NSGO EARLY PHASE CLINICAL TRIALS UPDATE

Niraparib and niraparib-bevacizumab combination against bevacizumab alone in Women with Homologous Recombination Deficient (HRD) platinum-sensitive epithelial ovarian, fallopian tube, or peritoneal cancer.

ENGOT-OV24 - NSGO / AVANOVA

EudraCT number: 2014-004269-26

ASCO 2016

Gynecologic Cancer

Session Type: Poster Session

Date and Time: 06/06/2016 1:00 PM - 4:30 PM

Abstract Title: *The ENGOT-OV24/AVANOVA1 trial*

Abstract ID: *5555*

Sponsor: NSGO

Project Manager: Louisa Boufercha

Statistitian: DePont Christensen

PI: Mirza

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ENGOT-OV24 - NSGO / AVANOVA

Phase 1 (Completed)

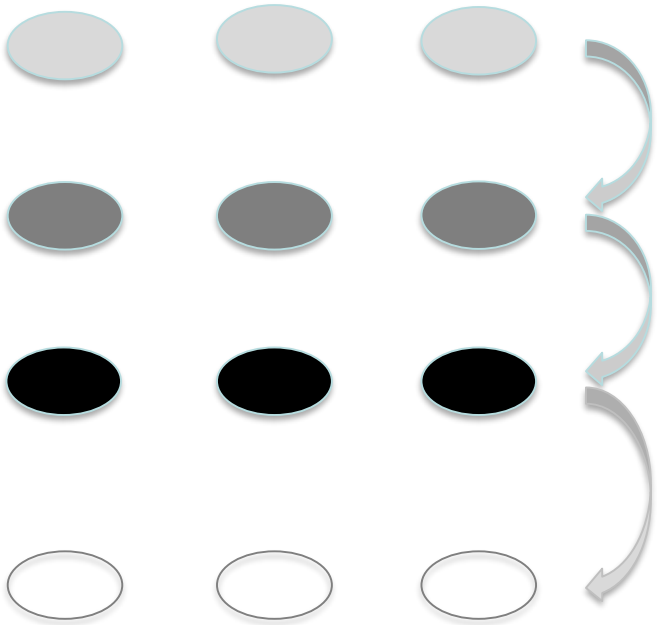
Dose Escalation from cohorts 1 to 2 to 3 to 4

