Updates in Platinum Resistant Ovarian Cancer & Low Grade Serous

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GOG Highlight Reel

Strategies in PROC

		Phase	Regimen	Prior total Therapies	Prior therapies for PROC	Tumor testing/ Prevalence
Taxanes	**GOG-3018 (OVAL)**	**3**	VB-111/placebo D1 (56 day cycle) +weekly paclitaxel vs. weekly Paclitaxel	≤ 5	<3	no
	GOG-3029 (INNOVATE-3)	**3**	TTFields >18 hr/day + weekly paclitaxel vs. weekly Paclitaxel	≤ 5	<3	no
	GOG-3044 (PROFECTA)	**2**	Afuresertib PO QD + Paclitaxel D1,8,15 Q3W vs. weekly Paclitaxel	1-3 prior platinum	0	yes
	GOG-3059 (Aravive)	**3**	AVB-S6-500 (D1 & 15) +Weekly paclitaxel (D 1, 8, 15 on a 28d cycle) vs. weekly Paclitaxel	1-4	not defined (no prior taxanes for recurrence	no
Antibody Drug Conjugates	**GOG-3045 (MIRASOL)**	**3**	Mirvetuximab vs Investigator Choice chemotherapy	1-3	Not defined	yes
	GOG-3048 (Mersana)	**1b**	XMT-1536 every 4 weeks	1-3 permis. Can be granted for 4 prior)	not defined (only 2 prior taxanes allowed)	no
Immunotherapy	**NRG-GY009**	**2/3**	PLD/Atezo (D1&15) vs. PLD/Bev(D1&15)/ Atezo (D1&15) vs. PLD/Bev (D1&15)	1-2	Not defined	no
	NRG-GY023	**2**	IC vs durva/cediranib vs olaparib/cediranib vs durva/cediranib/ olaparib	5 (prior bev req.)	4	no
Targeting Replication Stress/PARPi Resistance	**NRG-GY029**	**2**	IC vs olaparib and copanlisib (PARPI resistant)	Unlimited PSOC ≤ 2 PROC, bev req	≤ 2	no
	NRG-GY030	**2/3**	Gemcitabine vs. Gemcitabine + Berzosertib	Unlimited PSOC, 1 PROC, prior bev req	1	no

