# Onco-Gynécologie

Dr Anne Floquet, Oncologue médicale - Institut Bergonié (Bordeaux)

# Liens d’intérêt

- Astra Zeneca, GSK, MSD, Roche, Clovis Oncology, Pharma Mar

# SOLO 1

## Maintenance olaparib for patients with newly diagnosed advanced ovarian cancer and a BRCA mutation: 5-year follow-up from SOLO1

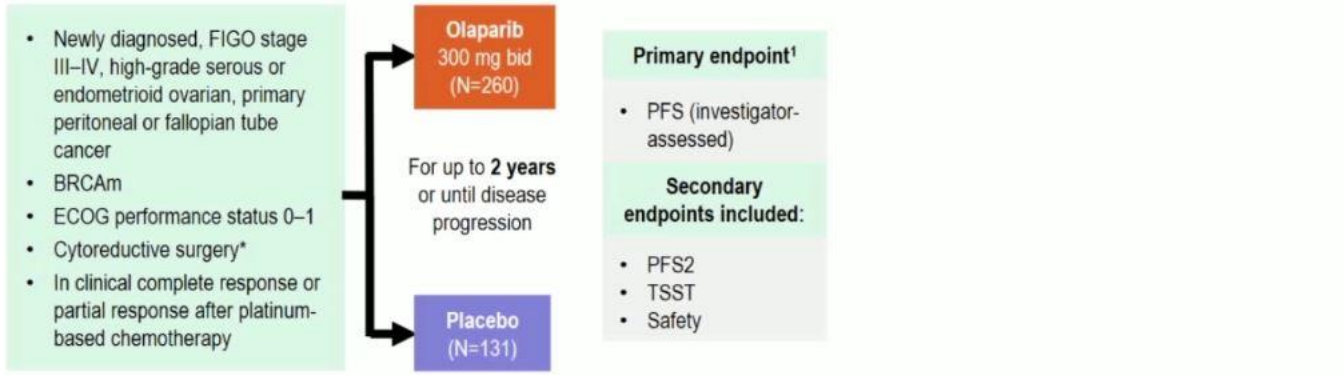
Susana Banerjee,[1] Kathleen Moore,[2] Nicoletta Colombo,[3] Giovanni Scambia,[4] Byoung-Gie Kim,[5] Ana Oaknin,[6] Michael Friedlander,[7] Alla Lisyanskaya,[8] Anne Floquet,[9] Alexandra Leary,[10] Gabe S Sonke,[11] Charlie Gourley,[12] Amit Oza,[13] Antonio González-Martín,[14] Carol Aghajanian,[15] William Bradley,[16] Eileen Holmes,[17] Elizabeth S Lowe,[18] Paul DiSilvestro[19]

*[1]The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, UK; [2]Stephenson Oklahoma Cancer Center, Oklahoma City, OK, USA; [3]University of Milan-Bicocca and Istituto Europeo di Oncologia, Milan, Italy; [4]Università Cattolica del Sacro Cuore-Fondazione Policlinico A. Gemelli, IRCCS, Rome, Italy; [5]Samsung Medical Center, Sungkyunkwan University School of Medicin Seoul, Korea; [6]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; [7]University of New Sou Wales Clinical School, Prince of Wales Hospital, Randwick, Australia; [8]St Petersburg City Oncology Dispensary, St Petersburg, Russia; [9]Institut Bergonié, Comprehensive Cancer Centre, Bordeaux, and Groupe d'Investigateurs Nationaux pour l'Etude des Cancers Ovariens, France; [10]Institut Gustave-Roussy, Villejuif, and Groupe d'Investigateurs Nationaux pour l'Etude des Cancers Ovariens, France; [11]The Netherlands Cancer Institute, Amsterdam, The Netherlands; [12]Cancer Research UK Edinburgh Centre, University of Edinburgh, Edinburgh, UK; [13]Princess Margaret Cancer Centre, Toronto, ON, Canada; [14]Clínica Universidad de Navarra, Madrid, Spain; [15]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [16]Froedtert and the Medical College of Wisconsin, Milwaukee, WI, USA; [17]AstraZeneca, Cambridge, UK; [18]AstraZeneca, Gaithersburg, MD, USA; [19]Women & Infants Hospital, Providence, RI, USA*

Conducted in partnership with the Gynecologic Oncology Group (GOG-3004)
ClinicalTrials.gov identifier: NCT01844986. This study was sponsored by AstraZeneca and is part of an alliance between AstraZeneca and Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA

## The SOLO1 trial[1]

5-year survival for newly diagnosed advanced ovarian cancer is 30-50% and patients are at high risk of relapse;[2,3] treatment goals in this setting include delay of recurrence and, for some patients, increased chance of cure

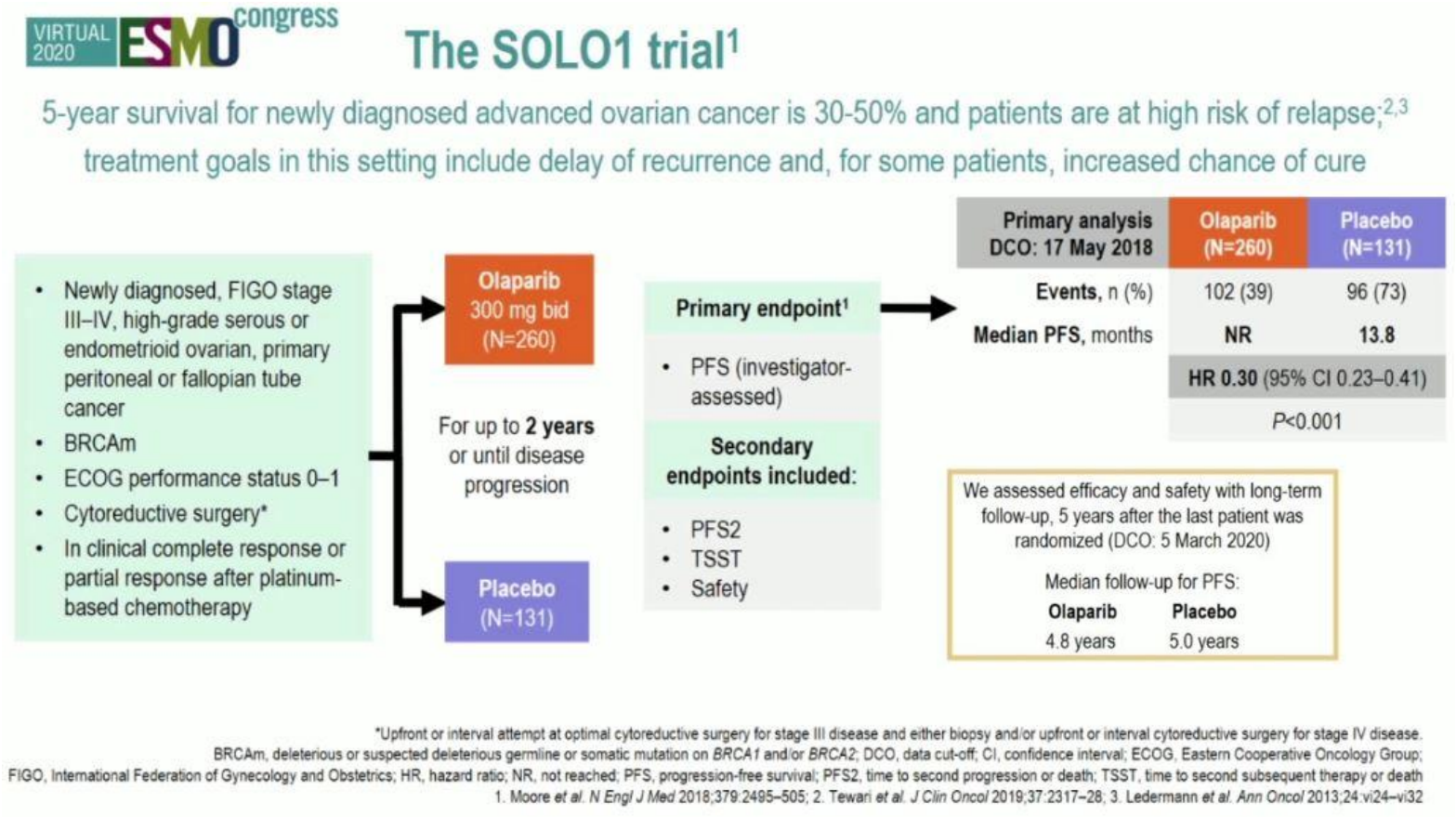



*Upfront or interval attempt at optimal cytoreductive surgery for stage III disease and either biopsy and/or upfront or interval cytoreductive surgery for stage IV disease.
BRCAm, deleterious or suspected deleterious germline or somatic mutation on *BRCA1* and/or *BRCA2*; ECOG, Eastern Cooperative Oncology Group; FIGO, International Federation of Gynecology and Obstetrics; PFS, progression-free survival; PFS2, time to second progression or death; TSST, time to second subsequent therapy or death

1. Moore *et al. N Engl J Med* 2018;379:2495–505; 2. Tewari *et al. J Clin Oncol* 2019;37:2317–28; 3. Ledermann *et al. Ann Oncol* 2013;24:vi24–vi32

*D'après la présentation du Dr Banerjee*

# SOLO 1

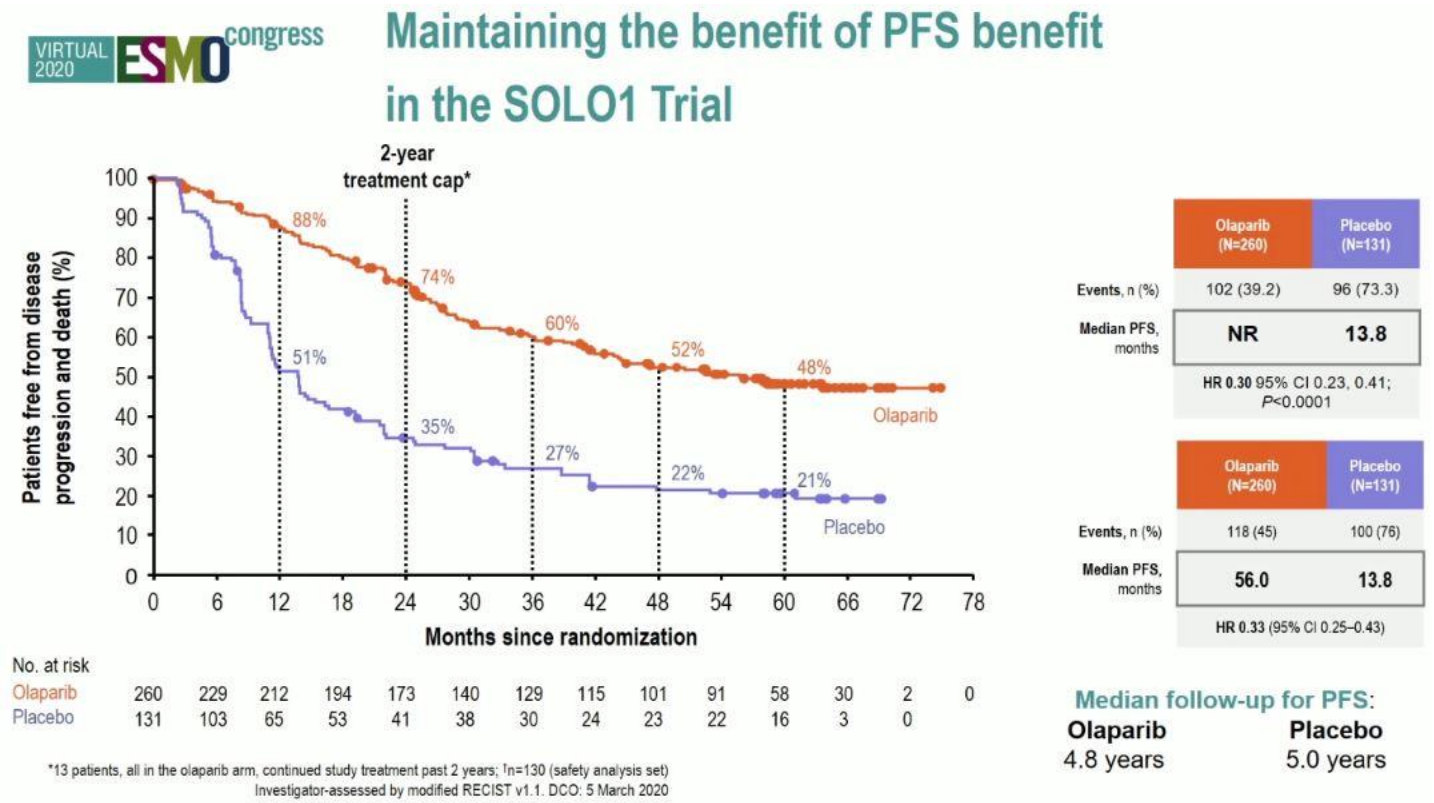



*D'après la présentation du Dr Banerjee*

# SOLO 1

**Changement de pratique confirmé**

**En attente de remboursement**




| | Olaparib (N=260) | Placebo (N=131) |
|---|---|---|
| Events, n (%) | 102 (39.2) | 96 (73.3) |
| Median PFS, months | NR | 13.8 |

HR 0.30 95% CI 0.23, 0.41; *P*<0.0001

| | Olaparib (N=260) | Placebo (N=131) |
|---|---|---|
| Events, n (%) | 118 (45) | 100 (76) |
| Median PFS, months | 56.0 | 13.8 |

HR 0.33 (95% CI 0.25–0.43)

**Median follow-up for PFS:**

**Olaparib** 4.8 years

**Placebo** 5.0 years

## Conclusion

- 1er essai avec Parpi en maintenance dans le cancer de l'ovaire avancé avec mutation BRCA montrant le maintien d'un bénéfice en SSP avec un recul aussi important
- Avec une magnitude jamais observée
- Plus de la moitié des patientes en RC et traitées par olaparib sont toujours contrôlées (courbes non montrées)
- Pas de nouveaux signaux de tolérance
  - SMD/LAM < 1,5 %

*D'après la présentation du Dr Banerjee*

# IMagyn 050

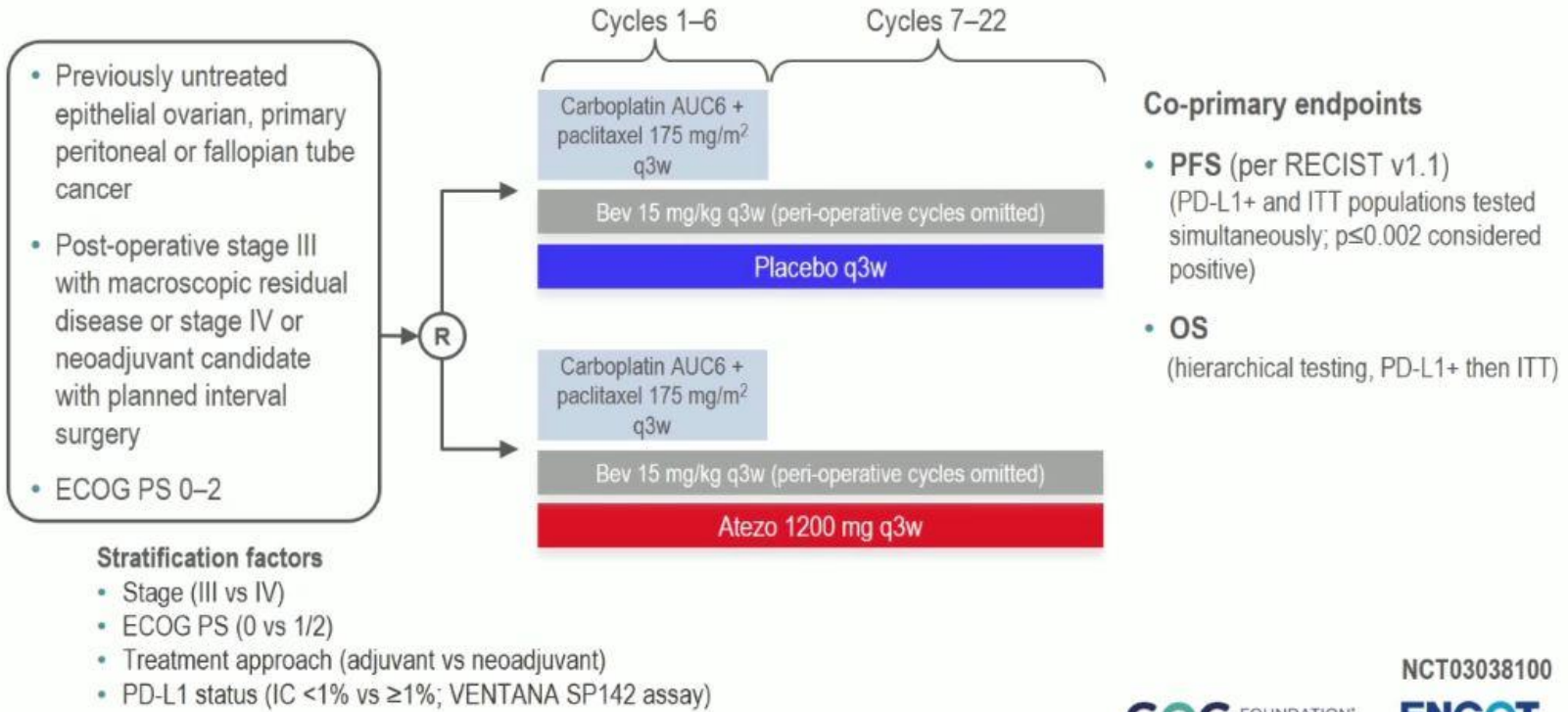
## Primary results from IMagyn050/GOG 3015/ENGOT-OV39, a double-blind placebo-controlled randomised phase 3 trial of bevacizumab-containing therapy ± atezolizumab for newly diagnosed stage III/IV ovarian cancer

K Moore[1], M Bookman[2], J Sehouli[3], A Miller[4], C Anderson[5], G Scambia[6], T Myers[7], C Taskiran[8], K Robison[9], J Maenpaa[10], L Willmott[11], N Colombo[12], J Thomes-Pepin[13], MA Gold[14], C Aghajanian[15], F Wu[16], L Molinero[16], V Khor[16], YG Lin[16], S Pignata[17]

