

AGO OP.7 / TRUST



TRUST – Trial on Radical Upfront Surgical Therapy

A close international cooperation



ENGOT ov33



Trial setting:

Pt with ovarian-, tube- or peritoneal carcinoma, FIGO Stage IIIB- IV

Sponsor:

AGO Study Group

Study design:

TRUST

Trial on Radical Uprfront Surgical Therapy



Pts. with ovarian-, fallopian-tube or peritoneal-cancer FIGO stage IIIB, IIIC and resectable stage IV



- *Primary Endpoint OS ITT population.*
- *Secondary Endpoints PFS, resection rates, morbidity and mortality after 6 months, QoL, „fragility Index“*
- *Strata: FIGO stage (III / IV), group/country, ECOG 0 vs 1/2*
- *Qualification process for participating centers to ensure high surgical quality*

S surgery
 C Carboplatin AUC5
 P Paclitaxel 175 mg/sq
 ➔ Bev. 15mg 15 mon
 suggested therapy, also weekly paclitaxel possible / or omission of Bev

TRUST-Quality Assurance Program



**STUDY OF
PRIMARY RADICAL CYTOREDUCTIVE SURGERY FOR
ADVANCED EPITHELIAL OVARIAN CANCER**

TRUST

Protocol ID:
AGO-OVAR OP.7

A prospectively randomised open multi-centre study
A project of the AGO study group

TRUST Quality Control Manual

Version: V01MASTER international
Date: 02.03.2016



Authors: S. Mahner, A. du Bois

Some of the site selection criteria...



- $\geq 50\%$ complete resection rate in upfront surgery for FIGO IIIB - IV pts („self-report“ by each center)
- ≥ 36 debulking-surgeries/year
- Upfront review of 24 surgery- and pathology reports from last year
 - Upper abdominal surgery must be established
 - Retroperitoneal surgery must be established
 - M'n'M management must be established
- Consent to be visited and audited by TRUST Quality committee delegates

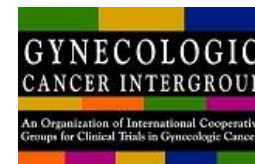




Ongoing Trials – status update

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Planned No. of pts: 686

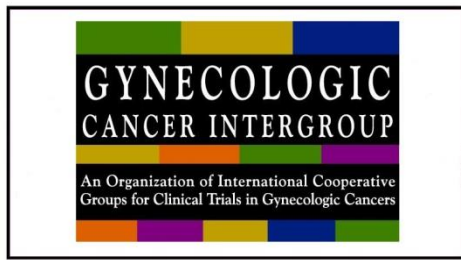
Current accrual: 112 (status May 26th, 2017)

First patient in: Aug 2016

Status International:



| Group | Country | # sites planned | Status |
|--------------|---------|-----------------|--|
| AGO | Germany | 8 sites | 8 sites active |
| | UK | 1 site | Ethics approval pending |
| GINECO | France | 4 sites | Activation of first site expected in June 2017 |
| MITO / MaNGO | Italy | 4 sites | Activation of first site expected in June 2017 |



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ENGOT Model A



Chemo-Bevacizumab +/- Atezolizumab in
recurrent ovarian cancer
– a randomised Phase III trial



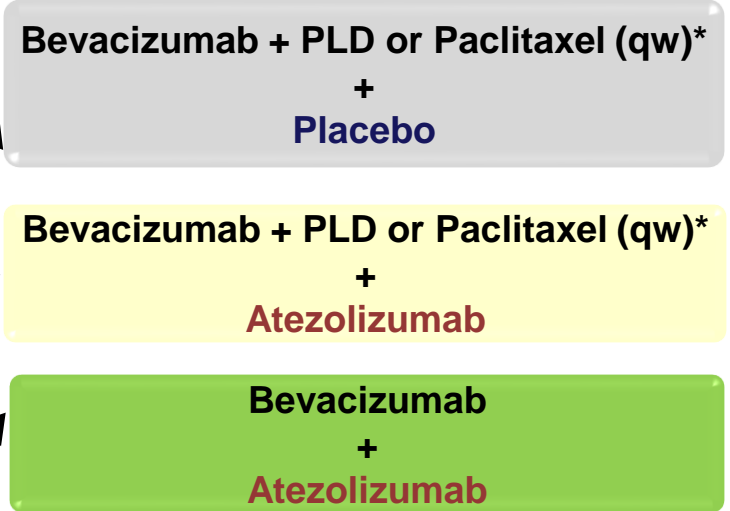
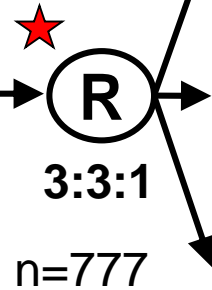


