological Oncology

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Clinical Trials Project

STUDY BOOK 3

Genetics and Pathology

for the participants of the Clinical Trials Project

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Educational Workshop on how to read and understand a CT protocol

- A clinical trial aims to find an answer to the main research question or hypothesis that the study intends to answer.
- The primary clinical research question that the researchers want to investigate is called the Objective of a trial – to address the scientific question by collecting appropriate data.
- The study Endpoints, on the other hand, are the specific response variables that are chosen and used to measure and evaluate this Objective.

Educational Workshop on how to read and understand a CT protocol

There are 3 phases in a randomized clinical trial:

- Phase 1 - only a small number of patients (20-60) to find the maximum tolerated dose and the safety of the drug.
- Phase II - focuses on the efficacy of the drug (20-100 patients involved). In rare cases a drug gets approval after a phase II study.
- Phase III focuses on comparing the standard of care with the study drug(s) (200-2000 patients involved). Most powerful study to get approval from the FDA in the US and EMA in Europe.

Educational Workshop on how to read and understand a CT protocol

Hypothesis: PRIMA/ENGOT-OV26/GOG-3012 was designed to test the efficacy and safety of niraparib after response to platinum-based chemotherapy in patients with newly diagnosed advanced ovarian cancer, including those at high risk of relapse (ClinicalTrials.gov: NCT02655016).

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How to read and understand a CT protocol – the PRIMA trial as an example.

In the PRIMA trial the PARP-inhibitor niraparib was used as maintenance treatment in first line high-grade serous or endometroid ovarian cancer.

Study Population

The study population had stage III or stage IV disease

Randomization

One arm to receive the new drug and one arm to receive the standard of care.

How to read and understand a CT protocol – the PRIMA trial as an example.

Stratification factor:

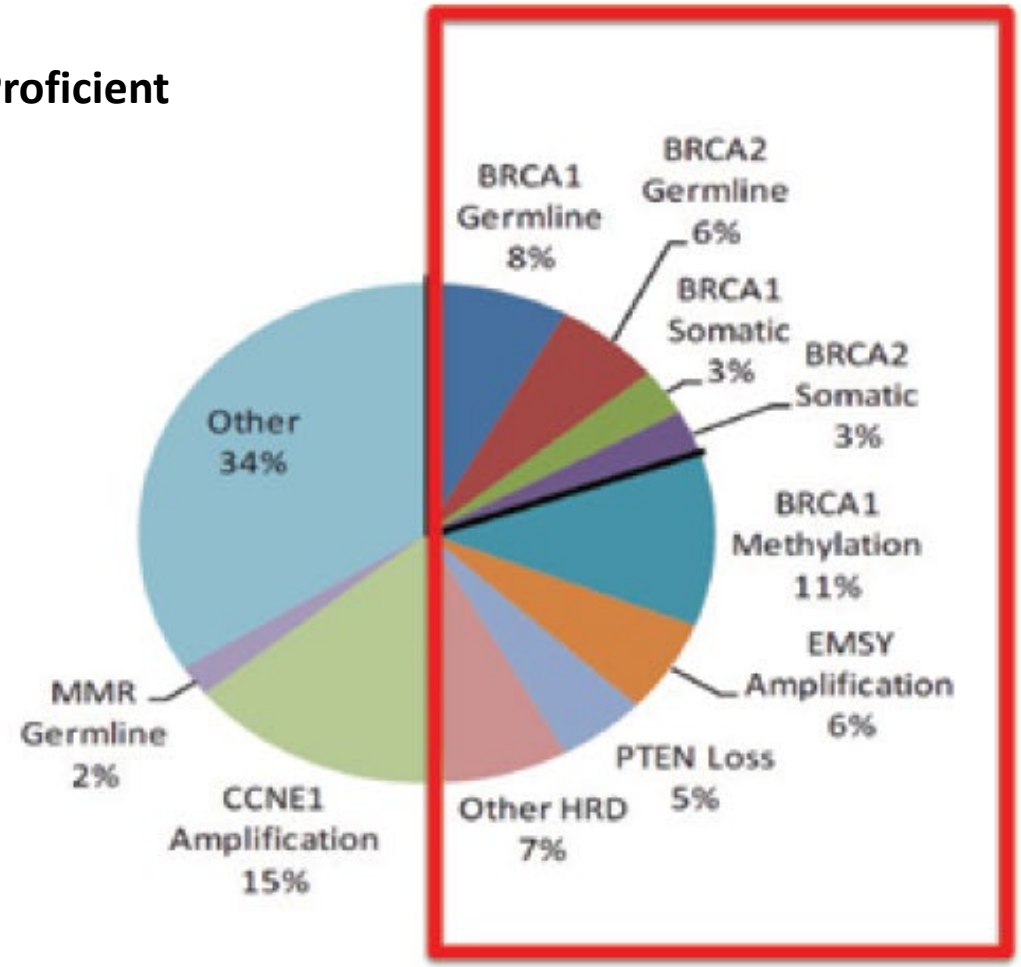
If we have red apples,
green apples and oranges
in a trial, we have to make sure
that there are equal numbers
of each in every arm.