[1]Stephenson Cancer Center at the University of Oklahoma Health Sciences Center, Oklahoma City, OK, and Sarah Cannon Research Institute, Nashville TN, USA; [2]Kaiser Permanente Northern California, San Francisco, CA, USA; [3]Charité-Medical University of Berlin (Campus Virchow Klinikum), Berlin, Germany; [4]Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA; [5]Willamette Valley Cancer Institute, Eugene, OR, USA; [6]Fondazione Policlinico Universitario Gemelli IRCCS, Rome, Italy; [7]Baystate Medical Center, Springfield, MA, USA; [8]Koc University School of Medicine and VKV American Hospital, Istanbul, Turkey; [9]Women and Infants Hospital, Providence, RI, USA; [10]Tampere University and University Hospital, Tampere, Finland; [11]Arizona Oncology Associates, PC, Phoenix, AZ, USA; [12]European Institute of Oncology, IRCCS, and University of Milan-Bicocca, Milan, Italy; [13]Minnesota Oncology, Maplewood, MN, USA; [14]Oklahoma Cancer Specialists, Tulsa, OK, USA; [15]Weill Cornell Medical College, New York, NY, USA; [16]Genentech, Inc., South San Francisco, CA, USA; [17]Istituto Nazionale Tumori IRCCS Fondazione G Pascale, Napoli, Italy

GOG FOUNDATION · IMagyn050 OVARIAN · ENGOT European Network of Gynaecological Oncological Trial groups

## Trial design




**Co-primary endpoints**

- **PFS** (per RECIST v1.1)
  (PD-L1+ and ITT populations tested simultaneously; p≤0.002 considered positive)
- **OS**
  (hierarchical testing, PD-L1+ then ITT)

**Stratification factors**

- Stage (III vs IV)
- ECOG PS (0 vs 1/2)
- Treatment approach (adjuvant vs neoadjuvant)
- PD-L1 status (IC <1% vs ≥1%; VENTANA SP142 assay)

NCT03038100

GOG FOUNDATION · ENGOT European Network of Gynaecological Oncological Trial groups

Atezo = atezolizumab; AUC = area under the curve; bev = bevacizumab; ECOG PS = Eastern Cooperative Oncology performance status; IC = immune cell; ITT = intent to treat; OS = overall survival; PFS = progression-free survival; q3w = every 3 weeks; RECIST = Response Evaluation Criteria in Solid Tumours

*D'après la présentation du Dr Moore*

# IMagyn 050

## Overall safety profile

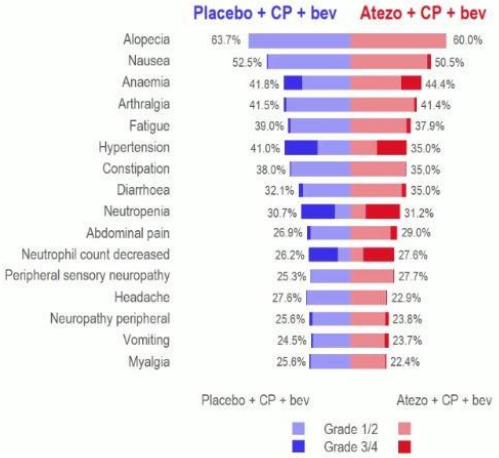
| AEs, n (%) | Placebo + CP + bev (n=644) | Atezo + CP + bev (n=642) |
|---|---|---|
| All-grade AEs | 643 (100) | 642 (100) |
| AE with fatal outcome | 8 (1) | 9 (1) |
| Related AE with fatal outcome | 5 (0.8) | 4 (0.6) |
| SAE | 211 (33) | 304 (47) |
| Related SAE | 135 (21) | 222 (35) |
| Grade 3/4 AE[a] | 471 (73) | 509 (79) |
| Related grade 3/4 AE | 429 (67) | 479 (75) |
| AE leading to any treatment discontinuation | 140 (22) | 167 (26) |
| AE leading to atezo/placebo discontinuation | 40 (6) | 98 (15) |
| AE leading to bev discontinuation | 109 (17) | 116 (18) |
| AE leading to atezo dose interruption | 385 (60) | 425 (66) |
| AESI for atezo | 336 (52) | 469 (73) |
| AESI with fatal outcome[b] | 0 | 1 (0.2) |
| Grade 3/4 AESI[a] | 38 (6) | 109 (17) |

- The addition of atezolizumab did not compromise delivery of backbone therapy

[a]Grade 3/4 AE refers to highest grade experienced. [b]The fatal AESI myasthenia gravis was considered by investigator as related to atezolizumab
AE = adverse event; AESI = adverse event of special interest; SAE = serious adverse event

## Most common AEs

Most common AEs (≥25% in either arm)




SAEs with ≥2% incidence in either arm

| SAEs | Placebo + CP + bev (n=644) | Atezo + CP + bev (n=642) |
|---|---|---|
| Febrile neutropenia | 3.7% | 8.4% |
| Pyrexia | 1.2% | 4.0% |

## AEs of special interest for atezolizumab (>2 patients in either arm)

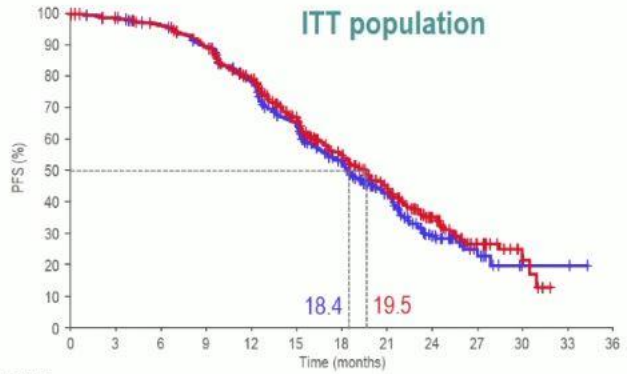
| Immune-mediated AEs by medical concept, n (%) | Placebo + CP + bev (n=644) | | Atezo + CP + bev (n=642) | |
|---|---|---|---|---|
| | Any grade | Grade 3/4[a] | Any grade | Grade 3/4[a] |
| Hepatitis | 14 (2.2) | 4 (0.6) | 17 (2.6) | 7 (1.1) |
| Pneumonitis | 4 (0.6) | 0 | 12 (1.9) | 1 (0.2) |
| Hypothyroidism | 83 (12.9) | 1 (0.2) | 166 (25.9) | 3 (0.5) |
| Hyperthyroidism | 23 (3.6) | 0 | 51 (7.9) | 0 |
| Adrenal insufficiency | 2 (0.3) | 0 | 5 (0.8) | 1 (0.2) |
| Infusion-related reactions | 49 (7.6) | 2 (0.3) | 78 (12.1) | 5 (0.8) |
| Colitis | 11 (1.7) | 7 (1.1) | 21 (3.3) | 11 (1.7) |
| Rash | 165 (25.6) | 6 (0.9) | 265 (41.3) | 41 (6.4) |
| Severe cutaneous reactions | 3 (0.5) | 0 | 15 (2.3) | 8 (1.2) |
| Myositis | 5 (0.8) | 0 | 4 ( 0.6) | 2 (0.3) |
| Meningoencephalitis[b] | 3 (0.5) | 0 | 3 ( 0.5) | 1 (0.2) |
| Pancreatitis | 0 | 0 | 5 ( 0.8) | 4 (0.6) |

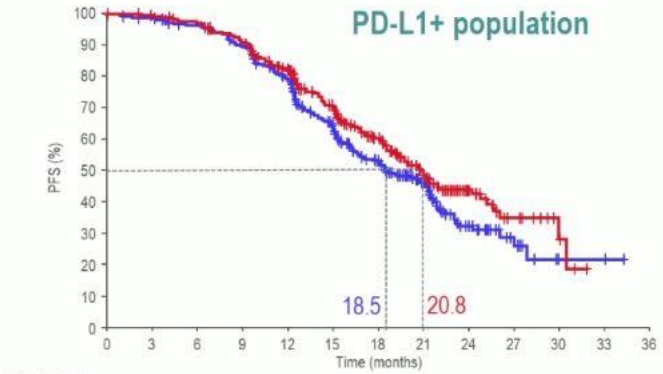
[a]Grade 3/4 AE refers to highest grade experienced. [b]No cases of meningitis, 1 patient with encephalitis, remaining events were photophobia. In the atezo arm there was one (fatal) case of myasthenia gravis and two cases of systemic immune activation (one grade 4, both resolved). Diabetes mellitus and rhabdomyolysis each occurred in 2 patients (0.3%) in the atezo arm (grade 3/4 in 1 patient; 0.2%) and there were three cases of diabetes mellitus (0.5%) in the placebo arm (no grade 3/4). Myocarditis and Guillain–Barré syndrome each occurred in 1 patient (0.2%) in each arm, at grade 3/4 in all cases except for myocarditis in the atezo arm. There were no cases of haemophagocytic lymphohistiocytosis or hypophysitis in either arm

*D'après la présentation du Dr Moore*

# IMagyn 050

## Progression-free survival



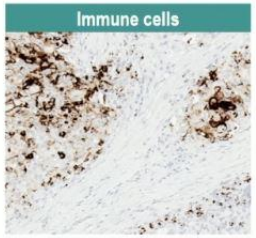




| PFS | ITT population | | PD-L1+ population | |
|---|---|---|---|---|
| | Placebo + CP + bev (n=650) | Atezo + CP + bev (n=651) | Placebo + CP + bev (n=393) | Atezo + CP + bev (n=391) |
| Patients with events, n (%) | 341 (52.5) | 323 (49.6) | 199 (50.6) | 167 (42.7) |
| Median PFS, months (95% CI) | 18.4 (17.2–19.8) | 19.5 (18.1–20.8) | 18.5 (16.6–21.4) | 20.8 (19.1–24.2) |
| Stratified HR (95% CI) | 0.92 (0.79–1.07) | | 0.80 (0.65–0.99) | |
| Stratified log-rank p-value | 0.2785 | | 0.0376 | |
| 2-year event-free rate (95% CI) | 29.1 (23.9–34.3) | 35.1 (30.0–40.3) | 32.2 (25.4–39.0) | 43.9 (37.2–50.5) |

CI = confidence interval; HR = hazard ratio

## VENTANA SP142 PD-L1 immunohistochemistry

**Ovarian cancer:**
PD-L1 expression mainly on IC




**IMagyn050 PD-L1 analyses**

Co-primary endpoint:

PD-L1 IC positive — IC ≥1%

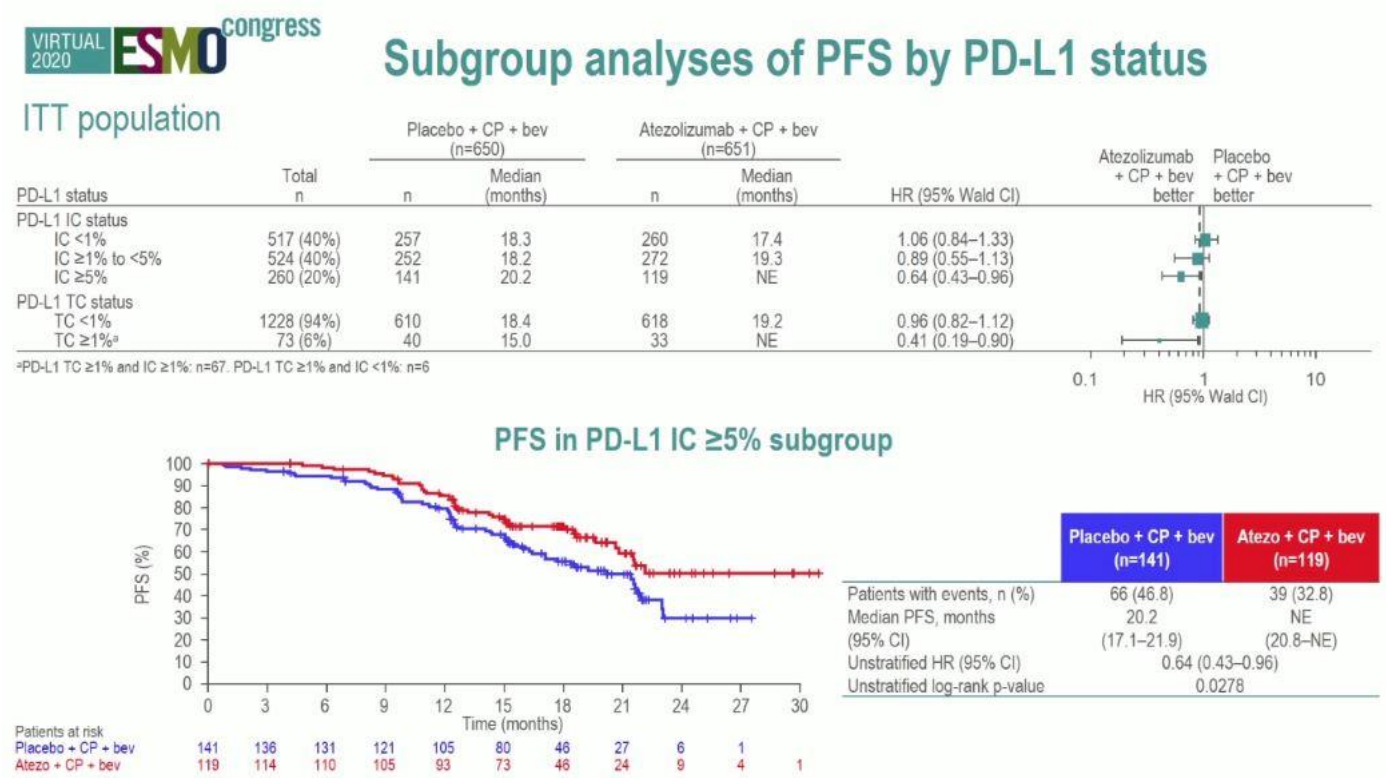
Exploratory analysis:

| | | | |
|---|---|---|---|
| PD-L1 IC negative | IC <1% | PD-L1 TC negative | TC <1% |
| IC positive-low | IC ≥1–<5% | TC positive | TC ≥1% |
| IC positive-high | IC ≥5% | | |

Scoring:
PD-L1 IC: area of PD-L1-stained tumour-infiltrating immune cells (ICs) as a percentage of tumour area
PD-L1 TC: percentage of PD-L1-stained tumour cells (TCs)

*D'après la présentation du Dr Moore*

# IMagyn 050




*D'après la présentation du Dr Moore*

# IMagyn 050

Pas de changement de pratique

## Conclusion:

➢ Essai négatif

L'ajout d' Atézolizumab à la combinaison CARTAX + Avastin n'augmente pas la SSP

**ITT pop**: med SSP: 19,5 m vs 18,4 m (standard)

HR =0.92 IC 95%[0,79-1,07]

**PDL1+ (≥1%) pop**: med SSP : 20,8 m vs 18,5 m (standard)

HR= 0.80 IC 95%[0,65-0,99]

Sous groupe exploratoire : PD-L1≥5% plus intéressant

➢ Toxicités: celles attendues

*D'après la présentation du Dr Moore*

# OVAIRE Rechute PS 6-12 mois
# INOVATYON

## INOVATYON study

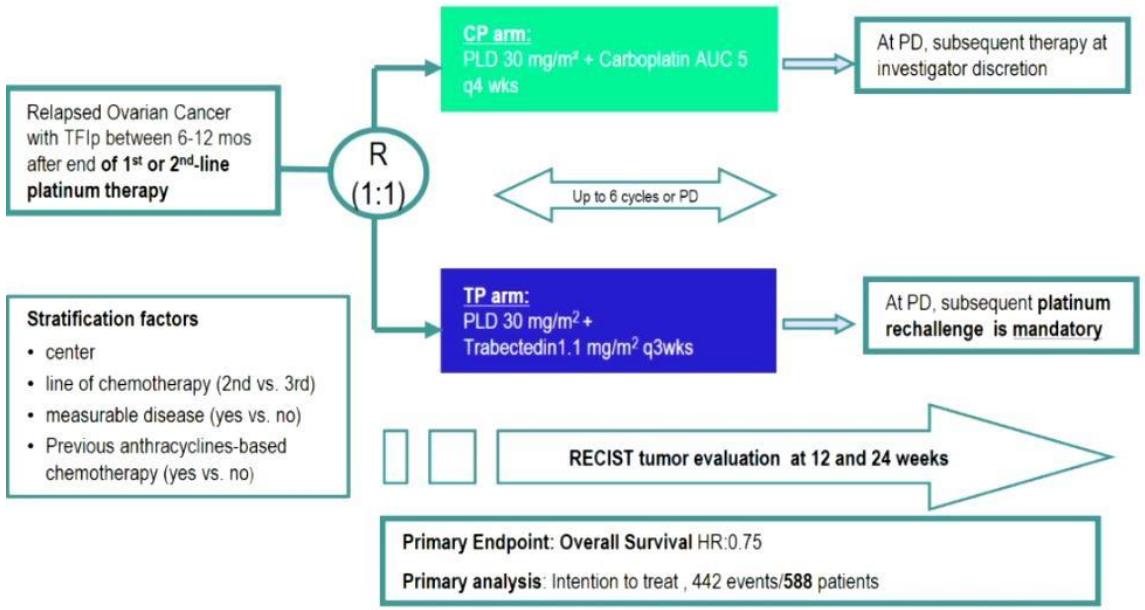
**INternational OVArian cancer patients Trial with YONdelis**

**Randomized phase III international study comparing trabectedin/PLD followed by platinum at progression vs Carboplatin/PLD in patients with recurrent ovarian cancer progressing within 6-12 months after last platinum line.**


N. Colombo[1], A. Gadducci[2], J. Sehouli[3], E. Biagioli[4], G.-B. Nyvang[5], S. Riniker[6], A. Montes[7], N. Ottevanger[8], A. G. Zeimet[9], I. Vergote[10], G. Funari[4], A. Baldoni[11], G. Tognon[12], A. De Censi[13], C. Churruca Galaz[14], R. Chekerov[3], J. Maenpaa[15], E. Rulli[4], R. Fossati[4], A. Poveda[16]

[1]*Gynecologic Cancer Program, European Institute of Oncology, IRCCS and University of Milano Bicocca, Milan, Italy,* [2]*University of Pisa, Italy,* [3]*Charité-Berlin University of Medicine, Germany,* [4]*Istituto di Ricerche Farmacologiche Mario Negri - IRCCS, Milano, Italy,* [5]*University Hospital, Odense, Denmark,* [6]*Kantonsspital St.Gallen, Switzerland,* [7]*Guy's & St Thomas' NHS Foundation Trust, London, United Kingdom,* [8]*Radboud University Medical Center, Nijmegen, Netherlands,* [9] *Medical University of Innsbruck, Austria* [10]*Gynecology, University Hospitals Leuven Belgium,* [11]*Istituto Oncologico Veneto, Padova, Italy,* [12]*ASST Spedali Civili-Università degli Studi di Brescia, Brescia, Italy,* [13]*E.O. Ospedali Galliera, Genova, Italy,* [14]*HU Donostia – Onkologikoa, Donostia-San Sebastian, Spain,* [15]*Tampere University Hospital, Finland,* [16]*Hospital Quirónsalud, Valencia, Spain*