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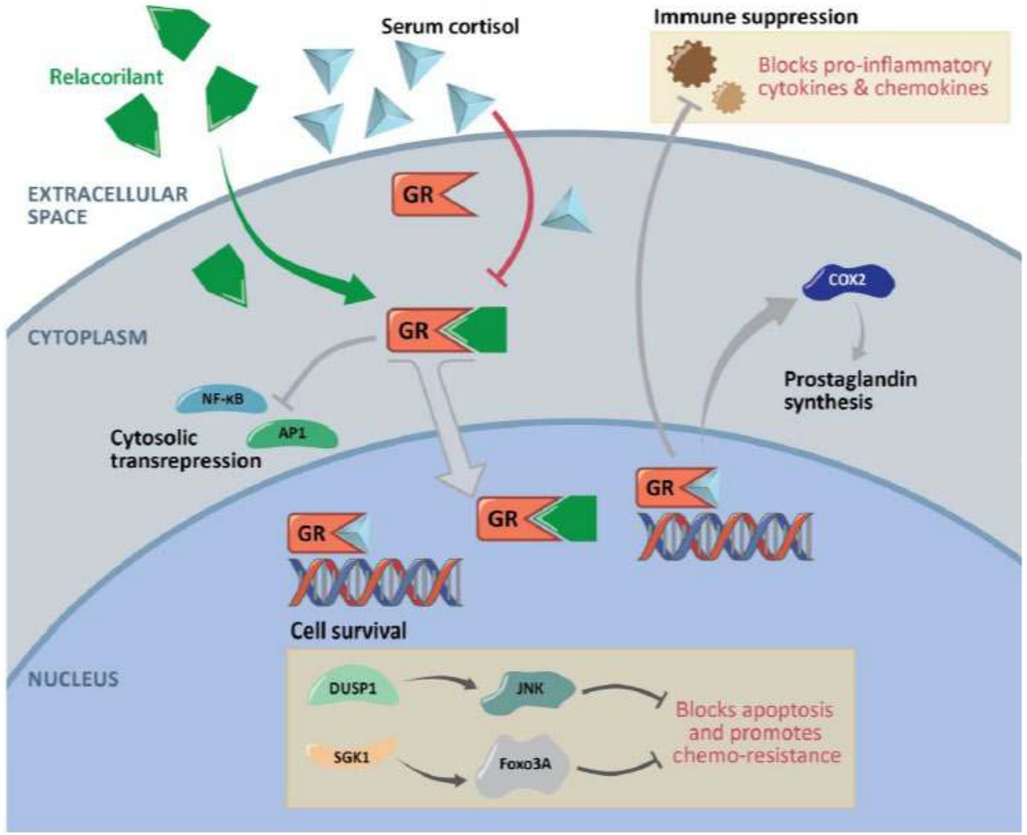
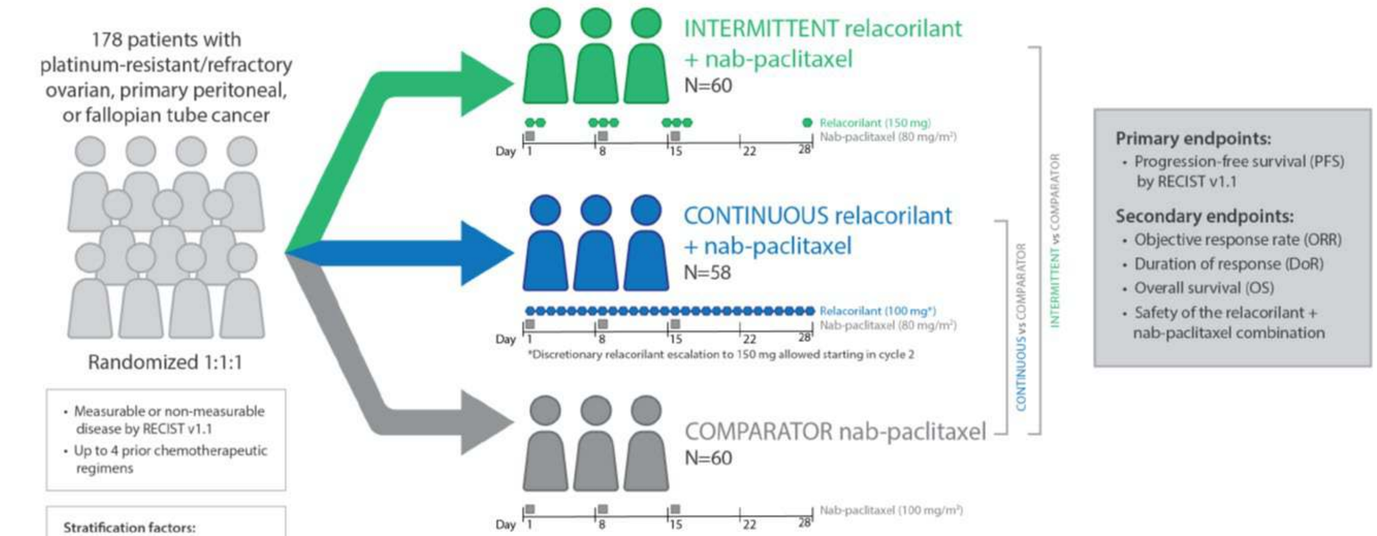
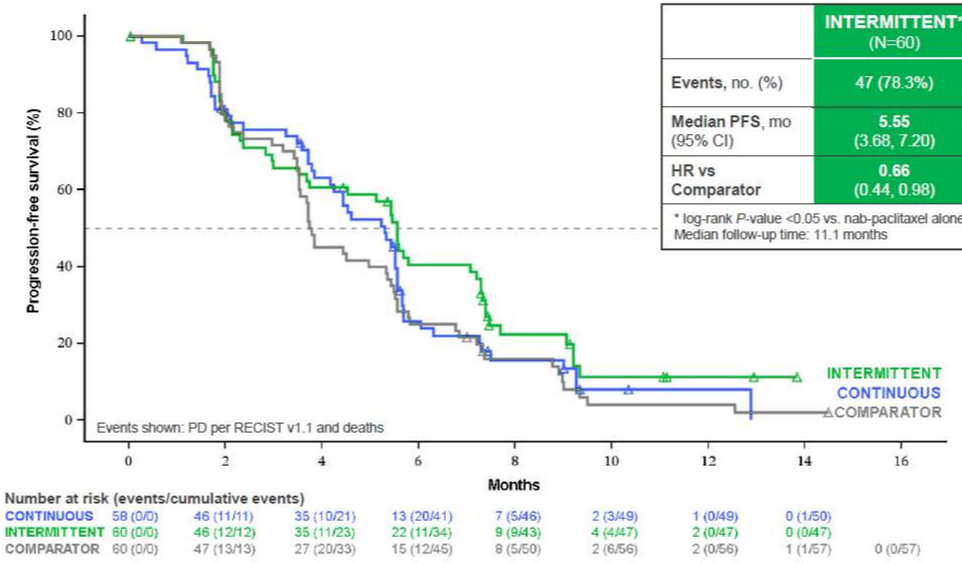
Synergy with taxanes: Relacorilant + Abraxane





