Evolution of data supporting the use of ADCs in GYN Cancers

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A GOG Foundation, Inc. Educational Program

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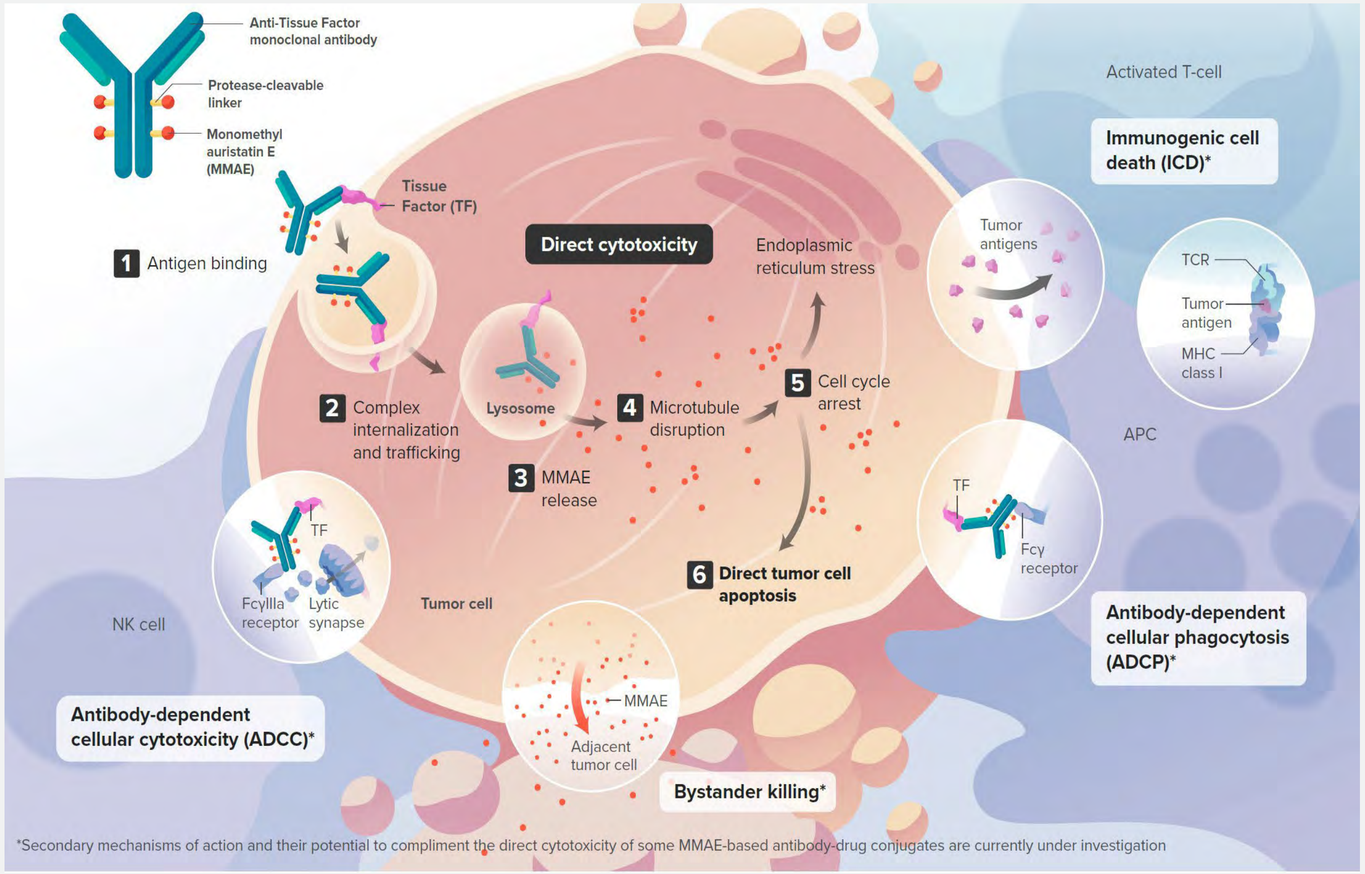
Agenda

- Cervical Cancer
  - Tisotumab Vedontin Monotherapy
    - 2nd line+*
  - Tisotumab Vedontin Combo therapy
    - 2nd line+
    - First line
- Ovarian Cancer
  - Mirvetuximab soravtansine Monotherapy
    - PROC*
    - PSOC
  - Mirvetuximab soravtansine Combo therapy
    - PROC
    - PSOC

*Accelerated Approval

Tisotumab Vedotin (TV)

- Tisotumab vedotin is an investigational antibody–drug conjugate directed to TF and covalently linked to the microtubule-disrupting agent, MMAE, via a protease-cleavable linker[1,2]
  - TF is a protein highly expressed in cervical cancer and other solid tumors[3-6]
- Multimodal MOA of tisotumab vedotin[1,2,7]
  - Direct cytotoxicity
  - Bystander killing
  - Immunogenic cell death
  - ADCC
  - ADCP



.ADCC, antibody-dependent cellular cytotoxicity; ADCP, antibody-dependent cellular phagocytosis; MMAE, monomethyl auristatin E; MOA, mechanism of action; TF, tissue factor

1. Breij EC et al. *Cancer Res*. 2014;74(4):1214-1226. 2. De Goeij BE et al. *Mol Cancer Ther*. 2015;14(5):1130-1140. 3. Forster Y et al. *Clin Chim Acta.* 2006;364:12-21. 4. Pan L et al. *Mol Med Rep*. 2019;19:2077-2086. 5. Cocco E et al. *BMC Cancer.* 2011;11:263. 6. Zhao X et al. *Exp Ther Med.* 2018;16:4075-4081. 7. Alley SC et al. AACR 2019; Abstract 221.

innovaTV 204/ GOG-3023/ENGOT-cx6

innovaTV 204 (NCT03438396) is a pivotal phase 2 single-arm, multicenter (United States and Europe) study evaluating tisotumab vedotin in patients with previously treated recurrent and/or metastatic cervical cancer

Key Eligibility Criteria

- Recurrent or extrapelvic metastatic cervical cancer
- Progressed during or after doublet chemotherapy[a] with bevacizumab (if eligible)
- Received ≤2 prior systemic regimens[b]
- ECOG PS 0-1

Enrolled: 102[c]
Treated: 101*

Tisotumab vedotin 2.0 mg/kg IV Q3W

Until PD or unacceptable toxicity

Tumor responses assessed using CT or MRI at baseline, every 6 weeks for the first 30 weeks, and every 12 weeks thereafter

Primary Endpoint
- ORR[d] per RECIST v1.1, assessed by radiographic review by IRC

Secondary Endpoints
- ORR, DOR, TTR, and PFS by IRC and investigator
- OS
- Safety

Exploratory Endpoints
- Biomarkers
- HRQoL

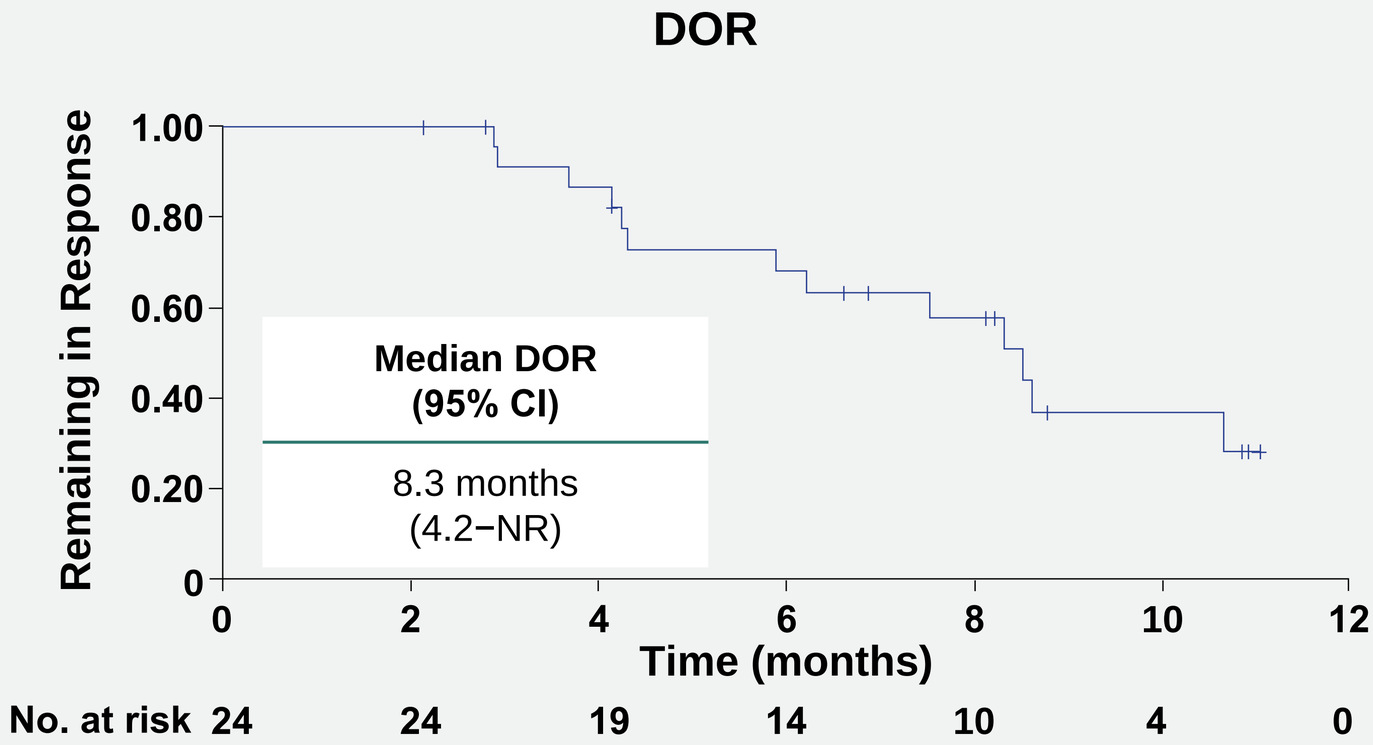
***Study sample size calculated assuming a confirmed ORR of 21% to 25% with tisotumab vedotin and to provide ≥80% power to exclude an ORR of ≤11%[e]**

R Coleman et al ESMO 2020

[a]Paclitaxel plus platinum (cisplatin or carboplatin) or paclitaxel plus topotecan. [b]Adjuvant or neoadjuvant chemotherapy or if administered with radiation therapy, was not counted as a prior systemic regimen. [c]June 2018 to April 2019. [d]Responses were confirmed by subsequent repeat imaging performed ≥4 weeks after initial response assessment. [e]Using one-sided exact binomial test at 0.025 significance level.
CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; HRQoL, health-related quality of life; IRC, independent review committee; IV, intravenous; MRI, magnetic resonance imaging; OS, overall survival; PD, progressive disease; Q3W, every 3 weeks; RECIST v1.1, Response Evaluation Criteria In Solid Tumors version 1.1; TTR, time to response.