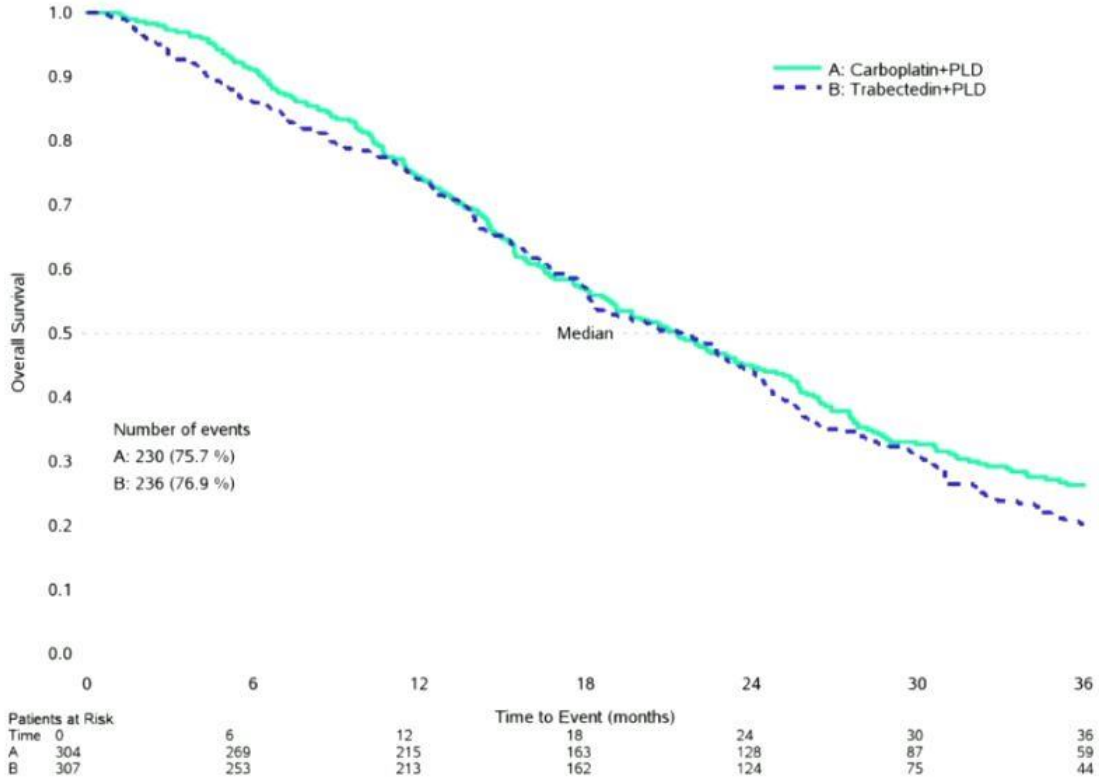

## Study Design




*D'après la présentation du Dr Colombo*

# OVAIRE Rechute PS 6-12 mois
# INOVATYON

## Primary Endpoint:Overall Survival




**Median follow-up:** 44mos

**Median OS (Q1-Q3):**

Carboplatin+PLD: 21.3 mos (11.8-37.0)

Trabectedin+PLD: 21.5 mos (11.6-32.4)

**HR OS [95% CI]; p-value :**

Trabectedin+PLD vs. Carboplatin+PLD

1.10 [0.92-1.32]; 0.284

*D'après la présentation du Dr Colombo*

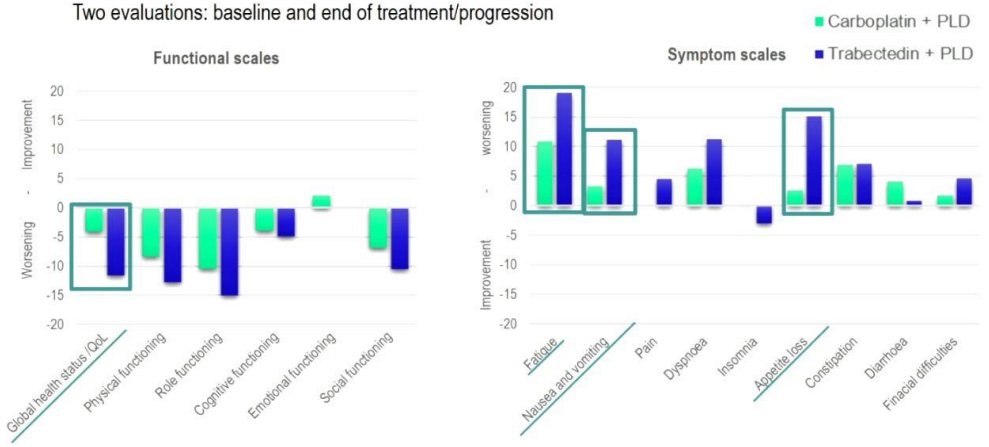
# OVAIRE Rechute PS 6-12 mois INOVATYON

## Treatment Compliance

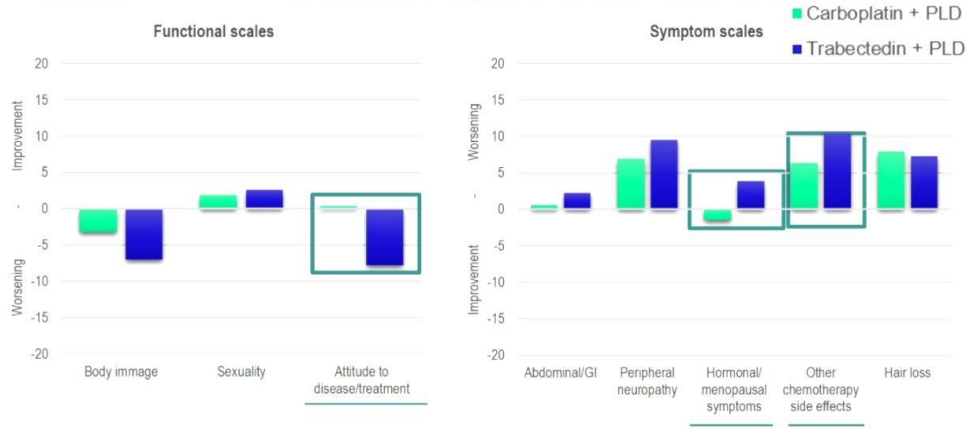
| | Carboplatin+PLD (N=304) | Trabectedin+PLD (N=307) |
|---|---|---|
| **Never started** - (%) | 3.3 | 1.0 |
| **Treatment interrupted >=6 cycles** - (%) | 68.1 | 53.4 |
| **Treatment interrupted < 6 cycles** - (%) | 28.3 | 45.6 |
| *Reason: -n (%)* | | |
| Disease progression | 55 (64.0) | 70 (50.0) |
| Unacceptable toxicity | 13 (15.1) | 27 (19.3) |
| Patient refusal/Consent withdrawn | 4 (4.6) | 13 (12.8) |
| Physician decision | 5 (5.8) | 8 (5.7) |
| Death | 5 (5.8) | 6 (4.3) |
| Intercurrent illness of sufficient severity | 1 (1.2) | 8 (5.7) |
| Lost to follow-up | - | 1 (0.7) |
| Screening failure | 1 (1.2) | - |
| Other | 2 (2.3) | 2 (1.4) |
| **Treatment ongoing** - (%) | 0.3 | - |

## Secondary Endpoint: Quality of life (EORTC - QLQ-C30)

Two evaluations: baseline and end of treatment/progression




## Secondary Endpoint: Quality of life (EORTC - QLQ-OV28)




*D'après la présentation du Dr Colombo*

# OVAIRE Rechute PS 6-12 mois INOVATYON

Pas de changement de pratique

## Conclusion

➢ Essai négatif

- L' objectif principal n'est pas atteint (HR:1.1, IC 95% [0.92-1.32], p=0,284)

Trabectédine+DoxLipeg suivi de platine à la rechute n'allonge pas la survie globale des patientes en comparaison de Carbo+DoxLipeg d'emblée suivi d'une autre chimio à la rechute

**Le traitement standard d'une 1ère ou 2ème rechute dans les 6-12 mois après platine reste…la reprise de la combo avec platine…**

➢ Et ce, avec un meilleur profil de tolérance (hématologie, GI, asthénie, hépatique) et de QDV

*D'après la présentation du Dr Colombo*

# Onco-Gynécologie

Dr Elise Deluche, Oncologue médicale – CHU Limoges

# Liens d’intérêt

- Novartis, Pfizer, Astra Zeneca

# OVAIRE Rechute <12 mois

# TAPAZ study

VIRTUAL 2020 ESMO congress

## Paclitaxel with or without pazopanib in ovarian cancer patients with relapse during bevacizumab maintenance therapy

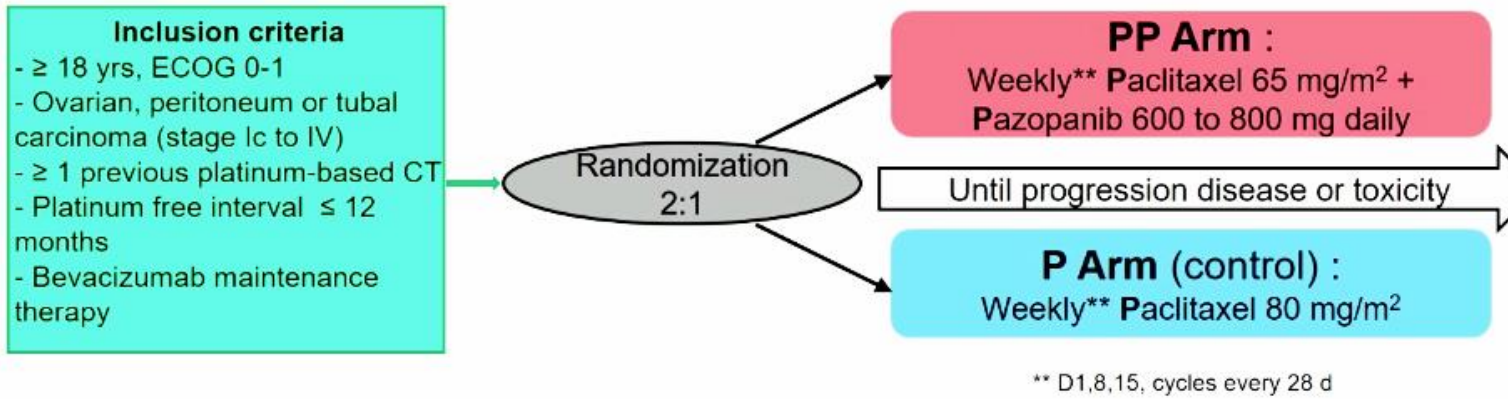
*The GINECO randomized phase 2 TAPAZ study*

E. Joly Lobbedez[2], M. Fabbro[2], D. Berton[3], J. Lequesne[4], A. Anota[5], A. Puszkiel[6], A. Floquet[7], M. Cancel[8], H. Bourgeois[9], I. Bengrine Lefevre[10], B. You[11], F. Pommeret[12], A. Lortholary[13], D. Spaeth[14], I. Martin-Babau[15], C. Abdeddaim[16], M.-C. Kaminsky-Forrett[17], D. Petran[18], M. Provansal Gross[19], P.-E. Brachet[1]

[1]Medical Oncology, Centre François Baclesse, Caen, France; [2]Medical Oncology, ICM Regional Cancer Institute of Montpellier, Montpellier, France; [3]Medical Oncology, Institut de Cancérologie de l'Ouest, Saint Herblain, France; [4]Clinical Research, Centre François Baclesse, Caen, France; [5]Methodology and Quality of Life in Oncology Unit (INSERM U1208) & French National Platform Quality of Life and Cancer, CHRU Besançon - Hopital Jean Minjoz, Besançon, France; [6]EMR UCBL/HCL 3738, Univ. Lyon, Université Claude Bernard Lyon 1, Faculté de médecine Lyon-Sud, Lyon, France; [7]Medical Oncology, Institute Bergonié, Bordeaux, France; [8]Medical Oncology, CHU Bretonneau Centre, Tours University, Tours, France; [9]Medical Oncology Department, Centre Jean Bernard - Clinique Victor Hugo and GINECO group France, Le Mans, France; [10]Medical Oncology, Centre Georges François Leclerc, Dijon, France; [11]Medical Oncology, Institut de Cancérologie des Hospices Civils de Lyon (HCL), CTD-ML, BRECO, Univ Lyon, Université Claude Bernard Lyon 1, Faculté de médecine Lyon-Sud, EMR UCBL/HCL 3738, Lyon, France; [12]Département de médecine oncologique, Gustave Roussy, Villejuif, France; [13]Oncologie, Centre Catherine de Sienne, Hopital privé du Confluent, Nantes, France; [14]Oncologie, Centre d'Oncologie de Gentilly, Nancy, France; [15]Medical Oncology, Centre Armoricain d'Oncologie CARIO-HCPA-BEC 22, Plerin, France; [16]Medical Oncology, Centre Oscar Lambret, Lille, France; [17]Medical Oncology, Institut de Cancérologie de Lorraine - Alexis Vautrin, Vandoeuvre les Nancy, France; [18]Medical Oncology, Hôpital de Mont de Marsan, Mont de Marsan, France; [19]Medical Oncology, Institute Paoli Calmettes, Marseille, France.

Florence JOLY LOBBEDEZ

Centre François Baclesse / GINECO Group




**Comments:**

- PFI <12mo (majority <6mo, 70%)
- Relapse DURING beva (MITO16, 72% relapsed after completion of beva)
- Lower dose of Pazopanib (600mg)
- LOWER dose of chemo in combination arm (65mg/m2 vs 80mg/m2)

# Rationnel

- MITO-16 : Augmentation de la PFS avec le re-challenge du bévacizumab

- ROC>6mo from platinum
- Prior Beva

R → 1:1
- Standard: Platinum doublet
- Experimental: Platinum doublet + Bev → Bev

| | Standard | Experimental | P |
|---|---|---|---|
| Median PFS | 8.8 mos | 11.8 mos | <0.001 |
| HR* (95%CI) | 0.51 (0.41-0.65) | | |

Pignata et al. ASCO 2018

- AGO-OVAR16: Augmentation de la PFS avec le pazopanib

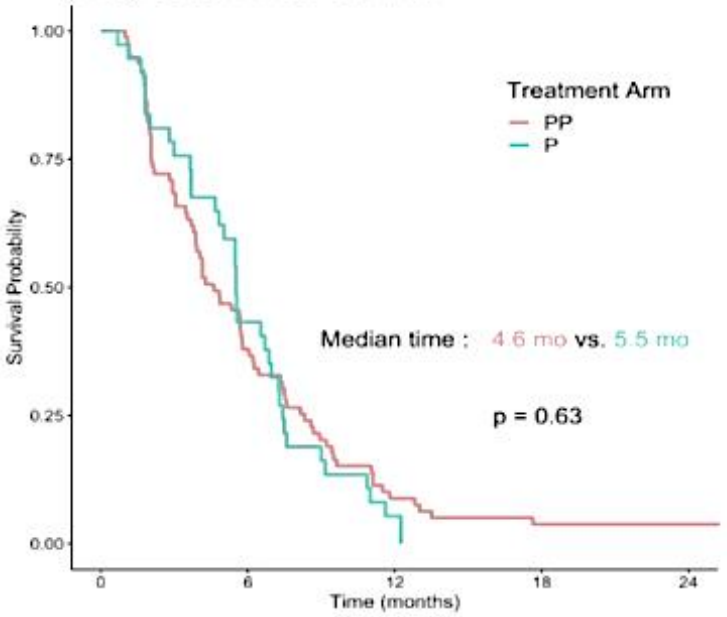
- St II-IV OC
- PDS or IDS
- Non-PD post platinum
- No bulky residual dis

Randomized AFTER chemo → 1:1
- Placebo
- Pazopanib 800mg once a day x 2 yrs

Dubois et al JCO 2014

# TAPAZ : Efficacy results

## Progression-Free Survival

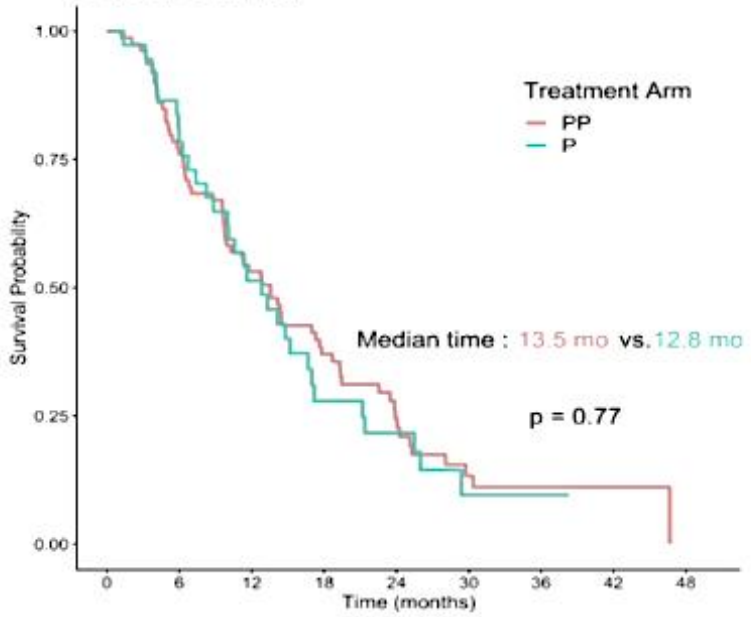



**Main endpoint**

4-months PFS rate :

- 57 % [95%CI 47-69] in PP arm
- 67.6% [54-84.5] in P arm

## Overall Survival




Median follow-up of 12.8 months

Case & Morgan design :
Z-test statistic -10.9<Rejection limit : H0 retained.
Median PFS 4.6 mo [3.9-6.1]

