MaNGO
Mario Negri Gynecologic Oncology

Novita' da ASCO

Dott.ssa Federica Tomao
IEO, Milano

XVIII ASSEMBLEA MANGO

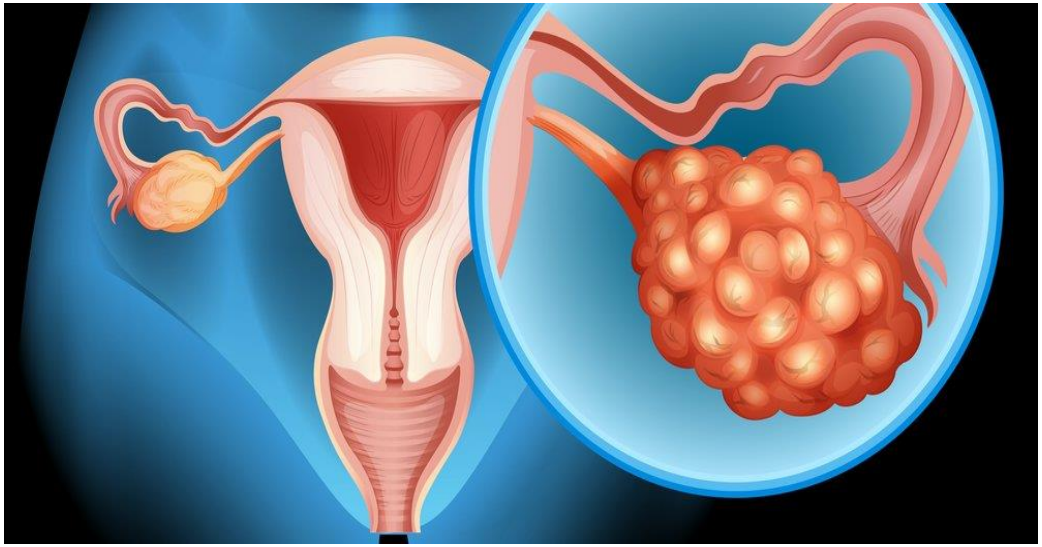
Ricerca Clinica e Traslazionale in Ginecologia Oncologica

MILANO, 2-3 LUGLIO 2021

Con il Patrocinio di:

AIOM Associazione Italiana di Oncologia Medica
FICOG | Federation of Italian Cooperative Oncology Groups
SOCIETA' ITALIANA DI CANCEROLOGIA
SIGO SOCIETA' ITALIANA DI GINECOLOGIA E OSTETRICIA
ACTO ALLEANZA CONTRO il TUMORE OVARICO

Ovarian cancer



2021 ASCO ANNUAL MEETING

GINECO

EFFICACY AND SAFETY RESULTS FROM NEOPEMBROV STUDY. A RANDOMIZED PHASE II TRIAL OF NEOADJUVANT CHEMOTHERAPY (CT) WITH OR WITHOUT PEMBROLIZUMAB (P) FOLLOWED BY INTERVAL DEBULKING SURGERY AND STANDARD SYSTEMIC THERAPY ± P FOR ADVANCED HIGH GRADE SEROUS CARCINOMA (HGSC). A GINECO STUDY.

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Isabelle Ray-Coquard, Centre Leon Bérard

May, 2021

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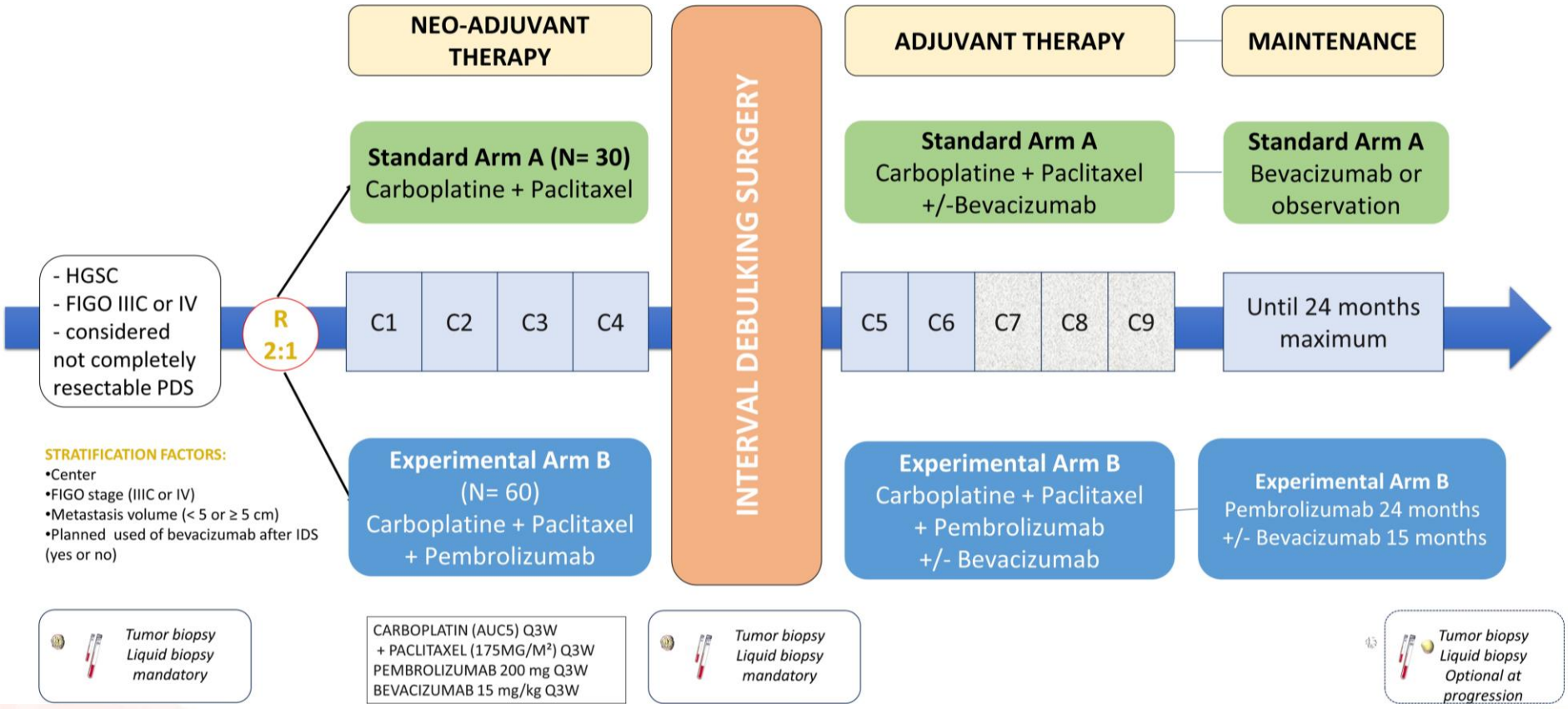
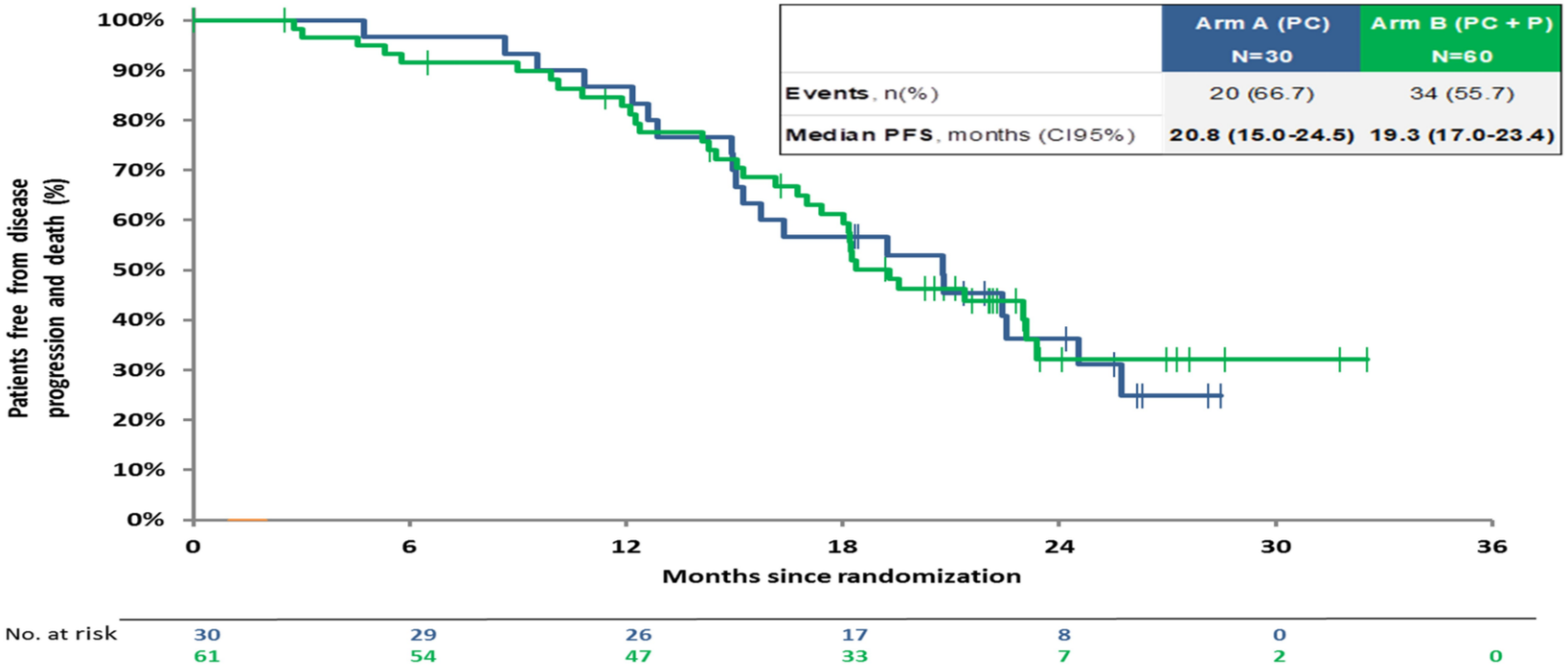
Study design



Response to CT +/- Bev +/- Pembro

	Arm A (CP ± Bev) N = 30	Arm B (CP+ P ± Bev) N = 61
Interval debulking surgery performed (%)		
Yes	29 (96.7)	58 (95.1)
No	1 (3.3)	3 (4.9)
Response at IDS (PCI Decrease)		
mean [std]	- 9.58 [8.58]	- 10.19 [9.27]
Not evaluable	3	6
Primary Endpoint (ITT) Rate of complete debulking % [95% CI]	***70% [53.5% -]***	***73.8% [62.9% -]***
Complete cytoreductive surgery (CC0)	21 (72.4)	45 (77.5)
CC1	0 N = 29	2 (3.4) N = 58
CC ≥ 3 or biopsies only	8 (27.6)	11 (18.9)
Response Rate after 4 cy NACT (RECIST) (%)		
Complete response	2 (6.9)	2 (3.3)
Partial response	16 (55.2)	42 (70.0)
Stable	11 (37.9)	14 (23.3)
Progression	0 (0.0)	2 (3.3)
Not evaluable	1	1
ORR (95% CI)	***62.1% [42.3-79.3]***	***73.3% [60.3-83.9]***
Best Overall Response (%)		
Complete response	22 (75.9)	45 (75.0)
Partial response	3 (10.3)	10 (16.7)
Stable	4 (13.8)	5 (8.3)
Not evaluable	1	1
CR+PR	*25 (83.3)*	*55 (90.1)*
Ca125 normalization	22 (73.3)	46 (75.4)

PFS



	Arm A (PC) N=30	Arm B (PC + P) N=60
Events, n(%)	20 (66.7)	34 (55.7)
Median PFS, months (CI95%)	**20.8 (15.0-24.5)**	**19.3 (17.0-23.4)**

Median Follow-up of 22 months (min=6.8, max = 32.5)

2021 ASCO ANNUAL MEETING

ENGOT European Network of Gynaecological Oncological Trial groups

GCIG GYNECOLOGIC CANCER INTERGROUP

AGO Study Group

GINECO ARCAGY

NSGO-CTU Nordic Society of Gynaecological Oncology - Clinical Trial Unit

Optimal treatment duration of bevacizumab combined with carboplatin and paclitaxel in patients with primary epithelial ovarian, fallopian tube or peritoneal cancer

A prospective randomized Phase III ENGOT/GCIG Study of the AGO Study Group, GINECO, NSGO
AGO-OVAR 17 BOOST / GINECO OV118 / ENGOT Ov-15 / NCT01462890

Performed according to ENGOT Model A. Financial support and drug supply provided by F. Hoffmann-La Roche Ltd.

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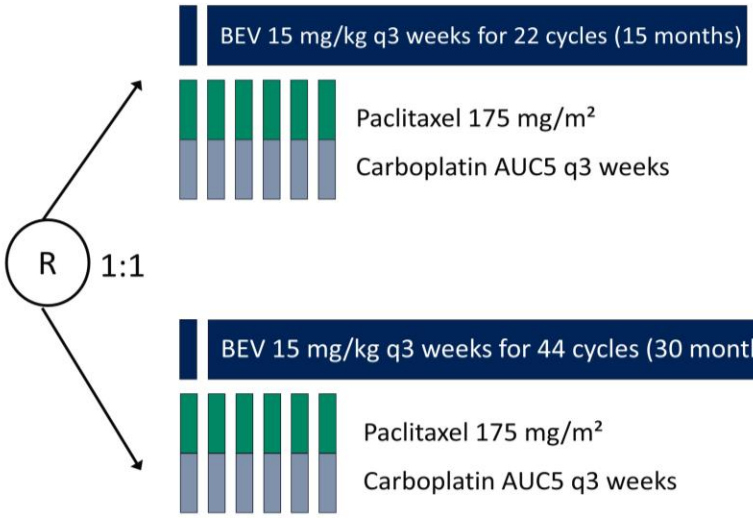
The study design

AGO-OVAR 17 BOOST / GINECO OV118 / ENGOT Ov-15

- Histologically confirmed epithelial ovarian, fallopian tube, or peritoneal cancer (excluding non-epithelial and borderline tumors)
- FIGO stage IIB–IV (any grade/ histologic subtype)
- Primary debulking surgery ≤8 weeks before treatment start, >4 weeks before first BEV dose
- Adequate coagulation parameters, bone marrow, liver, and renal function
- ECOG PS 0–2
- Standard BEV exclusion criteria

n= 927 Nov 2011 – Aug 2013



BEV15
(standard arm)

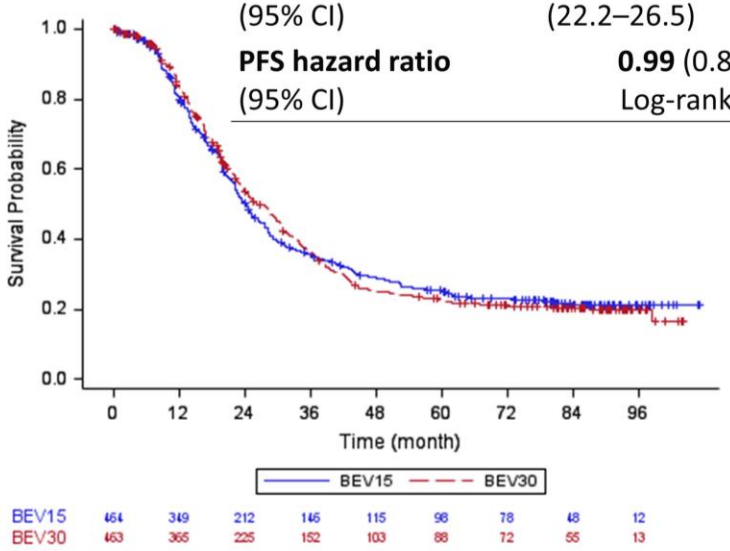
BEV30
(experimental arm)