Statistical assumptions

- **CONTINUOUS** vs COMPARATOR: 91 PFS events to detect a HR=0.56 (median PFS increase from 3.8 to 6.8 mo)
- **INTERMITTENT** vs COMPARATOR: 92 PFS events to detect a HR=0.7 (median PFS increase from 3.8 to 5.4 mo)

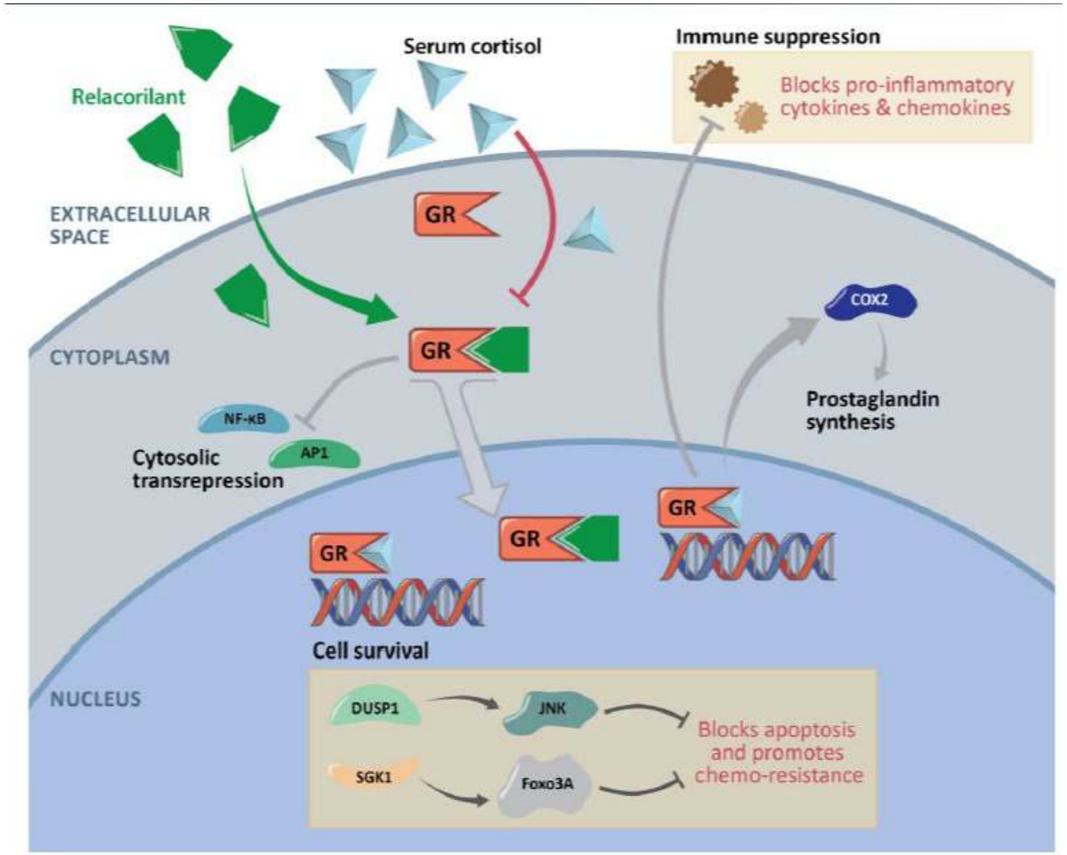


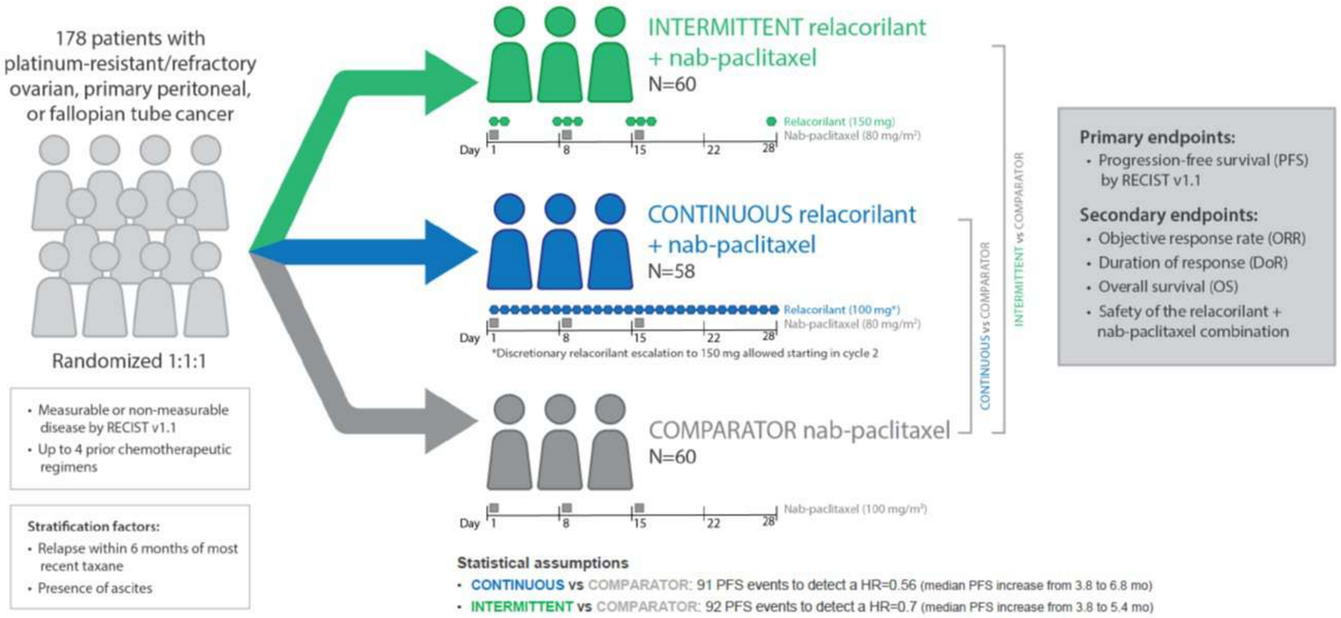