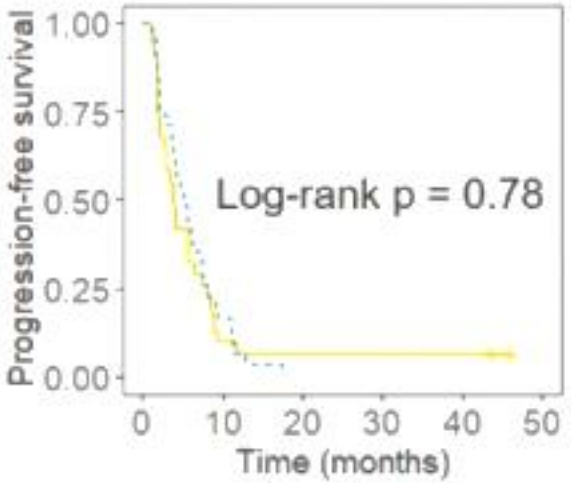
## **Safety:** Sig ↑ in toxicities

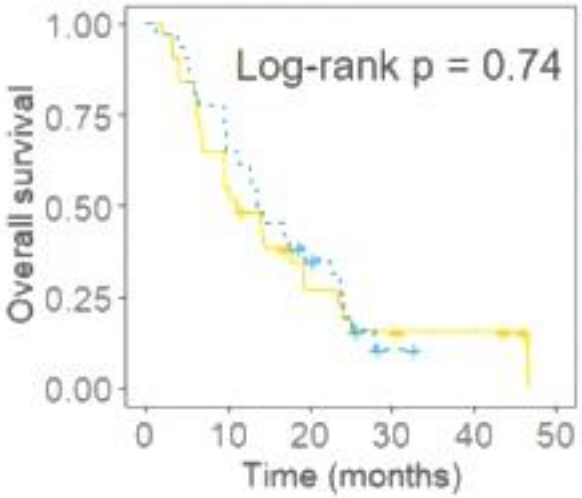
- **All grade ≥ 3 toxicities:**
  - 87% in PP arm
  - 70% in P arm *(p-value = 0.03)*
- **Grade 3 high blood pressure:**
  - 44% in PP arm
  - 8% in P arm *(p-value < 0.001)*
- **Grade ≥ 2 digestive events :**
  - 81% in PP arm
  - 59% in P arm *(p-value = 0.02)*
- **Grade ≥ 2 hepatic events:**
  - 32% in PP arm
  - 14% in P arm *(p-value = 0.04)*
- **2 toxic deaths in PP Arm**
  - pulmonary embolism
  - digestive perforation

# TAPAZ : Other secondary endpoints

## Pharmacokinetic relationships of pazopanib plasma exposure and outcomes (n= 62)

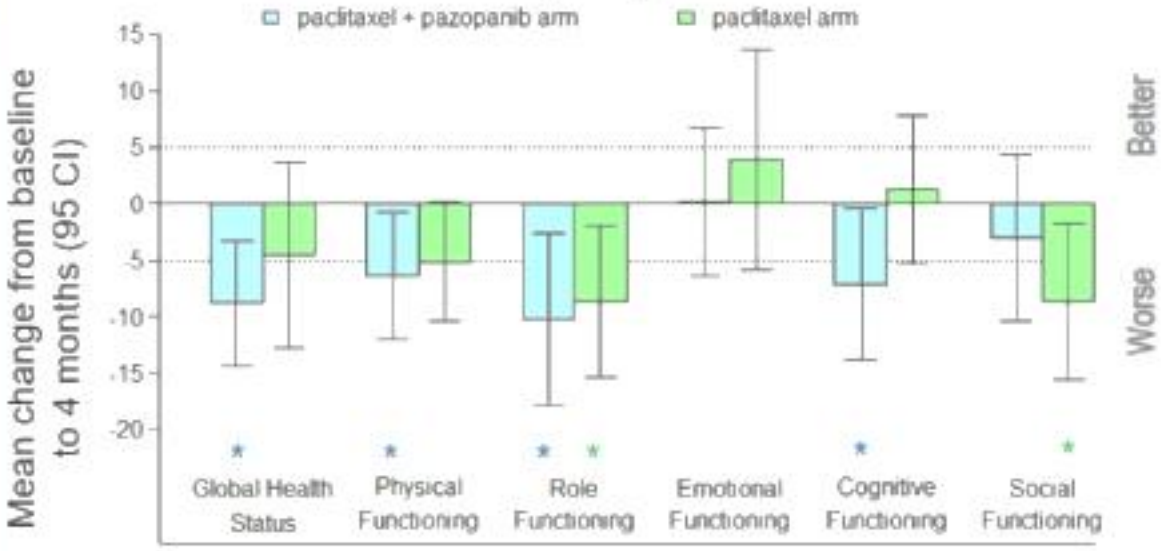
Pazopanib plasma exposure (AUC) cumulated over day 1 - 21 (Cycle 1) — < MEDIAN — >= MEDIAN

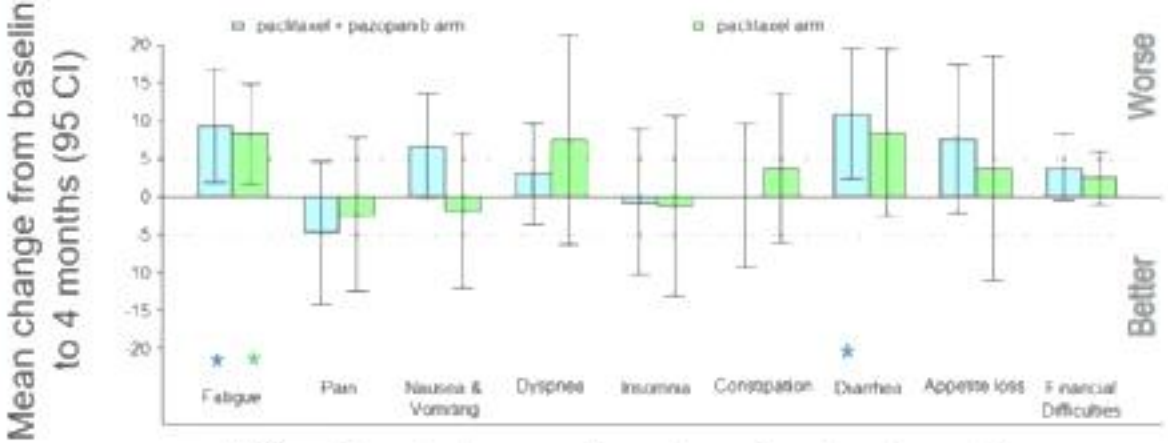



No significant relationship between pazopanib plasma exposure and efficacy (PFS or OS) was found

## Health-related quality of life at 4 months




* Significant change from baseline to 4 months

# OVAIRE Rechute <12 mois
# TAPAZ study

**Pas de changement de pratique**

## Conclusion :

- Essai négatif :
  - Pas de bénéfice de l'association pazopanib+ paclitaxel
  - Toxicités majeures
  - Impact négatif sur la QDV

## Perspective :

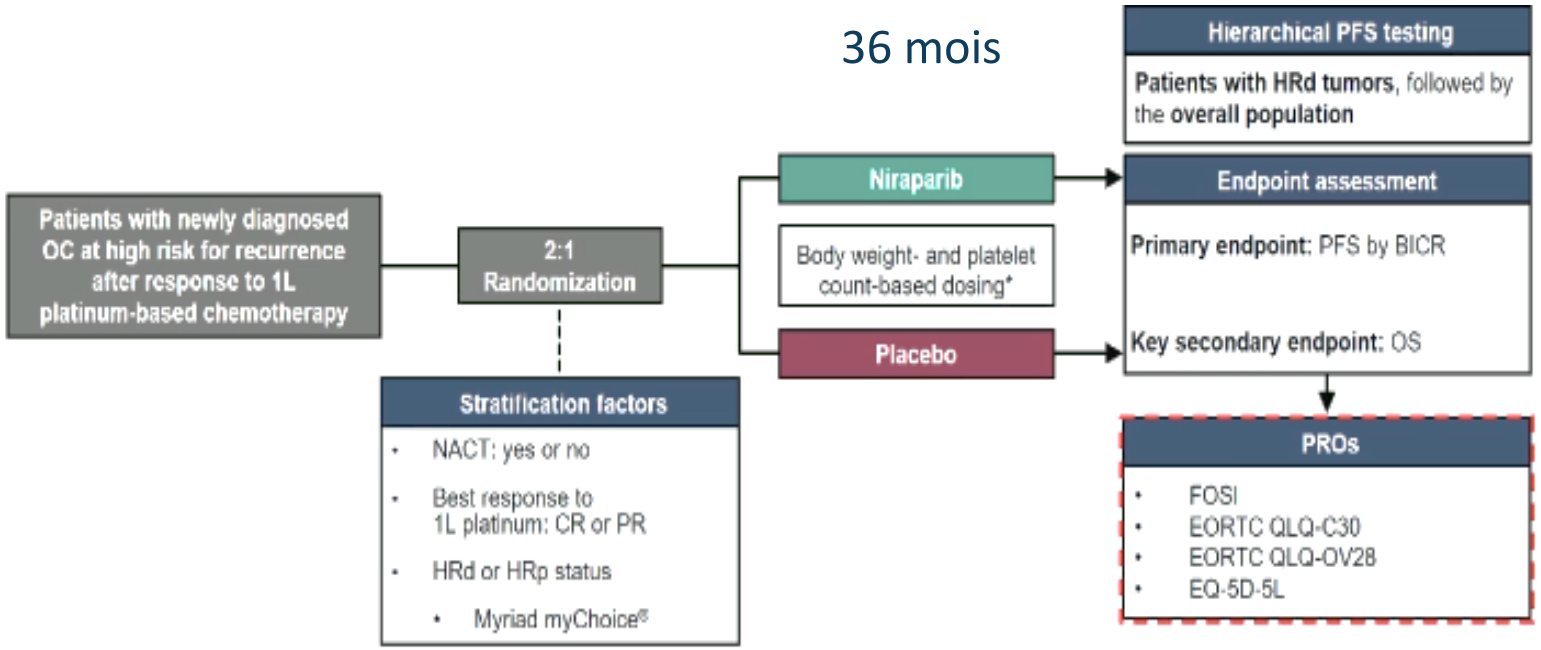
Etude MITO-11 (n = 76, pacli+ pazo) : 100% platine-résistance (vs 70%), pas de bévacizumab -> PFS : augmentée avec HR : 042

*D'après la présentation du Dr Colombo*

# OVAIRE 1ère ligne

# PRIMA study

36 mois




**Dose de Niraparib : 200 ou 300 mg selon le taux de plaquettes et le poids

VIRTUAL 2020 ESMO congress

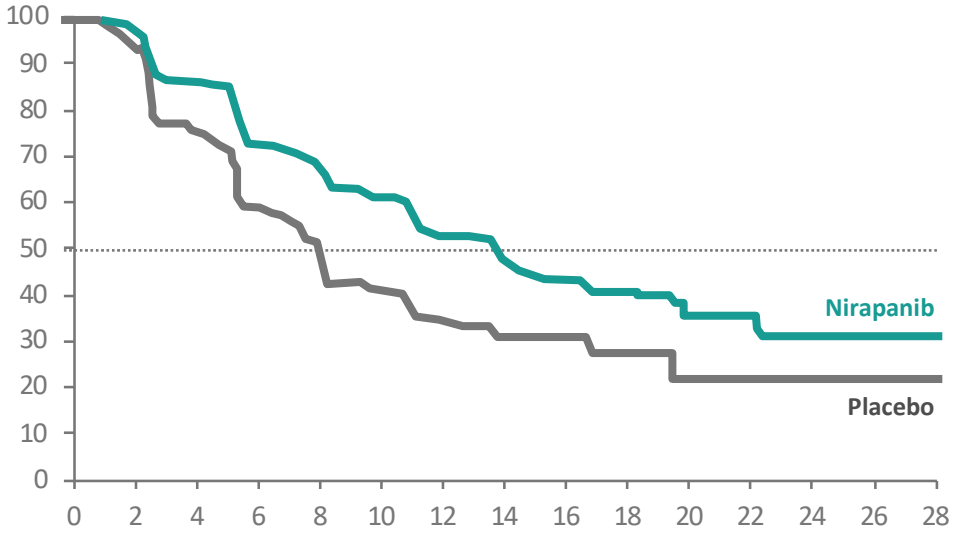
## Patient-Reported Outcomes in Patients Receiving Niraparib in the PRIMA/ENGOT-OV26/GOG-3012 Trial

Bhavana Pothuri

Gynecologic Oncology Group (GOG) and the Department of Obstetrics/Gynecology, Perlmutter Cancer Center, NYU Langone Health, New York, NY, USA

- **Population :**
  - **Stade III avec résidu tumoral ou inopérable**
  - **Stade IV (35%)**
- **Chimiothérapie sans bévacizumab**
- **Stratification : Chimio néo-adjuvante, réponse à la chimio (PR, CR), Statut HRD***
  - → 67% chimio néo-adjuvante
  - → 30% avec mutation *BRCA – 51% HRD*

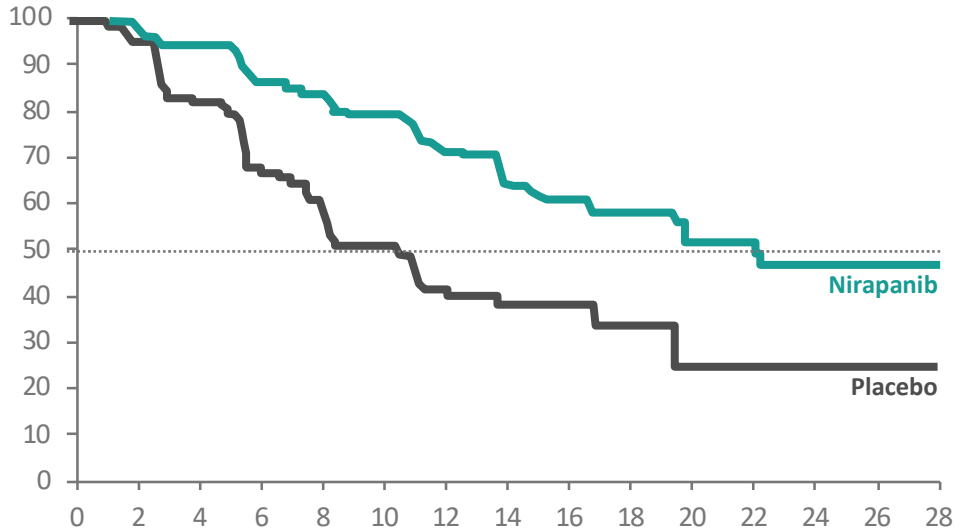
--> **Population de mauvais pronostic**




Initiation de PRIMA après la 1L CT

| | Médiane, SSP Mois (95% CI) | HR (IC95%) ; *p* |
|---|---|---|
| Nirapanib (N=487) | 13,8 (11,5 - 14,9) | 0,62 (0,50 - 0,76) ; *<0,001* |
| Placebo (N=246) | 8,2 (7,3 - 8,5) | |

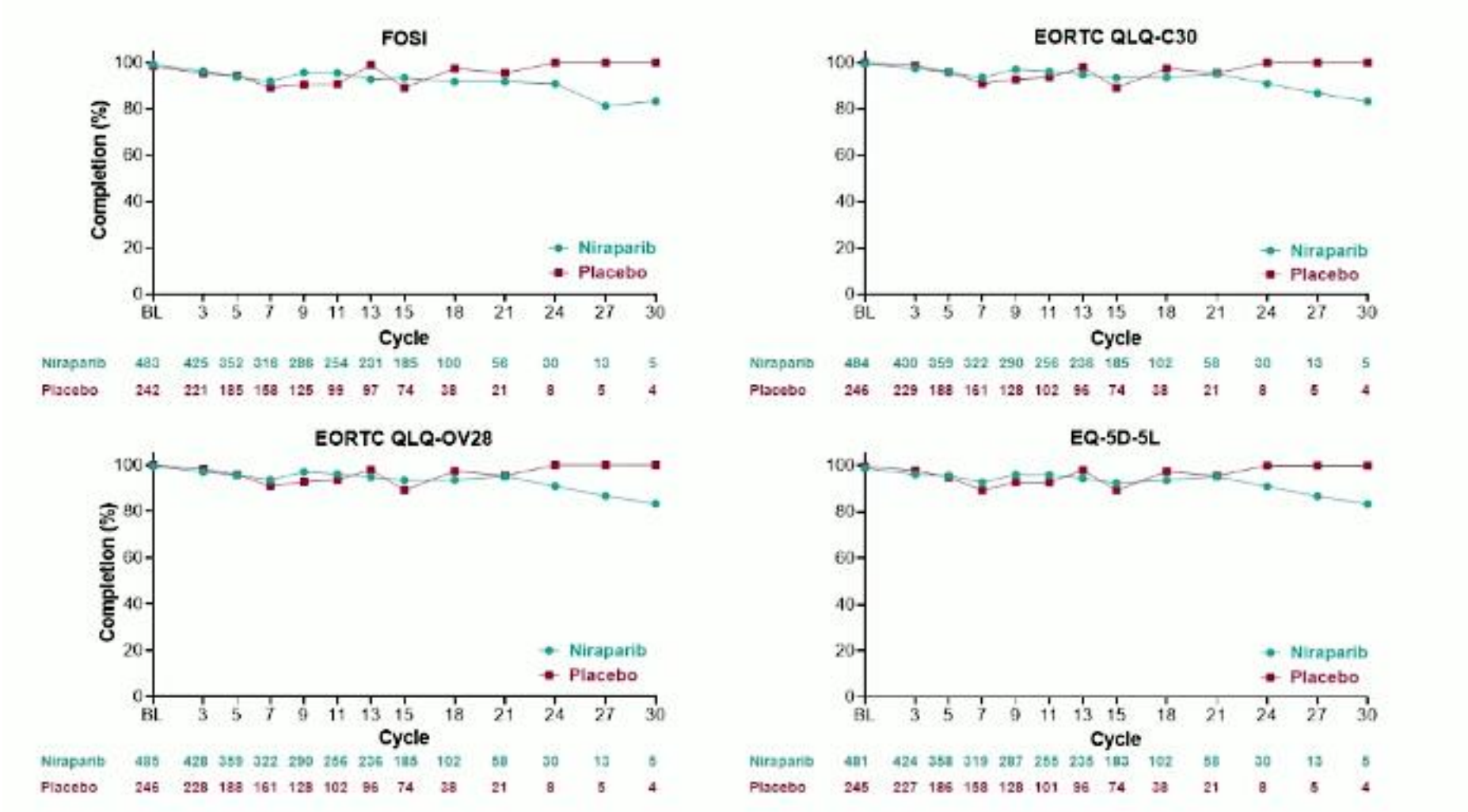
SSP dans la population globale, peu importe BRCA ou HRD