Stratification factors

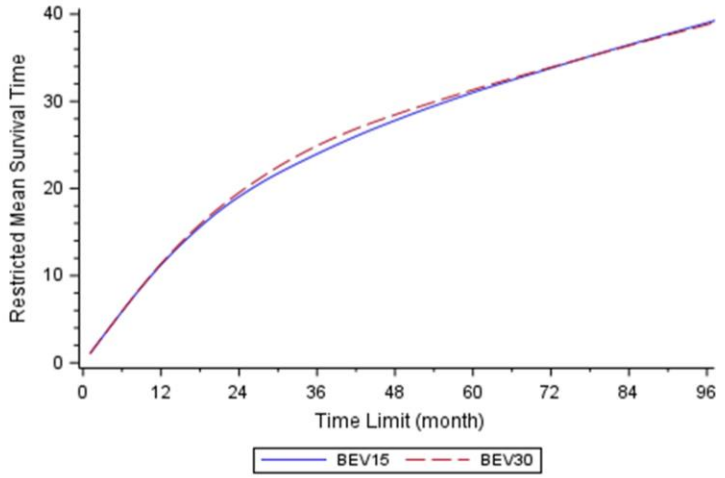
FIGO IIB–IIIC and no residual tumor
versus
FIGO IIB–IIIC with residual tumor *or* FIGO IV

PFS

	BEV15 n=464	BEV30 n=463
PFS events, n (%)	333 (72)	340 (73)
Median PFS, months (95% CI)	**24.2** (22.2–26.5)	**26.0** (23.7–29.7)
PFS hazard ratio (95% CI)	**0.99** (0.85–1.15) Log-rank p=0.90	

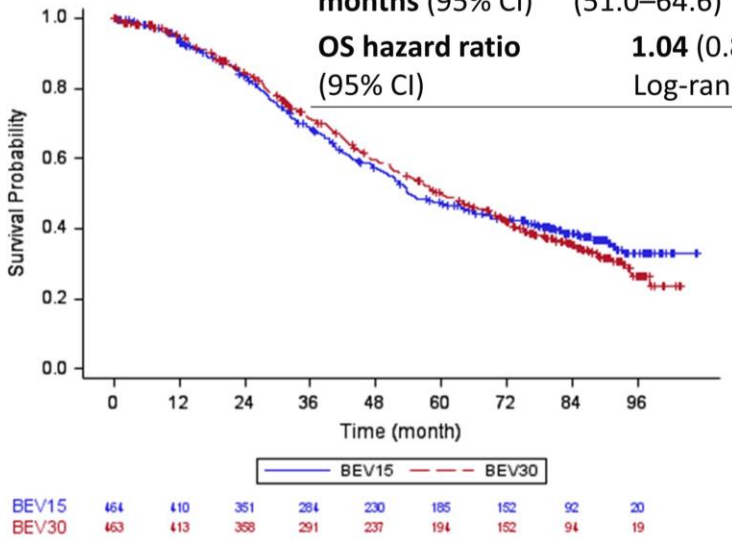


	BEV15 n=464	BEV30 n=463
Restricted mean PFS, months (95% CI)*	**39.5** (36.3–42.7)	**39.3** (36.2–42.4)
* Restricted at last event time	p=0.92	

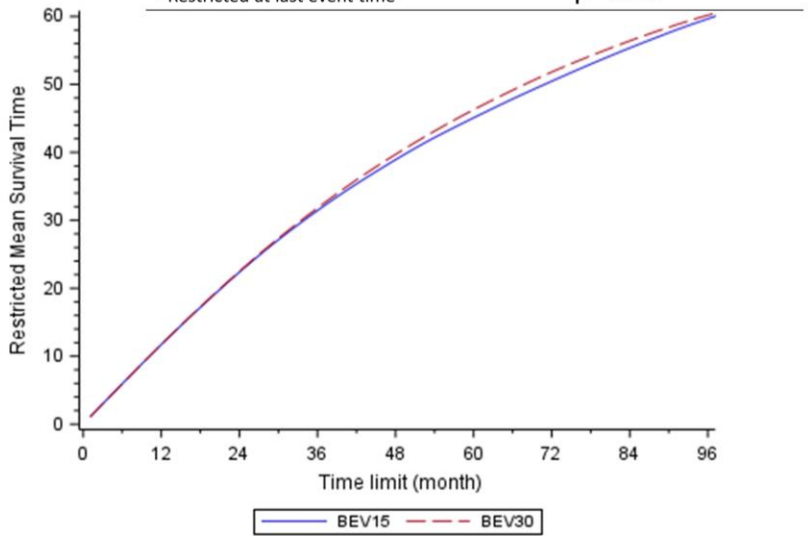


OS

	BEV15 n=464	BEV30 n=463
OS events, n (%)	257 (55)	275 (59)
Median OS, months (95% CI)	**54.3** (51.0–64.6)	**60.0** (54.0–68.6)
OS hazard ratio (95% CI)	**1.04** (0.87–1.23) Log-rank p=0.68	



	BEV15 n=464	BEV30 n=463
Restricted mean OS, months (95% CI)*	**60.4** (57.2–63.6)	**60.8** (57.8–63.8)
* Restricted at last event time	p=0.87	



MAINTENANCE GEMOGENOVATUCEL-T (GEM) IN NEWLY DIAGNOSED ADVANCED OVARIAN CANCER: EFFICACY ASSESSMENT OF HOMOLOGOUS RECOMBINATION PROFICIENT (HRP) PATIENTS IN THE PHASE IIB VITAL TRIAL

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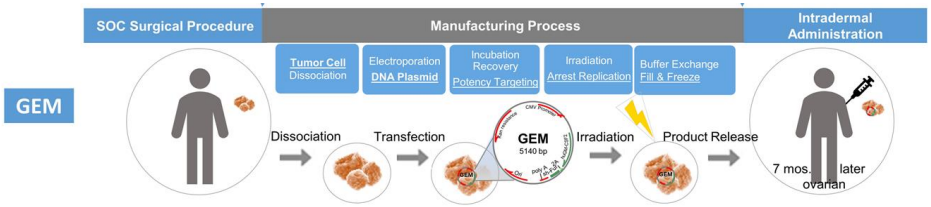
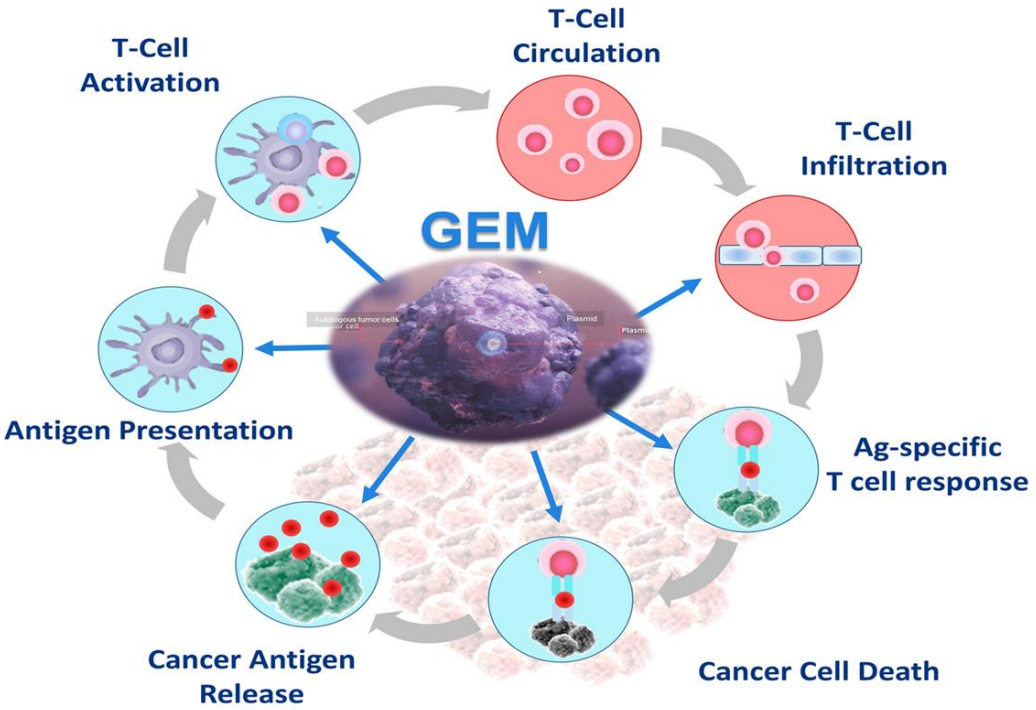
The role of GEM in the cancer immunity cycle





Methods: study design

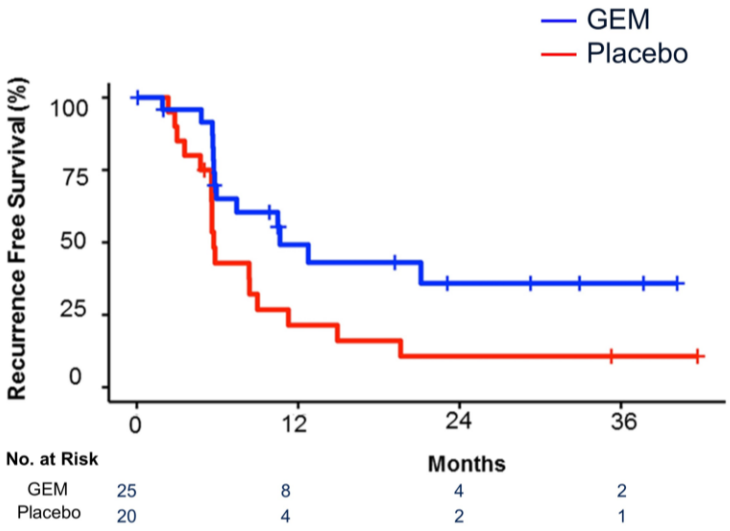
- ***VITAL Phase 2b study***
  - Double-blinded
  - Randomized GEM vs. Placebo in 1:1 fashion

- ***Patients***
  - Epithelial Ovarian Cancer (EOC)
  - Advanced Stage IIIb-IV
  - Clinical complete response (cCR) after 1L surgery + platinum/taxane

- ***Treatment***
  - GEM vaccine 1x10e7 cells/dose given via intradermal injection every 4 weeks (up to 12 doses)
  - Placebo given via intradermal injection every 4 weeks (up to 12 doses)

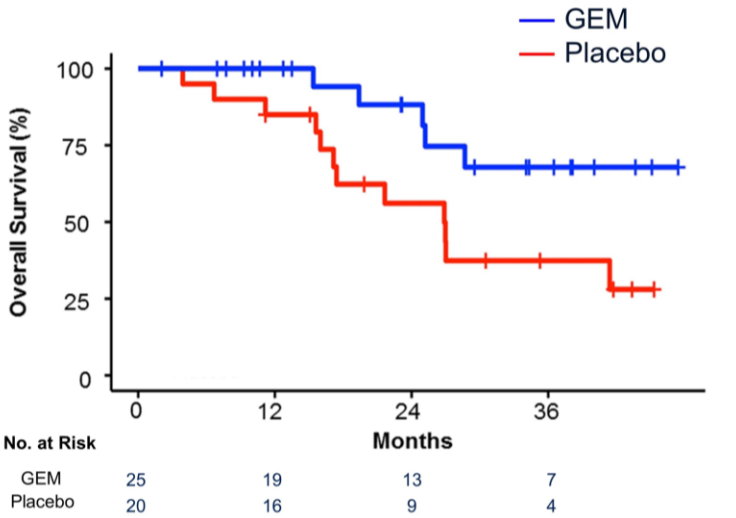
Results in HRP patients

RFS (from randomization)



Group	N	N (%)	Median RFS (mo)	HR	p-value* (log-rank)
GEM	25	13 (52)	10.6	0.386	0.007
Placebo	20	17 (85)	5.7		

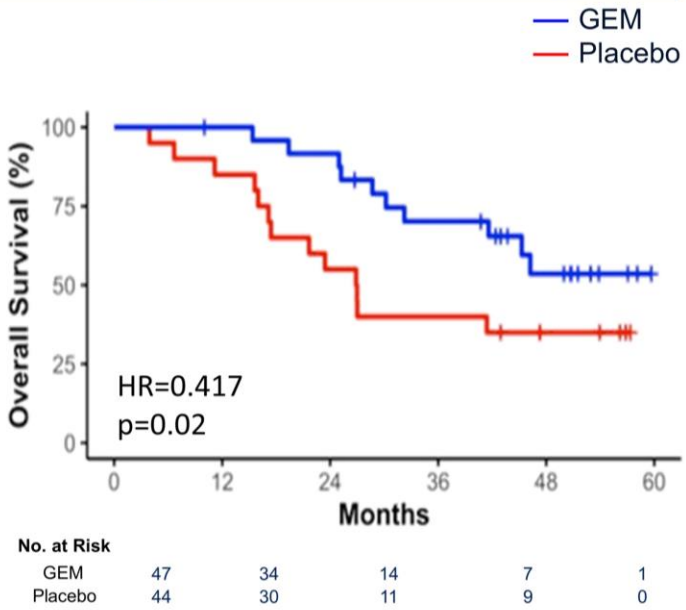
OS (from randomization)

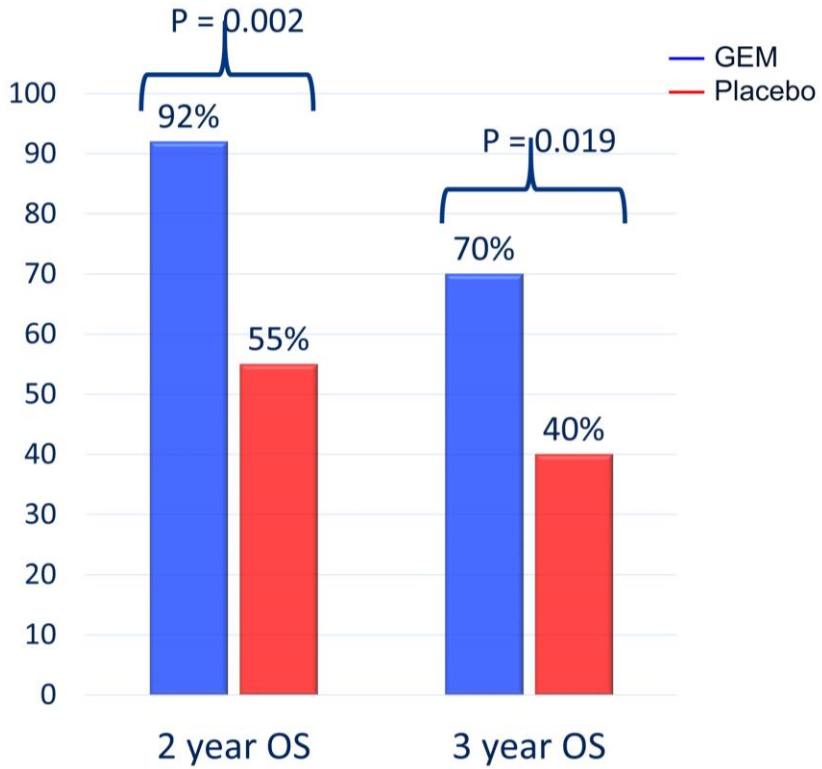


Group	N	N (%)	Median OS (mo)	HR	p-value* (log-rank)
GEM	25	5 (20)	NR	0.342	0.019
Placebo	20	12 (60)	26.9		

Updated survival in HRP patients (April 2021)

OS (from randomization)





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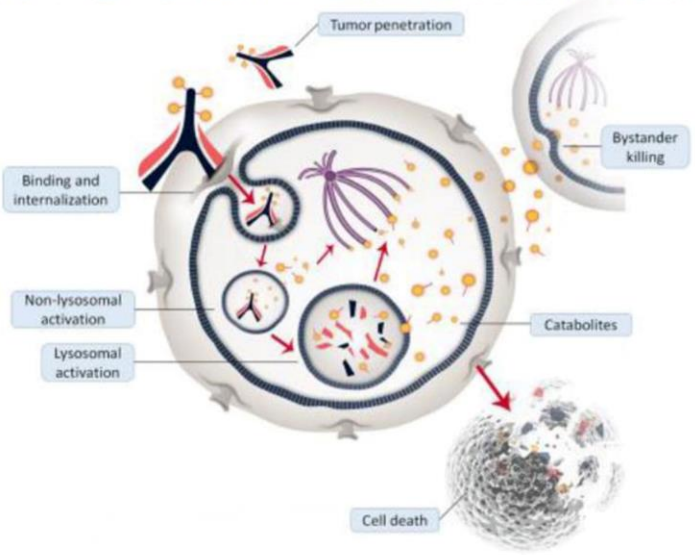
Mirvetuximab Soravtansine, a folate receptor alpha-targeting antibody drug conjugate, in combination with bevacizumab in patients with platinum-agnostic ovarian cancer: final analysis