	INTERMITTENT* (N=60)	CONTINUOUS (N=58)	COMPARATOR (N=60)
Events, no. (%)	47 (78.3%)	50 (86.2%)	57 (95.0%)
Median PFS, mo (95% CI)	**5.55** (3.68, 7.20)	5.29 (3.84, 5.55)	3.76 (3.52, 5.36)
HR vs Comparator	**0.66** (0.44, 0.98)	0.83 (0.56, 1.22)	N/A

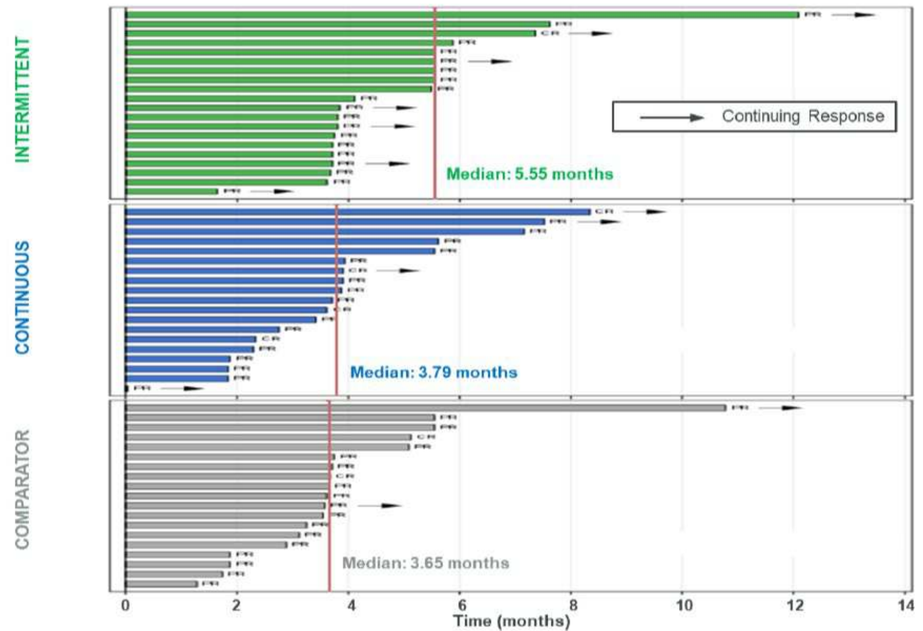
* log-rank *P*-value <0.05 vs. nab-paclitaxel alone
Median follow-up time: 11.1 months