Initiation de PRIMA après la 1L CT

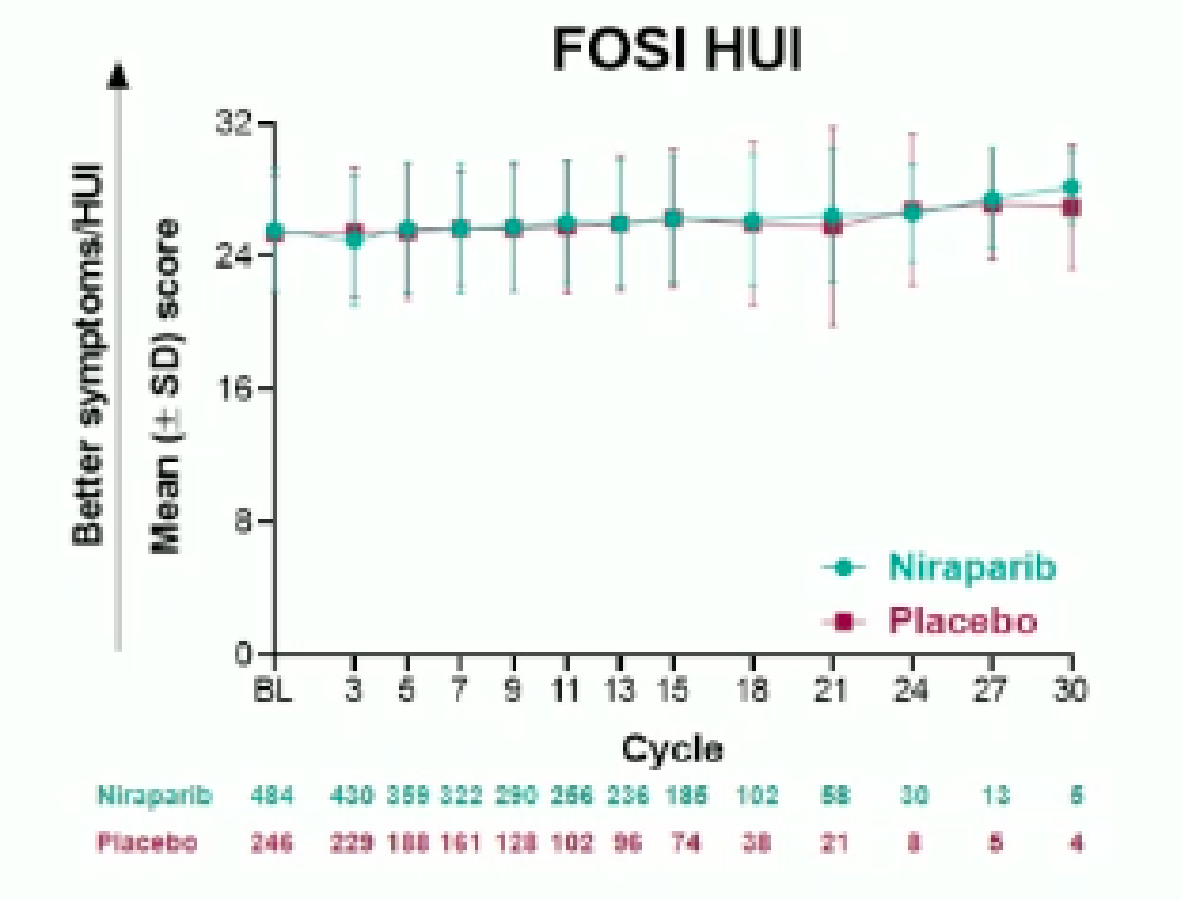
| | Médiane SSP Mois (IC 95%) | HR (IC 95%I) ; *p* |
|---|---|---|
| Nirapanib (N=247) | 21,9 (19,3 - NE) | 0,43 (0,31 - 0,59) ; *<0,001* |
| Placebo (N=126) | 10,4 (8,1 - 12,1) | |

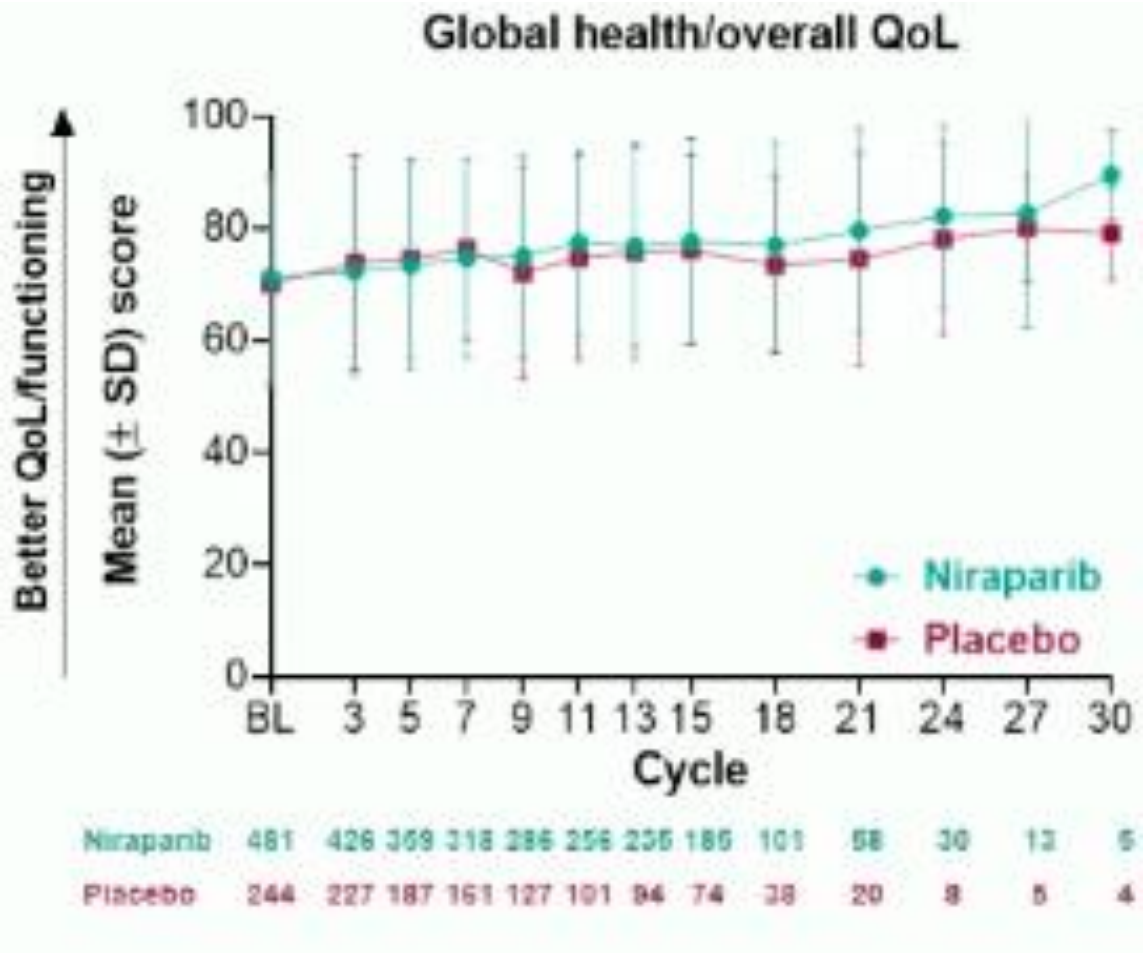
**SSP dans le groupe HRD positif**

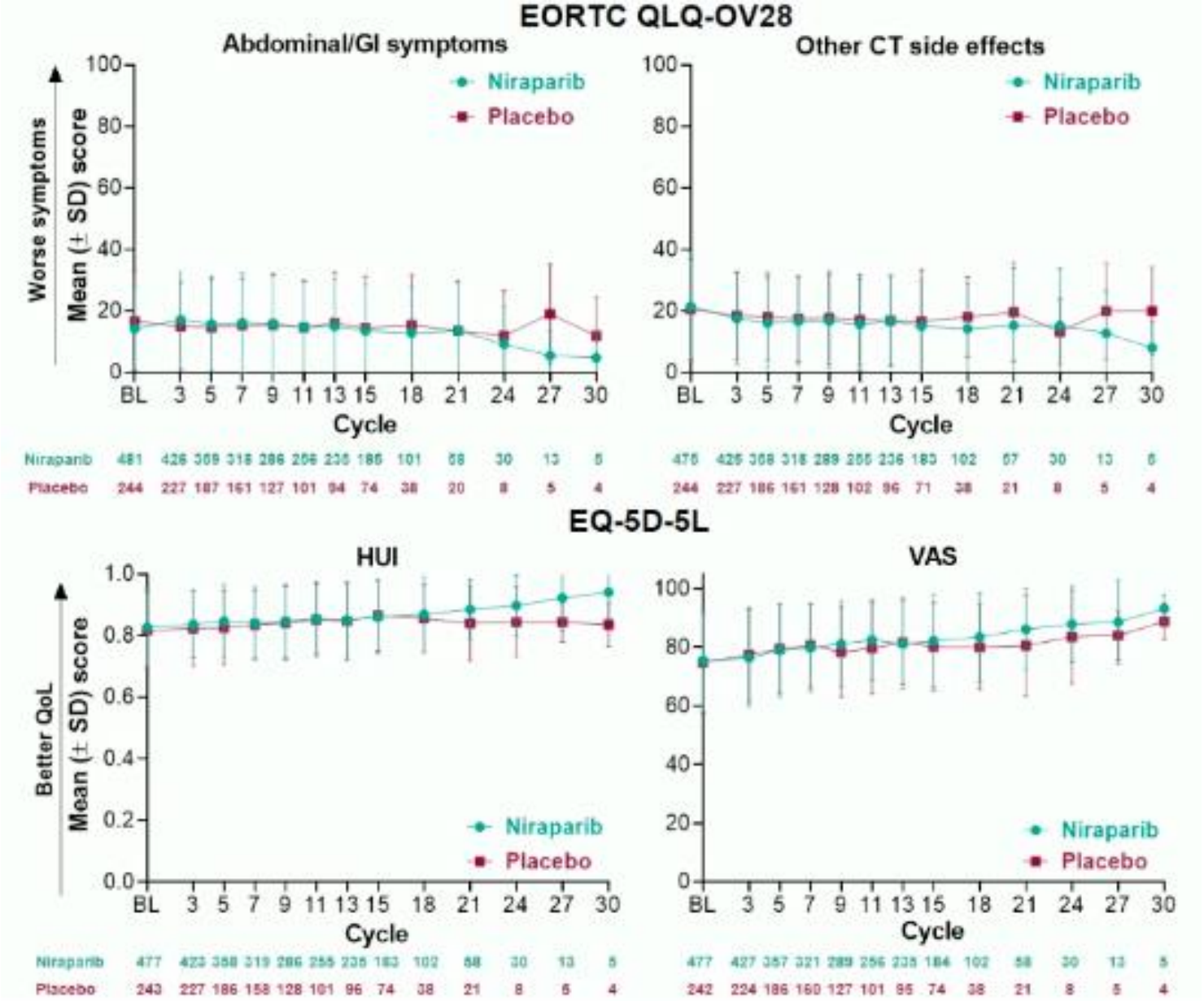



Bonne compliance au traitement par les patientes

# EORTC QLQ-C30






Pas de dégradation de la QDV

VIRTUAL 2020 ESMO congress

# How strong are these results?

Discussion Dr JOLLY

## Methodology : Good tools ? Good endpoints ?

| | Velia | Prima | Comments |
|---|---|---|---|
| **Tools** | EQ-5D<br>Fosi 18 | EQ-5D – EORTC-QLQC30<br>Fosi 8 - EORTC- Ov | General QoL, Symptoms related to disease ☺<br>No Specific evaluation of fatigue and self reported toxicities ☹ |
| **Administration** | Every 2 months until progression or up to 2 yrs | Every 2 months 56 wks then 3 months and after discontinuation | During and after tt ☺<br>Enough to capture the impact on day to day life? ☹ |
| **Compliance** | ? | > 80% | High quality of monitoring ☺ |
| **Endpoints** | Secondary | Secondary | 😐 |
| **Main QoL hypothesis** | Disease related symptoms (DRS) in m-BRCA and the whole population | No defined specific domain (all the domains) | What is the most pertinent endpoint? ☺<br>- Disease symptom oriented<br>- Toxicity oriented<br>- Global/social QoL |
| **Definition of the difference clinically significative** | Fosi - DRS : 3 points (8%) | Fosi : 2 pts (6%)<br>EORTC: 10 (10%) | Definition of the difference ☺<br>How to chose the difference significative? ☺<br>(Would the results different if a 2 points of difference was chosen in the Velia study) |
| **Analysis** | Intent to treat<br>Mixed models (no info of deal with missing data) | Intent to treat<br>Mixed models (no info of deal with missing data) | Adapted statistics ☺<br>However had we enough power to conclude ? ☹ |

# OVAIRE Rechute <12 mois
# TAPAZ study

changement de pratique

## Conclusion :

- Essai positif :
  - Bénéfice du niraparib
  - Impact sur la QDV : pas de détérioration de la QDV

*D'après la présentation du Dr Colombo*

# OPTIONS

| | |
|---|---|
| **Chirurgie + Chimiothérapie** | **Maintenance** |
| | **Olaparib** (cp, 300 mg pour 2 ans) : BRCA muté **(SOLO1) : ESMO 2018** |
| **Bévacizumab** | **Bévacizumab** 15 mois |
| | **+/- OLAPARIB si BRCA muté ou BRCA HRD ?? (PAOLA)** |
| **Pas de bévacizumab** | **PRIMA**<br>**ATU de cohorte pour le niraparib : 36 mois-** Début le 12/08/2020<br>Absence de mutation du gène BRCA, en réponse (réponse complète ou partielle) à une première ligne de chimiothérapie à base de platine et non éligible au bévacizumab |

# GCO-002 CACOVID-19 study


- **The GCO-002 CACOVID-19 study** (NCT04397575): a French nationwide retro-prospective cohort of COVID-19 patients with solid tumors
- Cohort set up on April 4, 2020 by the Groupes Coopérateurs en Oncologie (GCO), a French consortium of academic cooperative groups in oncology
- Patients with solid tumours and COVID-19 diagnosed between **March 1 and June 11, 2020** were analysed
- **COVID-19 diagnosis:** confirmation of SARS-CoV-2 infection by RT-PCR on nasopharyngeal swabs and/or imaging consistent with COVID-19 pneumonia on CT-scan or highly suggestive symptoms combined with positive SARS-CoV-2 serology
- **Primary endpoint:** all-cause mortality
- **Secondary endpoints:**
  - COVID-19 severity = admission to an ICU and/or mechanical ventilation and/or death
  - impact of COVID-19 on cancer treatment

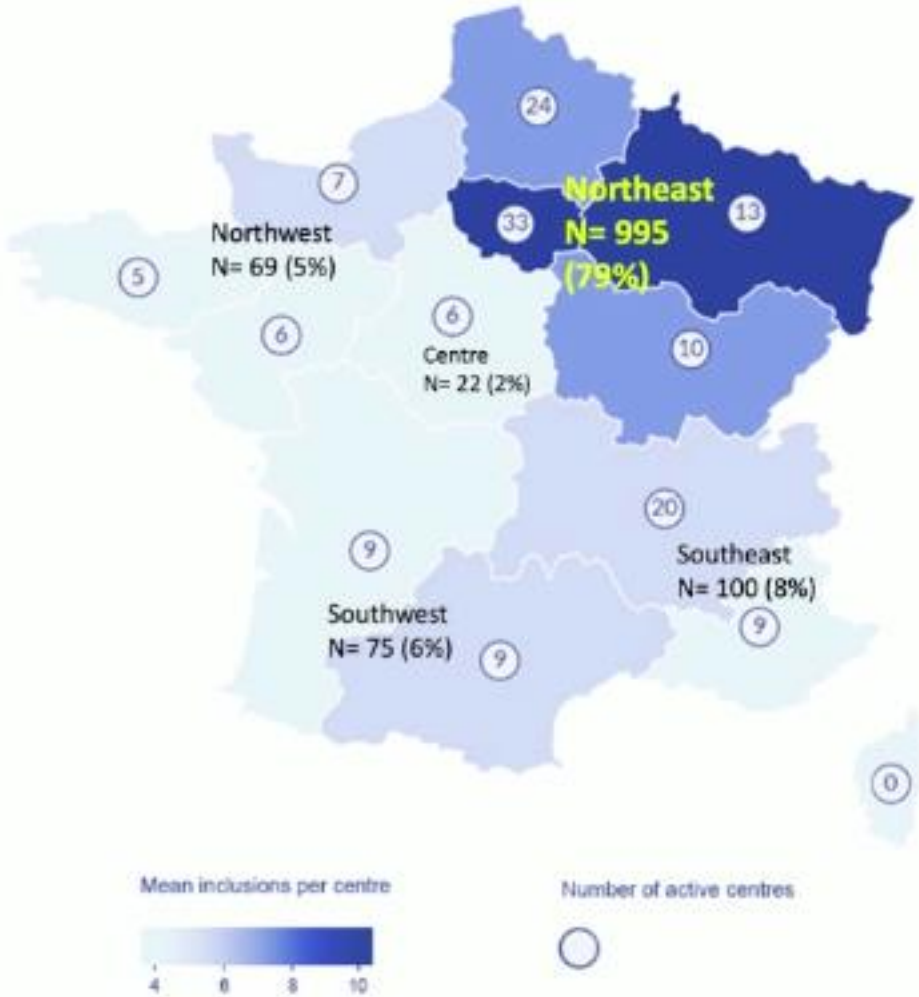
From April 4 to June 11, 2020: **1,289 pts (153 institutions)** were included

- Median age: 67 years, Male: 62%
- Most common region of residence: Northeast (n = 995, 79%).
- Obesity (BMI ≥ 30): n=183 (16%)
- Former/Current smoker: n=574 (52%)
- Comorbidities:

- ≥ 1 comorbidity: n=1,114 (86%), ≥ 4 comorbidities: n= 324 (25%)
- Most common: hypertension 46%, diabetes 21% and COPD 12%

- ECOG PS 0-1: n=547 (59%)

Geographic distribution of cancer patients with COVID-19 and participating institutions



# TUMOUR CHARACTERISTICS AND OUTCOME

| Cancer Type | |
|---|---|
| Digestive | 470 (36%) |
| Thoracic | 311 (24%) |
| Gynaecological | 252 (20%) |
| Breast Cancer | 173 (68.7%) |
| Other gynaecological | 79 (31.3%) |
| Head and neck | 104 (8%) |
| Central nervous system | 65 (5%) |
| Genitourinary | 65 (5%) |
| Dermatological | 14 (1%) |
| Others | 6 (<1%) |

Metastatic stage: n= 758 (59%)

| Anticancer treatment during 3 months before COVID-19 diagnosis | |
|---|---|
| ***Systemic therapy*** | ***755 (59%)*** |
| cytotoxic chemotherapy | 577 (45%) |
| immunotherapy | 110 (8%) |
| targeted therapy | 181 (14%) |
| hormone therapy | 57 (4%) |
| ***local therapy*** | |
| radiotherapy | 133 (10%) |
| surgery | 56 (4%) |