David M. O'Malley[1], Ana Oaknin[2], Ursula A. Matulonis[3], Gina M. Mantia-Smaldone[4], Peter Lim[5], Cesar Castro[6], Diane Provencher[7], Sanaz Memarzadeh[8], Patrick Zweidler-McKay[9], Jiuzhou Wang[9], Brooke Esteves[9], Kathleen N. Moore[10] Lucy Gilbert[11]

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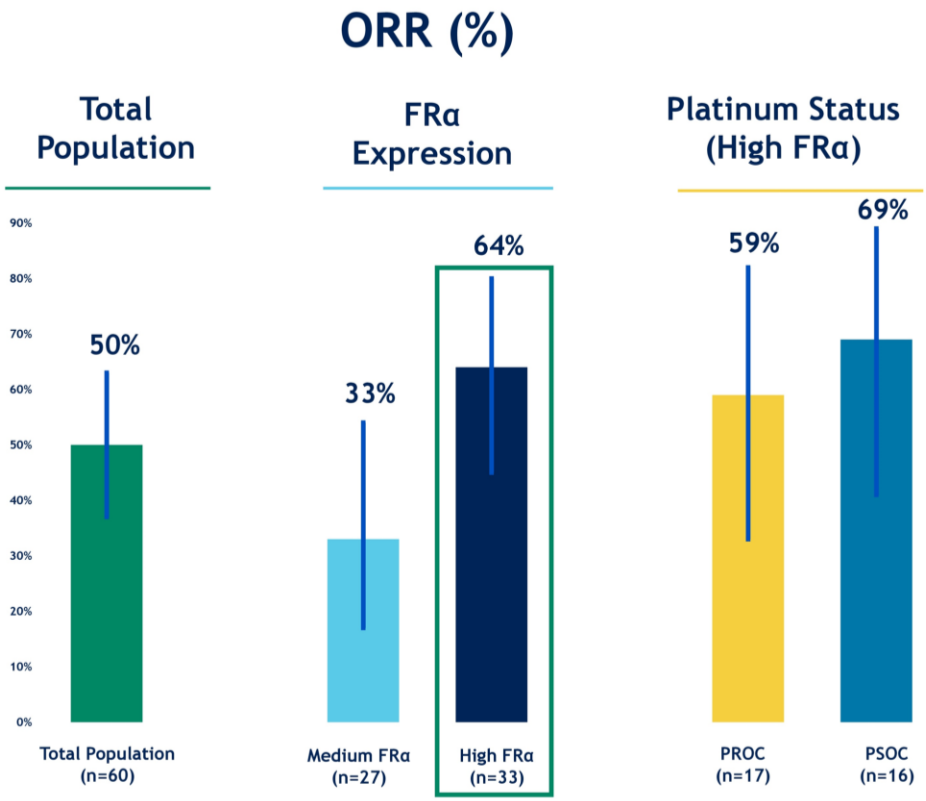
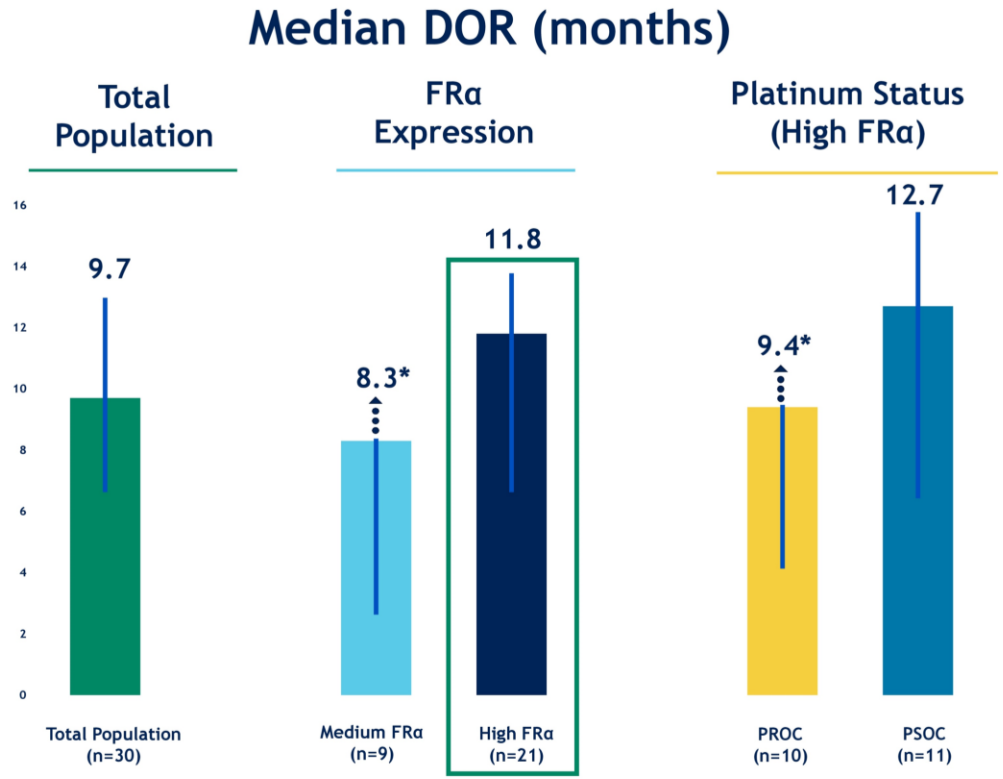
Confirmed ORR by FRα and platinum status



- **50% ORR** (30/60) for overall cohort
- **64% ORR** (21/33) in high FRα tumors
  - **59% ORR** (10/17) in PROC subset
  - **69% ORR** (11/16) in PSOC subset

Median DOR by FRα and platinum status

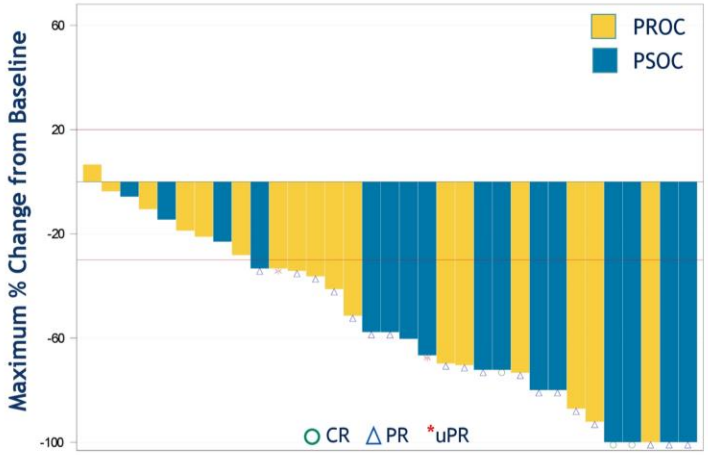


- **9.7 mo mDOR** for overall cohort
- **11.8 mo mDOR** in high FRα tumors
  - **9.4 mo mDOR** in PROC subset
  - **12.7 mo mDOR** in PSOC subset

*Upper limit of 95% confidence interval not reached

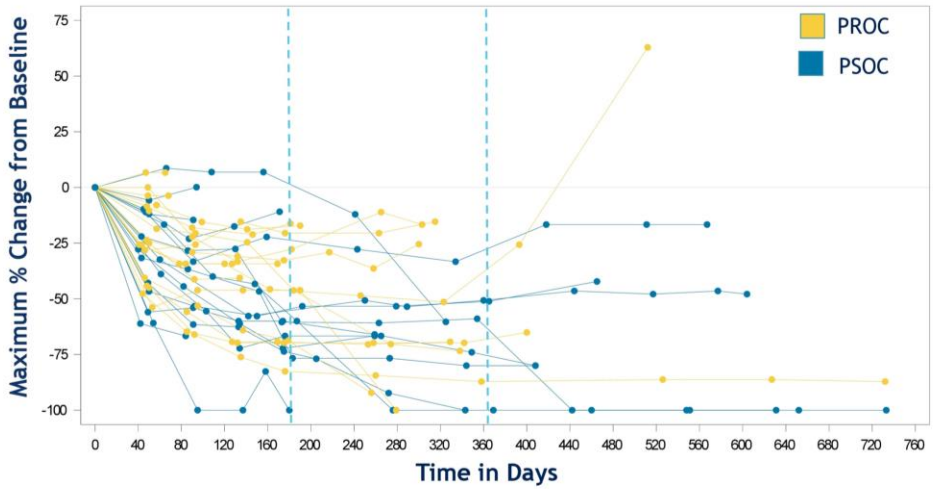
High FRα tumors showed a deep response and durable benefit

Maximum % Change from Baseline



- **97% (32/33)** of patients demonstrated tumor burden reduction

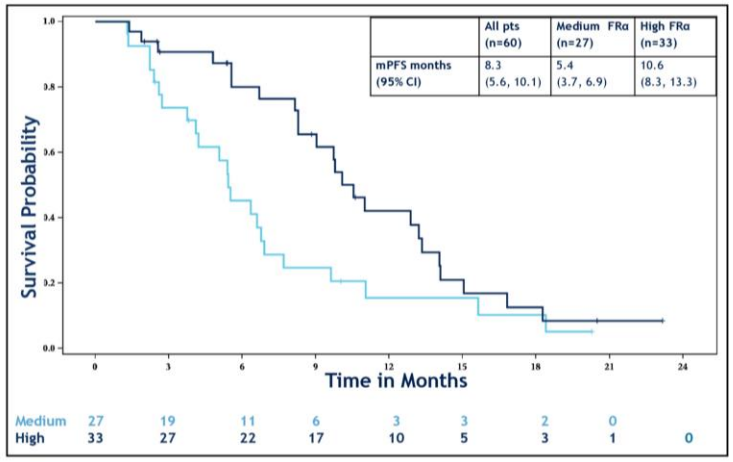
Percent Change and Duration from Baseline



- Rapid tumor shrinkage, with early responses
- Durable benefit in both PSOC and PROC

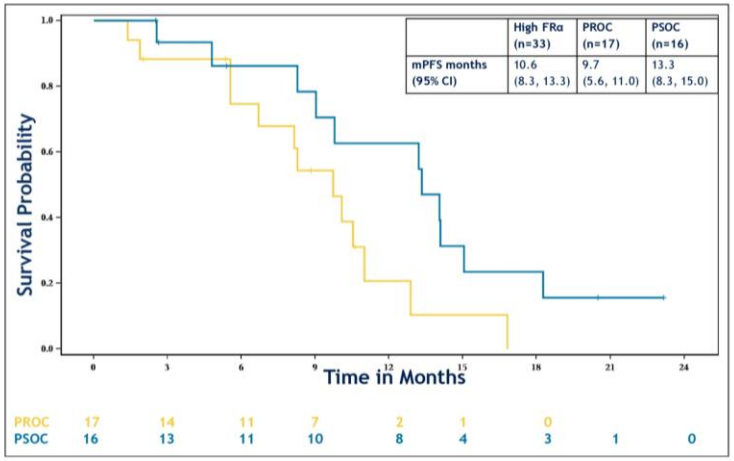
Longer PFS in high FRα tumors regardless of platinum status

Medium and High FRα Tumors



- mPFS 10.6 months in high FRα tumors
- mPFS 5.4 months in medium FRα tumors
- High FRα 6-month and 12-month PFS rate of 80% and 42%, respectively

High FRα Tumors (PROC and PSOC)



- mPFS 9.7 months in high FRα PROC tumors
- mPFS 13.3 months in high FRα PSOC tumors

mPFS = median progression free survival

Treatment-Related emergent AE > 20%

N=60	All Grades	Grade 3/4
Adverse Event	N (%)	N (%)
Diarrhea^	37 (62)	1 (2)
Blurred vision	36 (60)	0 (0)
Fatigue^	36 (60)	2 (3)
Nausea	34 (57)	0 (0)
Keratopathy†	26 (43)	0 (0)
Peripheral neuropathy*	24 (40)	1 (2)
Dry eye	20 (33)	3 (5)
Decreased appetite	20 (33)	0 (0)
Hypertension^	19 (32)	10 (17)
Headache	17 (28)	0 (0)
AST increased	17 (28)	2 (3)
Vomiting	17 (28)	0 (0)
Abdominal pain	16 (27)	0 (0)
Visual acuity reduced	14 (23)	0 (0)
Thrombocytopenia	14 (23)	2 (3)
Neutropenia	13 (22)	8 (13)
ALT increased	13 (22)	3 (5)
Dysphonia^	13 (22)	0 (0)
Asthenia	13 (22)	0 (0)
Weight decrease^	13 (22)	1 (2)

- **Most AEs were low grade**
  - GI and Ocular were most frequent
  - Ocular AE class effect of ADC manageable with eye drops
- **Grade 3+ events were infrequent**
  - 17% hypertension
  - 13% neutropenia
- **Eighteen patients (30%) discontinued BEV and/or MIRV** due to treatment-related AEs
  - Discontinuations occurred after a median of 13 cycles of treatment
  - Discontinuations by agent
    - MIRV: 23%
    - BEV: 18%

AE rates are similar for MIRV/BEV compared with MIRV alone (n=243 from FORWARD I), when adjusted for exposure
^Exceptions (p <0.05, not adjusted for multiplicity testing) include Diarrhea, Fatigue, Hypertension, Dysphonia, and Weight Decrease

EFFORT: EFFICACY OF ADAVOSERTIB IN PARP RESISTANCE: A RANDOMIZED 2-ARM NON-COMPARATIVE PHASE II STUDY OF ADAVOSERTIB WITH OR WITHOUT OLAPARIB IN WOMEN WITH PARP-RESISTANT OVARIAN CANCER

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Robert L. Coleman[2], Bryan Fellman[1], Ying Yuan[1], Anil Sood[1], Pamela Soliman[1], Alexi Wright[3], Neil Horowitz[3], Susana Campos[3], Panagiotis Konstantinopoulos[3], Charles Levenback[1], David Gershenson[1], Karen Lu[1], Virginia Bayer[1], Sobiya Tukdi[1], Alexis Rabbit[3], Lone Ottesen[4], Robert Godin[4], Gordon Mills[5], Joyce F. Liu[3]