Cohort 1
Niraparib 100mg + Bev 15mg

Cohort 2
Niraparib 200mg + Bev 15mg

Cohort 3
Niraparib 300mg + Bev 15mg

Cohort 4
Niraparib 300mg + Bev 7.5mg



No Dose Limiting Toxicity
Escalate to cohort 2

No Dose Limiting Toxicity
Escalate to cohort 3

Bev related toxicity
Consider cohort 4

Recommended Phase 2 Dose (RP2D) of bevacizumab-niraparib combination

Niraparib 300mg daily + Bevacizumab 15mg/kg q 3 wks

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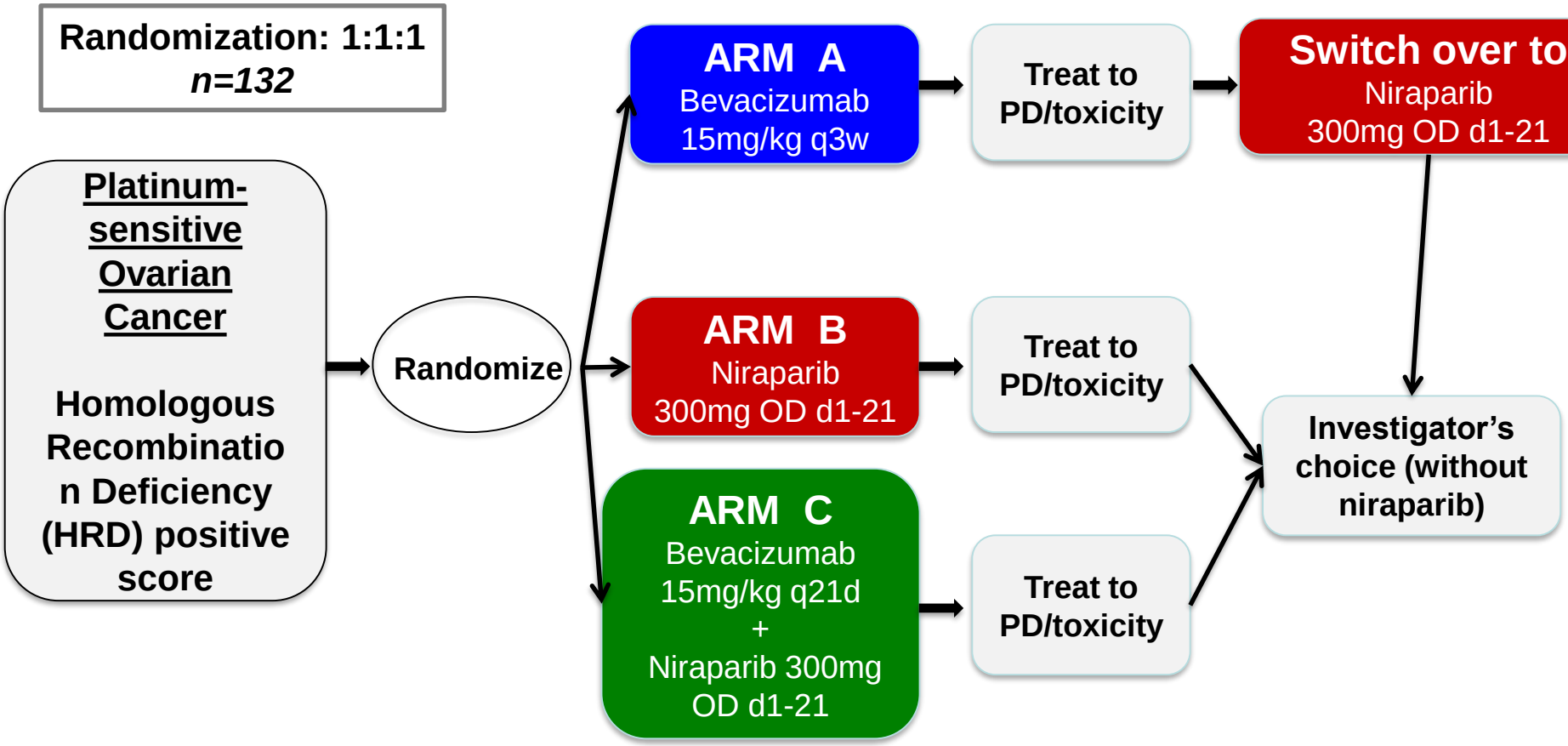
Phase 2 design



Stratifications

- **BRCA status: BRCA mutated vs. non-carrier**
- **Prior receipt of anti-angiogenic therapy (yes/no)**
- **Prior lines of therapy: 1-3 vs > 3 lines**

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Study Status

Part 1	**Completed**
Part 2	**Screening in DK**
	Activations ongoing in SWE
	Submissions completed in (NOR, FIN)
	FDA & IRB submissions in May

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A Phase 2 Randomized Umbrella Trial in Recurrent Ovarian Cancer

NSGO-OV-UMB1

ENGOT-OV30

Sponsor: Nordic Society of Gynaelogical Oncology (NSGO)
Study Chair: MR Mirza

Lead Investigators by participating groups:

MR Mirza:	Nordic Society of Gynaecological Oncology (NSGO)
C Gourley:	The Scottish Gynaecological Cancer Trials Group (SGCTG)
A Oza:	The Princess Margaret Hospital Consortium (PMHC)
I Vergote:	Belgian Gynaelogical Onology Group (BGOG)
M Friedlander:	The Australia New Zealand Gynaecological Oncology Group (ANZGOG)
J Barek:	Cooperative Ovarian Cancer Group for Immunotherapy (COGI)
K Fujiwara:	Gynecologic Oncology Trial and Investigation Consortium (GOTIC)
SY Ryu:	Korean Gynaelogical Onology Group (KGOG)
G Coukos	Ludvig Cancer Research Centre, Switzerland