Median follow-up from COVID-19 diagnosis: 34 days

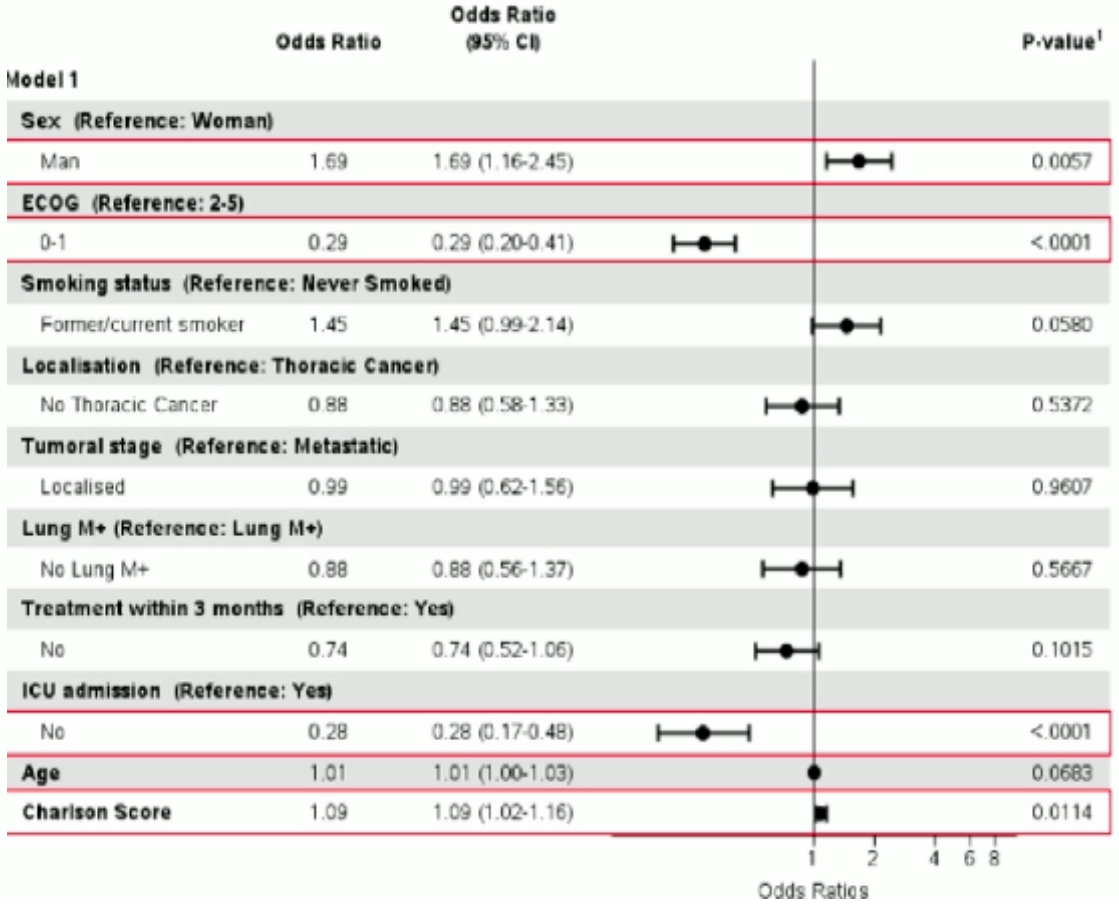
| COVID-19 COMPLICATIONS | |
|---|---|
| Admission to hospital[1] | 734 (65%) |
| Admission to ICU[1] | 110 (10%) |
| O2 requirement[2] | 412 (42%) |
| Mechanical ventilation[2] | 49 (5%) |
| Death[3] | 370 (29%) |
| COVID-19 severity = O2 or ICU admission or death | 424 (33%) |

[1] excludes 164 cases [2] excludes 300 cases with missing data

[3] After a median of 10 days

The systemic anticancer treatment was interrupted or stopped following COVID-19 diagnosis in 431 (39%) pts

# RISK FACTORS FOR ALL-CAUSE MORTALITY



# COVID et CANCER

## Conclusion

- Facteurs pronostiques classiques : état général, sexe, comorbidités
- Pas de surmortalité sur le critère : âge et cancer thoracique
- Biais de sélection
- Evaluation de l'impact de l'arrêt des traitements et/ou report

*D'après la présentation du Dr Colombo*

# Onco-Gynécologie

Dr Elise Deluche, Oncologue médicale - CHU Limoges

# Liens d’intérêt Dr Deluche

- Novartis, Pfizer, Astra Zeneca

# OVAIRE Rechute <12 mois

# TAPAZ study

VIRTUAL 2020 ESMO congress

## Paclitaxel with or without pazopanib in ovarian cancer patients with relapse during bevacizumab maintenance therapy

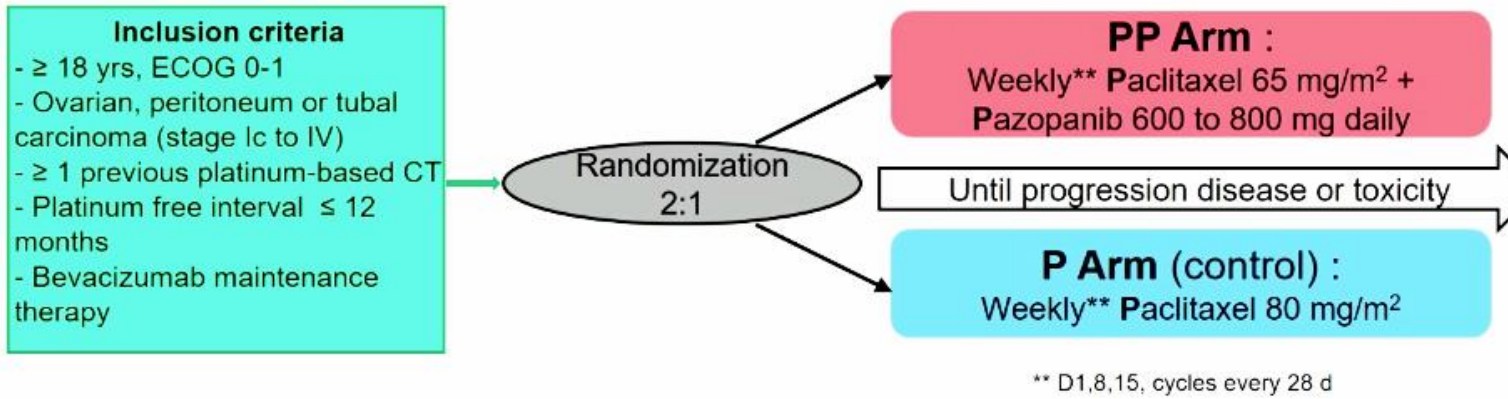
*The GINECO randomized phase 2 TAPAZ study*

E. Joly Lobbedez[2], M. Fabbro[2], D. Berton[3], J. Lequesne[4], A. Anota[5], A. Puszkiel[6], A. Floquet[7], M. Cancel[8], H. Bourgeois[9], I. Bengrine Lefevre[10], B. You[11], F. Pommeret[12], A. Lortholary[13], D. Spaeth[14], I. Martin-Babau[15], C. Abdeddaim[16], M.-C. Kaminsky-Forrett[17], D. Petran[18], M. Provansal Gross[19], P.-E. Brachet[1]

[1]Medical Oncology, Centre François Baclesse, Caen, France; [2]Medical Oncology, ICM Regional Cancer Institute of Montpellier, Montpellier, France; [3]Medical Oncology, Institut de Cancérologie de l'Ouest, Saint Herblain, France; [4]Clinical Research, Centre François Baclesse, Caen, France; [5]Methodology and Quality of Life in Oncology Unit (INSERM U1208) & French National Platform Quality of Life and Cancer, CHRU Besançon - Hopital Jean Minjoz, Besançon, France; [6]EMR UCBL/HCL 3738, Univ. Lyon, Université Claude Bernard Lyon 1, Faculté de médecine Lyon-Sud, Lyon, France; [7]Medical Oncology, Institute Bergonié, Bordeaux, France; [8]Medical Oncology, CHU Bretonneau Centre, Tours University, Tours, France; [9]Medical Oncology Department, Centre Jean Bernard - Clinique Victor Hugo and GINECO group France, Le Mans, France; [10]Medical Oncology, Centre Georges François Leclerc, Dijon, France; [11]Medical Oncology, Institut de Cancérologie des Hospices Civils de Lyon (HCL), CTD-ML, BRECO, Univ Lyon, Université Claude Bernard Lyon 1, Faculté de médecine Lyon-Sud, EMR UCBL/HCL 3738, Lyon, France; [12]Département de médecine oncologique, Gustave Roussy, Villejuif, France; [13]Oncologie, Centre Catherine de Sienne, Hopital privé du Confluent, Nantes, France; [14]Oncologie, Centre d'Oncologie de Gentilly, Nancy, France; [15]Medical Oncology, Centre Armoricain d'Oncologie CARIO-HCPA-BEC 22, Plerin, France; [16]Medical Oncology, Centre Oscar Lambret, Lille, France; [17]Medical Oncology, Institut de Cancérologie de Lorraine - Alexis Vautrin, Vandoeuvre les Nancy, France; [18]Medical Oncology, Hôpital de Mont de Marsan, Mont de Marsan, France; [19]Medical Oncology, Institute Paoli Calmettes, Marseille, France.

Florence JOLY LOBBEDEZ

Centre François Baclesse / GINECO Group




**Comments:**

- PFI <12mo (majority <6mo, 70%)
- Relapse DURING beva (MITO16, 72% relapsed after completion of beva)
- Lower dose of Pazopanib (600mg)
- LOWER dose of chemo in combination arm (65mg/m2 vs 80mg/m2)

# Rationnel

- MITO-16 : Augmentation de la PFS avec le re-challenge du bévacizumab

- ROC>6mo from platinum
- Prior Beva

R → 1:1
- Standard: Platinum doublet
- Experimental: Platinum doublet + Bev → Bev

| | Standard | Experimental | P |
|---|---|---|---|
| Median PFS | 8.8 mos | 11.8 mos | <0.001 |
| HR* (95%CI) | 0.51 (0.41-0.65) | | |

Pignata et al. ASCO 2018

- AGO-OVAR16: Augmentation de la PFS avec le pazopanib

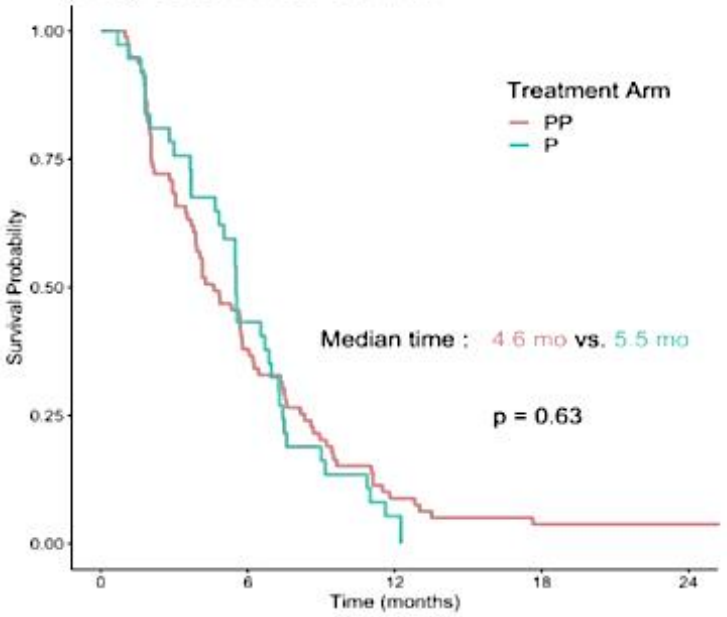
- St II-IV OC
- PDS or IDS
- Non-PD post platinum
- No bulky residual dis

Randomized AFTER chemo → 1:1
- Placebo
- Pazopanib 800mg once a day x 2 yrs

Dubois et al JCO 2014

# TAPAZ : Efficacy results

## Progression-Free Survival

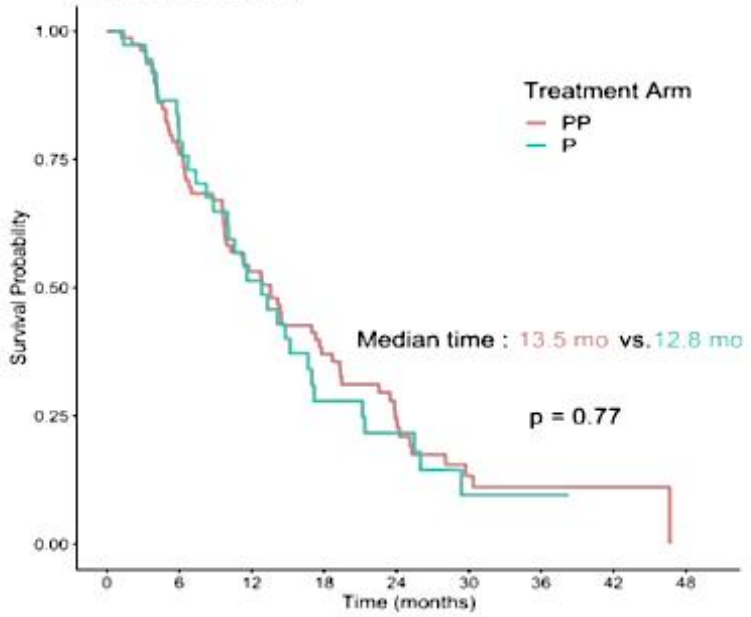



**Main endpoint**

4-months PFS rate :

- 57 % [95%CI 47-69] in PP arm
- 67.6% [54-84.5] in P arm

## Overall Survival




Median follow-up of 12.8 months

Case & Morgan design :
Z-test statistic -10.9<Rejection limit : H0 retained.
Median PFS 4.6 mo [3.9-6.1]

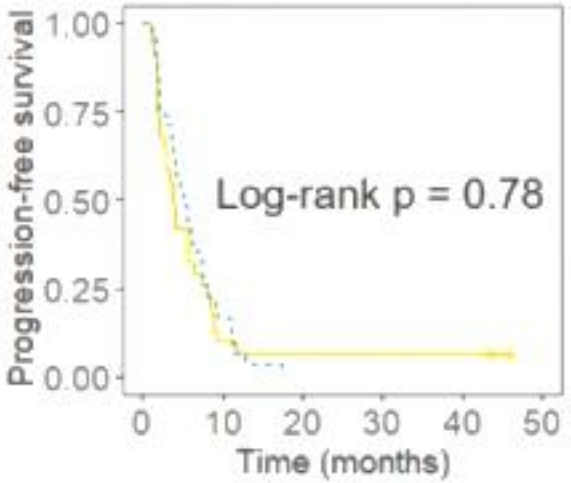
## **Safety:** Sig ↑ in toxicities

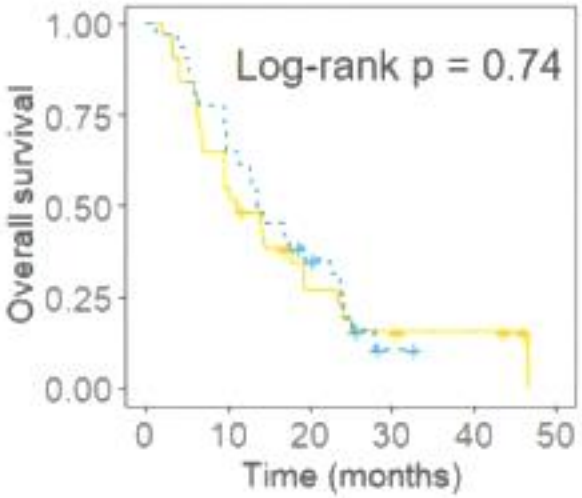
- **All grade ≥ 3 toxicities:**
  - 87% in PP arm
  - 70% in P arm *(p-value = 0.03)*
- **Grade 3 high blood pressure:**
  - 44% in PP arm
  - 8% in P arm *(p-value < 0.001)*
- **Grade ≥ 2 digestive events :**
  - 81% in PP arm
  - 59% in P arm *(p-value = 0.02)*
- **Grade ≥ 2 hepatic events:**
  - 32% in PP arm
  - 14% in P arm *(p-value = 0.04)*
- **2 toxic deaths in PP Arm**
  - pulmonary embolism
  - digestive perforation

# TAPAZ : Other secondary endpoints

## Pharmacokinetic relationships of pazopanib plasma exposure and outcomes (n= 62)

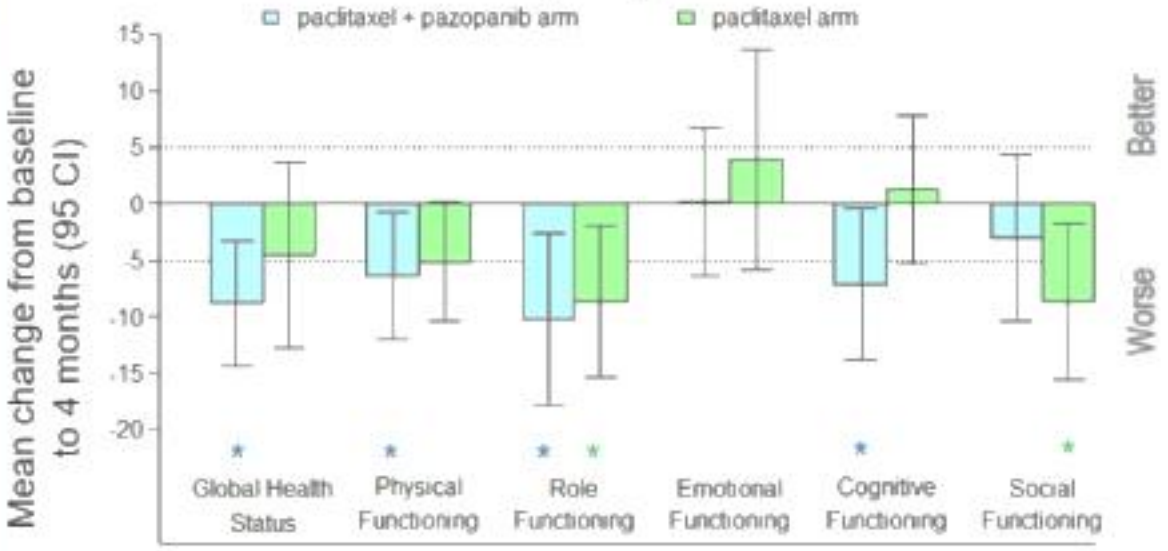
Pazopanib plasma exposure (AUC) cumulated over day 1 - 21 (Cycle 1) — < MEDIAN — >= MEDIAN