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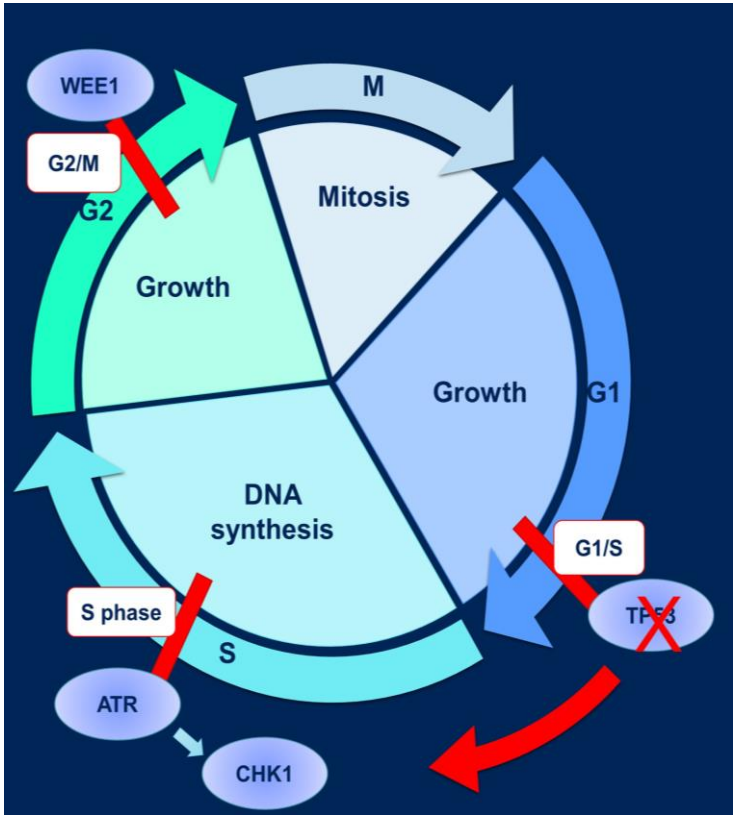
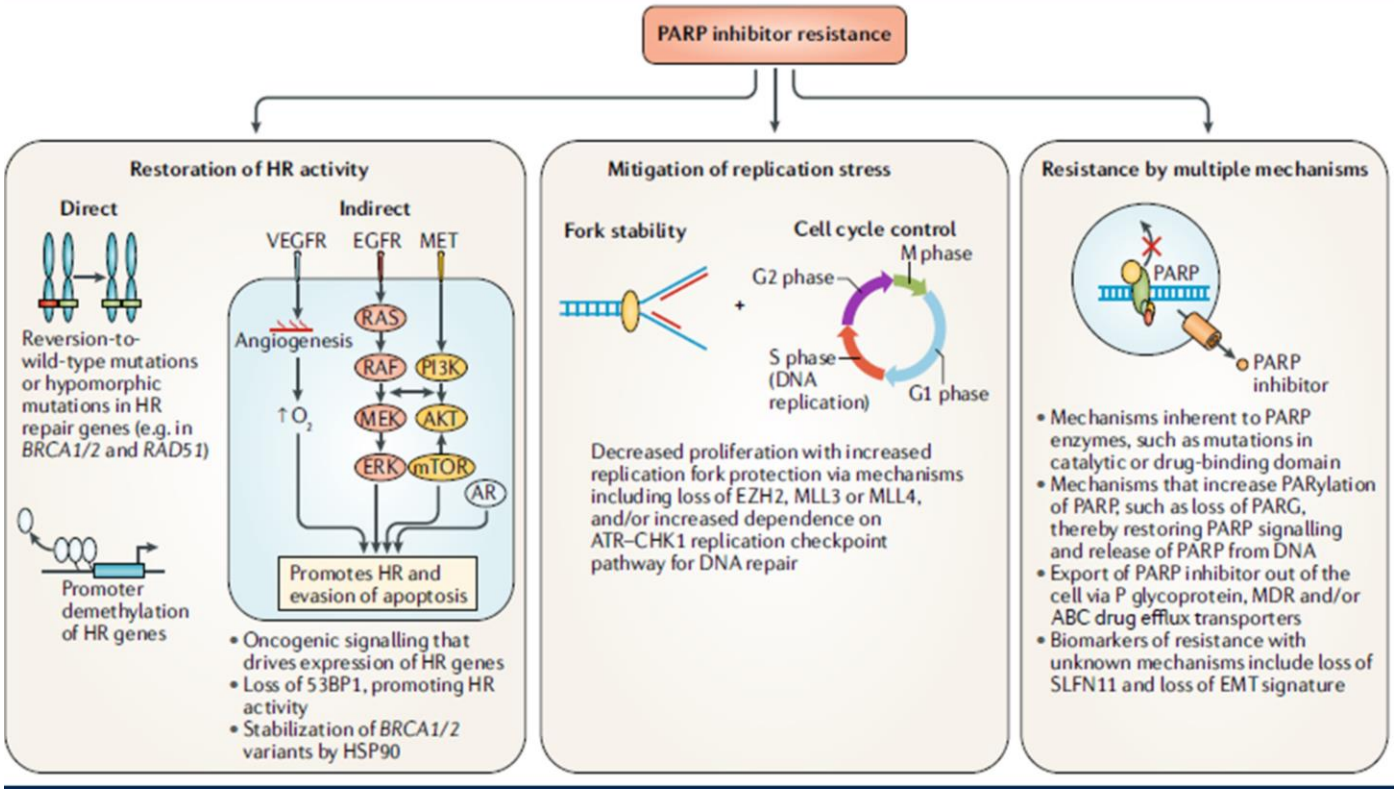
Synthetic lethality: p53 mutation and WEE1 inhibition

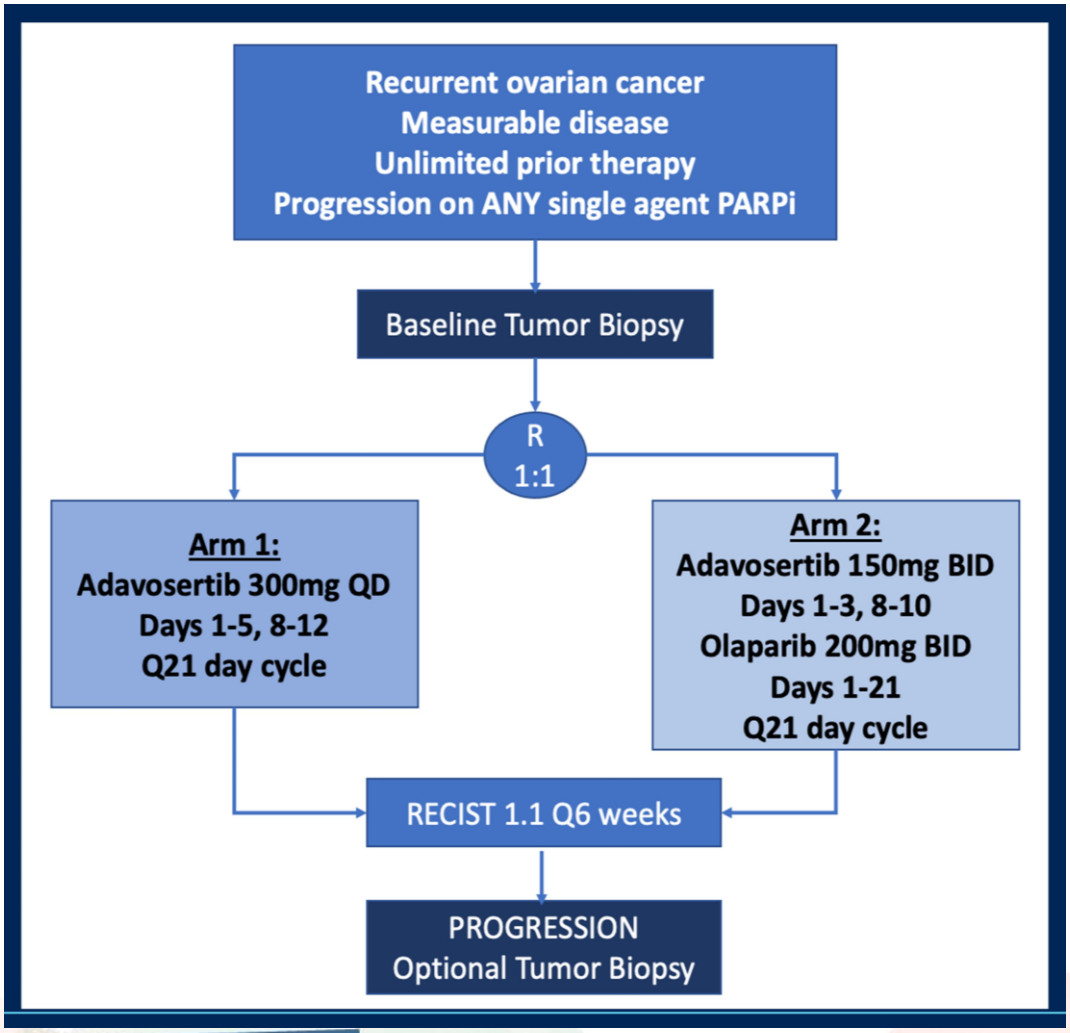
- WEE1 regulates the G2/M checkpoint
- Cells with p53 mutation/loss lose G1/S checkpoint
- Increases replication stress
- Increases dependence on G2/M checkpoint



PARP Inhibitor Resistance Mechanism



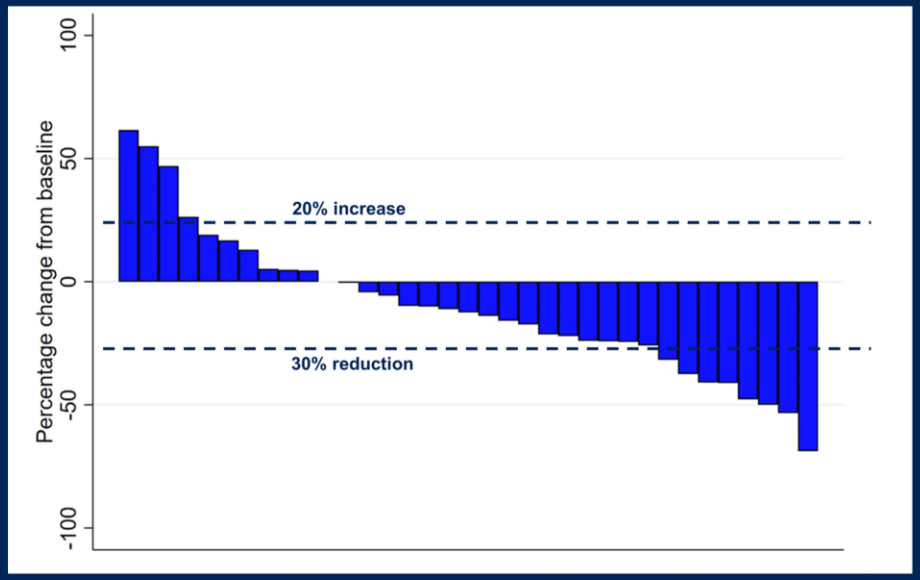
Study design



Primary end point: ORR

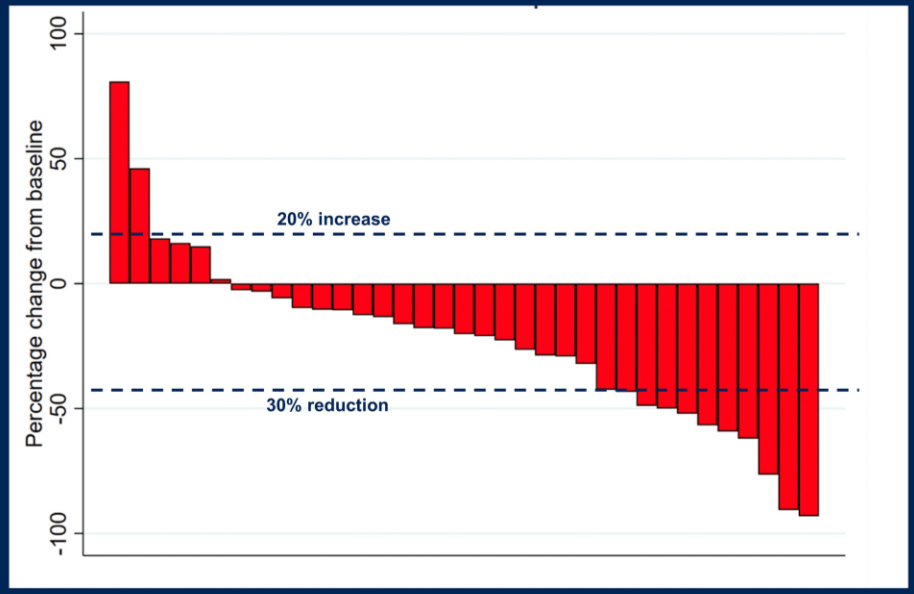
Response to therapy

Adavosertib Alone



ORR: 23%
DOR 5.5 months

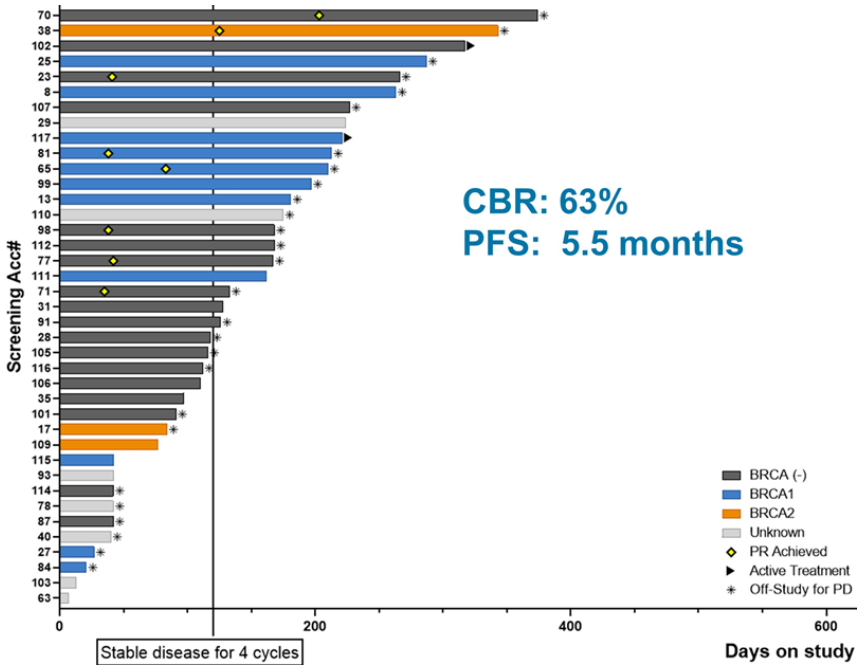
Adavosertib and Olaparib



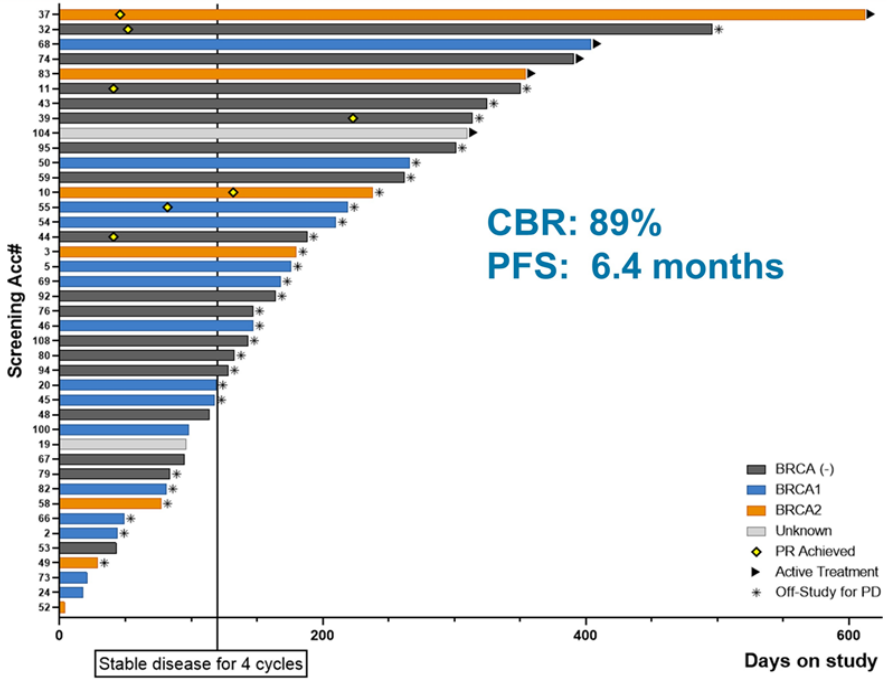
ORR: 29%
DOR 5.5 months

Response to therapy (clinical benefit rate and PFS)

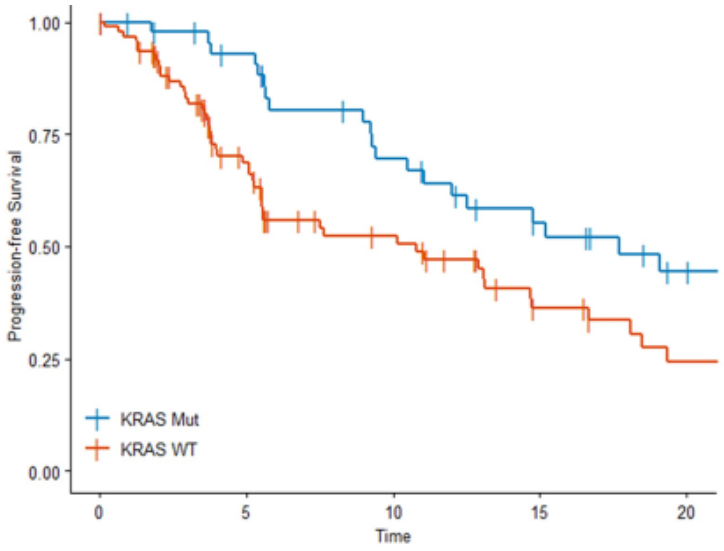
Adavosertib Alone



Adavosertib and Olaparib

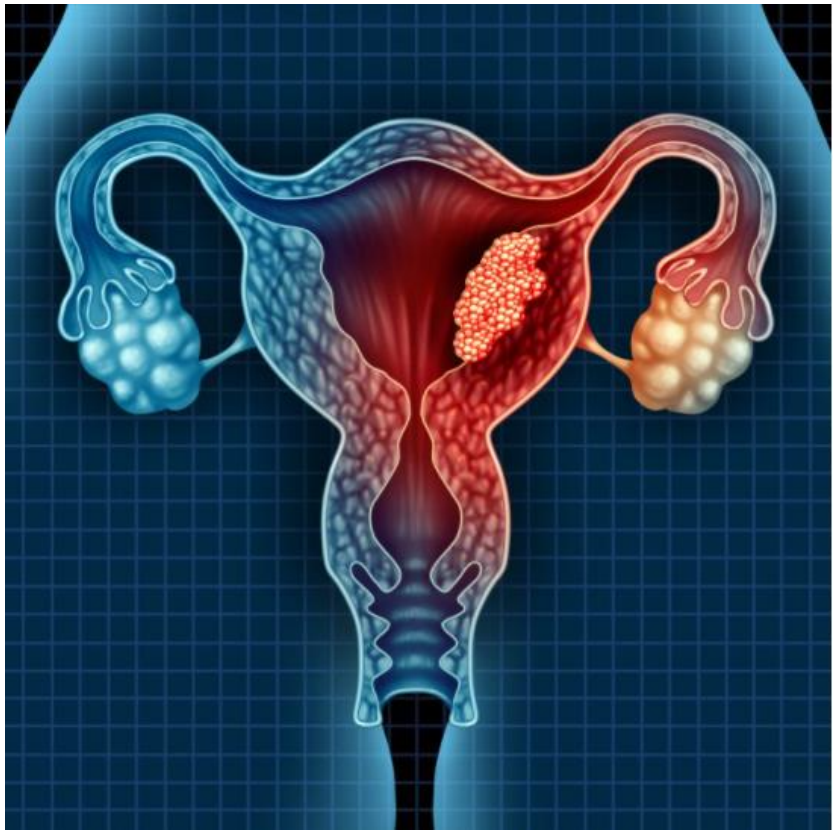


MOLECULAR RESULTS AND POTENTIAL BIOMARKERS IDENTIFIED FROM MILO/ENGOT-OV11 PHASE 3 STUDY OF BINIMETINIB VS PHYSICIANS CHOICE OF CHEMOTHERAPY (PCC) IN RECURRENT LOW-GRADE SEROUS OVARIAN CANCER