Antitumor Activity by IRC Assessment

	N=101
Confirmed ORR (95% CI),[a] %	**24 (15.9−33.3)**
CR, n (%)	7 (7)
PR, n (%)	17 (17)
SD, n (%)	49 (49)
PD, n (%)	24 (24)
Not evaluable, n (%)	4 (4)
Disease control rate (95% CI),[b] %	72 (62.5−80.7)

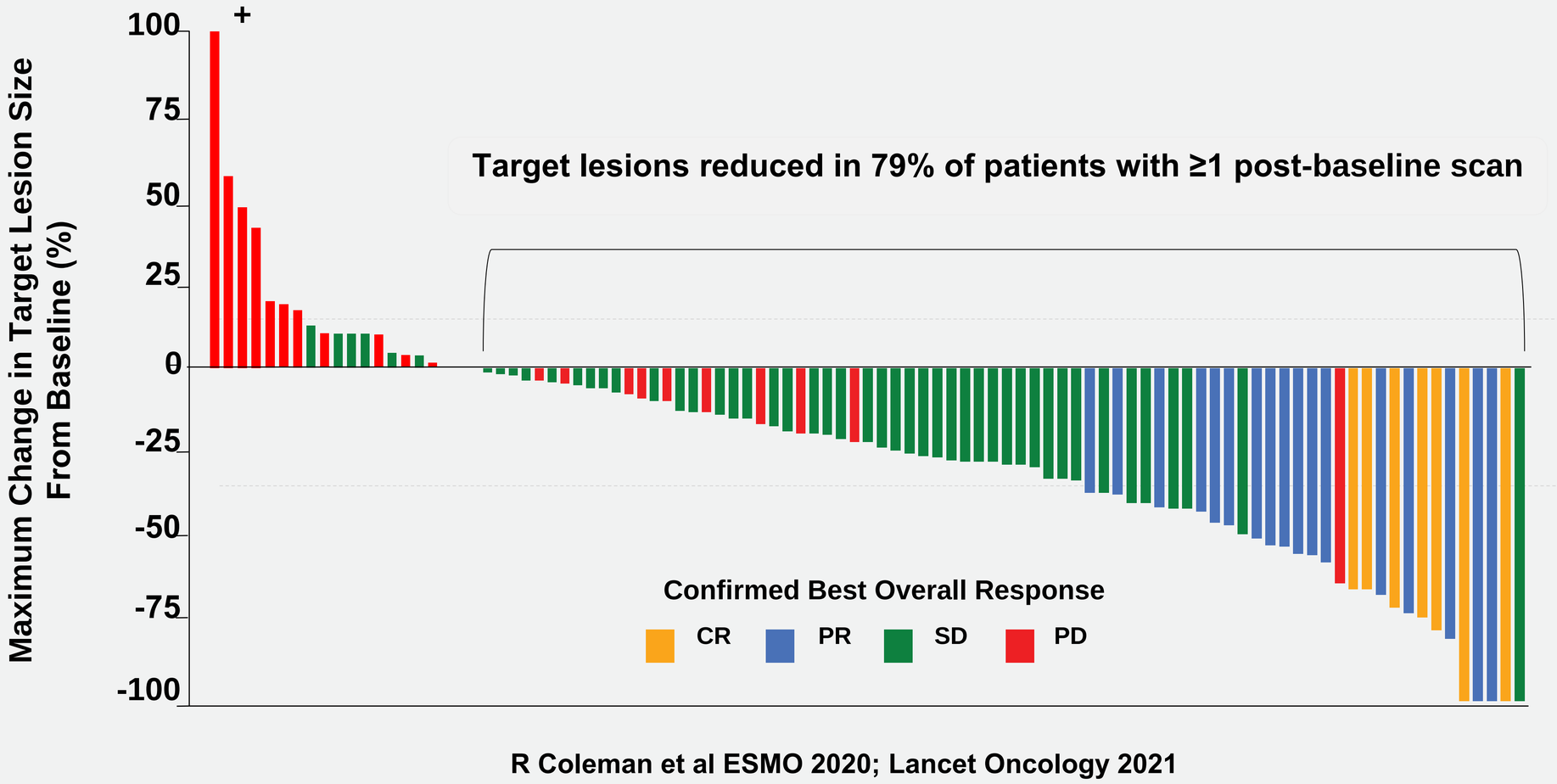


Clinically meaningful and durable responses were observed

R Coleman et al ESMO 2020; Lancet Oncology 2021

Data cutoff: February 06, 2020. Median duration of follow-up: 10.0 months.
[a]Based on the Clopper-Pearson method. [b]Patients with a confirmed response (CR or PR confirmed at least 4 weeks later) or SD (as measured at least 5 weeks after the first dose of tisotumab vedotin).
CI, confidence interval; CR, complete response; DOR, duration of response; IRC, independent review committee; NR, not reached; ORR, objective response rate; PD, disease progression; PR, partial response; SD, stable disease.

Maximum Change in Target Lesion Size by IRC Assessment



R Coleman et al ESMO 2020; Lancet Oncology 2021

Data cutoff: February 06, 2020. Median duration of follow-up: 10.0 months. + indicates a change greater than 100%. Horizontal dashed lines indicate 20% increase and 30% decrease in target lesion diameters from baseline for RECIST v1.1 assessment. Colored bars represent the best overall confirmed response. CR, PR, SD, and PD were based on RECIST v1.1 as evaluated by IRC.

CR, complete response; IRC, independent review committee; PD, disease progression; PR, partial response; RECIST v1.1, Response Evaluation Criteria In Solid Tumors version 1.1; SD, stable disease.

Genmab Announces Very Favorable Topline Results from Phase 2 Clinical Trial of Tisotumab Vedotin in Recurrent or Metastatic Cervical Cancer

Jun 29, 2020 at 10:29 PM CEST

Genmab and Seagen Announce FDA Accelerated Approval for TIVDAK™ (tisotumab vedotin-tftv) in Previously Treated Recurrent or Metastatic Cervical Cancer

September 20, 2021 17:00 ET | Source: Genmab A/S

GOG-3057/innovaTV 301/ ENGOT cx12

Phase 3, randomized trial of Tisotumab Vedotin vs Investigator's choice chemotherapy in 2nd or 3rd line recurrent cervical cancer

Primary endpoints: Overall survival
Secondary endpoints: PFS (Inv), Confirmed ORR (Inv), Safety, PRO, TTR, DOR
Exploratory endpoints: PK, biomarkers

- **Progressed during or after 1L chemo of taxane/platin or tax/topo w/wo Bev for metastatic/ recurrent cxca**
- **1 or 2 prior lines for metastatic or recurrent disease**
- **Measurable disease**

1:1
R
N= 482

Tisotumab Vedotin 2 mg/kg Q3W

Investigator's choice chemo

Options (provided by Sponsor, if needed):
- Topotecan 1,5 mg/m² d1-5 q3wks*
- Irinotecan 100 or 125 mg/m² d1,8,15,22 q6wks*
- Gemcitabine 1000 mg/m² d1,8 q3wks*
- Vinorelbine 30 mg/m² d1,8 q3wks*
- Pemetrexed 500 mg/m² d1 q3wks*

*** Fast reduction rules will be applied**

Imaging: q 6 wks for 30 wks, then q 12 wks until radiographic PD

OS

Stratification:
- ECOG (0 vs 1)
- Region
- Prior PD-1 or PD-L1 therapy Y/N
- Prior Bev Y/N

Planned No. of patients: 482

https://www.clinicaltrials.gov/ct2/show/NCT04697628

GOG-3024/ InnovaTV 205/ENGOT-cx8/

Phase 1/2 study of TV monotherapy or in combination with other cancer agents in cervical cancer

Patient population

Metastatic or recurrent cervical cancer (N=~140)

Part 1: Dose Escalation

- **Arm A: TV (ED) Q3W + Bevacizumab (ED)**
- **Arm B: TV (ED) Q3W + Pembrolizumab (FD)**
- **Arm C: TV (ED) Q3W + Carboplatin (FD)**

Part 2: Dose Expansion

- **Arm D: TV (RP2D) Q3W + Carboplatin**
- **Arm E: TV (RP2D) Q3W + Pembrolizumab**
- **Arm F: TV (RP2D) Q3W + Pembrolizumab**
- **Arm G: TV QW for 3 weeks and 1 week off (28-day treatment cycle)**

Objectives

PRIMARY ENDPOINT
Part 1: Safety and tolerability
Part 2: ORR (RECIST)

SECONDARY ENDPOINT
Part 1: Anti-tumor activity
Part 2: Safety, tolerability, DOR, TTR, PFS, OS, PK

NCT03786081
EUCTR: 2017-004758-40

KEY ELIGIBILITY CRITERIA

- **Recurrent or metastatic cervical cancer**
- **Progressed on or after standard of care or ineligible/intolerant to SOC (Arms A, B, and C only)**
- **No prior systemic therapy (Arms D and E only)**
- **Progressed after at least 1 but no more than 2 prior standard of care therapies (Arm F and G only)**
- **ECOG 0-1**

Abbreviations: ED=Escalating Dose; FD=Fixed Dose

https://clinicaltrials.gov/ct2/show/NCT03786081. Accessed April 16, 2020.