How to read and understand a CT protocol – the PRIMA trial as an example.

Define the study population – **in this case patients with stage III and stage IV disease - BRCAmut, HRD positive, HRD negative.**

Then there are the **Key inclusion criteria and Key exclusion criteria**. Can also be called **the eligibility criteria.**

HR Proficient



Around 50% of high grade serous carcinomas show HRD, Homologous recombination deficiency

Testing HRD in tumor tissue to predict response to Chemotherapy and PARP inhibition

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PRIMA Was Designed to Address the Unmet Need in 1L Advanced OC

Hypothesis: PRIMA/ENGOT-OV26/GOG-3012 was designed to test the efficacy and safety of niraparib therapy after response to platinum-based chemotherapy in patients with newly diagnosed advanced ovarian cancer, induding those at high risk of relapse (ClinicalTrials.gov: NCT02655016)

Key Inclusion Criteria

- High grade serous or endometroid pathology
- Stage III: PDS with visible residual disease post surgery, NACT, or inoperable
- Stage IV: PDS regardless of residual disease, NACT, or inoperable
- CR or PR following platinum first-line treatment
- Tissue for homologous recombination testing was required at screening (Myriad MyChoice)

Key Exclusion Criteria

- Patients with Stage III disease who have had complete cytoreduction (i.e., no visible residual disease) after PDS

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1L, first-line; CR, complete response; NACT, neoadjuvant chemotherapy; OC, ovarian cancer; PDS, primary debulking surgery; PR, partial response