Binimetinib Treatment Group		
	N(%)	Median PFS months (95% CI)
All Patients	144	12.9 (9.4, 18.1)
KRAS mutation	46 (32%)	17.7 (12, NR)
KRAS WT	98 (68%)	10.8 (5.6, 16.7)
PCC Treatment Group		
All Patients	71	11.9 (9.1, 24.6)
KRAS mutation	24 (34%)	14.6 (9.4,NR)
KRAS WT	47 (66%)	11.5 (5.7, 26.6)

Endometrial cancer



VICTORIA: A MULTICENTRIC, RANDOMIZED, OPEN-LABEL, PHASE I/II OF VISTUSERTIB COMBINED WITH ANASTROZOLE IN PATIENTS WITH HORMONE RECEPTOR-POSITIVE ADVANCED OR RECURRENT ENDOMETRIAL CANCER

Heudel P, Frenel JS, Dalban C, Bazan F, Joly F, Arnaud A, Abdeddaim C, Chevalier A, Augereau P, Pautier P, Chakiba C, You B, Lancry Lecomte L, Garin G, Marcel V, Diaz JJ, Treilleux I, Pérol D, Fabbro M, Ray-Coquard I

Study design

A multicenter, non-comparative, randomized, open label, Phase I/II

Eligibility criteria

- ER+ and/or PR+ advanced or recurrent endometrial cancer
- ≤ 1 prior CT and ≤ 2 prior endocrine therapy excluding aromatase inhibitor
- RECIST V1.1 evaluable disease
- ECOG PS 0 or 1
- Tumor lesion accessible for on-treatment biopsy (week 8)

R* 2:1

Vistusertib
(125 mg BiD, 2d ON/5d OFF, po)
+ Anastrozole
(1 mg/d, po)

Anastrozole
(1 mg/d, po)

Primary endpoint

Progression-free rate at 8 weeks (PFR-8W) centrally assessed

Secondary endpoints

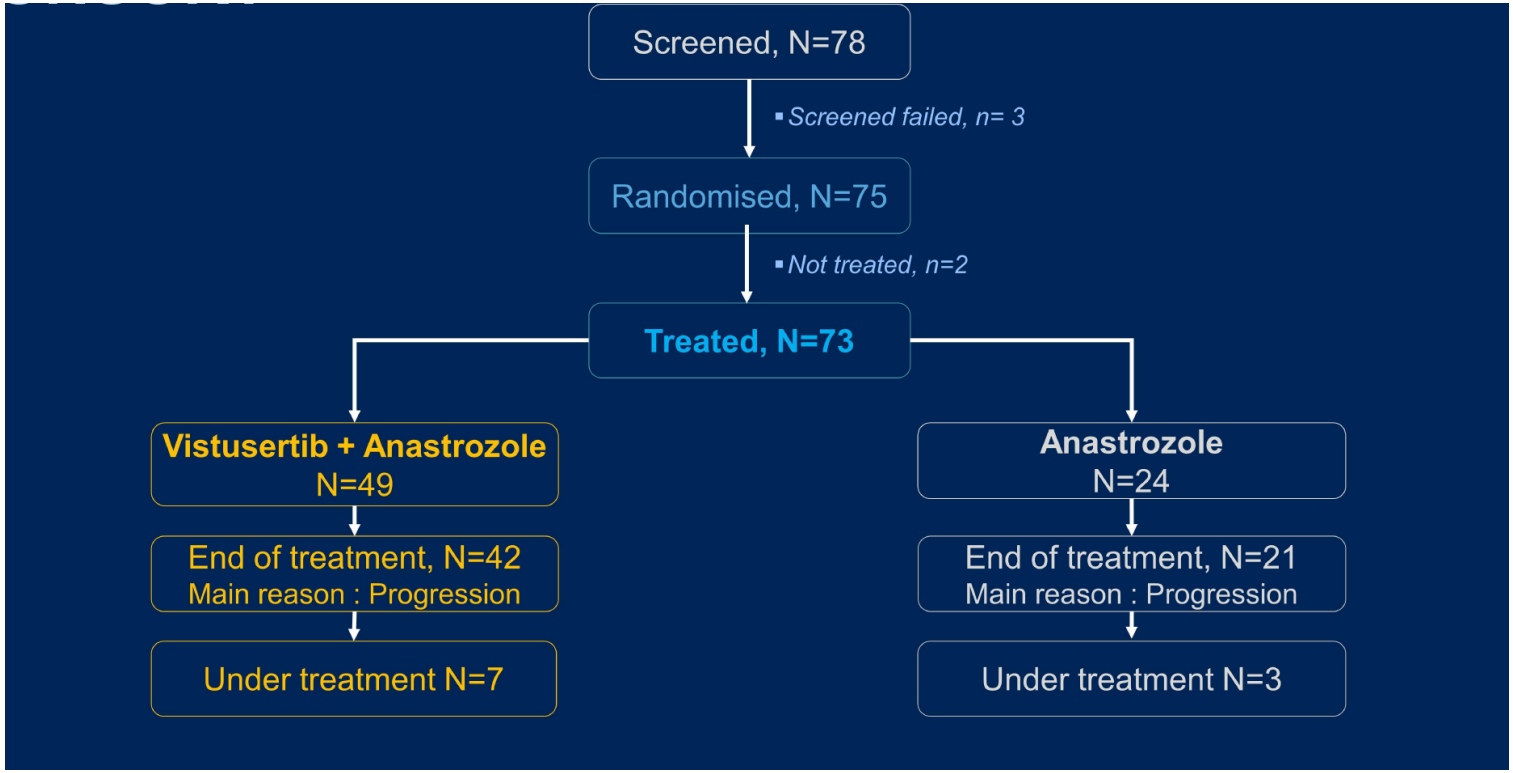
- ORR, DoR, PFS, OS
- Safety (NCI-CTCAE V4.03)
- Translational researches

* Randomization was stratified by n° of prior CT line (0 vs. 1)

The planned sample size (n=46) in Vistusertib arm was based on a Simon's two-stage (optimal) design by using P_0: 40%; P_1: 60%, α: 0.05 and β: 0.20.

Decisions rules were the following: Stage I : PFR-8W ≥ 8/16 → Stage II ; Stage II: PFR-8W ≥ 24/46 → Further interest

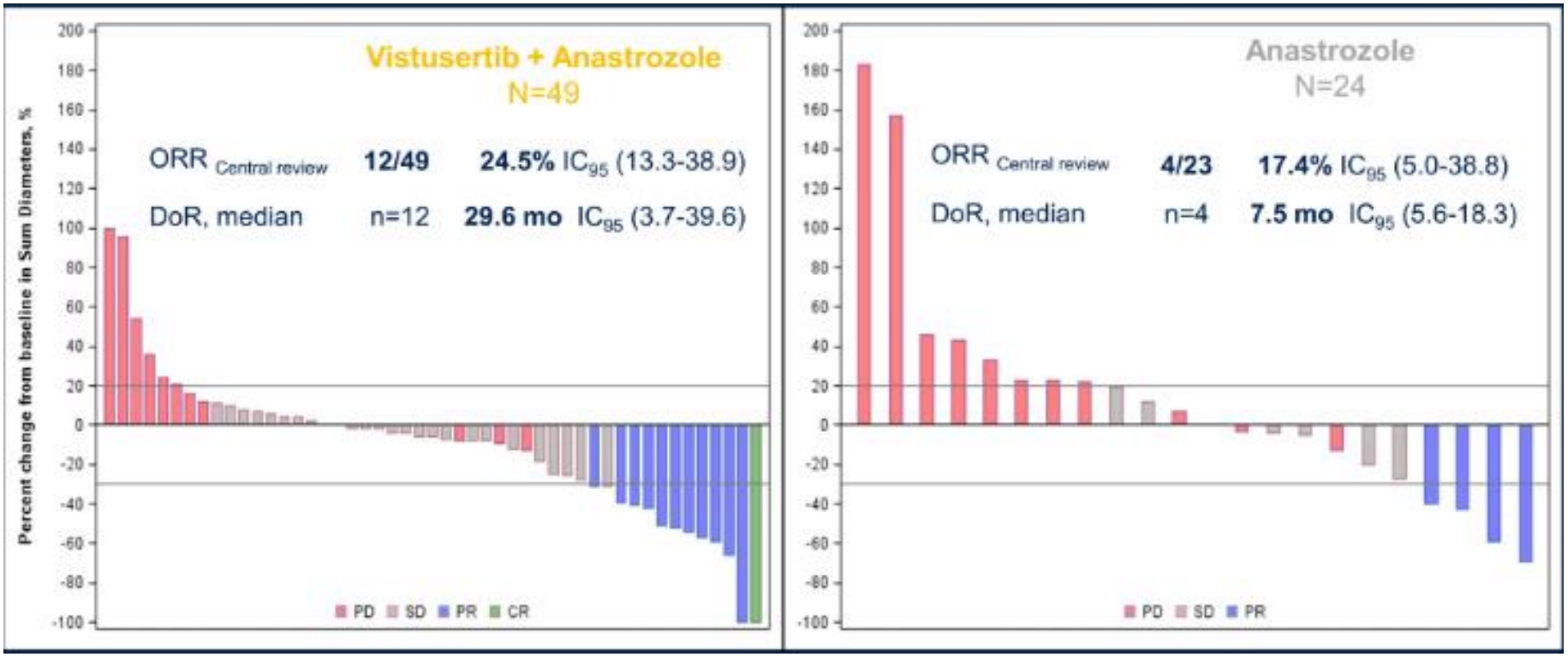
Consort


Screened, N=78
Screened failed, n= 3
Randomised, N=75
Not treated, n=2
Treated, N=73
Vistusertib + Anastrozole
N=49
End of treatment, N=42
Main reason : Progression
Under treatment N=7
Anastrozole
N=24
End of treatment, N=21
Main reason : Progression
Under treatment N=3

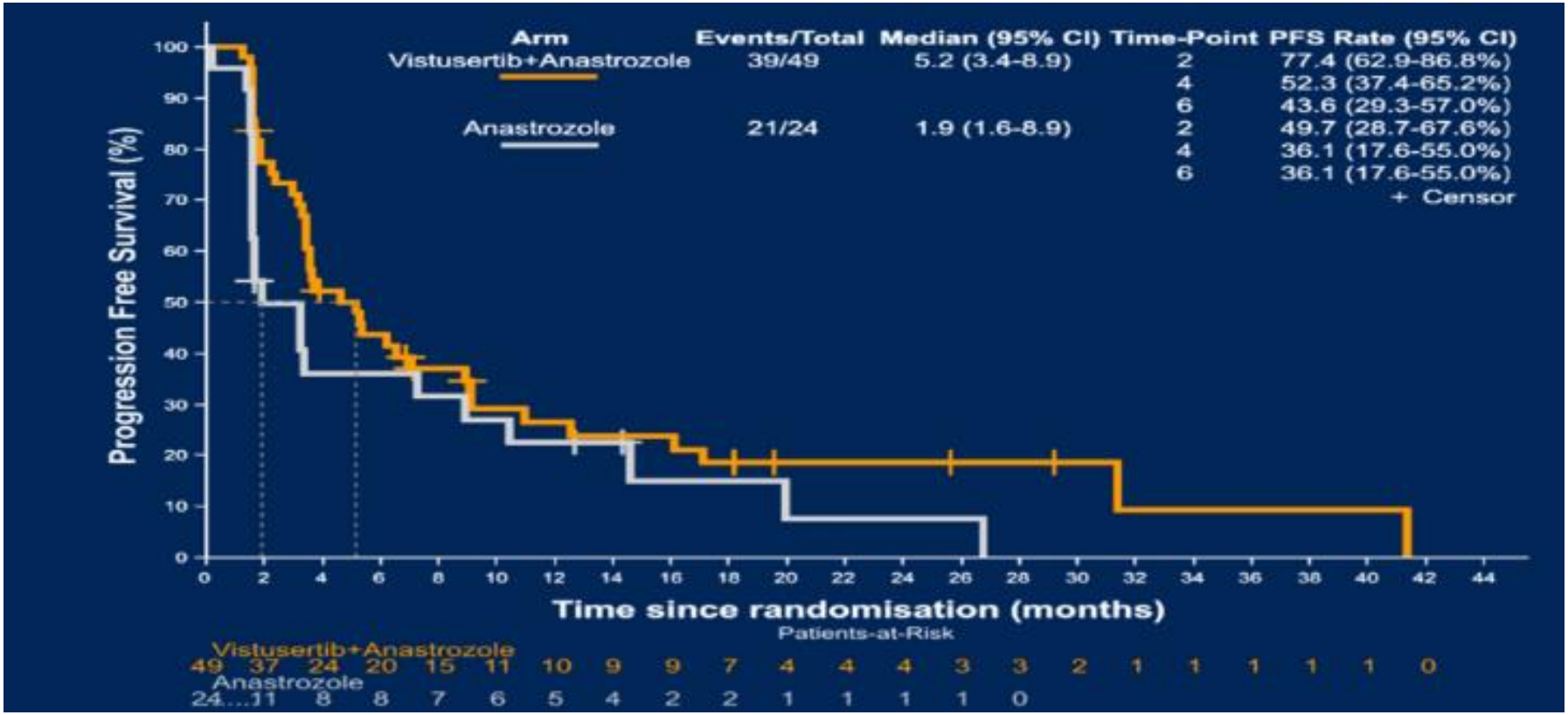
Primary objective: progression free rate at 8 weeks

	Vistusertib + Anastrozole N=49		Anastrozole N=24	
PFR-8W central review	**33 / 49**	**(67.3%)**	**9 / 23**	**(39.1%)**
95% unilateral CI	[54.7% ; -]		[22.2% ; -]	
PFR-8W investigator	**34 / 49**	**(69.4%)**	**11 / 24**	**(45.8%)**
95% unilateral CI	[56.8% ; -]		[28.2% ; -]	

Secondary objective: waterfall (ORR & DoR)



PFS


Arm
Events/Total
Median (95% CI)
Time-Point
PFS Rate (95% CI)
Vistusertib+Anastrozole
39/49
5.2 (3.4-8.9)
2
77.4 (62.9-86.8%)
4
52.3 (37.4-65.2%)
6
43.6 (29.3-57.0%)
Anastrozole
21/24
1.9 (1.6-8.9)
2
49.7 (28.7-67.6%)
4
36.1 (17.6-55.0%)
6
36.1 (17.6-55.0%)
+ Censor
Progression Free Survival (%)
Time since randomisation (months)
Patients-at-Risk
Vistusertib+Anastrozole
49 37 24 20 15 11 10 9 9 7 4 4 4 3 3 2 1 1 1 1 1 0
Anastrozole
24 11 8 8 7 6 5 4 2 2 1 1 1 1 0