ENGOT PI =Vergote
GOG PI = Monk

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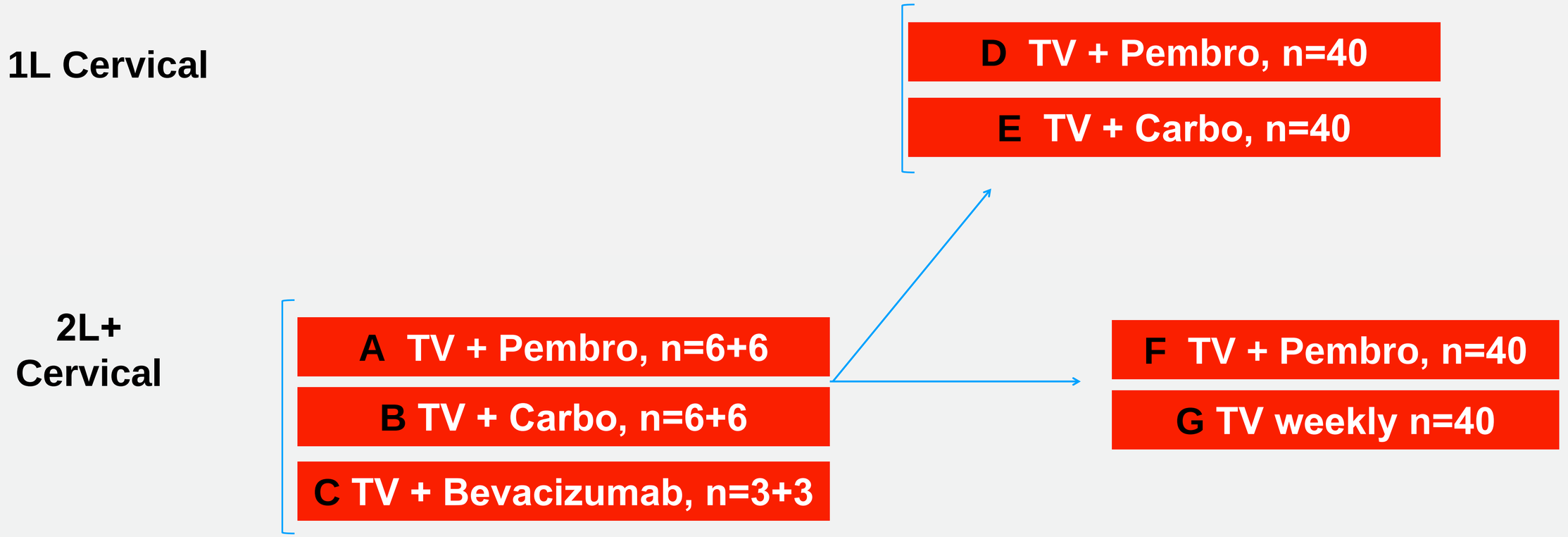
GOG 3024-innovaTV 205/ENGOT-cx8 :

Phase 1b/2 Study to Assess the Safety, Tolerability and Preliminary Antitumor Activity of Tisotumab Vedotin When Administered with Chemotherapy, Bevacizumab, and CPI in Cervical Cancer (innovaTV 205)



Modified form Leslie Randal

NCT03786081
Brad Monk US PI

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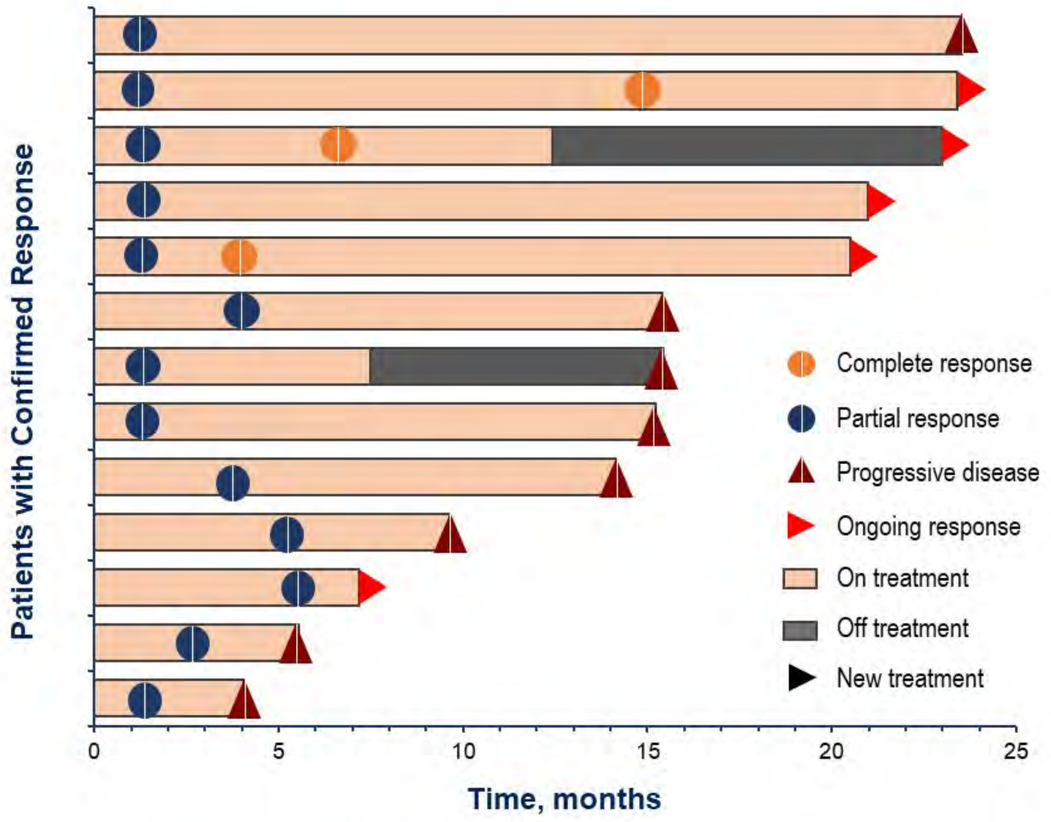
Anti-tumor activity – 2L/3L TV + Pembro

Efficacy parameter	2L/3L TV + Pembro (N = 34*) Median f/u: 15.0 months
Confirmed ORR, % [95% CI]	38.2 [22.2 – 56.4]
Complete response	3 (8.8)
Partial response	10 (29.4)
Stable disease	12 (35.3)
Progressive disease	7 (20.6)
Not evaluable	2 (5.9)
DCR[a], % [95% CI]	73.5 [55.6 – 87.1]
Median DOR[b], months [95% CI]	14.0 [2.8 – NR]
Median time to response, months (range)	1.4 (1.3 – 5.8)
Median PFS[c], months [95% CI]	5.6 [2.7 – 14.2]
Median OS[d], months [95% CI]	15.3 [9.9 – NR]

+, censored; NR, not reached
*1 patient was excluded from the full analysis set as they had no target lesions at baseline.
[a]Defined as SD (at least 5 weeks after the first dose of study treatment) or confirmed CR or PR.
[b]5 patients are censored; [c]10 patients are censored; [d]14 patients are censored

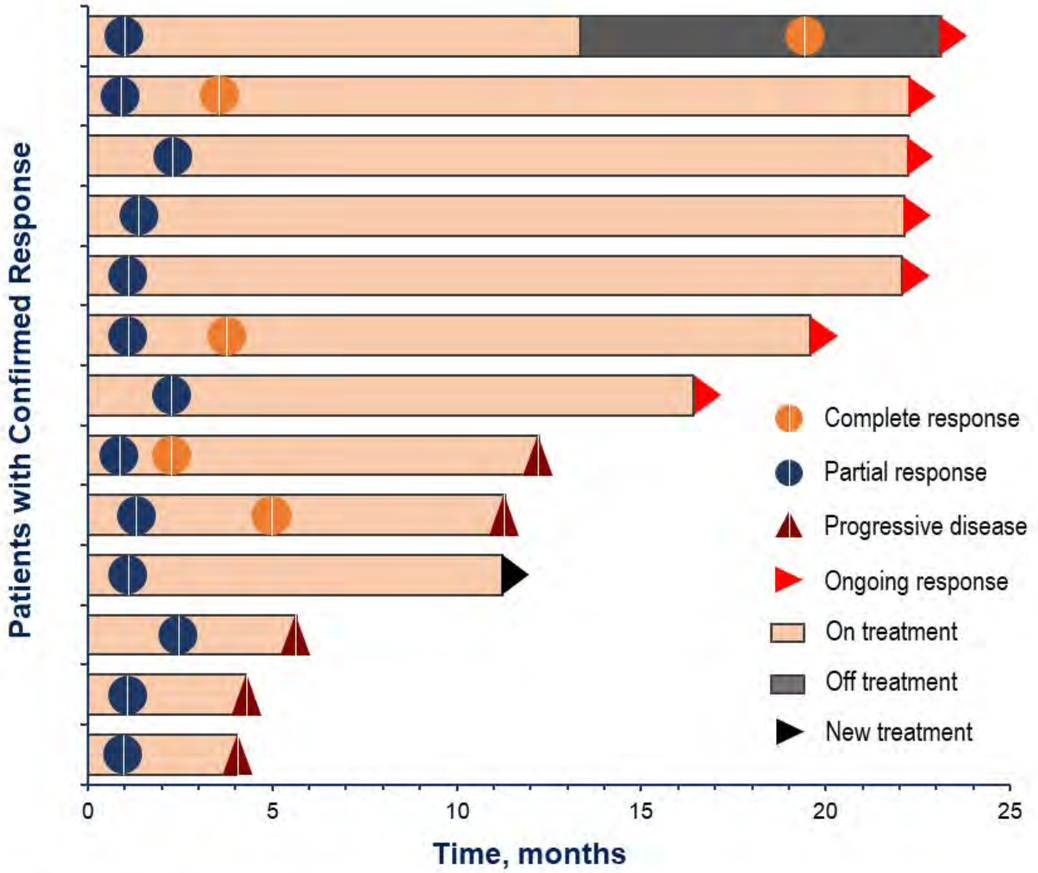


With 15 months median follow-up, compelling, durable preliminary efficacy was observed in 2L/3L with ~40% of responders ongoing in response

Anti-tumor activity – 1L TV + Pembro

Efficacy parameter	1L TV + Pembro (N = 32*) Median f/u: 18.8 months
Confirmed ORR, % [95% CI]	40.6 [23.7 – 59.4]
Complete response	5 (15.6)
Partial response	8 (25.0)
Stable disease	14 (43.8)
Progressive disease	1 (3.1)
Not evaluable	4 (12.5)
DCR[a], % [95% CI]	84.4 [67.2 – 94.7]
Median DOR[b], months (range)	NR (2.8 – 21.9+)
Median time to response, months (range)	1.4 (1.2 – 2.8)
Median PFS[c], months [95% CI]	5.3 [4.0 – 12.2]
Median OS[d], months (range)	NR (0.5 – 24.9+)

+, censored; NR, not reached.
*1 patient was excluded from the full-analysis set due to receiving incorrect study drug.
[a]Defined as SD (at least 5 weeks after the first dose of study treatment) or confirmed CR or PR.
[b]8 patients are censored; [c]12 patients are censored;[d]19 patients are censored.