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Suported by: OVA CURE

NSGO-OV-UMB1

Endpoints

Primary endpoint:
Progression-Free Survival (PFS) by RECIST

Secondary endpoints:
PFS by Immune-RECIST
PFS at 9 months
PFS at 12 months
Median PFS
PFS in each group according to trial stratification factors
Overall survival for each experimental arm
Objective response rate (ORR)
Disease control rate (DCR) (CR+PR+SD)
Duration of (Overall) Response
Patient Related Outcomes (PROs)
Safety and tolerability.

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NSGO-OV-UMB1
Key Inclusion Criteria

- **Relapsed ovarian cancer with TFIchemo either < 6months or ≥ 6months. Patients with TFIchemo of ≥ 6months must have received 3 courses of chemotherapy.**

- **High-grade serious, endometriod, undifferentiated. Apart from these types a limited number of low grade serious carcinoma, clear-cell carcinoma and mucinous carcinoma can be enrolled in this study - maximum of 5 patients per study cohort.**

- **Patient agrees to undergo all analysis (blood, serum, tissue) including tumor biopsy.**

- **ECOG performance status 0-1**
- **Serum albumin >30g/l.**

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NSGO-OV-UMB1

3:1 randomization
In each cohort
Cross-over in Standard arm permitted

Relapsed ovarian cancer

Tumor biopsy

Cohort A — Coordinating Lead Group SGCTG
Durvalumab

Standard of care

Cohort B — Coordinating Lead Group PMHC
Durva + AZD5069

Standard of care

Cohort C — Coordinating Lead Group NSGO
Durva + AZD9150

Standard of care

PET-CT, tumor, blood, plasma and serum samples

Tumor biopsy At progression

Next-Generation Sequencing if required

PET-CT, tumor, blood, plasma and serum samples

Treatment until disease progression

Continous blood, plasma and serum samples

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Suported by:

NSGO-OV-UMB1
Experimental Treatment Arms

Abbreviations: C=cycle; D=day; IBW=ideal body weight; IV=intravenous; PO=by mouth.

	7-day Lead-In							Treatment Cycle 1 (and beyond) 28 days																													
								C1 Week 1							C1 Week 2							C1 Week 3							C1 Week 4							
	D -7	D -6	D -5	D -4	D -3	D -2	D -1	D 1							D 8							D 15							D 22							
Treatment cohort A: MEDI4736 alone																																				
MEDI4736 (10mg/kg IV)								x														x														
Treatment cohort B: AZD5069 in combination with MEDI4736																																				
AZD5069 (mg BID, PO)	x x	x x	x x	x x	x x	x x	x x	x x	x x	x x	x x	x x	x x	x x	x x	x x	x x	x x	x x	x x	x x	x x	x x	x x	x x	x x	x x	x x	x x	x x	x x	x x	x x	x x	x x	x x
Medi4736 (mg/kg IV)								x														x														
Treatment cohort C: AZD9150 in combination with MEDI4736																																				
AZD9150 (mg/kg IBW IV)	x		x		x			x							x							x							x							
Medi4736 (mg/kg IV)								x														x														

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NSGO-OV-UMB1
Study Status

Initial grant from AZ received

Kickoff meeting of Steering Committee Meeting (Feb 20, 2016, London)

Major grant application for study cohorts A-C submitted (March 1, 2016)

Distribution of responsibilities being agreed between the lead groups & sponsor (NSGO)