Adverse events

Incidence, N (%)	Vistusertib + Anastrozole N=49		Anastrozole N=24	
Grade	Any	3/4	Any	3/4
Nausea	25 (51.0%)	1 (2.0%)	2 (8.3%)	0 (0.0%)
Fatigue	34 (69.4%)	4 (8.2%)	7 (29.2%)	0 (0.0%)
Vomiting	11 (22.4%)	1 (2.0%)	1 (4.2%)	0 (0.0%)
Diarrhea	20 (40.8%)	1 (2.0%)	3 (12.5%)	0 (0.0%)
Arthralgia	11 (22.4%)	0 (0.0%)	7 (29.2%)	0 (0.0%)
Lymphocytes count decreased	17 (34.7%)	10 (20.4%)	3 (12.5%)	2 (8.3%)
Hyperglycemia	15 (30.6%)	6 (12.2%)	2 (8.3%)	0 (0.0%)
Anemia	13 (26.5%)	2 (4.1%)	1 (4.2%)	0 (0.0%)
At least one serious AE	20 (40.8%)		3 (12.5 %)	
At least one SAE related to VISTUSERTIB				
- Sponsor	10 (20,4%)		-	
- Investigator	11 (22,4%)		-	

PERTUZUMAB PLUS TRASTUZUMAB IN PATIENTS WITH UTERINE CANCER WITH *ERBB2* OR *ERBB3* AMPLIFICATION, OVEREXPRESSION OR MUTATION: RESULTS FROM THE TARGETED AGENT PROFILING AND UTILIZATION REGISTRY (TAPUR™) STUDY

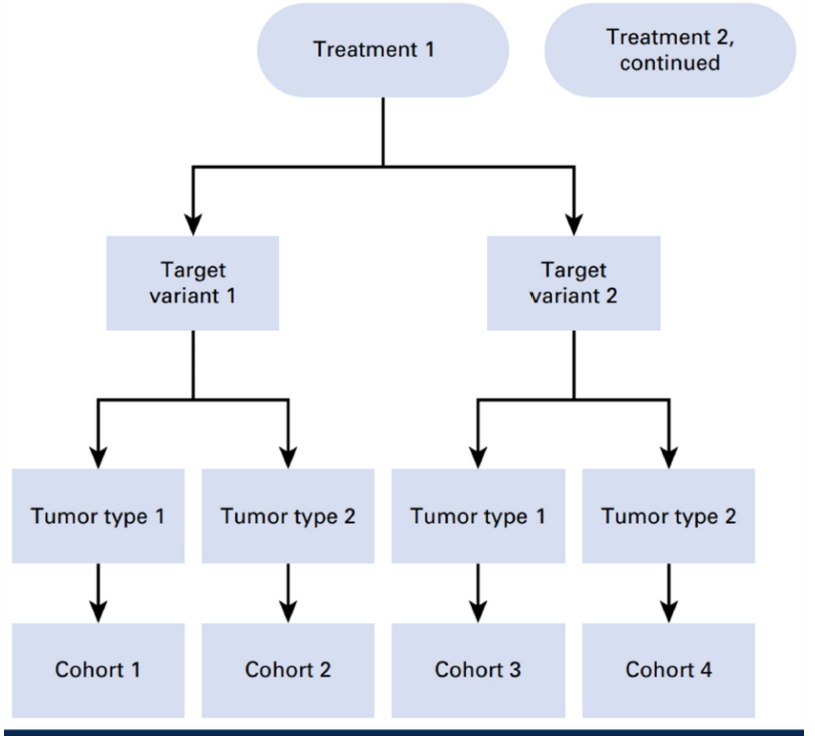
ASCO TAPUR™
Targeted Agent and Profiling Utilization Registry Study

Hussein Moustapha Ali-Ahmad, MD, Michael Rothe, MS, Pam K. Mangat, MS, Elizabeth Garrett-Mayer, PhD, Eugene R. Ahn, MD, John Chan, MD, Michael L. Maitland, MD, PhD, Ani S. Balmanoukian, MD, Sapna R. Patel, MD, Zachary Reese, MD, Charles W. Drescher, MD, Charles A. Leath III, MD, Rui Li, MD, Apostolia Maria Tsimberidou, MD, PhD, Richard L. Schilsky, MD, FACP, FSCT, FASCO

June 7, 2021

Tapur study

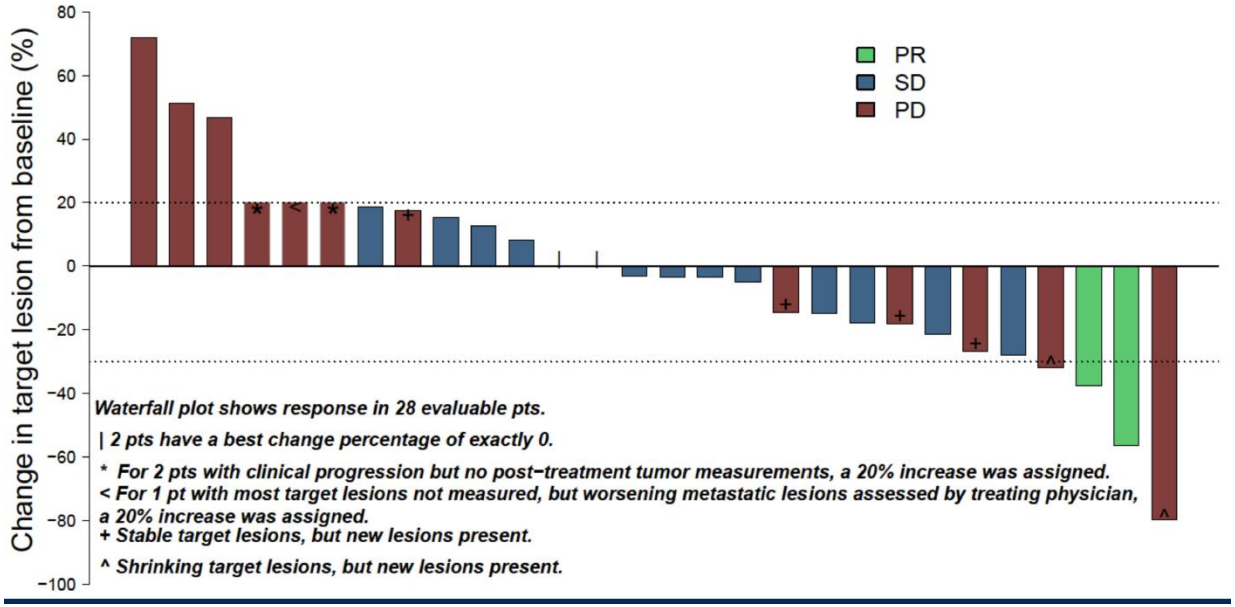
- Non-randomized, phase II, basket trial
- 18 treatments
- 85+ genomic targets
- All solid tumors
- Pre-specified genomic matching rule and eligibility criteria
- Virtual molecular tumor board



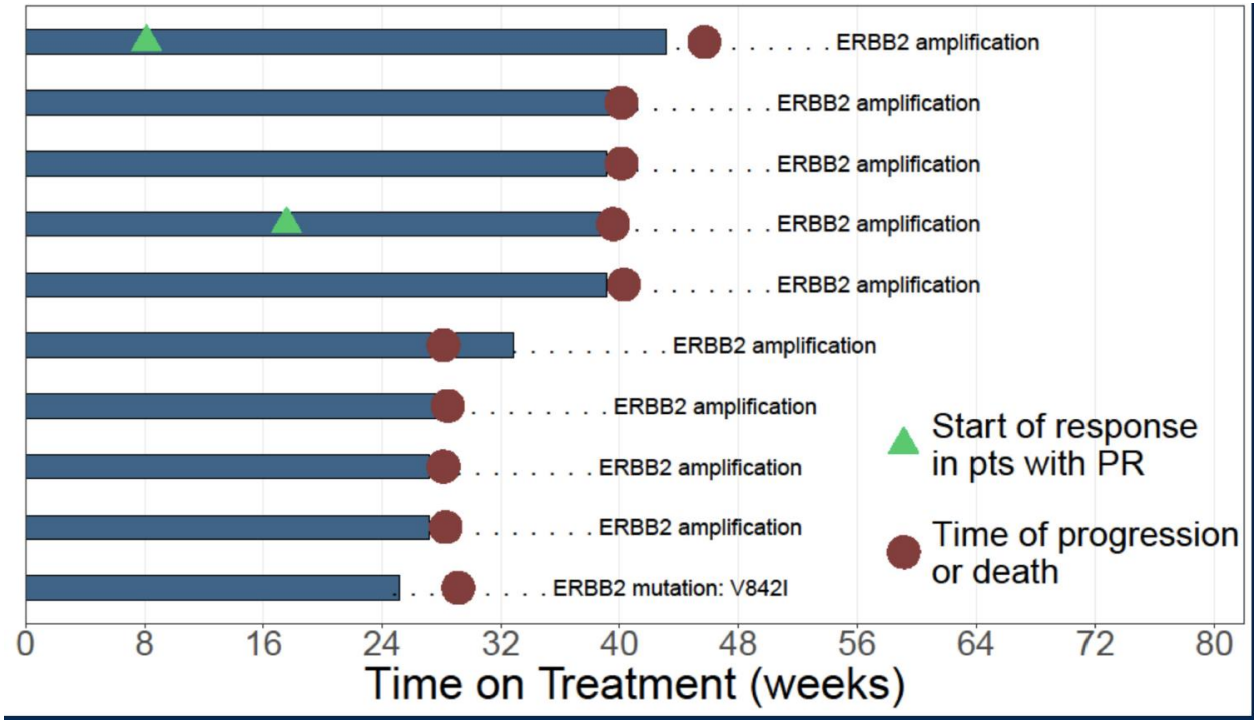
Efficacy outcomes

Efficacy Outcomes (N=28)	
DC rate, % (95% CI)	37 (21, 50)
OR rate, % (95% CI)	7 (1, 24)

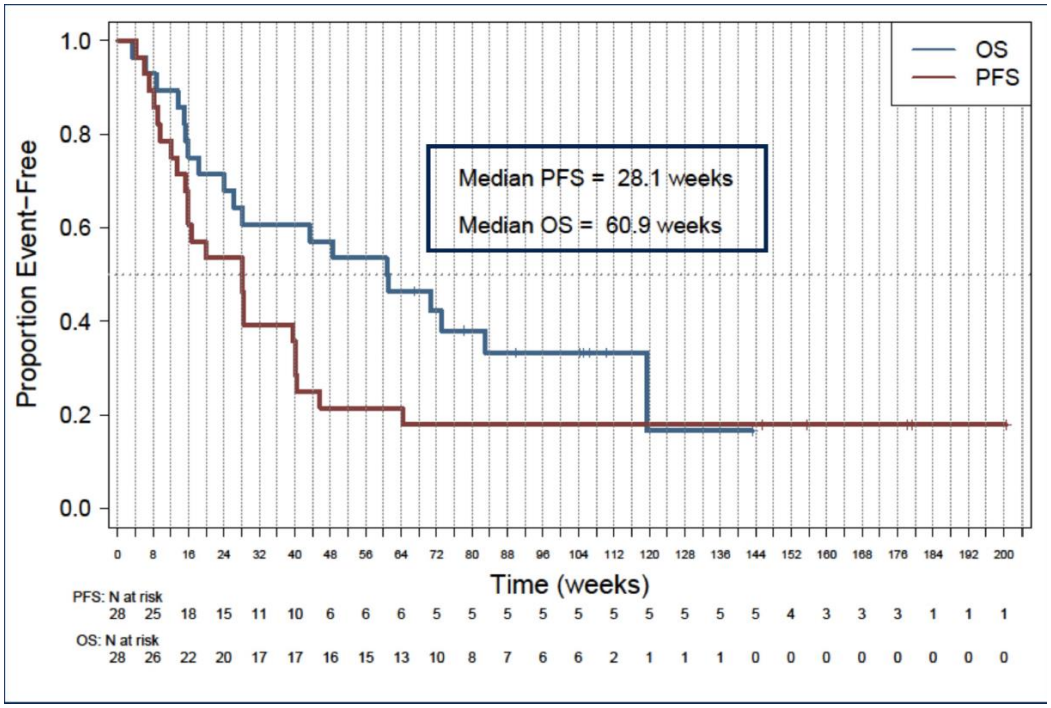
Best percent change from baseline target lesion size (n=28)



Time on treatment in pts with SD16+ or OR (n=10)

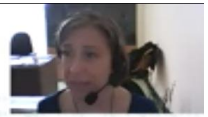


Progression free survival and Overall Survival (n=28)



Toxicity

- 1 patient experienced grade 3 muscle weakness at least possibly related to Pertuzumab + Trastuzumab
- No other treatment related grade 3-4 Aes or SAEs reported.



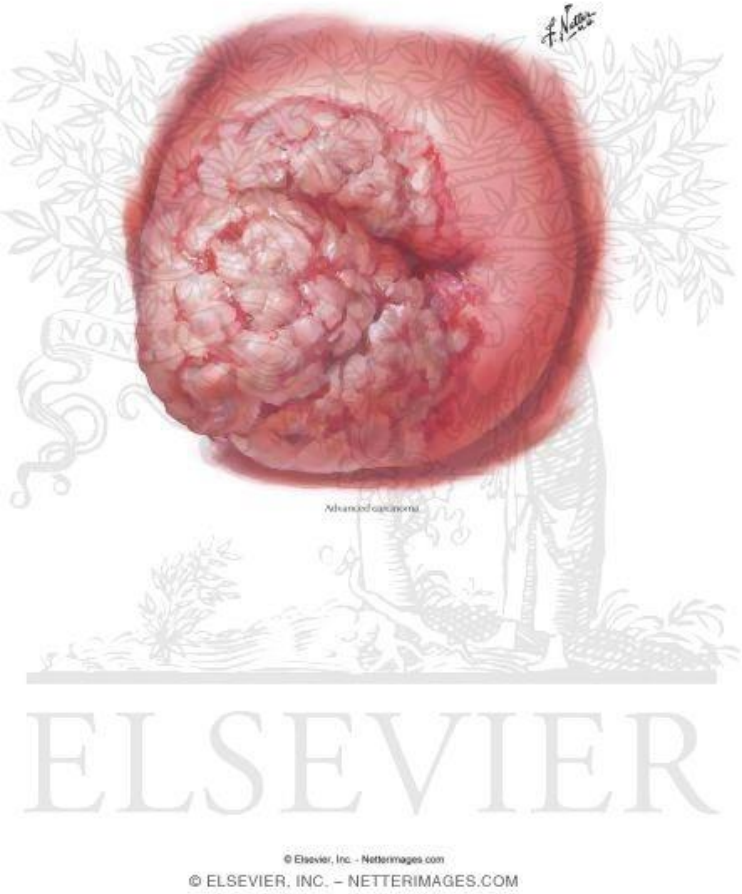
2021 ASCO ANNUAL MEETING

HEALTH-RELATED QUALITY OF LIFE IN ADVANCED ENDOMETRIAL CANCER PATIENTS TREATED WITH LENVATINIB + PEMBROLIZUMAB OR TREATMENT OF PHYSICIAN'S CHOICE

Domenica Lorusso[1], Nicoletta Colombo[2], Antonio Casado Herraez[3], Alessandro Santin[4], Emeline Colomba[5], David Scott Miller[6], Keiichi Fujiwara[7], Sandro Pignata[8], Sally E. Baron-Hay[9], Isabelle Laure Ray-Coquard[10], Ronnie Shapira-Frommer[11], Yong Man Kim[12], Mary McCormack[13], Steven Bird[14], Vimalanand S. Prabhu[14], Allison Martin Nguyen[14], Qi Zhao[15], Lea Dutta[15], Vicky Makker[16]

[1]Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy; [2]University of Milan-Bicocca, European Institute of Oncology IRCCS, Milan, Italy; [3]San Carlos University Teaching Hospital, Madrid, Spain; [4]Yale University School of Medicine, New Haven, CT, USA; [5]Gustave Roussy Cancerology Institute, Villejuif, GINECO Group, France; [6]University of Texas Southwestern Medical Center, Dallas, TX, USA; [7]Saitama Medical University International Medical Center, Hidaka, Japan; [8]Istituto Nazionale Tumori IRCCS-Fondazione G. Pascale, Naples, Italy; [9]Royal North Shore Hospital, St Leonards, Australia; [10]Centre Léon Bérard, University Claude Bernard, Lyon, GINECO Group, France; [11]Sheba Medical Center, Ramat, Israel; [12]Asan Medical Center, University of Ulsan, Seoul, Korea, Republic of South Korea; [13]University College London Hospitals NHS Foundation Trust, London, UK; [14]Merck & Co., Inc., Kenilworth, NJ, USA; [15]Eisai Inc., Woodcliff Lake, NJ, USA; [16]Memorial Sloan Kettering Cancer Center, New York, NY, USA.