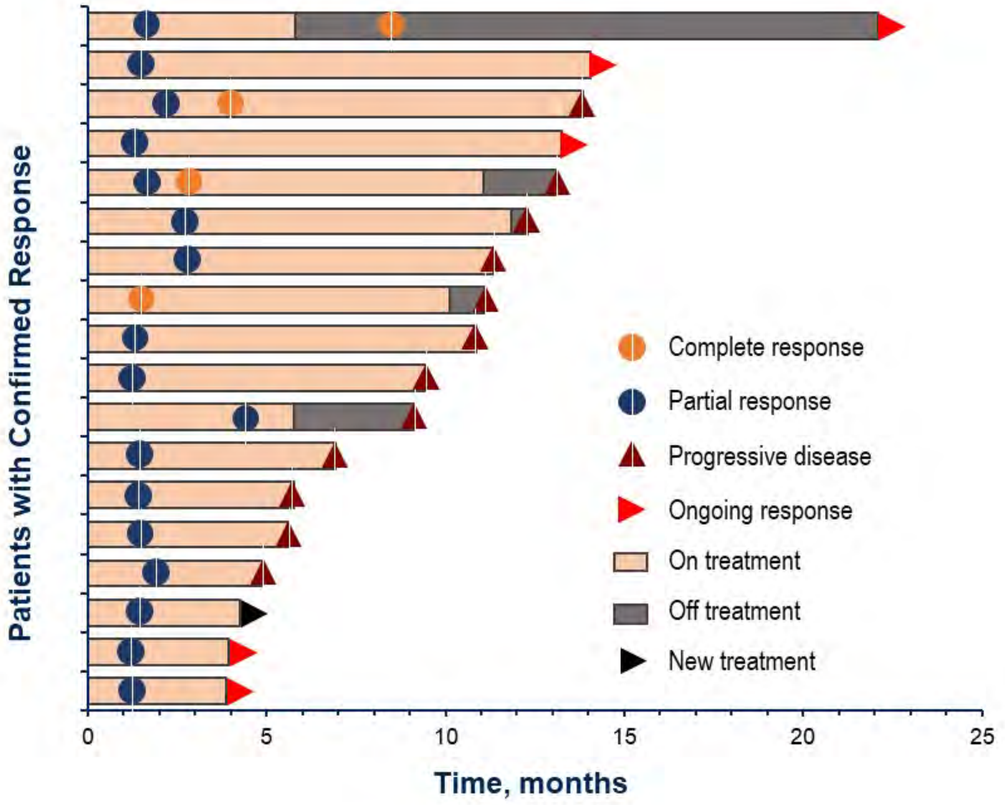
With 18.8 months median follow-up, compelling, durable preliminary efficacy was observed in 1L with >50% of responders with ongoing response

DCR, disease control rate; f/u, follow-up; TV, tisotumab vedotin.

Anti-tumor activity – 1L TV + Carbo

Efficacy parameter	1L TV + Carbo (N = 33) Median f/u: 14.6 months
Confirmed ORR, % [95% CI]	54.5 [36.4 – 71.9]
Complete response	4 (12.1)
Partial response	14 (42.4)
Stable disease	12 (36.4)
Progressive disease	2 (6.1)
Not evaluable	1 (3.0)
DCR[a], % [95% CI]	90.9 [75.7 – 98.1]
Median DOR[b], months [95% CI]	8.6 [4.2; 11.5]
Median time to response, months (range)	1.4 (1.1 – 4.4)
Median PFS[c], months [95% CI]	6.9 [4.0 – 11.1]
Median OS[d], months (range)	NR (0.8+ – 22.1+)

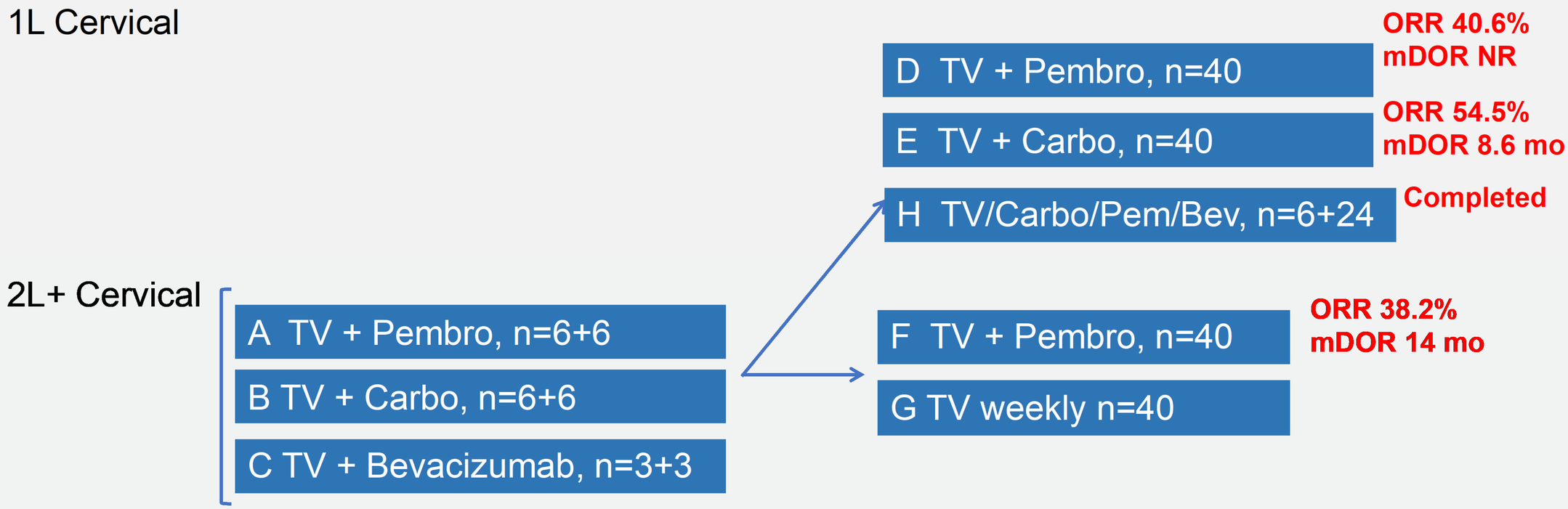
+, censored; NR, not reached.
[a]Defined as SD (at least 5 weeks after the first dose of study treatment) or confirmed CR or PR.
[b]4 patients are censored; [c]9 patients are censored; [d]22 patients are censored.



Compelling antitumor activity was observed in 1L patients with >50% experiencing a response and >90% with disease control

DCR, disease control rate; f/u, follow-up; TV, tisotumab vedotin.

ENGOT-cx8/GOG 3024-innovaTV 205 : Phase 1b/2 Study to Assess the Safety, Tolerability and Preliminary Antitumor Activity of Tisotumab Vedotin When Administered with Chemotherapy, Bevacizumab, and CPI in Cervical Cancer (innovaTV 205)



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NCT03786081
Brad Monk US PI

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Ovarian Cancer

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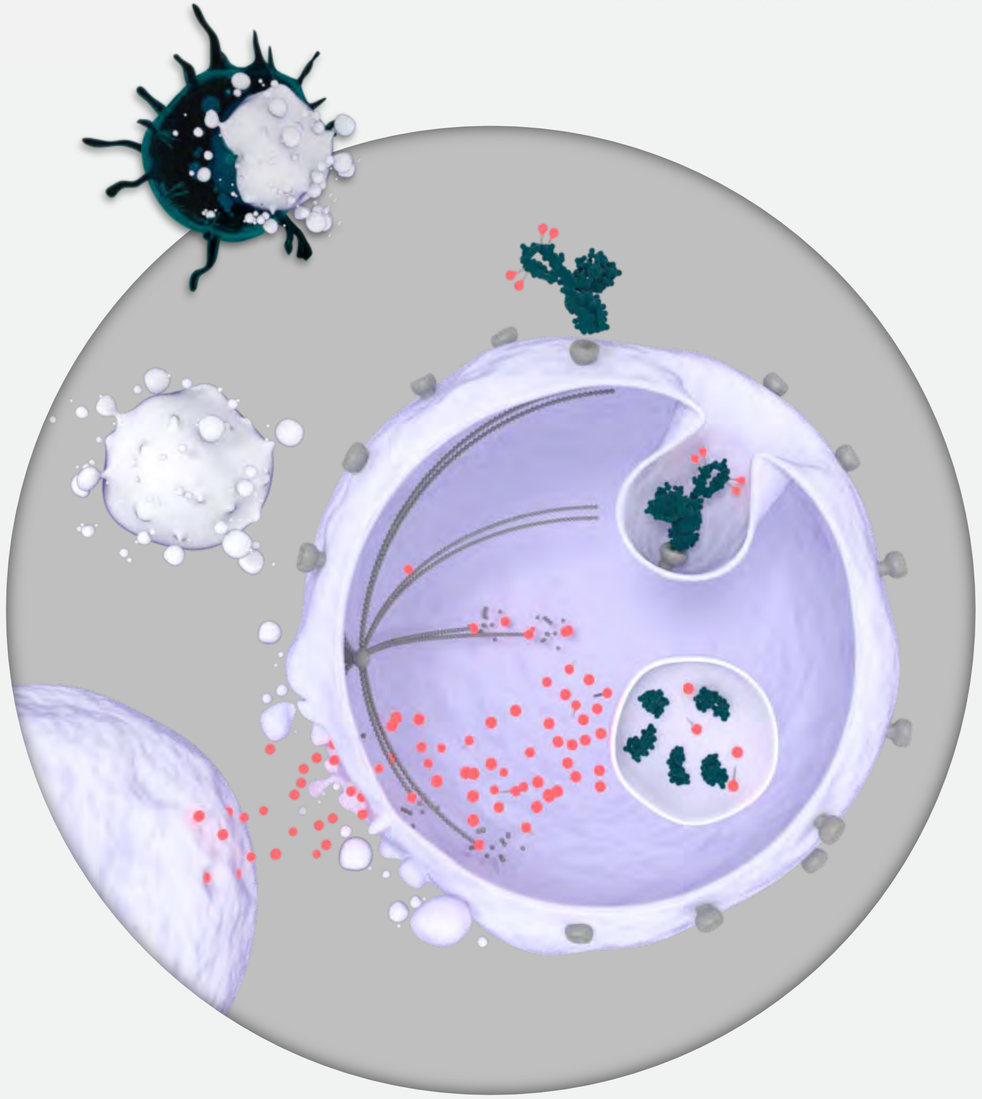
Mirvetuximab soravtansine (Mirv)