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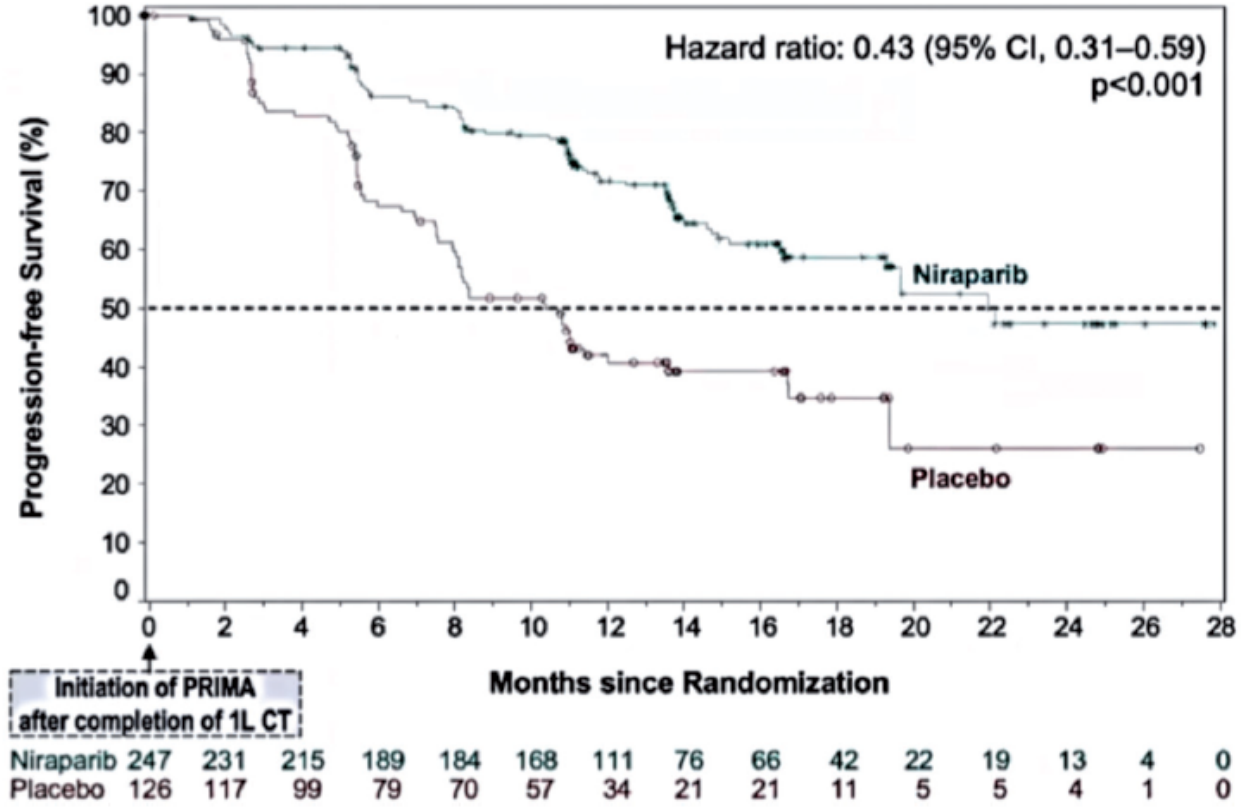
Patients at 50% mark – HRD



57% reduction in hazard of relapse or death with niraparib

	Niraparib (n=247)	Placebo (n=126)
Median PFS		
months (95% CI)	21.9 (19.3–NE)	10.4 (8.1–12.1)
Patients without PD or death (%)		
6 months	86%	68%
12 months	72%	42%
18 months	59%	35%

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1L, first-line; CI, confidence interval; CT, chemotherapy; HR, homologous recombination; NE, not estimable; PD, progressive disease; PFS, progression-free survival; Sensitivity analysis of PFS by the investigator was similar to and supported the BICR analysis.