Cervical cancer



2021 ASCO ANNUAL MEETING

Adjuvant chemotherapy following chemo-radiation as primary treatment for locally advanced cervical cancer compared to chemo-radiation alone: The randomised phase 3 OUTBACK Trial (ANZGOG 0902, RTOG 1174, NRG 0274)

Mileshkin L, Moore KN, Barnes EH, Narayan K, Diamante K, Fyles A, Gaffney DK, Khaw P, Brooks S, Thompson S, Huh W, Carlson JM, Matthews C, Rischin D, Stockler M, Monk BJ

ANZGOG

GCIG GYNECOLOGIC CANCER INTERGROUP

MaNGO

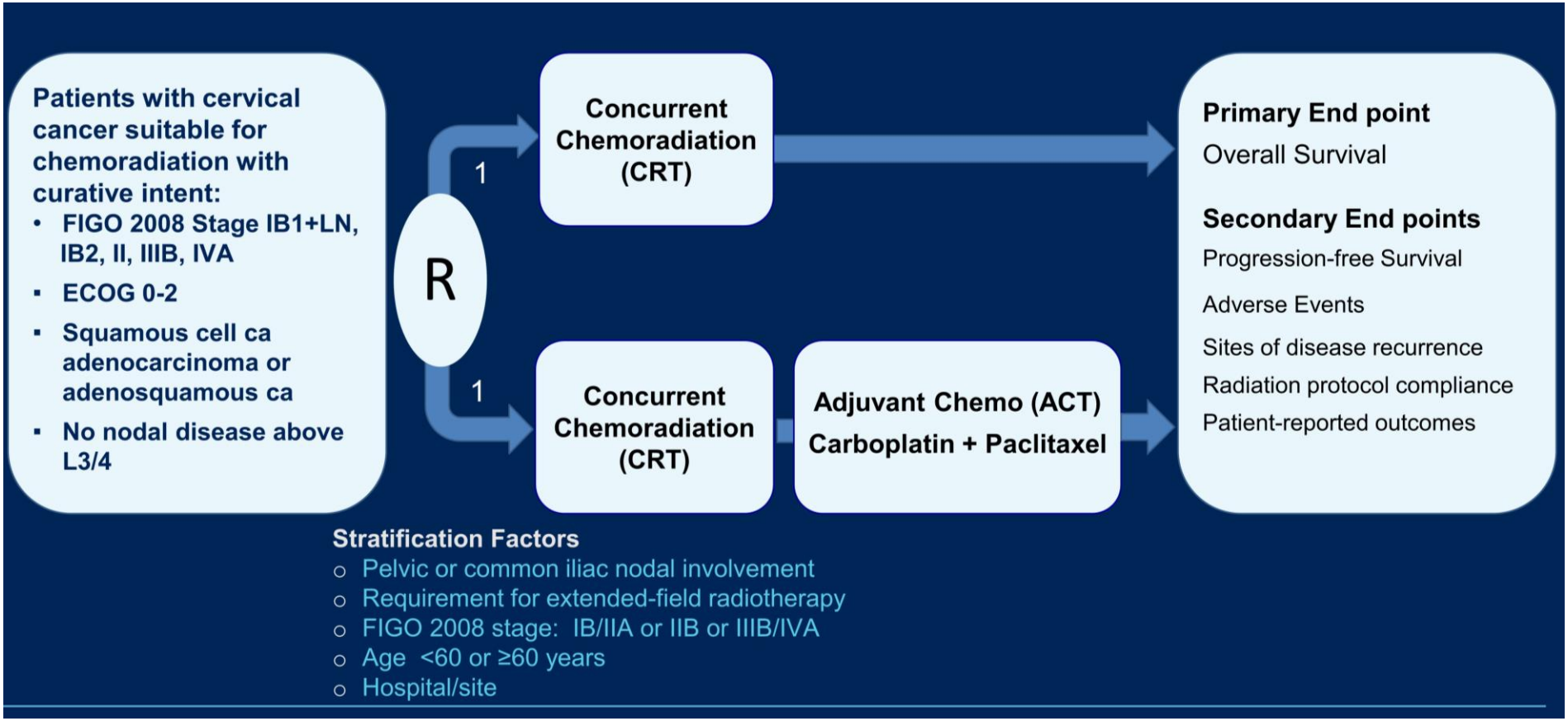
Ricerca Clinica e Traslazionale in Ginecologia Oncologica

NRG ONCOLOGY

Advancing Research. Improving Lives.™

NHMRC Clinical Trials Centre

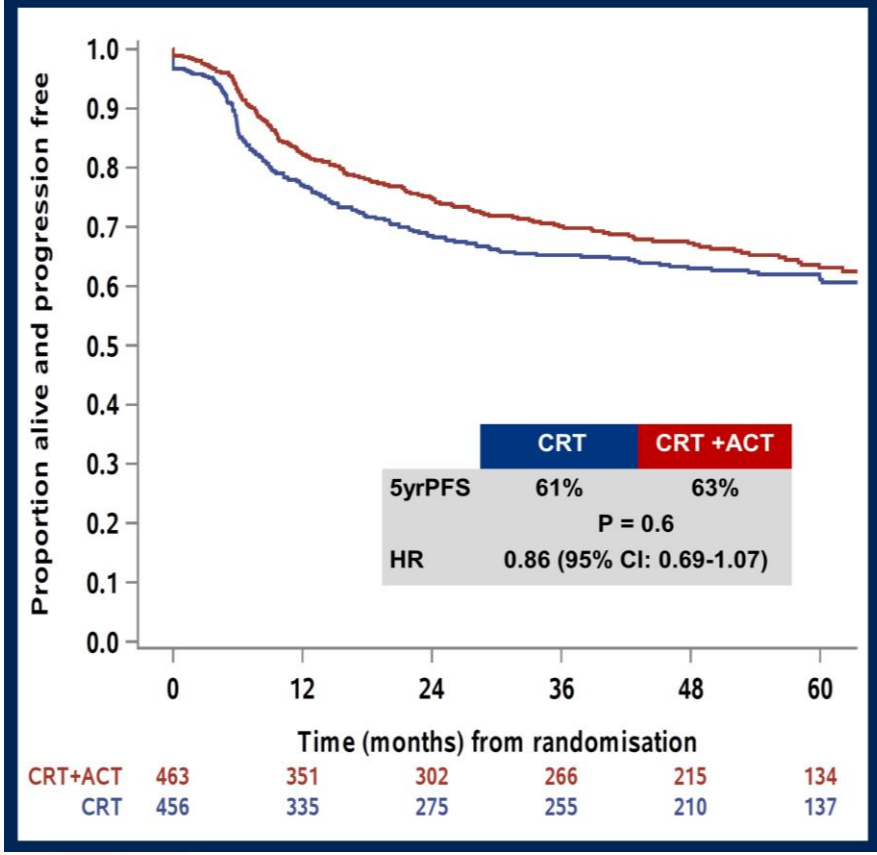
The study design



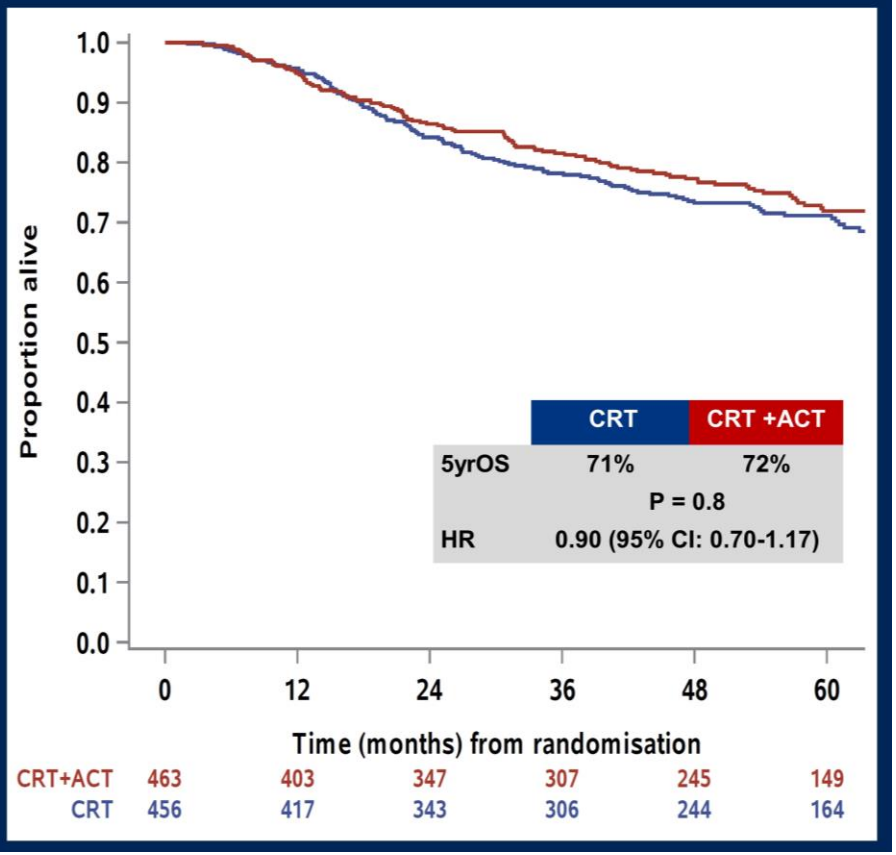
By courtesy of the Authors

Outcomes

Progression-Free Survival

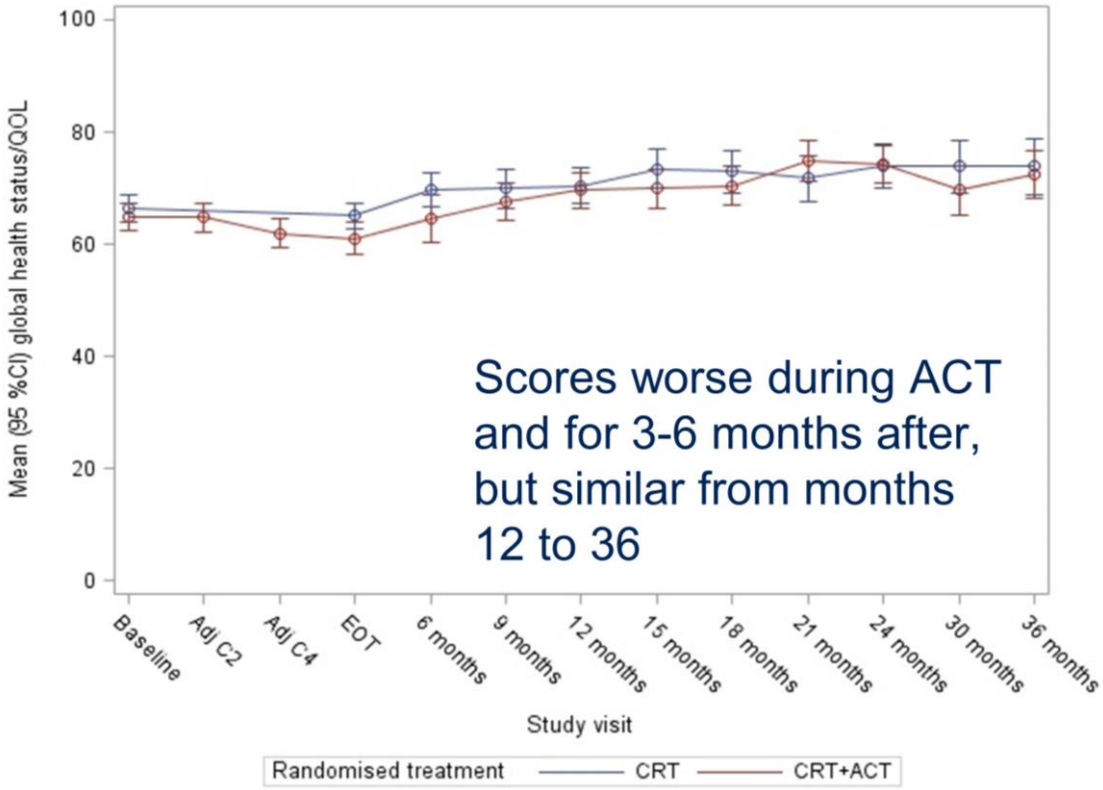


Overall Survival



By courtesy of the Authors

Quality of Life



By courtesy of the Authors

EVALUATION OF BINTRAFUSP ALFA, A BIFUNCTIONAL FUSION PROTEIN TARGETING TGF-β AND PD-L1, IN CERVICAL CANCER: DATA FROM PHASE 1 AND PHASE 2 STUDIES

Authors: Julius Strauss, Fadi S. Braiteh, Emiliano Calvo, Maria De Miguel, Andres Cervantes, William Jeffery Edenfield, Tianhong Li, Marika Anna Rasschaert, Tjoung-Won Park-Simon, Federico Longo, Luis G. Paz-Ares, Alexander I. Spira, Genevieve Jehl, Isabelle Dussault, Laureen S. Ojalvo, James L. Gulley, Suzanne Wendy Allan