- MIRV is an antibody-drug conjugate (ADC) comprising an FRα-binding antibody, cleavable linker, and a maytansinoid DM4 payload[3]
- Ovarian cancer cells overexpress FRα (*FOLR1* gene); FRα expression is associated with poor clinical outcomes[4-6]

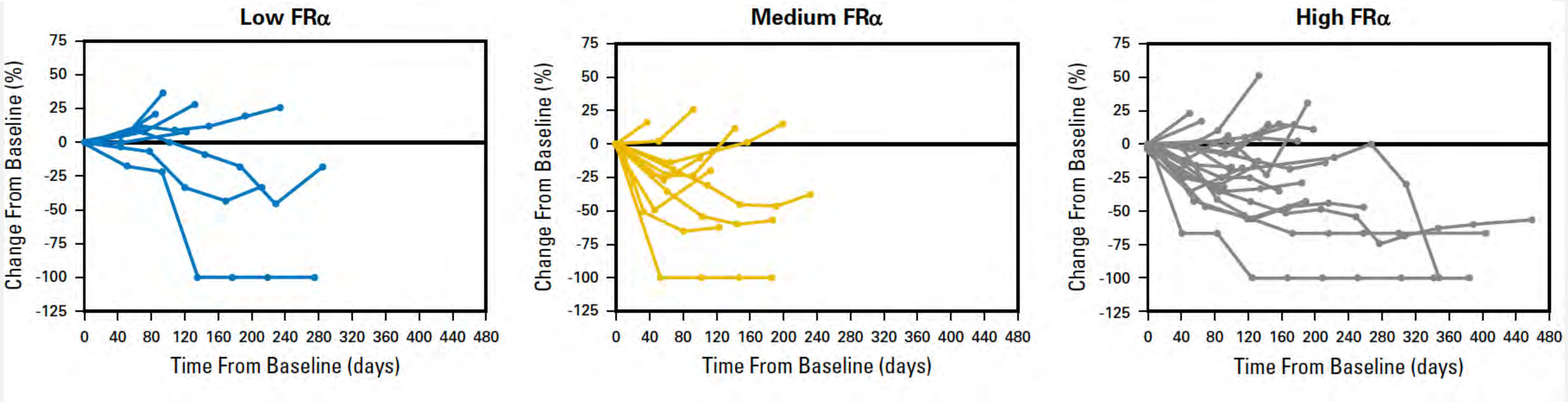
3. Moore KN, et al. *Cancer.* 2017;123(16):3080-3087. 4. Crane LM, et al. *Cell Oncol (Dordr).* 2012;35(1):9-18. 5. Kalli KR, et al. *Gynecol Oncol.* 2008;108(3):619-626. 6. Chen YL, et al. *Mol Oncol.* 2012;6(3):360-369.

Mirvetuximab soravtansine – FIH/Expansion

Table 3. Summary of Efficacy Measures Grouped by FRα Expression

FRα Expression	No. of Patients	CR	PR	SD	PD	ND	ORR (%)	95% CI
Low	9	0	2	6	0	1	22.2	2.8 to 60.0
Medium	14	0	4	8	2	0	28.6	8.4 to 58.1
High	23	1	5	14	2	1	26.1	10.2 to 48.4
Total	46	1	11	28	4	2	26.1	14.3 to 41.1

Abbreviations: CR, complete response; FRα, folate receptor alpha; ND, not determined; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease.



Moore KN, Martin LP, O'Malley DM, Matulonis UA, Konner JA, Perez RP, Bauer TM, Ruiz-Soto R, Birrer MJ. Safety and Activity of Mirvetuximab Soravtansine (IMGN853), a Folate Receptor Alpha-Targeting Antibody-Drug Conjugate, in Platinum-Resistant Ovarian, Fallopian Tube, or Primary Peritoneal Cancer: A Phase I Expansion Study. *J Clin Oncol.* 2017 Apr 1;35(10):1112-1118.

Moore K, Borghaei H, O'Malley D, Jeong W, Seward S, Bauer T, Perez R, Matulonis U, Running K, Zhang X, Ponte J, Ruiz-Soto R, Birrer M. Phase I dose-escalation study of mirvetuximab soravtansine (IMGN853), a folate receptor alpha-targeting antibody-drug conjugate, in patients with solid tumors. *Cancer*, 2017 Aug;123(16):3080-3087. PMID: 28440955

STUDY DESIGN

FORWARD I

- Platinum-resistant ovarian cancer
- FRα-positive tumor expression
  - Medium (50-74% cells positive)
  - High (≥75% cells positive)
- ECOG performance status 0 or 1
- 1-3 prior therapies

Statistical Assumptions

- Hochberg procedure
- α=0.05 (two-sided), power = 90%
  HR=0.58; control arm mPFS 3.5 mos

Mirvetuximab Soravtansine (n=248)

6 mg/kg (adjusted ideal body weight) once every 3 weeks

2:1 Randomization

Stratification Factors:
FRα expression (medium or high)
Prior therapies (1 and 2, or 3)
Choice of chemotherapy

Investigator's Choice Chemotherapy
Paclitaxel, PLD†, or Topotecan (n=118)

***Paclitaxel**: 80 mg/m² weekly*
***PLD**: 40 mg/m² once every 4 weeks*
***Topotecan**: 4 mg/m² on Days 1, 8, and 15 every 4 weeks; or 1.25 mg/m² on Days 1-5 every 3 weeks*

Primary Endpoint

Progression-free survival (PFS; by BIRC*) for ITT and high FRα populations

*BIRC = Blinded Independent Review Committee; analyzed by Hochberg procedure

Secondary Endpoints

Overall response rate (ORR)
Overall survival (OS)
Patient reported outcomes (PRO)

BARCELONA 2019 ESMO congress

†Pegylated liposomal doxorubicin
ClinicalTrials.gov Identifier: NCT02631876

Moore, K, ESMO 2019

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Efficacy Results at a Glance

Intent to treat (ITT) population

Endpoint	Treatment effect size	p-value
PFS by BIRC*	HR: 0.981 mPFS: 4.1 vs 4.4	0.897
ORR by BIRC	22% vs 12%	0.015
DOR (mos)	HR = 0.982 5.7 vs 7.3	0.974
OS	HR: 0.815 mOS: 16.4 vs 14.0	0.248
PFS by INV	HR: 0.809 mPFS: 4.3 vs 4.2	0.116
ORR by INV	29% vs 16%	0.008
CA125 ORR	51% vs 27%	0.0002

FRα high subgroup

Endpoint	Treatment effect size	p-value**
PFS by BIRC	HR: 0.693 mPFS: 4.8 vs 3.3	0.049
ORR by BIRC	24% vs 10%	0.014
DOR (mos)	HR= 0.598 5.7 vs 4.2	0.374
OS	HR: 0.618 mOS: NR* vs 11.8	0.033
PFS by INV	HR: 0.667 mPFS: 5.0 vs 4.2	0.018
ORR by INV	29% vs 13%	0.007

**Nominal P value

*BIRC = Blinded Independent Review Committee NS based on Hochberg Procedure

Efficacy Results ORR and DOR

Intent to treat (ITT) population

Endpoint	Treatment effect size	p-value**
ORR by BIRC*	22% vs 12%	0.015
DOR (mos)	HR = 0.982 5.7 vs 7.3	0.974
ORR by INV	29% vs 16%	0.008

FRα high subgroup

Endpoint	Treatment effect size	p-value**
ORR by BIRC*	24% vs 10%	0.014
DOR (mos)	HR= 0.598 5.7 vs 4.2	0.374
ORR by INV	29% vs 13%	0.007

Moore, K, ESMO 2019

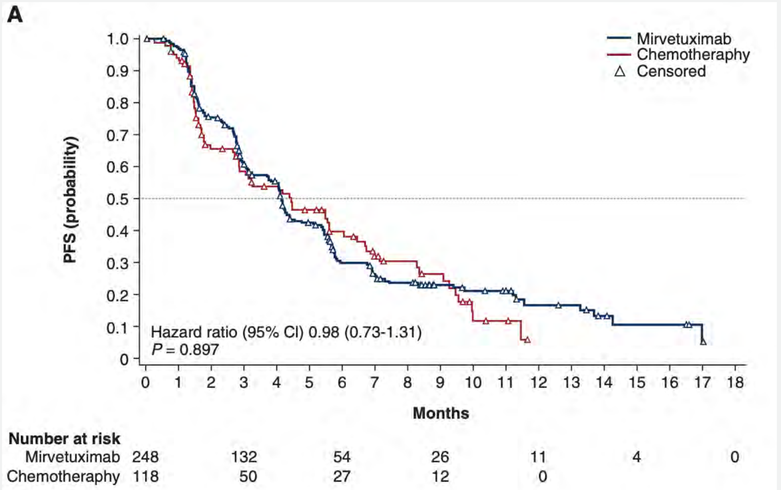
*BIRC = Blinded Independent Review Committee

**NS per Hochberg procedure

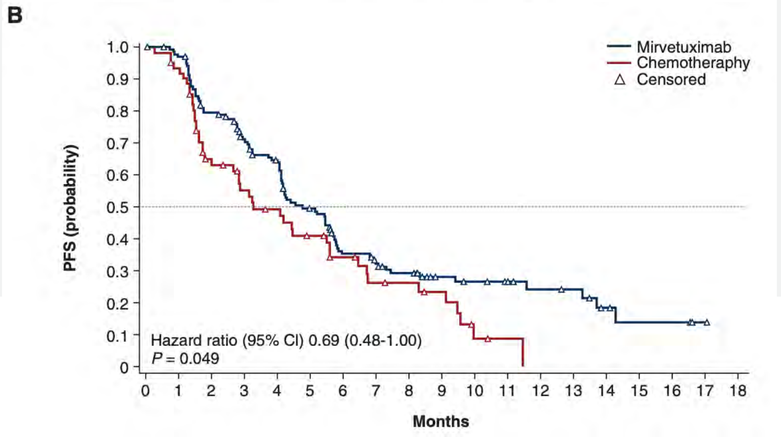
Moore KM et al; Annals of Oncology; 32 (6) 2021

FORWARD-1

- Negative for primary objectives
- Not statistically significant for HIGH FRa
- FRa predictive marker for Mirv
- FRa prognostic markers