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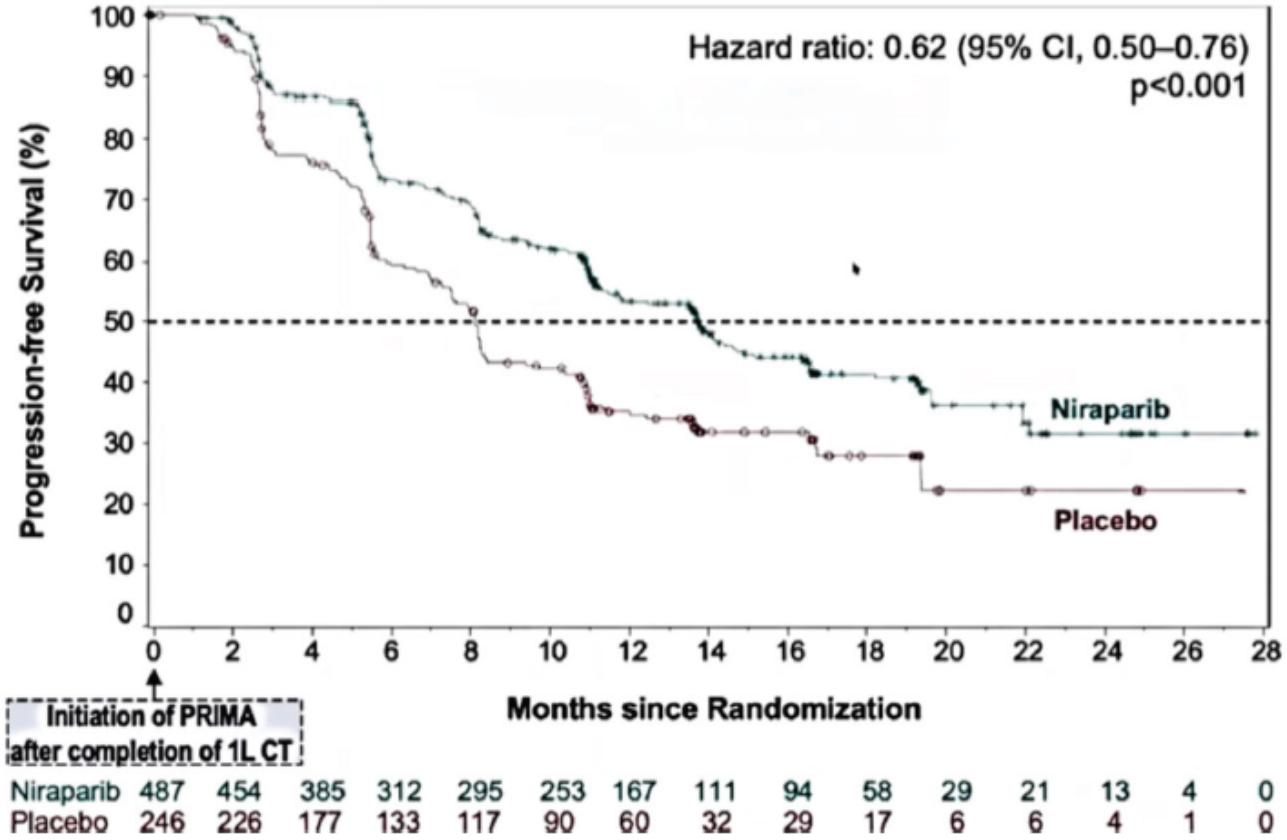
Patients at 50% mark – Overall population



38% reduction in hazard of relapse or death with niraparib

	Niraparib (n=487)	Placebo (n=246)
Median PFS		
months (95% CI)	13.8 (11.5–14.9)	8.2 (7.3–8.5)
Patients without PD or death (%)		
6 months	73%	60%
12 months	53%	35%
18 months	42%	28%

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1L, first-line; CI, confidence interval; CT, chemotherapy; PD, progressive disease; PFS, progression-free survival; Discordance in PFS event between investigator assessment vs BICR = 12%.

How to read and understand a CT protocol

- What does it mean if the trial is double-blinded?
- What is the informed consent?
- Can you opt out of a trial at any time?
- When will you know if you received placebo or the study drug?
- Could you think of a trial where the patient would know if she was in the trial arm?
- Would it be possible for the patient to cross-over to the trial arm?

How to read and understand a CT protocol

- Quality of life. What is used to measure QoL in a trial? – PRO, PROM, EORTC – Study Book 1
- The study population can be called the ITT-population (Overall Population – All-Comers) in a trial
- PFS - Progression-free Survival
- OS – Overall survival
- What does it mean to the patient if the HR of the PFS is e.g. 0.40?

Your task when the two lectures are finished:

You can find a lot of information just by reading the study description.

- The Objective – what you want to demonstrate with the trial
- The endpoints – primary and secondary if both are mentioned
- Study population – ITT population (Overall population, All Comers)
- Inclusion criteria (exclusion criteria if mentioned)
- How is the randomization done? How many arms are there?
- Stratification if mentioned
- Means to measure QoL if mentioned
- Statistical considerations HR (the hazard ratio)
- Was it a positive or a negative trial?

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3 groups – Ovarian, endometrial and cervical cancer
3 different trials – Ovarian, endometrial and cervical cancer
10 patient experts to help you find:

- The Objective
- Endpoints – primary and secondary
- Study population
- Inclusion criteria
- Means to measure QoL, if mentioned
- Statistical Considerations – HR (the hazard ratio)
- Was it a positive or a negative trial?

Presentation of your findings!