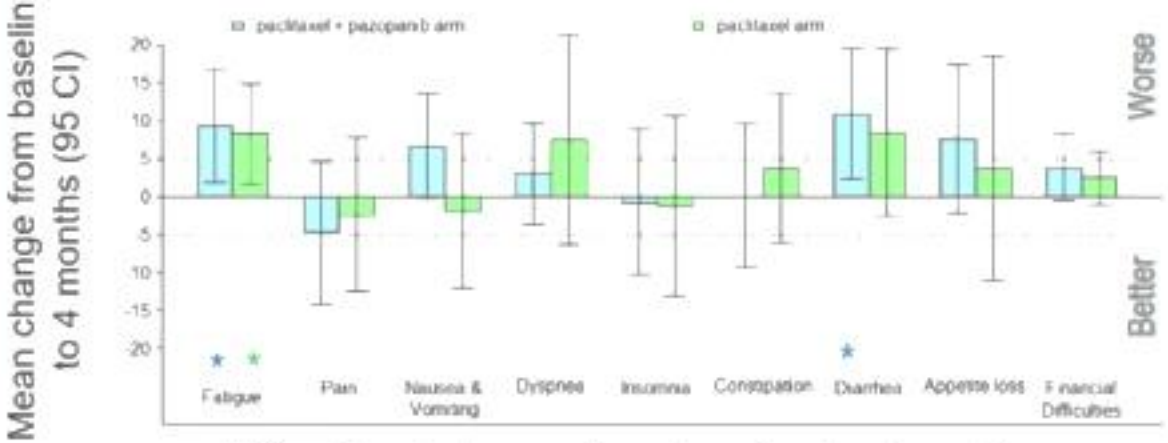



No significant relationship between pazopanib plasma exposure and efficacy (PFS or OS) was found

## Health-related quality of life at 4 months




* Significant change from baseline to 4 months

# OVAIRE Rechute <12 mois
# TAPAZ study

**Pas de changement de pratique**

## Conclusion :

- Essai négatif :
  - Pas de bénéfice de l'association pazopanib+ paclitaxel
  - Toxicités majeures
  - Impact négatif sur la QDV

## Perspective :

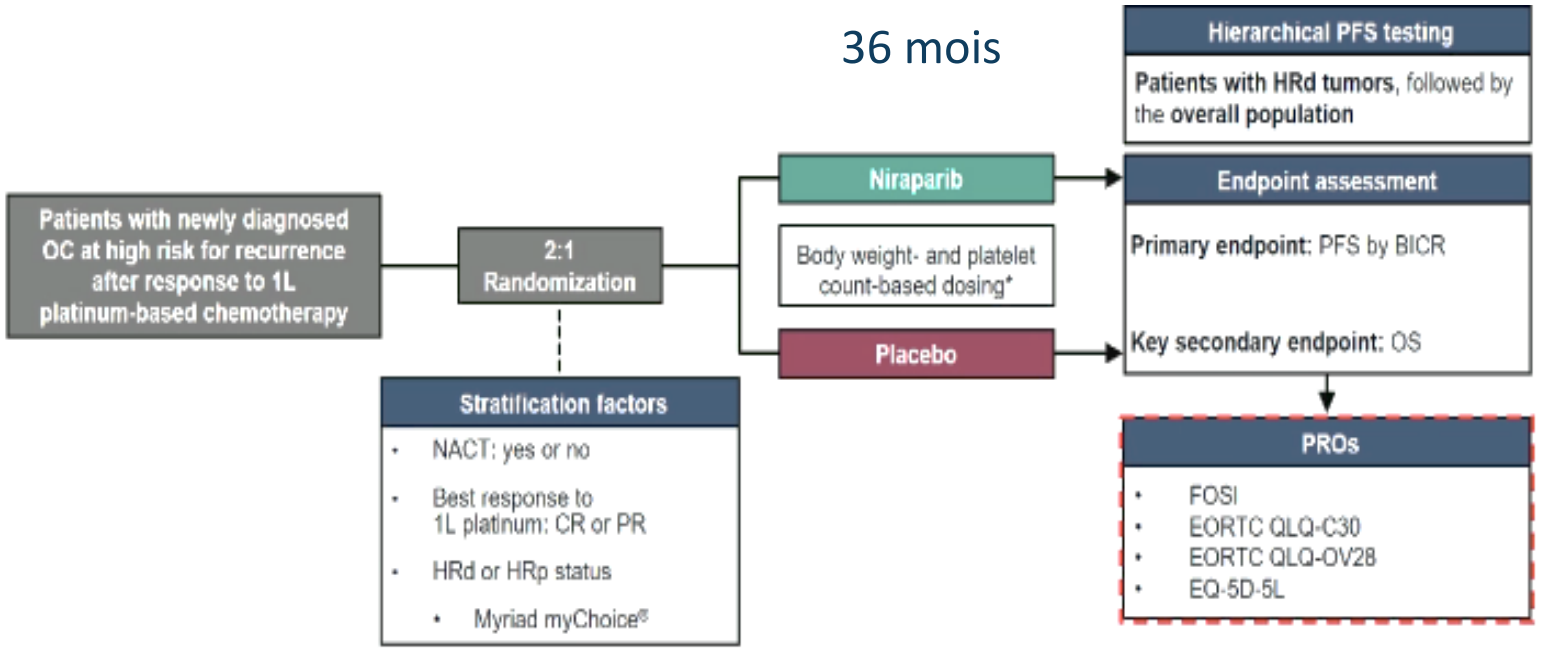
Etude MITO-11 (n = 76, pacli+ pazo) : 100% platine-résistance (vs 70%), pas de bévacizumab -> PFS : augmentée avec HR : 042

*D'après la présentation du Dr Colombo*

# OVAIRE 1ère ligne

# PRIMA study

36 mois




**Dose de Niraparib : 200 ou 300 mg selon le taux de plaquettes et le poids

VIRTUAL 2020 ESMO congress

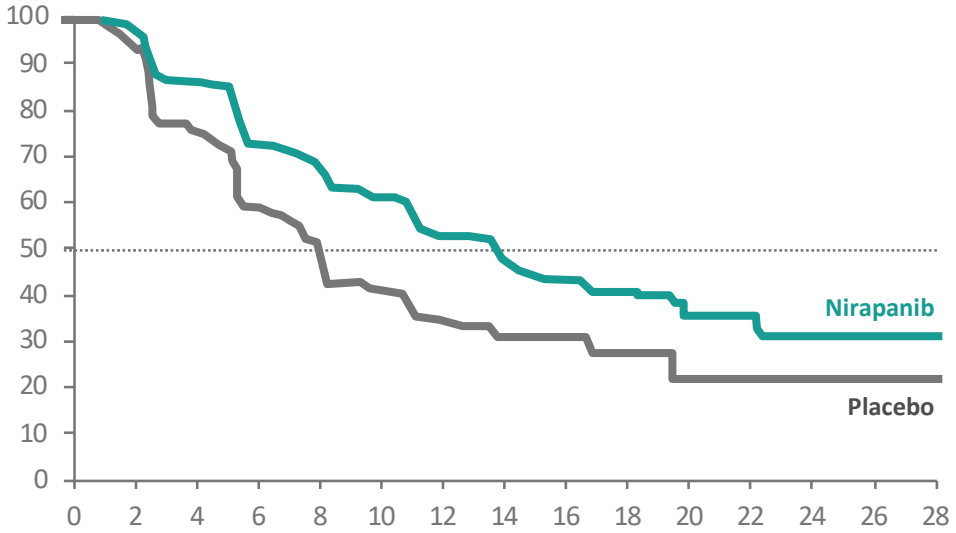
## Patient-Reported Outcomes in Patients Receiving Niraparib in the PRIMA/ENGOT-OV26/GOG-3012 Trial

Bhavana Pothuri

Gynecologic Oncology Group (GOG) and the Department of Obstetrics/Gynecology, Perlmutter Cancer Center, NYU Langone Health, New York, NY, USA

- **Population :**
  - **Stade III avec résidu tumoral ou inopérable**
  - **Stade IV (35%)**
- **Chimiothérapie sans bévacizumab**
- **Stratification : Chimio néo-adjuvante, réponse à la chimio (PR, CR), Statut HRD***
  - → 67% chimio néo-adjuvante
  - → 30% avec mutation *BRCA – 51% HRD*

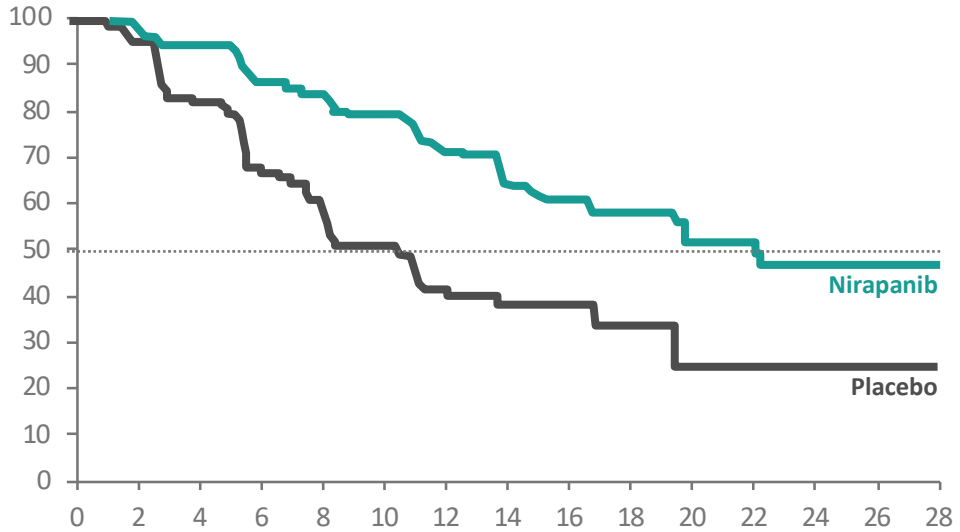
--> **Population de mauvais pronostic**




Initiation de PRIMA après la 1L CT

| | Médiane, SSP Mois (95% CI) | HR (IC95%) ; *p* |
|---|---|---|
| Nirapanib (N=487) | 13,8 (11,5 - 14,9) | 0,62 (0,50 - 0,76) ; *<0,001* |
| Placebo (N=246) | 8,2 (7,3 - 8,5) | |

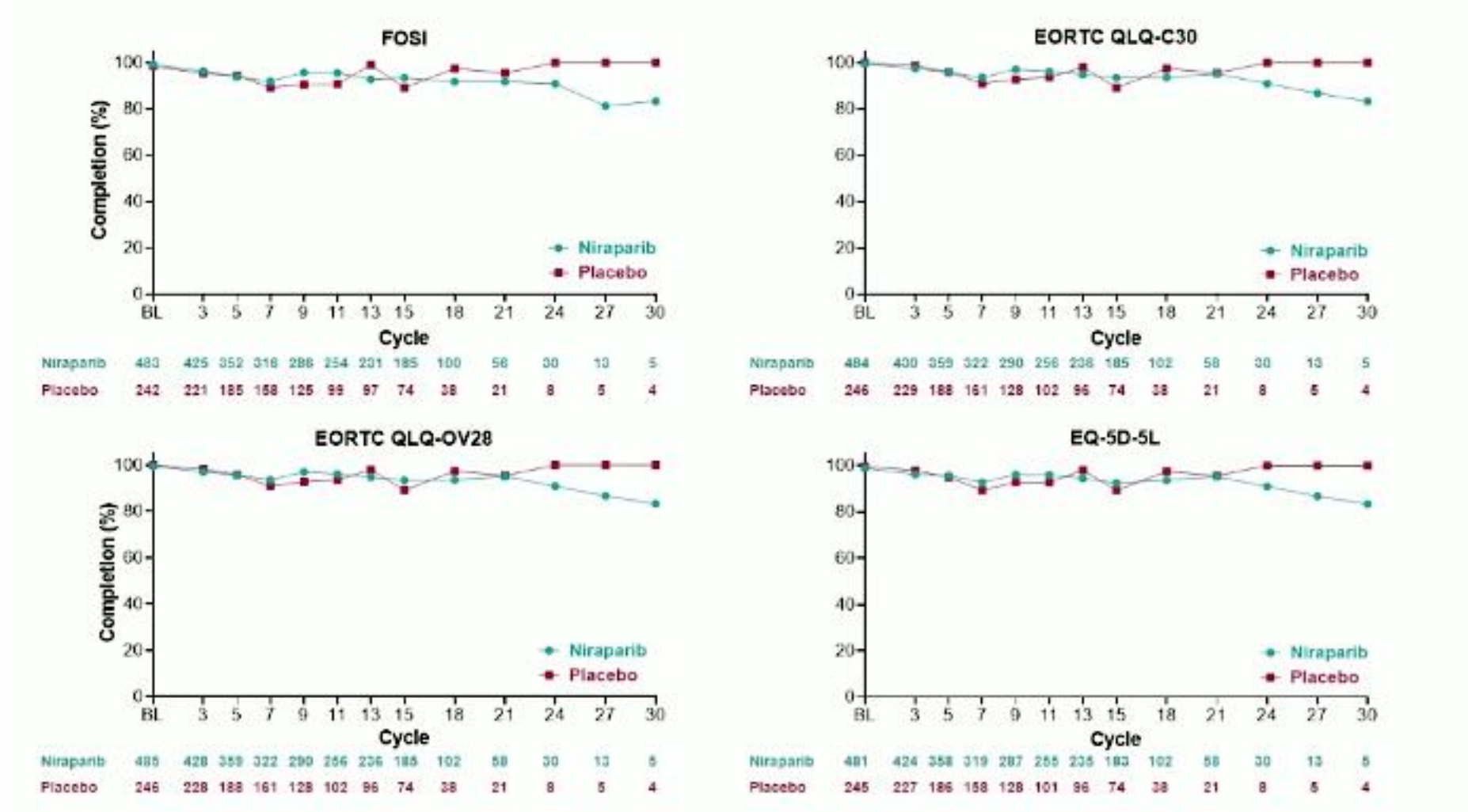
SSP dans la population globale, peu importe BRCA ou HRD




Initiation de PRIMA après la 1L CT

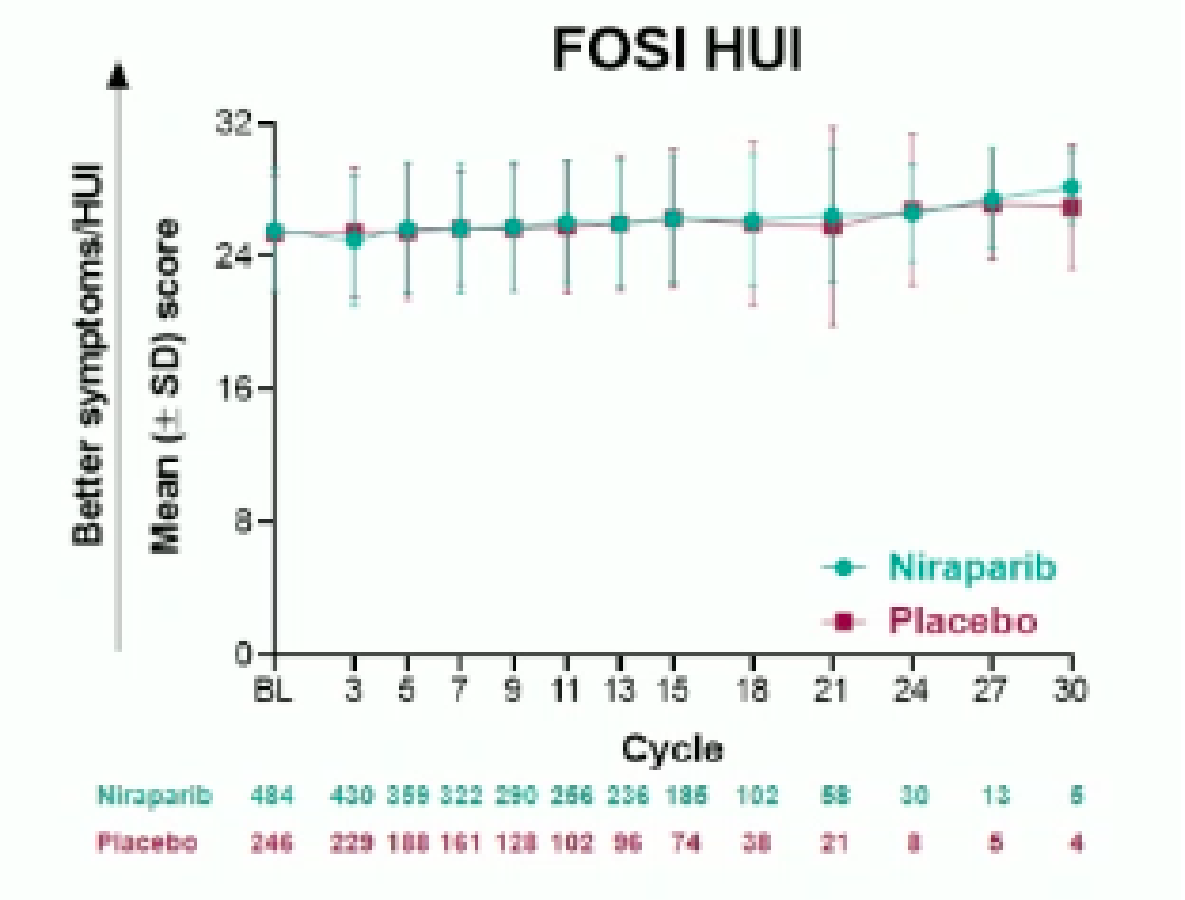
| | Médiane SSP Mois (IC 95%) | HR (IC 95%I) ; *p* |
|---|---|---|
| Nirapanib (N=247) | 21,9 (19,3 - NE) | 0,43 (0,31 - 0,59) ; *<0,001* |
| Placebo (N=126) | 10,4 (8,1 - 12,1) | |