ITT



HIGH FRa

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MIRASOL STUDY DESIGN

PHASE 3 REGISTRATION TRIAL FOR MIRVETUXIMAB USING PS2+ SCORING IN FRα HIGH PATIENTS

GOG 3045

MIRASOL

ENROLLMENT AND KEY ELIGIBILITY

- **430 patients/330 events for PFS by INV**
- **FRα-high by PS2+ scoring**
- **Platinum resistant disease (<6 months PFI)**
- **Prior Bev and PARP allowed**
- **BRCAmut patients allowed**

Completed Enrollment
PI: K Moore

1:1 RANDOMIZATION

Mirvetuximab Soravtansine

STRATIFICATION FACTORS
IC Chemotherapy Choice (Paclitaxel, PLD, Topotecan)
Prior Therapies (1 vs 2 vs 3)

Investigator's Choice Chemotherapy
Paclitaxel, PLD†, or Topotecan

PRIMARY ENDPOINT
PFS by INV; BICR* for sensitivity analysis

SECONDARY ENDPOINTS
ORR by INV, OS, and PRO

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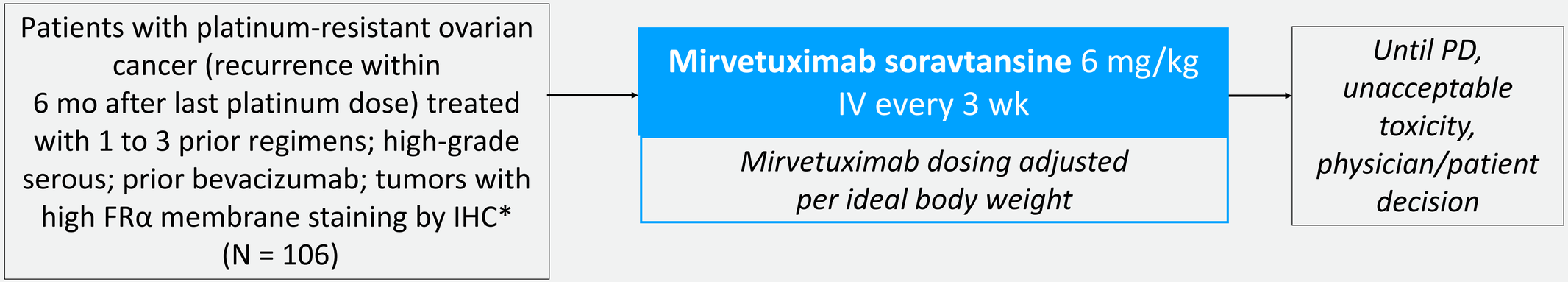
Mirvetuximab Soravtansine in Platinum-Resistant OC With High FRα Expression (SORAYA): Study Design



*High expression defined as ≥75% of cells staining positive with ≥2+ staining intensity.

- **Primary endpoints**: ORR by investigator
- **Secondary endpoints**: DoR

- Primary cancer diagnosis was epithelial ovarian cancer in 80%; 97% had stage III-IV disease at diagnosis
- 80% had unknown *BRCA* mutation status
- 100% had prior bevacizumab and 48% had previous PARP inhibitor

NCT04296890. Moore. Ann Oncol.2021;32:757. Matulonis. SGO 2022. Abstr 242.

Phase III SORAYA Study of Mirvetuximab Soravtansine: Efficacy Summary

Outcome	Investigator-Assessed (N = 105)	BICR-Assessed (N = 95)
ORR, n (%) [95% CI]	34 (32.4) [23.6-42.2]	30 (31.6) [22.4-41.9]
Best overall response, n %		
CR	5 (4.8)	5 (5.3)
PR	29 (27.6)	25(26.3)
SD	48 (45.7)	53 (55.8)
PD	20 (19.0)	8 (8.4)
Not evaluable	3 (2.9)	4 (4.2)
Median DoR, mo (95% CI)	6.9 (5.6-8.1)	11.7 (5.0-NR)
Median PFS, mo (95% CI)	4.3 (3.7-5.1)	5.5 (3.8-6.9)

- Clinically meaningful activity seen in patients with FRα-high platinum-resistant OC
- Consistent antitumor activity regardless of prior number of therapies or prior PARPi
  - **ORR if 1-2 lines of therapy:** 35.3% (range: 22.4%-49.9%)
  - **ORR if 3 lines of therapy:** 30.2% (range: 18.3%-44.3%)
  - **ORR if prior exposure to PARP inhibitor (yes vs no):** 38.0% (range: 24.7%-52.8%) vs 27.5% (range: 15.9%-41.7%)
- Overall median duration of response and by prior PARP inhibitor was comparable between those with 1-2 prior lines vs 3 prior lines of therapy

Matulonis. SGO 2022. Abstr 242.

FDA grants accelerated approval to mirvetuximab soravtansine-gynx for FRα positive, platinum-resistant epithelial ovarian, fallopian tube, or peritoneal cancer

On November 14, 2022, the Food and Drug Administration granted accelerated approval to mirvetuximab soravtansine-gynx (Elahere, ImmunoGen, Inc.) for adult patients with folate receptor alpha (FRα) positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have received one to three prior systemic treatment regimens. Mirvetuximab soravtansine-gynx is a folate receptor alpha directed antibody and microtubule inhibitor conjugate. Patients are selected for therapy based on an FDA-approved test.

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-mirvetuximab-soravtansine-gynx-fra-positive-platinum-resistant. Accessed 23 Jan 2023

Mirv + Bev (FORWARD-2)

Characteristic		MIRV+BEV (N=126)
Age, median (range)	Age in years	62 (39–83)
Primary cancer diagnosis, n (%)[a]	Epithelial ovarian	93 (74)
	Primary peritoneal	27 (21)
	Fallopian tube	5 (4)
FRα expression, n (%)[b]	High	62 (49)
	Medium	51 (40)
	Low	13 (10)
No. prior lines of systemic therapy, n (%)	1	27 (21)
	2	41 (33)
	3	**29 (23)**
	≥4	**29 (23)**
	Median (range)	2 (1–8)
Prior exposure, n (%)	**Bevacizumab**	**66 (52)**
	PARPi	34 (27)
Platinum-free interval, n (%)[c,d]	**≤6 months**	**94 (75)**
	>6–12 months	23 (18)
	>12 months	8 (6)
ECOG performance status	0	82 (65)
	1	44 (35)

- **Efficacy and safety of MIRV in combination with bevacizumab (BEV) in patients with recurrent FRα-expressing ovarian cancer**
- **46% had ≥ 3 prior lines of therapy**
- **52% had received prior Bev**
- **75% had most recent PFI of ≤ 6 months**

D O'Malley, et al IGCS 2022

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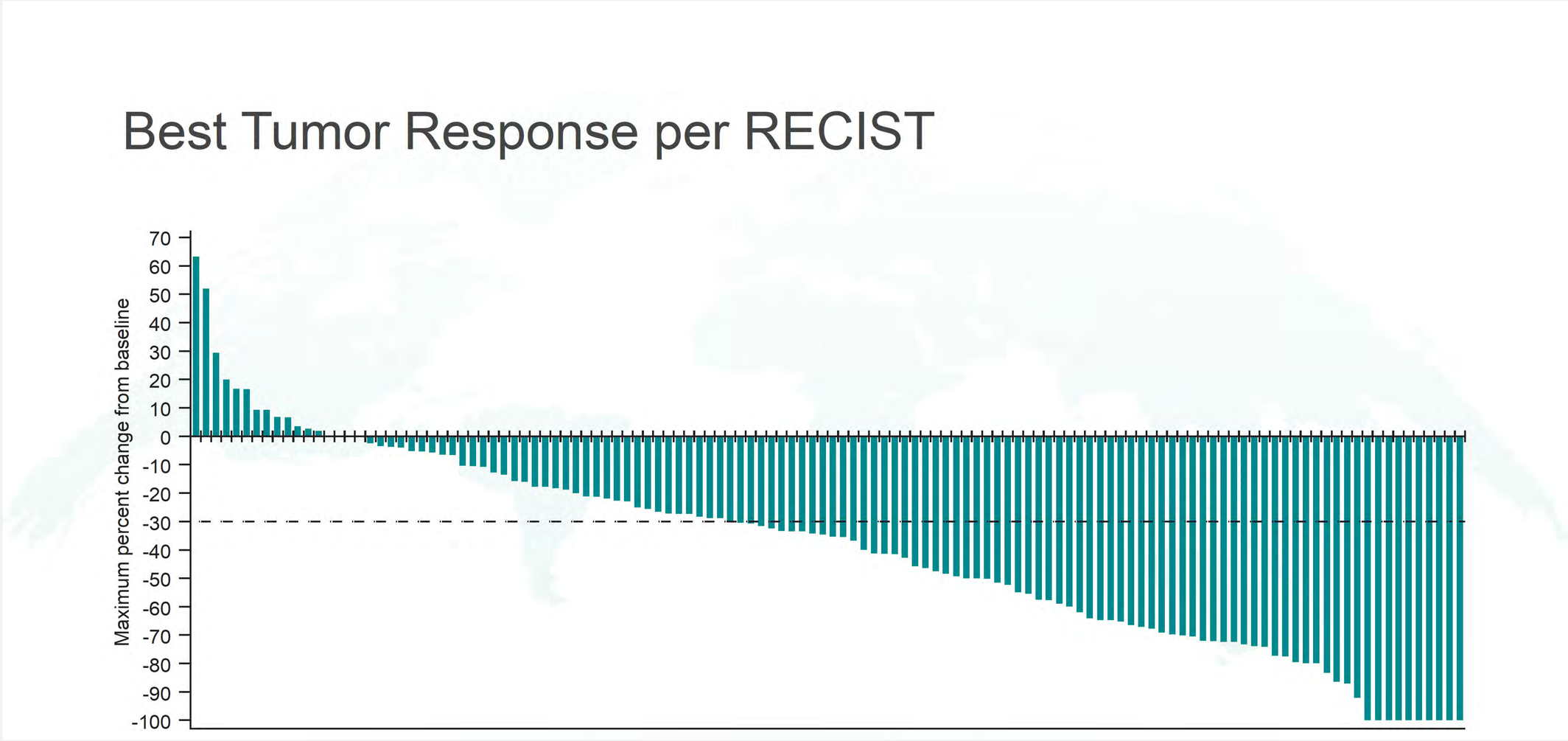
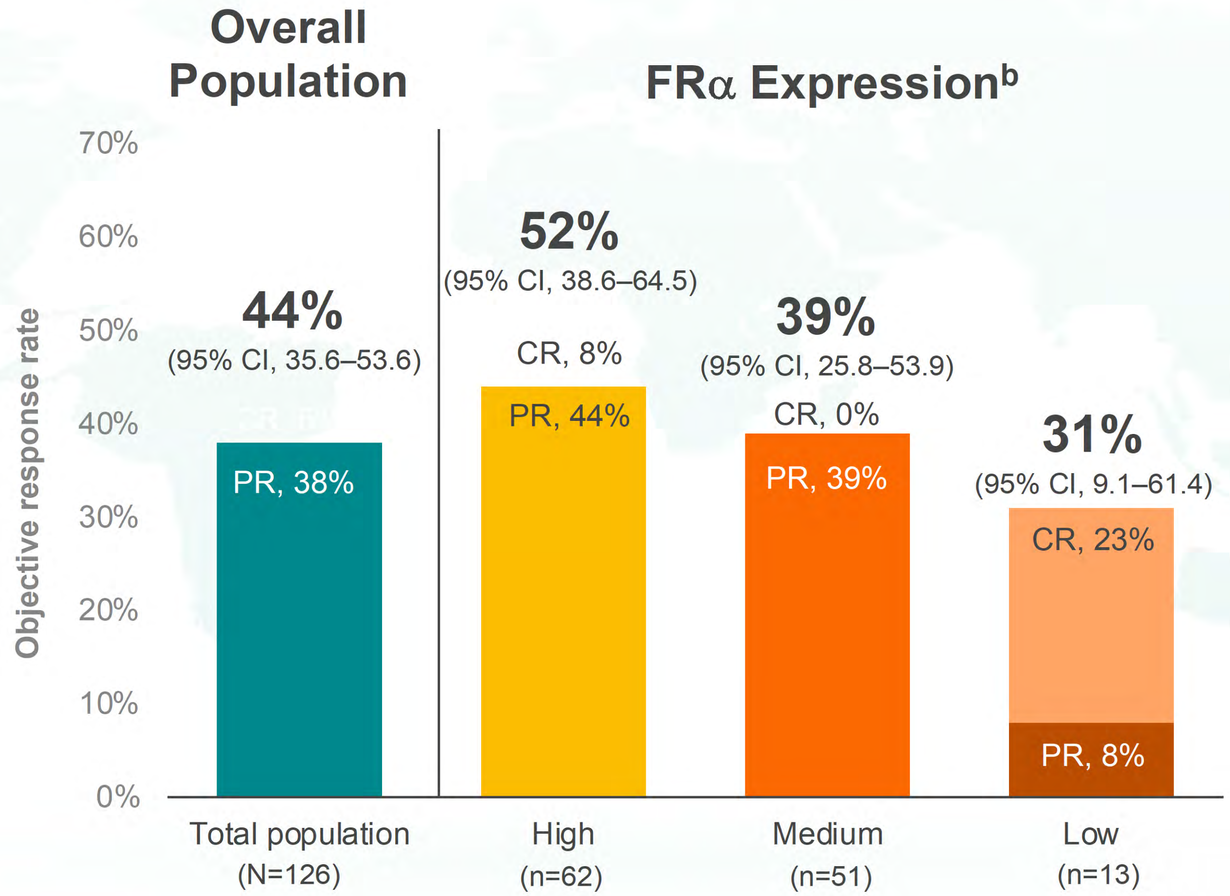
Mirv + Bev (FORWARD-2)