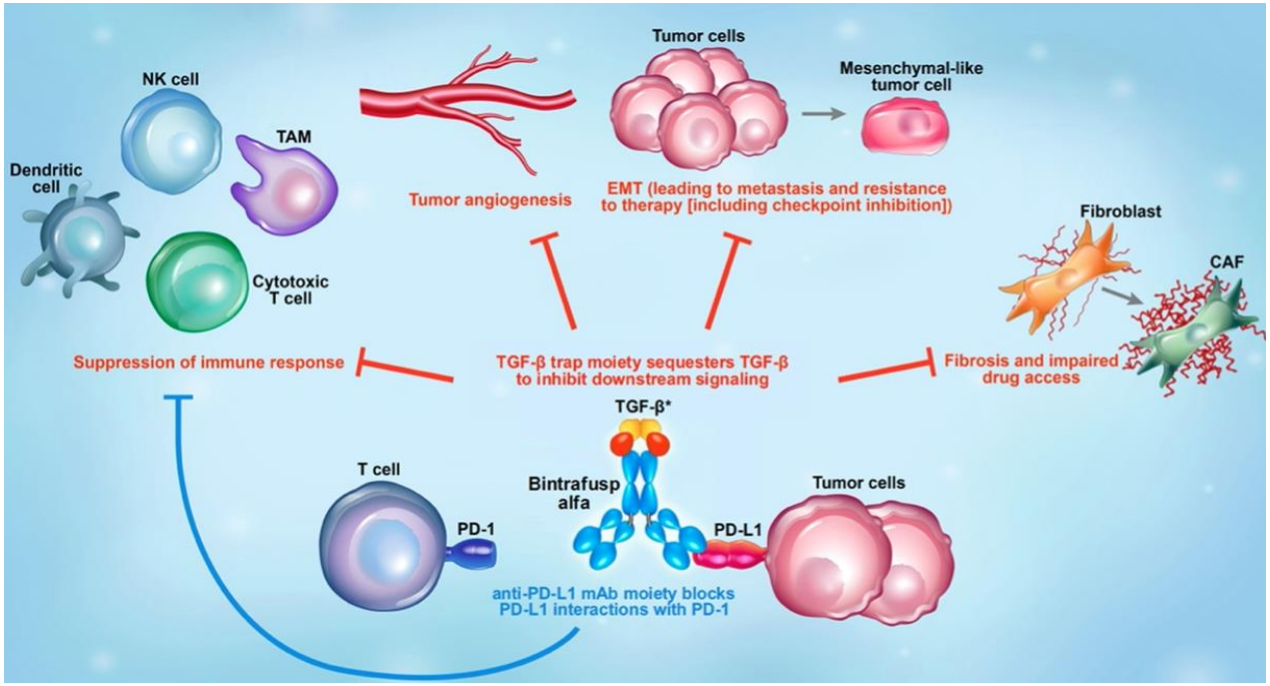
2021 ASCO ANNUAL MEETING

MaNGO

Ricerca Clinica e Traslazionale in Ginecologia Oncologica

XVIII ASSEMBLEA MANGO
MILANO, 2-3 LUGLIO 2021

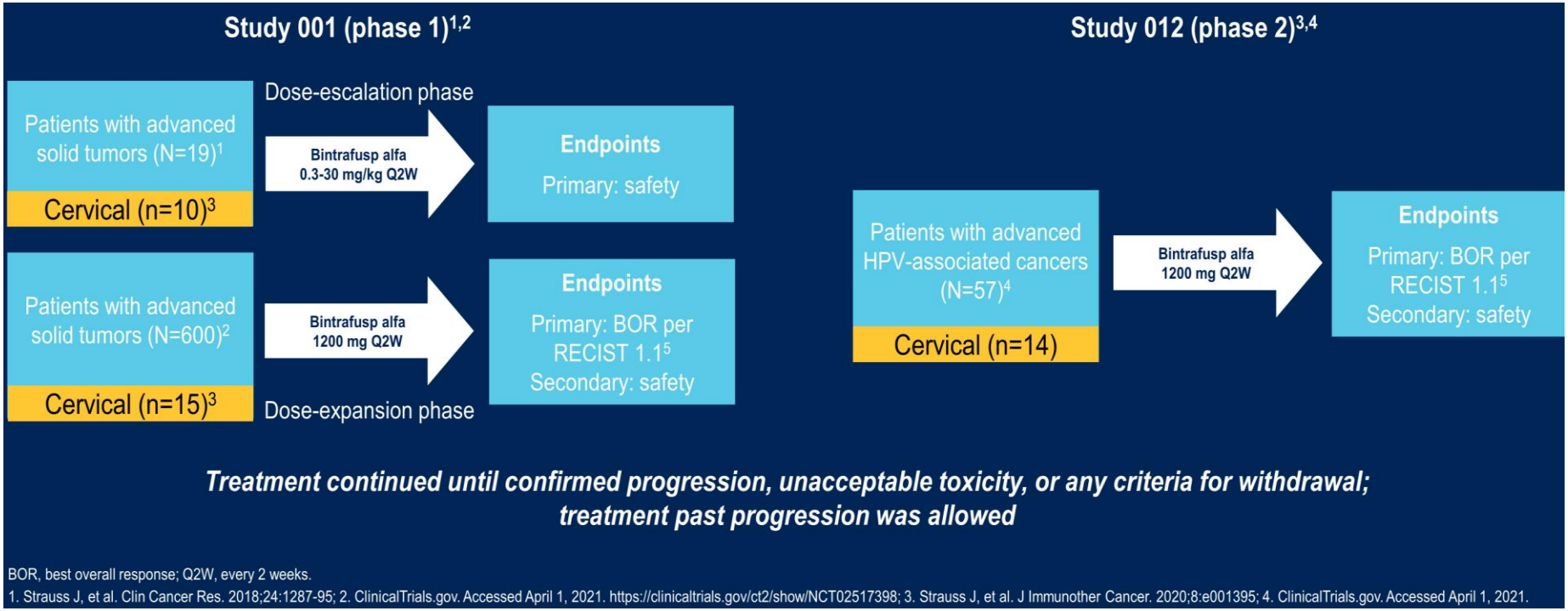
Bintrafusp alfa: a TGF-β AND PD-1 Inhibitor



- Inhibition of TGF-β activity while simultaneously blocking an additional immunosuppressive cellular mechanism, eg PD-L1 pathway, may provide a novel treatment approach
- Bintrafusp alfa is a first-in-class bifunctional fusion protein composed of the extracellular domain of the TGF-bRII receptor fused to a human IgG1 mAb blocking PD-L1

Birrer MJ, ESMO 2018
Lan Y, Sci Transl Med, 2018
Knudson KM et al, Oncoimmunology 2018

Study design



BOR, best overall response; Q2W, every 2 weeks.

1. Strauss J, et al. Clin Cancer Res. 2018;24:1287-95; 2. ClinicalTrials.gov. Accessed April 1, 2021. https://clinicaltrials.gov/ct2/show/NCT02517398; 3. Strauss J, et al. J Immunother Cancer. 2020;8:e001395; 4. ClinicalTrials.gov. Accessed April 1, 2021.

Results

	All patients N=39
BOR, n (%)	
CR	2 (5.1)
PR	9 (23.1)
SD	3 (7.7)
PD	20 (51.3)
Not evaluable	5 (12.8)
Delayed PR	1 (2.6)
Confirmed ORR (CR + PR), n (%)	11 (28.2)
95% CI	15.0-44.9
DCR (CR + PR + SD), n (%)	14 (35.9)
Total clinical response rate (ORR + delayed PR), n (%)	12 (30.8)
Duration of response (confirmed ORR), median (range), months	11.7 (1.4-41.2)
Durable response ≥6 months, n/n (%)	8/11 (72.7)
Durable response ≥12 months, n/n (%)	5/11 (45.5)
Ongoing response, n/n (%)	5/11 (45.5)
Duration of ongoing response (range), months	1.4-41.2

Results

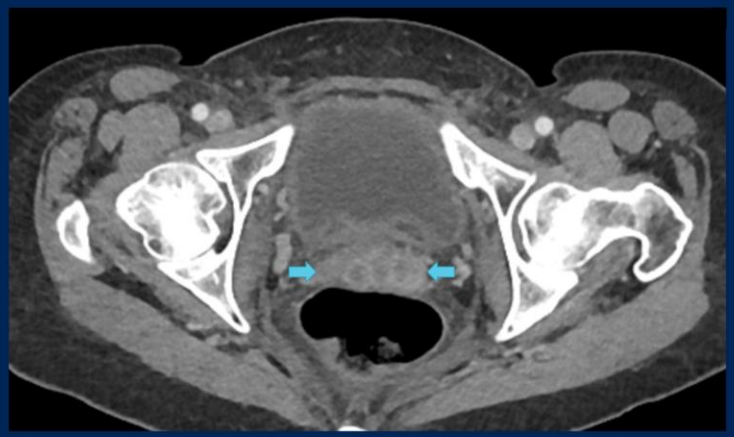
	Tumor histology		Prior bevacizumab use	
	Squamous cell carcinoma n=24	Adenocarcinoma n=12	Yes n=25	No n=14
BOR, n (%)				
CR	1 (4.2)	1 (8.3)	2 (8.0)	0
PR	5 (20.8)	4 (33.3)	4 (16.0)	5 (35.7)
SD	3 (12.5)	0	2 (8.0)	1 (7.1)
PD	11 (45.8)	7 (58.3)	14 (56.0)	6 (42.9)
Not evaluable	4 (16.7)	0	3 (12.0)	2 (14.3)
Delayed PR*	1 (4.2)	0	1 (4.0)	0
Confirmed ORR (CR + PR), n (%)	6 (25.0)	5 (41.7)	6 (24.0)	5 (35.7)
95% CI	9.8-46.7	15.2-72.3	9.4-45.1	12.8-64.9

- Responses occurred irrespective of tumor histology or prior bevacizumab use

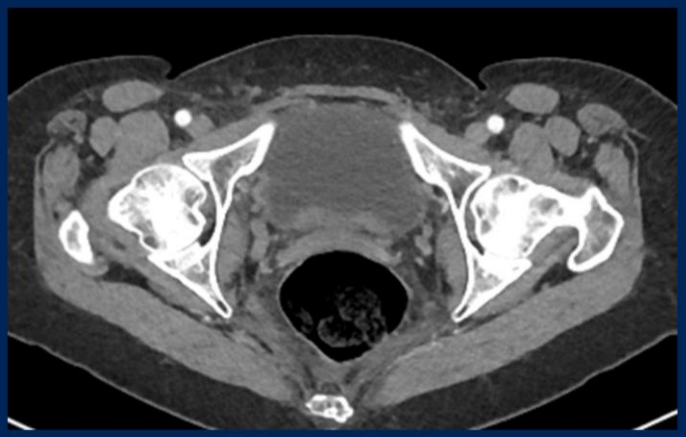
ORR on tumor irradiated lesions

Tumor reduction in target lesions in previously irradiated regions

- 4 patients had target lesions in previously irradiated regions; tumor reduction was observed in 3 different patients (2 in the cervix and 1 in the iliac node)

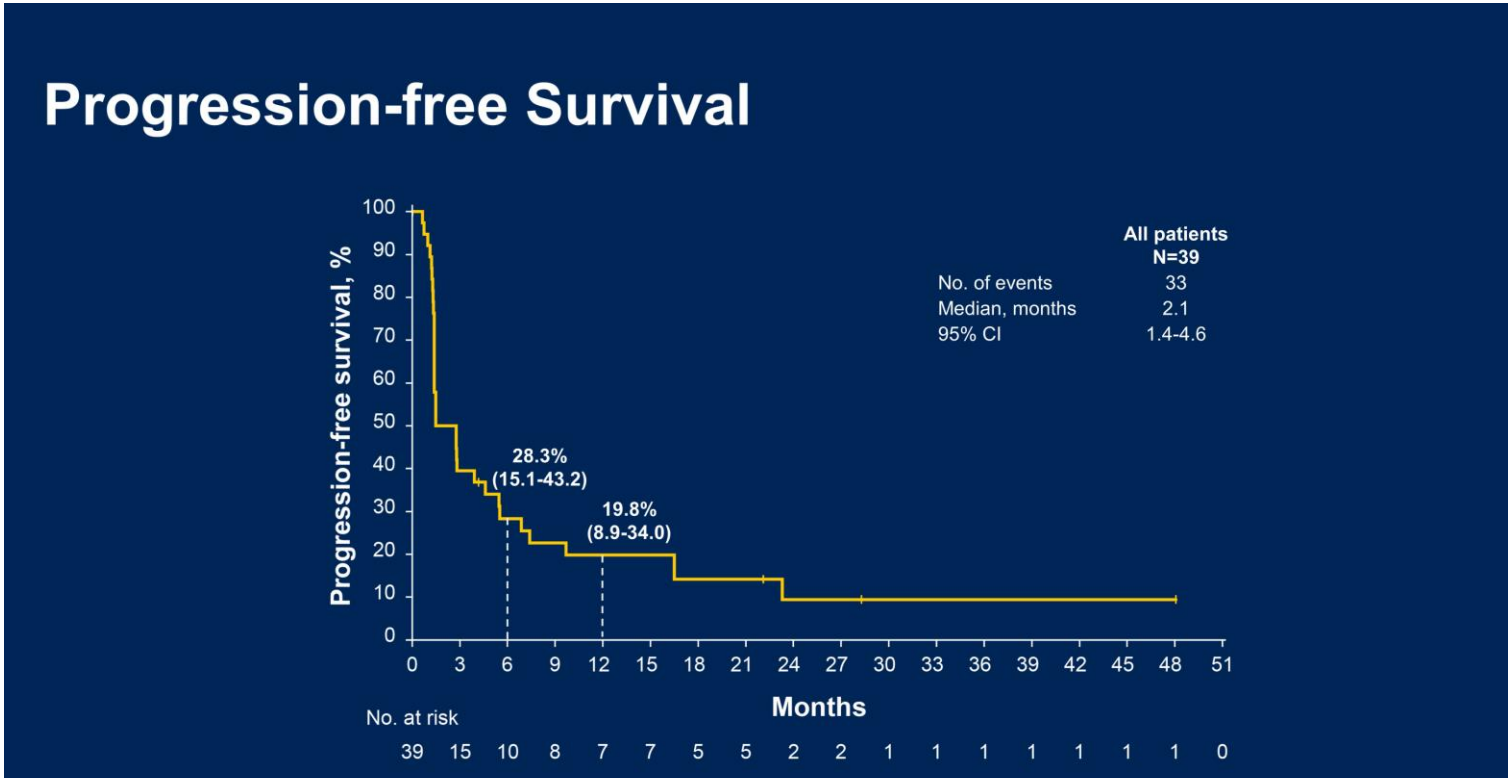


Baseline

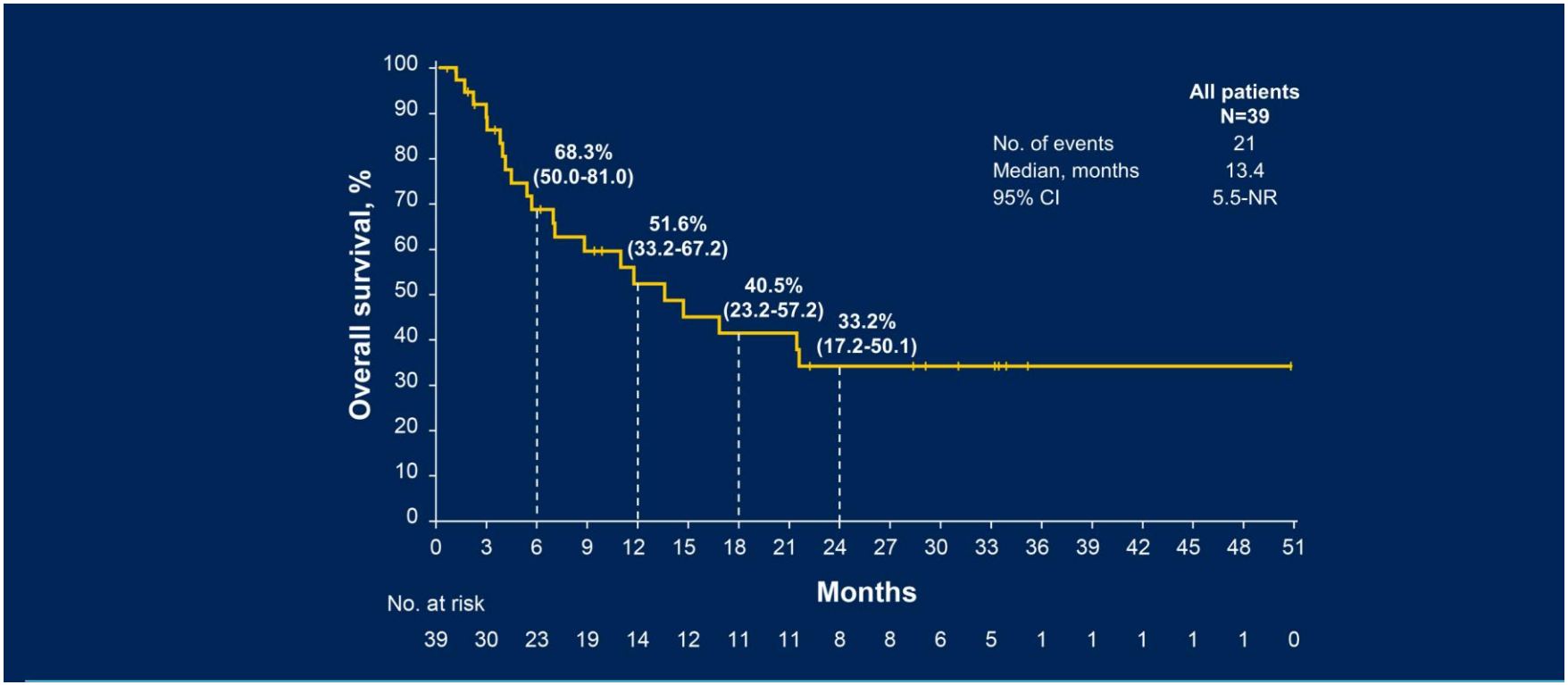


Post treatment

PFS


Progression-free Survival
Progression-free survival, %
100
90
80
70
60
50
40
30
20
10
0
28.3%
(15.1-43.2)
19.8%
(8.9-34.0)
All patients
N=39
No. of events 33
Median, months 2.1
95% CI 1.4-4.6
0 3 6 9 12 15 18 21 24 27 30 33 36 39 42 45 48 51
Months
No. at risk
39 15 10 8 7 7 5 5 2 2 1 1 1 1 1 1 1 0

OS


Overall survival, %
100
90
80
70
60
50
40
30
20
10
0
68.3%
(50.0-81.0)
51.6%
(33.2-67.2)
40.5%
(23.2-57.2)
33.2%
(17.2-50.1)
All patients
N=39
No. of events 21
Median, months 13.4
95% CI 5.5-NR
0 3 6 9 12 15 18 21 24 27 30 33 36 39 42 45 48 51
Months
No. at risk
39 30 23 19 14 12 11 11 8 8 6 5 1 1 1 1 1 0

thank you

MaNGO
Milan Negri Gynecology Oncology

Ricerca Clinica e Traslazionale
in Ginecologia Oncologica

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MILANO, 2-3 LUGLIO 2021