Planned submissions June 2016

Next wave of molecules/combinations under discussion

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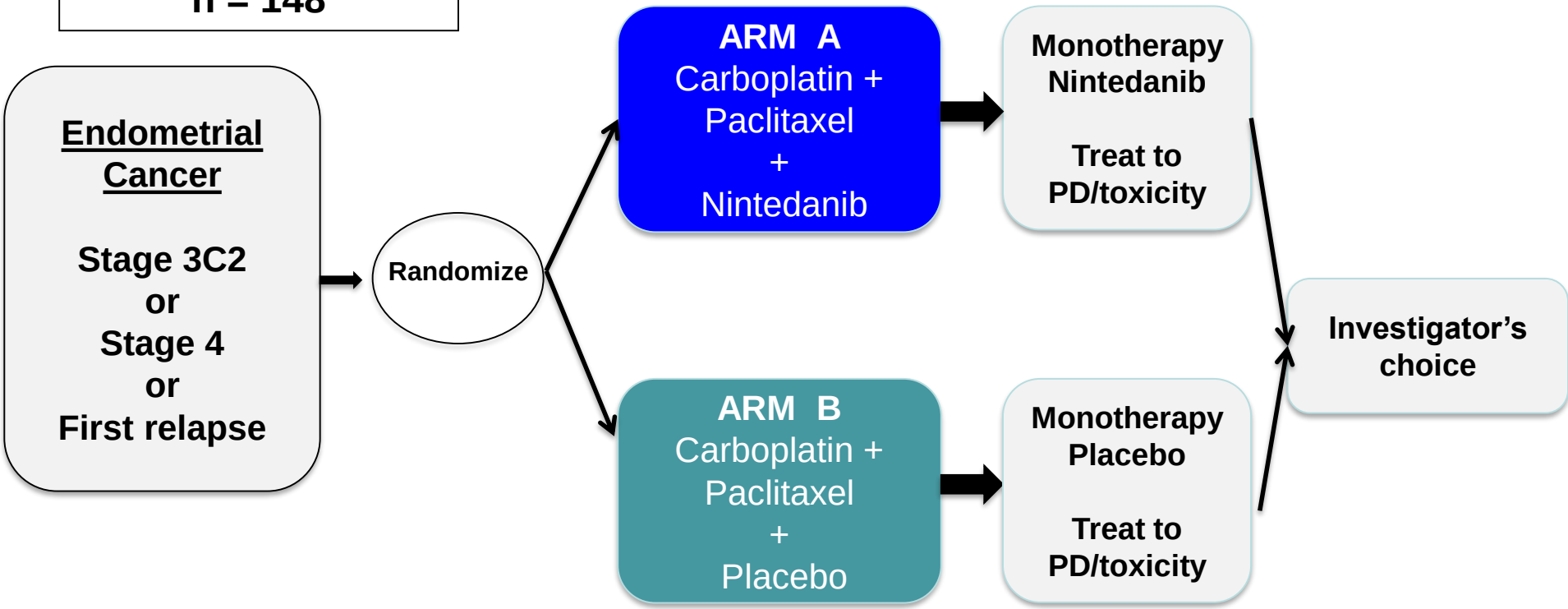
A randomized double-blind placebo-controlled phase II trial of first-line combination chemotherapy with Nintadenib for patients with advanced or recurrent endometrial cancer

ENGOT-EN1 / FANDANGO

NCT02730416

Randomization: 1:1
n = 148



Sponsor: NSGO
Project Manager: Christina Jederud
Statistitian: DePont Christensen
PI: Mirza

Stratifications
- stage of disease (stage 3C2 vs. stage 4 vs. recurrent disease)
- Prior adj chemotherapy (yes/no)
- Disease status (Measurable disease vs. non-measurable)

A randomized double-blind placebo-controlled phase II trial of first-line combination chemotherapy with Nintadenib for patients with advanced or recurrent endometrial cancer