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ENGOT model A
Sponsor AGO Study Group

- epithelial ovarian, fallopian tube or primary peritoneal cancer
- **1st or 2nd relapse:**
TFI p < 6 months
- **OR 3rd relapse**
- **Prior Bevacizumab allowed**
- Bev and atezolizumab specific exclusion criteria
- Archival **and** recent biopsy mandatory
- PS 0/1, life expectancy 3 months +

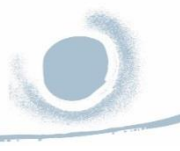


- Strata:
- Number of prior treatment lines (1-2 vs 3)
 - Planned chemotherapy (PLD vs paclitaxel)
 - Prior use of bevacizumab

* In arm 1 and 2 cohorts capping: 50% PLD and 50% paclitaxel

PLD, pegylated liposomal doxorubicin; PS: performance status

Mandatory Biopsy



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Primary endpoint Overall Survival

Alternative Scenario II after TC (1/17; Roche – study duration 3 instead of 4 years, decrease sample size)

Phase III confirmatory comparison of arms A and B;
additional exploratory arm C which will only be used for unpowered non-confirmatory comparisons.

Assumptions for sample size planning:

24 months accrual, 12 months follow-up after inclusion of last patient,
i.e. expected OS readout 36 months after randomization of the first patient

Power of 80% and two-sided significance level of 0.05 for the comparison of A and B

Median OS of 15 months in A and 20 months in B, i.e. hazard ratio of 0.75

constant hazards, i.e. exponential distribution

With these assumptions **631 (i.e. about 315 per arm) evaluable patients are needed** for the comparison of arms A and B in order to observe **380 OS events** and achieve a power of 80%.

About 100 patients should be added for arm C.

We suggest a 3:3:1 randomization, thus 105 patients in arm C.

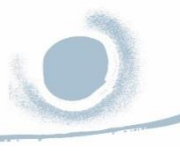
This sums up to about 735 patients.

Adjusting for 5% drop-out (and rounding to the next number divisible by 3+3+1=7)

777 patients should be randomized.

Recruiting 777 patients within 24 months translates to an average accrual of about 32.4 patients per month.

Final OS analysis should be performed after observation of 380 events in arms A and B combined.



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Primary endpoint: Overall Survival

Co-Primary endpoint: Progression free survival

Main secondary endpoints:

- QoL/PROs including pre-defined subgroups (symptomatic vs asymptomatic) and subdomains (EORTC C-30, OV28, EQ-5D-5L, PRO-CTCAE) and time until definitive deterioration including TUDD
- Overall response rate (ORR) and duration of response (DOR)
- Efficacy regarding OS, PFS, ORR/DOR depending on PD-L1 status and Teff cell signature high/low (cut- offs might be amended as there is at the moment no clear definition)
- Safety

Further planned analyses:

- Time from randomization to start of first subse-quent therapy (TFST)
- Time from randomization to start of second subse-quent therapy (TSST)

Preplanned subgroups for analysis of primary and secondary objectives:

- HRD / BRCA status
- Line of therapy
- Platinum-free-interval
- Abdominal Symptoms
- Definition of response: RECIST 1.1 vs irRC (Im-mune-related Response Criteria) vs CA125 in conjunction with MBO criteria.
- Stratified by initial lymphocyte count or lympho-cyte/neutrophile ratio or similar aspects

Multiple translationale objectives

Exploratory endpoint:

- To describe the results of an open-label chemo-free arm (arm C) regarding safety, efficacy (OS, PFS, ORR, DOR) and QoL



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Status 5/17

Synopsis approved by Roche

To do: Finalization of study protocol

Interested Groups:

All ENGOT-Groups (19!)

ANZGOG

Princes Margret Hospital Consortium, Toronto

To do: Feasibility questionnaire to interested groups