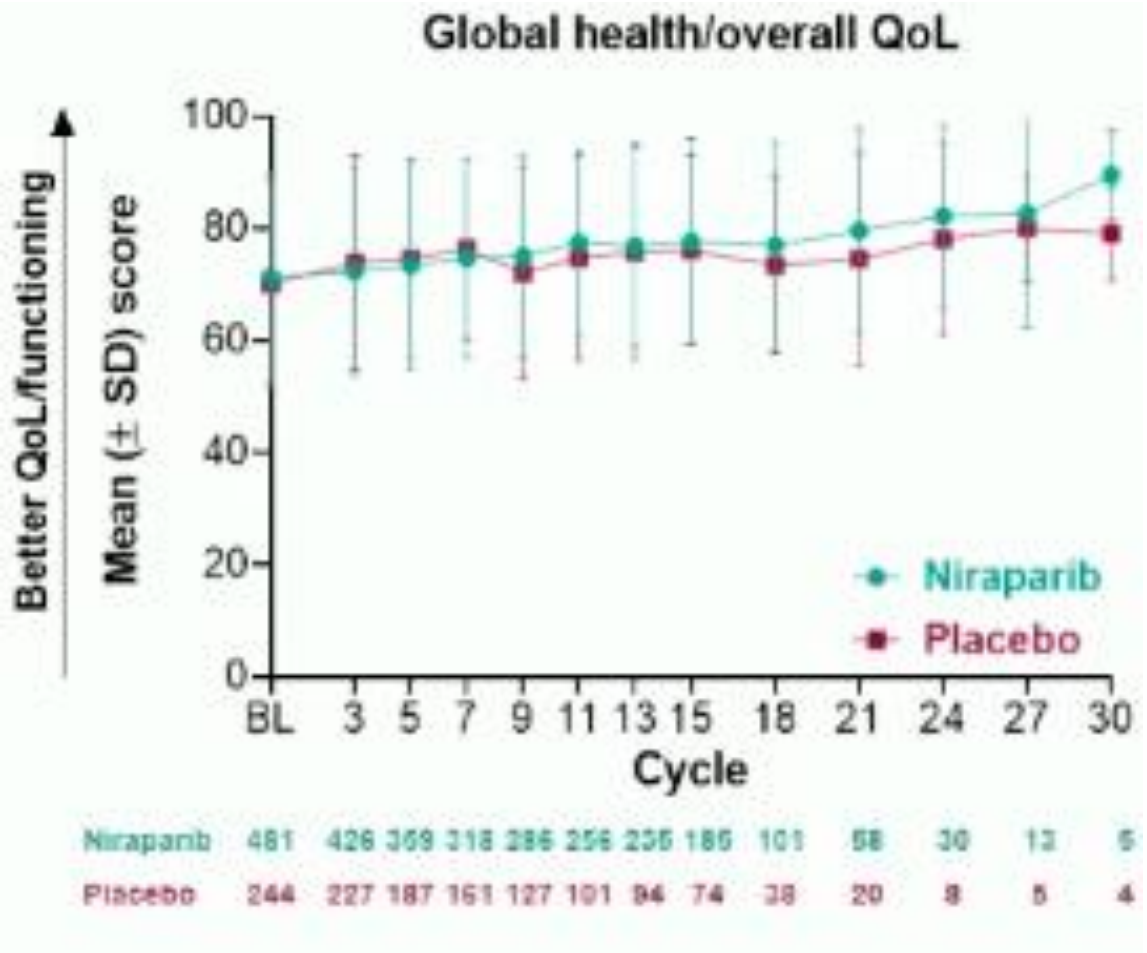
**SSP dans le groupe HRD positif**

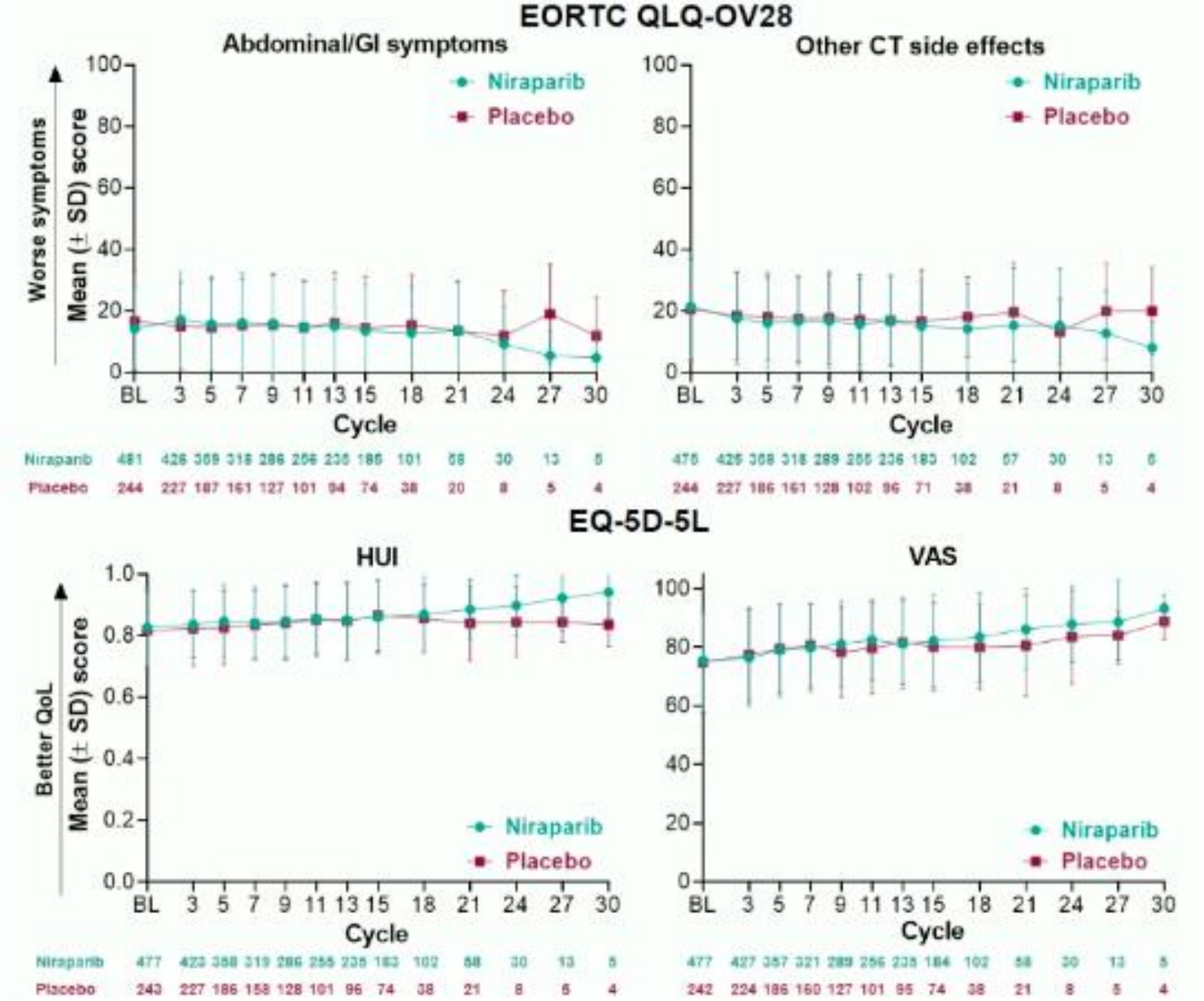



Bonne compliance au traitement par les patientes

# EORTC QLQ-C30






Pas de dégradation de la QDV

VIRTUAL 2020 ESMO congress

# How strong are these results?

Discussion Dr JOLLY

## Methodology : Good tools ? Good endpoints ?

| | Velia | Prima | Comments |
|---|---|---|---|
| **Tools** | EQ-5D<br>Fosi 18 | EQ-5D – EORTC-QLQC30<br>Fosi 8 - EORTC- Ov | General QoL, Symptoms related to disease ☺<br>No Specific evaluation of fatigue and self reported toxicities ☹ |
| **Administration** | Every 2 months until progression or up to 2 yrs | Every 2 months 56 wks then 3 months and after discontinuation | During and after tt ☺<br>Enough to capture the impact on day to day life? ☹ |
| **Compliance** | ? | > 80% | High quality of monitoring ☺ |
| **Endpoints** | Secondary | Secondary | 😐 |
| **Main QoL hypothesis** | Disease related symptoms (DRS) in m-BRCA and the whole population | No defined specific domain (all the domains) | What is the most pertinent endpoint? ☺<br>- Disease symptom oriented<br>- Toxicity oriented<br>- Global/social QoL |
| **Definition of the difference clinically significative** | Fosi - DRS : 3 points (8%) | Fosi : 2 pts (6%)<br>EORTC: 10 (10%) | Definition of the difference ☺<br>How to chose the difference significative? ☺<br>(Would the results different if a 2 points of difference was chosen in the Velia study) |
| **Analysis** | Intent to treat<br>Mixed models (no info of deal with missing data) | Intent to treat<br>Mixed models (no info of deal with missing data) | Adapted statistics ☺<br>However had we enough power to conclude ? ☹ |

# OVAIRE Rechute <12 mois
# TAPAZ study

changement de pratique

## Conclusion :

- Essai positif :
  - Bénéfice du niraparib
  - Impact sur la QDV : pas de détérioration de la QDV

*D'après la présentation du Dr Colombo*

# OPTIONS

| | |
|---|---|
| **Chirurgie + Chimiothérapie** | **Maintenance** |
| | **Olaparib** (cp, 300 mg pour 2 ans) : BRCA muté **(SOLO1) : ESMO 2018** |
| **Bévacizumab** | **Bévacizumab** 15 mois |
| | **+/- OLAPARIB si BRCA muté ou BRCA HRD ?? (PAOLA)** |
| **Pas de bévacizumab** | **PRIMA**<br>**ATU de cohorte pour le niraparib : 36 mois-** Début le 12/08/2020<br>Absence de mutation du gène BRCA, en réponse (réponse complète ou partielle) à une première ligne de chimiothérapie à base de platine et non éligible au bévacizumab |

# GCO-002 CACOVID-19 study


- **The GCO-002 CACOVID-19 study** (NCT04397575): a French nationwide retro-prospective cohort of COVID-19 patients with solid tumors
- Cohort set up on April 4, 2020 by the Groupes Coopérateurs en Oncologie (GCO), a French consortium of academic cooperative groups in oncology
- Patients with solid tumours and COVID-19 diagnosed between **March 1 and June 11, 2020** were analysed
- **COVID-19 diagnosis:** confirmation of SARS-CoV-2 infection by RT-PCR on nasopharyngeal swabs and/or imaging consistent with COVID-19 pneumonia on CT-scan or highly suggestive symptoms combined with positive SARS-CoV-2 serology
- **Primary endpoint:** all-cause mortality
- **Secondary endpoints:**
  - COVID-19 severity = admission to an ICU and/or mechanical ventilation and/or death
  - impact of COVID-19 on cancer treatment

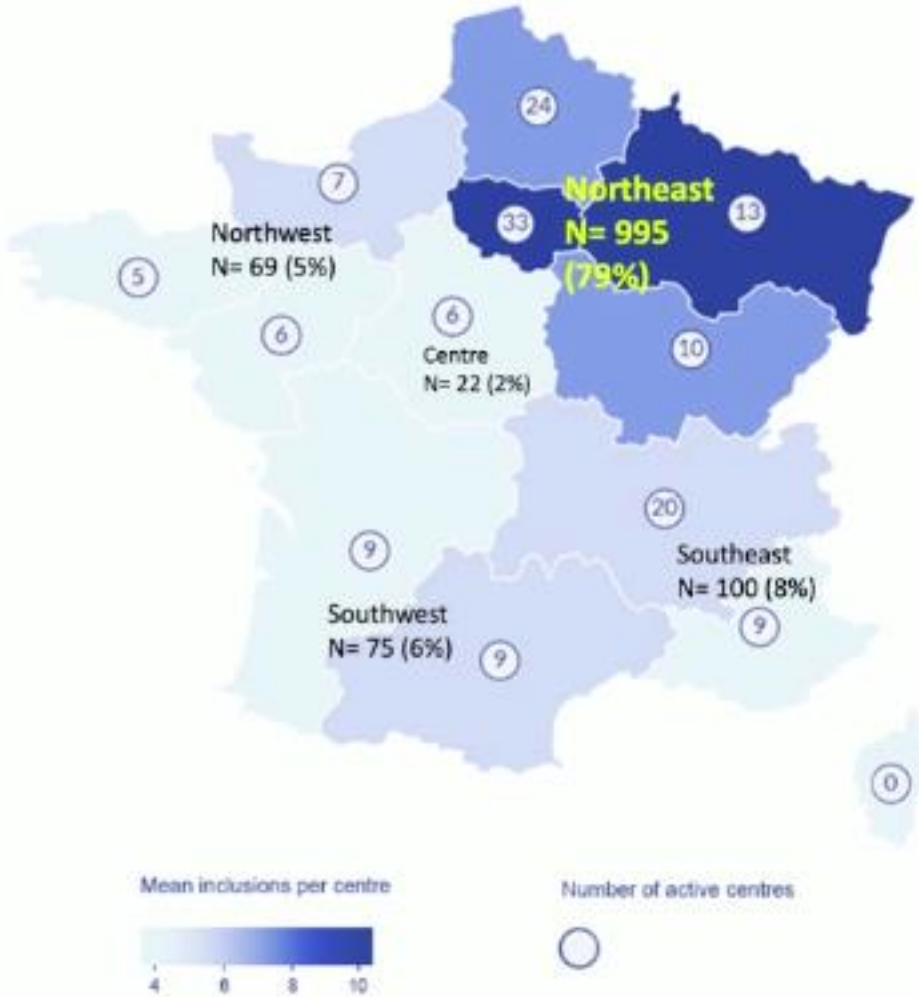
From April 4 to June 11, 2020: **1,289 pts (153 institutions)** were included

- Median age: 67 years, Male: 62%
- Most common region of residence: Northeast (n = 995, 79%).
- Obesity (BMI ≥ 30): n=183 (16%)
- Former/Current smoker: n=574 (52%)
- Comorbidities:

- ≥ 1 comorbidity: n=1,114 (86%), ≥ 4 comorbidities: n= 324 (25%)
- Most common: hypertension 46%, diabetes 21% and COPD 12%

- ECOG PS 0-1: n=547 (59%)

Geographic distribution of cancer patients with COVID-19 and participating institutions



# TUMOUR CHARACTERISTICS AND OUTCOME

| Cancer Type | |
|---|---|
| Digestive | 470 (36%) |
| Thoracic | 311 (24%) |
| Gynaecological | 252 (20%) |
| Breast Cancer | 173 (68.7%) |
| Other gynaecological | 79 (31.3%) |
| Head and neck | 104 (8%) |
| Central nervous system | 65 (5%) |
| Genitourinary | 65 (5%) |
| Dermatological | 14 (1%) |
| Others | 6 (<1%) |

Metastatic stage: n= 758 (59%)

| Anticancer treatment during 3 months before COVID-19 diagnosis | |
|---|---|
| ***Systemic therapy*** | ***755 (59%)*** |
| cytotoxic chemotherapy | 577 (45%) |
| immunotherapy | 110 (8%) |
| targeted therapy | 181 (14%) |
| hormone therapy | 57 (4%) |
| ***local therapy*** | |
| radiotherapy | 133 (10%) |
| surgery | 56 (4%) |

Median follow-up from COVID-19 diagnosis: 34 days

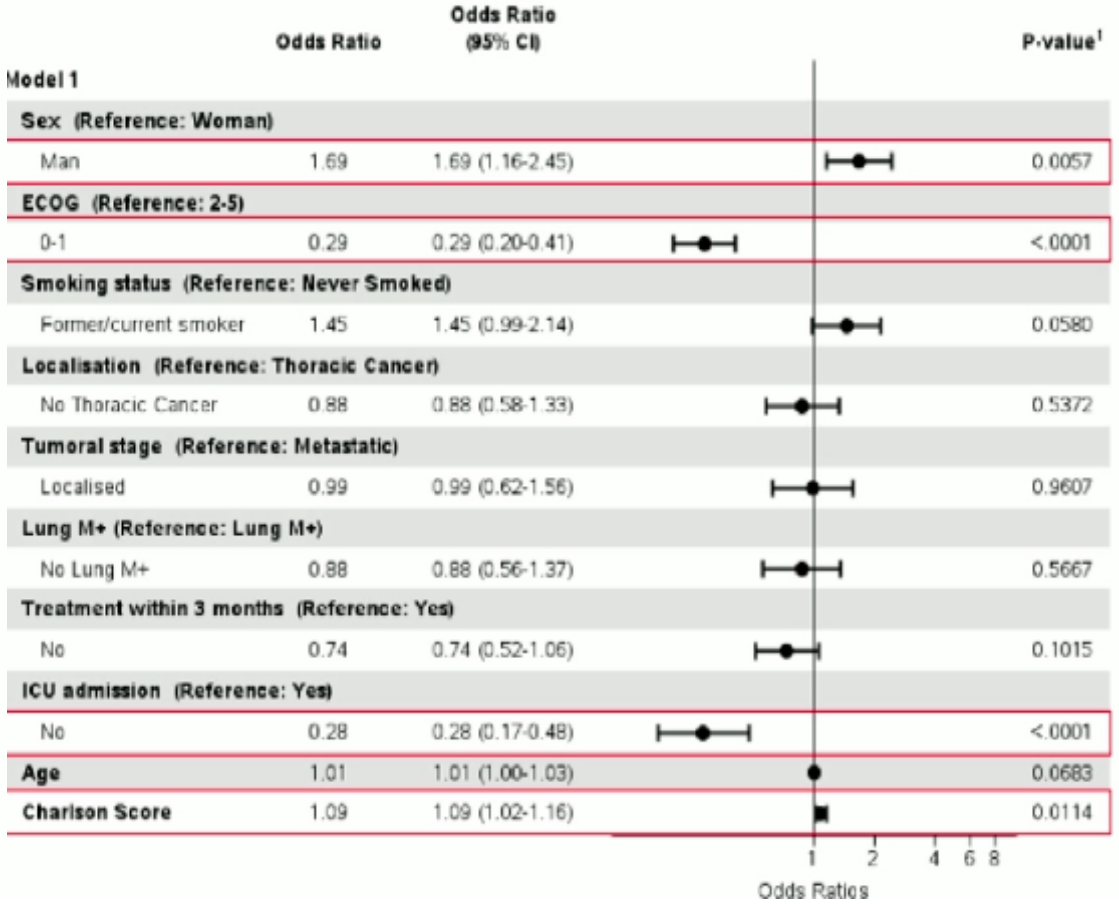
| COVID-19 COMPLICATIONS | |
|---|---|
| Admission to hospital[1] | 734 (65%) |
| Admission to ICU[1] | 110 (10%) |
| O2 requirement[2] | 412 (42%) |
| Mechanical ventilation[2] | 49 (5%) |
| Death[3] | 370 (29%) |
| COVID-19 severity = O2 or ICU admission or death | 424 (33%) |

[1] excludes 164 cases [2] excludes 300 cases with missing data

[3] After a median of 10 days

The systemic anticancer treatment was interrupted or stopped following COVID-19 diagnosis in 431 (39%) pts

# RISK FACTORS FOR ALL-CAUSE MORTALITY



# COVID et CANCER

## Conclusion

- Facteurs pronostiques classiques : état général, sexe, comorbidités
- Pas de surmortalité sur le critère : âge et cancer thoracique
- Biais de sélection
- Evaluation de l'impact de l'arrêt des traitements et/ou report

*D'après la présentation du Dr Colombo*

# Merci pour votre attention