ENGOT-EN1 / FANDANGO

Study Status

Feasibility in collaborative groups completed

Intergroup contracts being signed

NSGO site-contracts being signed

Submissions DK (DHMA & VEK) **– completed**

Submissions SE (CA & EC) **– completed**

Submissions to other countries to follow

(GSO(FIN, NOR, BEL) **GINECO, NOGGO)**

ALMAC (drug supply): ready by mid July 2016

Expected first patient in: August/September 2016

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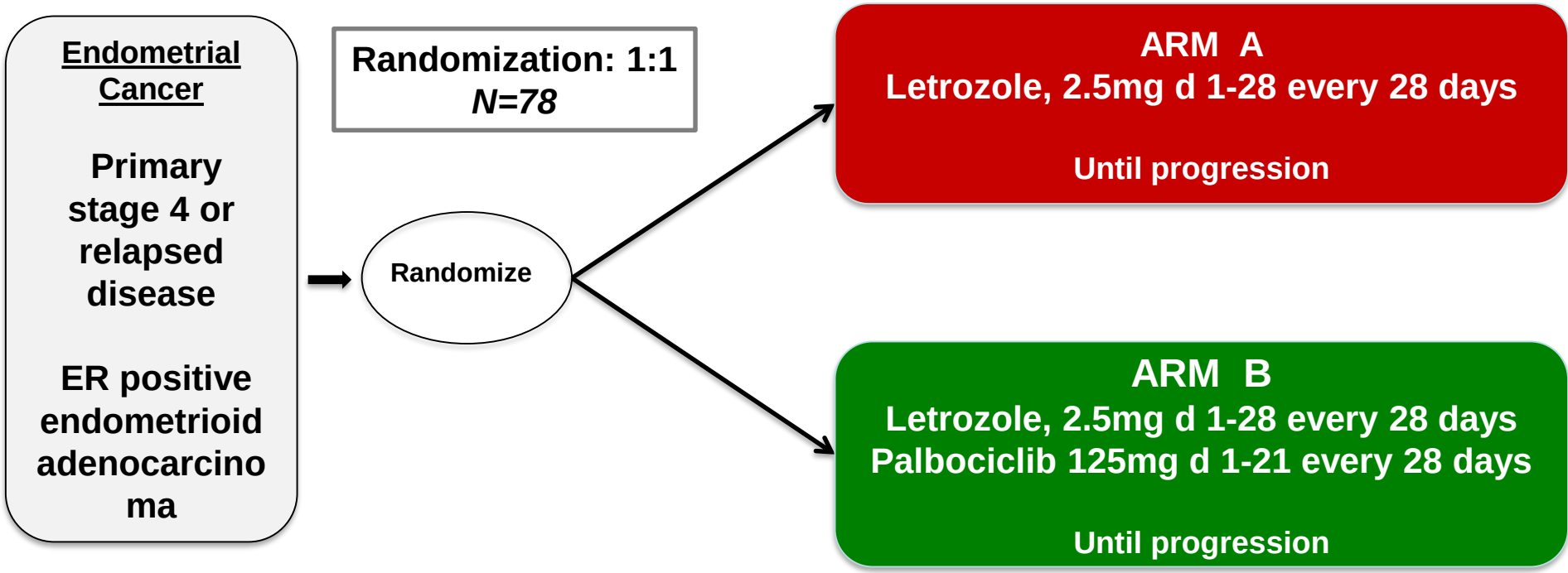
A randomized phase II trial of Palbociclib in combination with letrozole versus letrozole for patients with oestrogen receptor positive recurrent endometrial cancer.

ENGOT-EN3-NSGO/PALEO

NCT02730429



Sponsor: NSGO
Project Manager: Joan Løhndorf
Statistitian: DePont Christensen
PI: Mirza

Stratification:

- Number of prior lines of therapy (primary advanced disease vs. 1st relapse vs. ≥2 relapses)
- Measurable vs. evaluable disease
- Prior use of MPA/Megace (prior MPA/Megace use capped to a maximum of 50%)

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A randomized phase II trial of Palbociclib in combination with letrozole versus letrozole for patients with oestrogen receptor positive recurrent endometrial cancer.

ENGOT-EN3-NSGO/PALEO

Study Status

Feasibility is being performed

Planned Submission starts in May-June 2016

Planned first Patient in: October 2016

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