D O'Malley, et al IGCS 2022

ORR[a] in the Overall Population and by FRα Expression Level Subgroups



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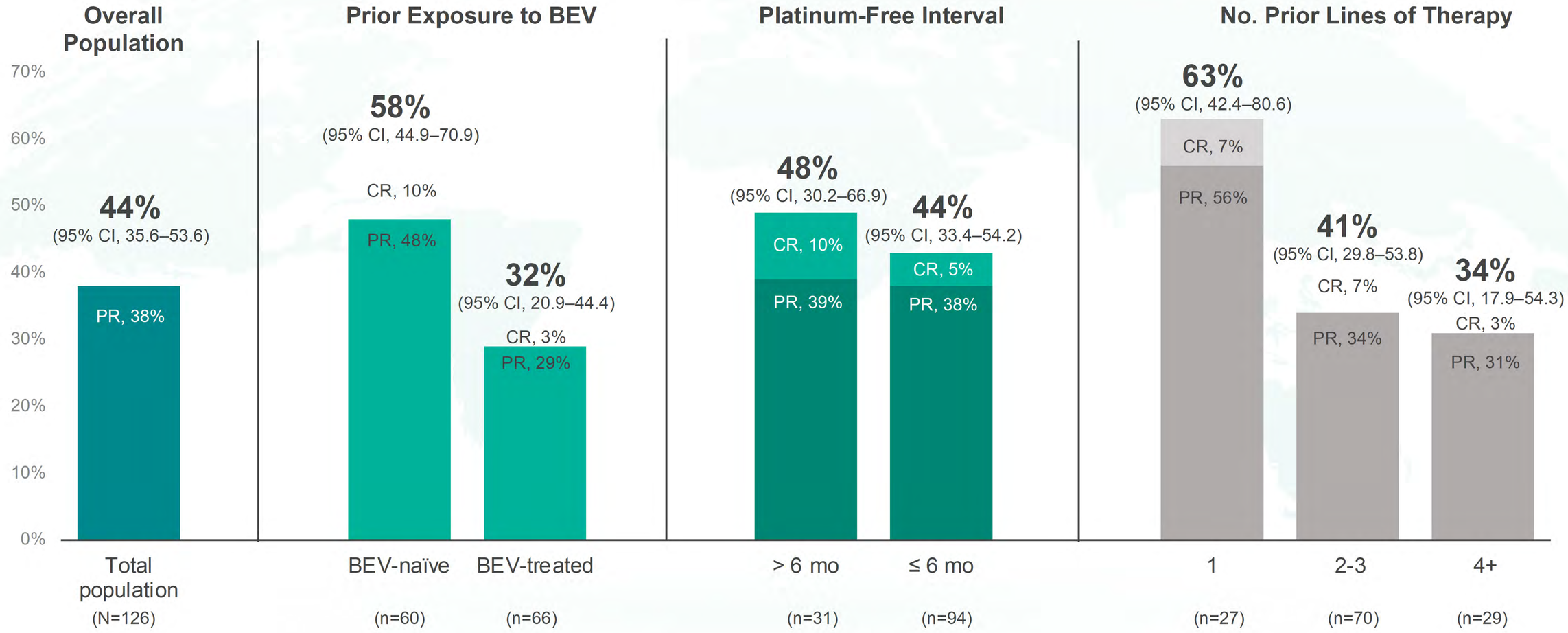
ORR[a] in Subgroups by BEV Treatment Status, Platinum-Free Interval, and Prior Lines of Therapy



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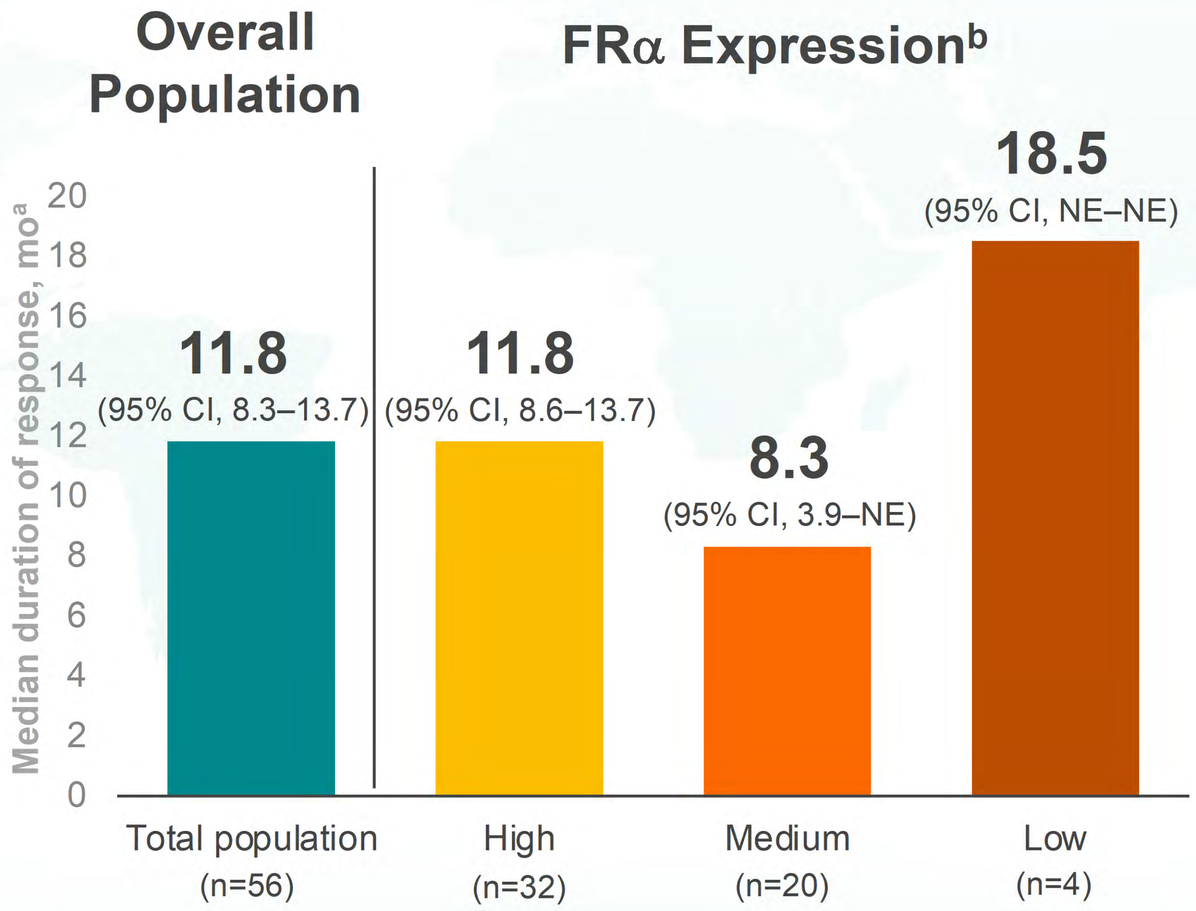
Median DOR[a] in Responders: Overall Population and by FRα Expression Level Subgroups



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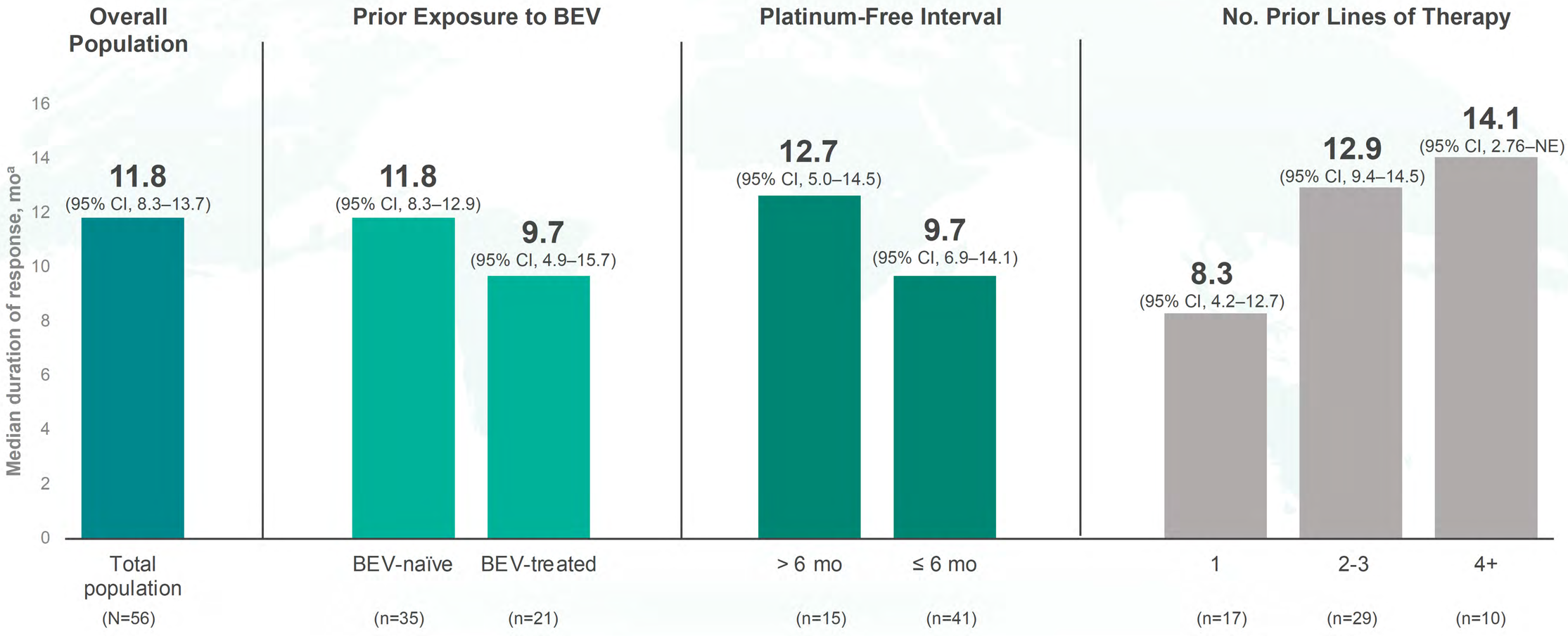
Median DOR[a] in Responders: Subgroups by BEV Treatment Status, Platinum Status, and Lines of Therapy



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NCCN Guidelines Jan 2023

Targeted Therapy

Dabrafenib + trametinib (for *BRAF* V600E-positive tumors)[x,28]

Entrectinib or larotrectinib (for *NTRK* gene fusion positive tumors)[x]

Mirvetuximab soravtansine-gynx/bevacizumab (for *FRα*-expressing tumors) (category 2B)[i,x,47, 48]

Selpercatinib (for *RET* gene fusion-positive tumors)[x,29]

For low-grade serous carcinoma:

- Trametinib[30]
- Binimetinib (category 2B)[31,32]

X: **Validated molecular testing should be performed in a CLIA-approved facility using the most recent available tumor tissue. Tumor molecular analysis is recommended to include, at a minimum, tests to identify potential benefit from targeted therapeutics that have tumor-specific or tumor-agnostic benefit including, but not limited to, BRCA1/2, HRD status, MSI, MMR, TMB, BRAF, FRα, RET, and NTRK if prior testing did not include these markers. More comprehensive testing may be particularly important in LCOC with limited approved therapeutic options. (See OV-B).**

NCCN guidelines 2023, accessed Jan 2023

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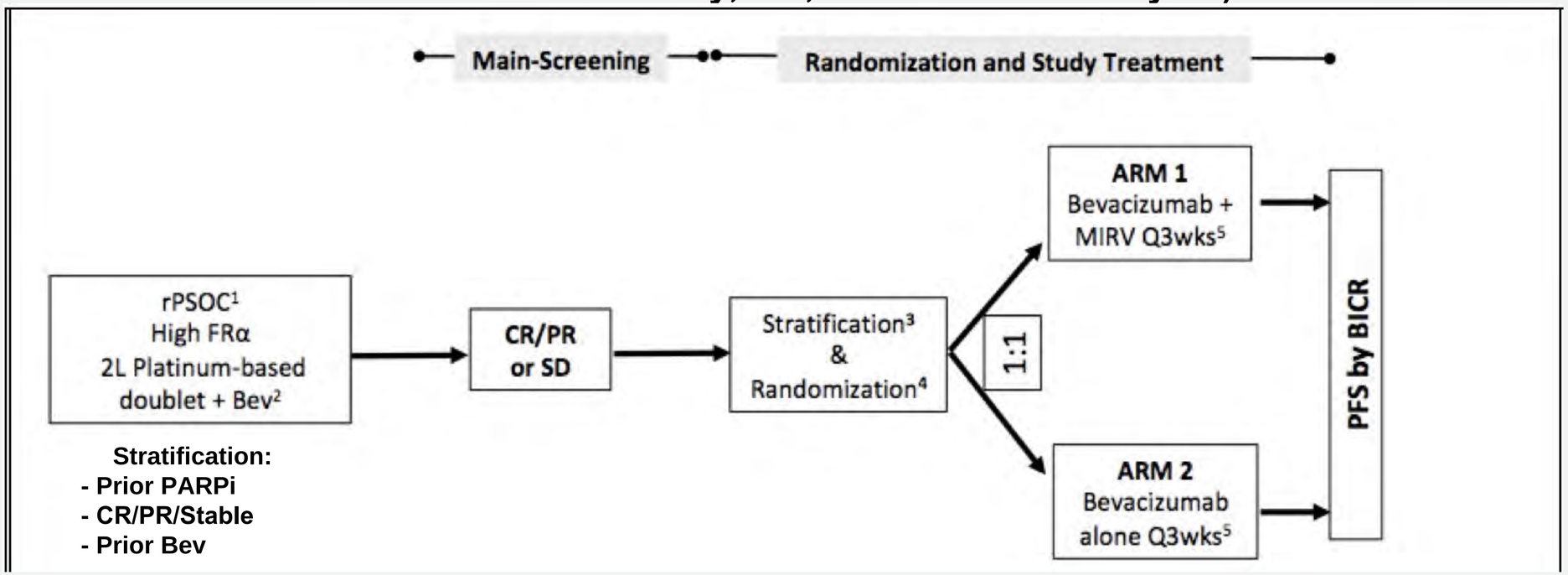
GOG-3078 (GLORIOSA)

Randomized multicenter, open-label, phase 3 study of bevacizumab with or without mirvetuximab soravtansine for patients with FRα–positive recurrent platinum-sensitive epithelial ovarian cancer, fallopian tube, or primary peritoneal cancers who have not progressed after second line platinum-based chemotherapy plus bevacizumab (PI: David O'Malley, MD, Co-PI: Tashanna Myers)



- High grade epithelial ovarian, tubal or primary peritoneal cancer
- Platinum + chemo + Bevacizumab for planned 6 cycles (min of 4 and max of 8) including at least 3 of cycles of Bev
- Need to have a CR, PR, or stable disease after platinum regimen
- Treatment until progressive disease, unacceptable toxicity, withdrawal or death
- Maintenance to must begin within 12 weeks of completing platinum doublet

PSOC – Mirv Mono Therapy

Characteristic	N = 31
Age, years	
Median (range)	59 (44-83)
Primary diagnosis, n (%)	
Epithelial ovarian cancer	20 (65)
Fallopian tube cancer	10 (32)
Other: Omentum	1 (3)
ECOG PS, n (%)	
0	22 (71)
1	9 (29)
No. of prior systemic therapies, n (%)	
1-2	23 (74)
≥3	8 (26)
FRα expression,[a] n (%)	
≥75%	18 (58)
50-74%	12 (39)
25-49%	1 (3)
Prior exposure, n (%)	
Taxane	31 (100)
Bevacizumab	10 (32)
PARP inhibitor	8 (26)

Endpoint	N = 31
Confirmed objective response rate, n (%)	15 (48)
95% CI	(30, 67)
Best overall response, n (%)	
Complete response	3 (10)
Partial response	12 (39)
Stable disease	14 (45)
Progressive disease	2 (6)
Not evaluable	0 (0)
Median duration of response, (months)	12.7
95% CI	(5.0, 14.5)
Median progression-free survival, (months)	9.6
95% CI	(5.4, 14.1)

PSOC, platinum-sensitive ovarian cancer.

L Gilbert … DM O'Malley, et al, IGCS 2022, Gyn Onc 2023

GOG FOUNDATION

PICCOLO

SINGLE-ARM TRIAL FOR MIRVETUXIMAB IN FRα-HIGH PATIENTS WITH PLATINUM-SENSITIVE OVARIAN CANCER

Completed Enrollment

PI: Angeles Alvarez-Secord

PRIMARY ENDPOINT
ORR by Investigator

SECONDARY ENDPOINT
DOR by Investigator

ENROLLMENT AND KEY ELIGIBILITY
~75 patients
Platinum-sensitive ovarian cancer
2 or more prior systemic treatments
At least 2 prior platinum-containing regimens
Prior PARPi required if BRCA+
Appropriate for single-agent therapy

GOG FOUNDATION®

Conclusions

- Cervical Cancer
  - Tisotumab Vedontin Monotherapy
    - 2nd line+*^
      - Ongoing phase III
  - Tisotumab Vedontin Combo therapy
    - 2nd line+
    - First line
- Ovarian Cancer
  - Mirvetuximab soravtansine Monotherapy
    - PROC*^
    - PSOC
      - Completed phase II
  - Mirvetuximab soravtansine Combo therapy
    - PROC^
    - PSOC
      - Ongoing phase III

*Accelerated Approval
^NCCN guidelines