Lorusso et al. ESMO 2021

Synergy with taxanes: Relacorilant + Abraxane







	ORR	
	n (%)	95% CI
INTERMITTENT	20 (35.7%)	(23.4, 49.6)
CONTINUOUS	19 (35.2%)	(22.7, 49.4)
COMPARATOR	19 (35.8%)	(23.1, 50.2)

While ORR was similar, DoR was **significantly improved** in the INTERMITTENT regimen.
HR 0.36, 95% CI (0.16-0.77), *P*=0.006

Lorusso et al. ESMO 2021

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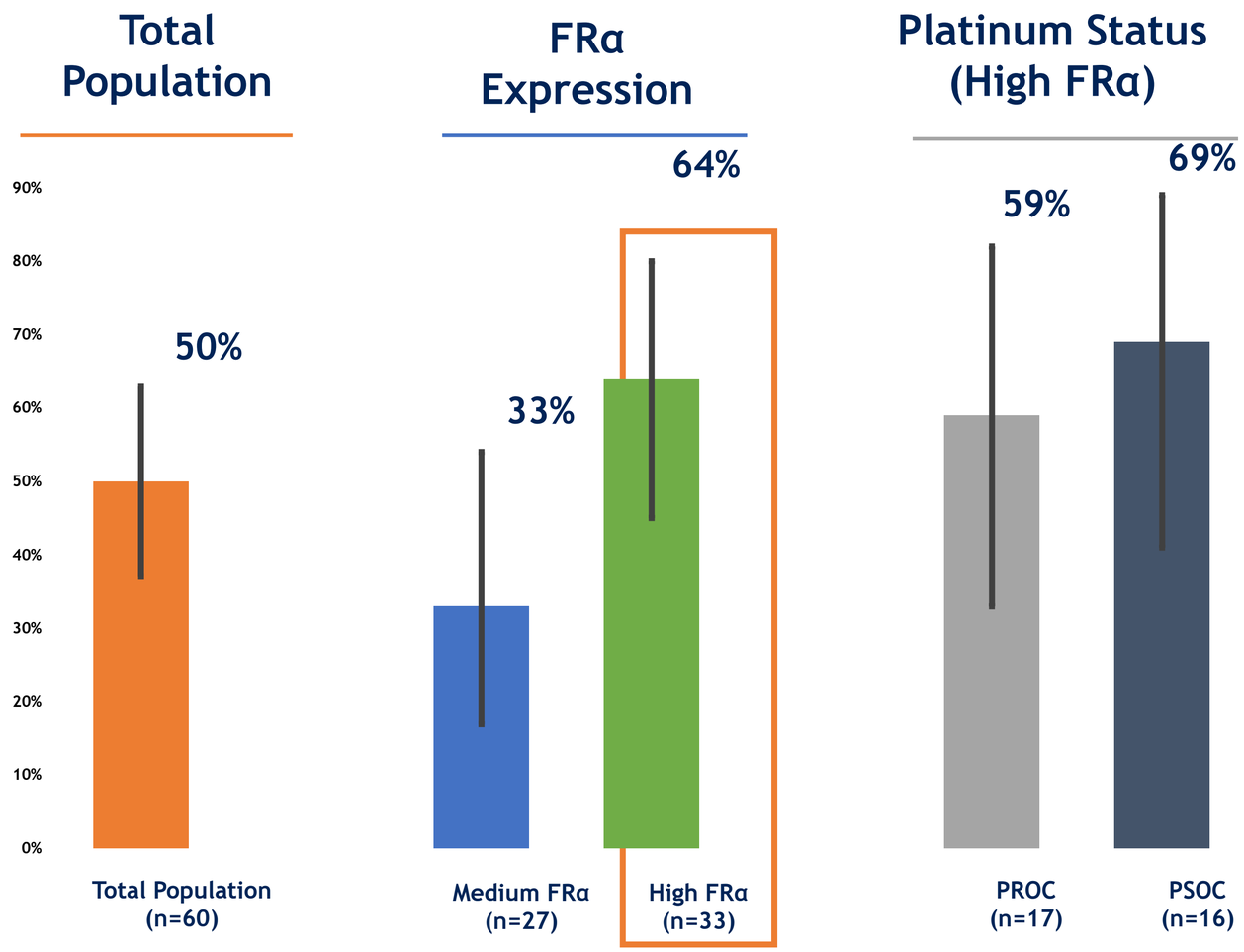
Antibody Drug Conjugates: Mirvetuximab + Bevacizumab

ORR (%)

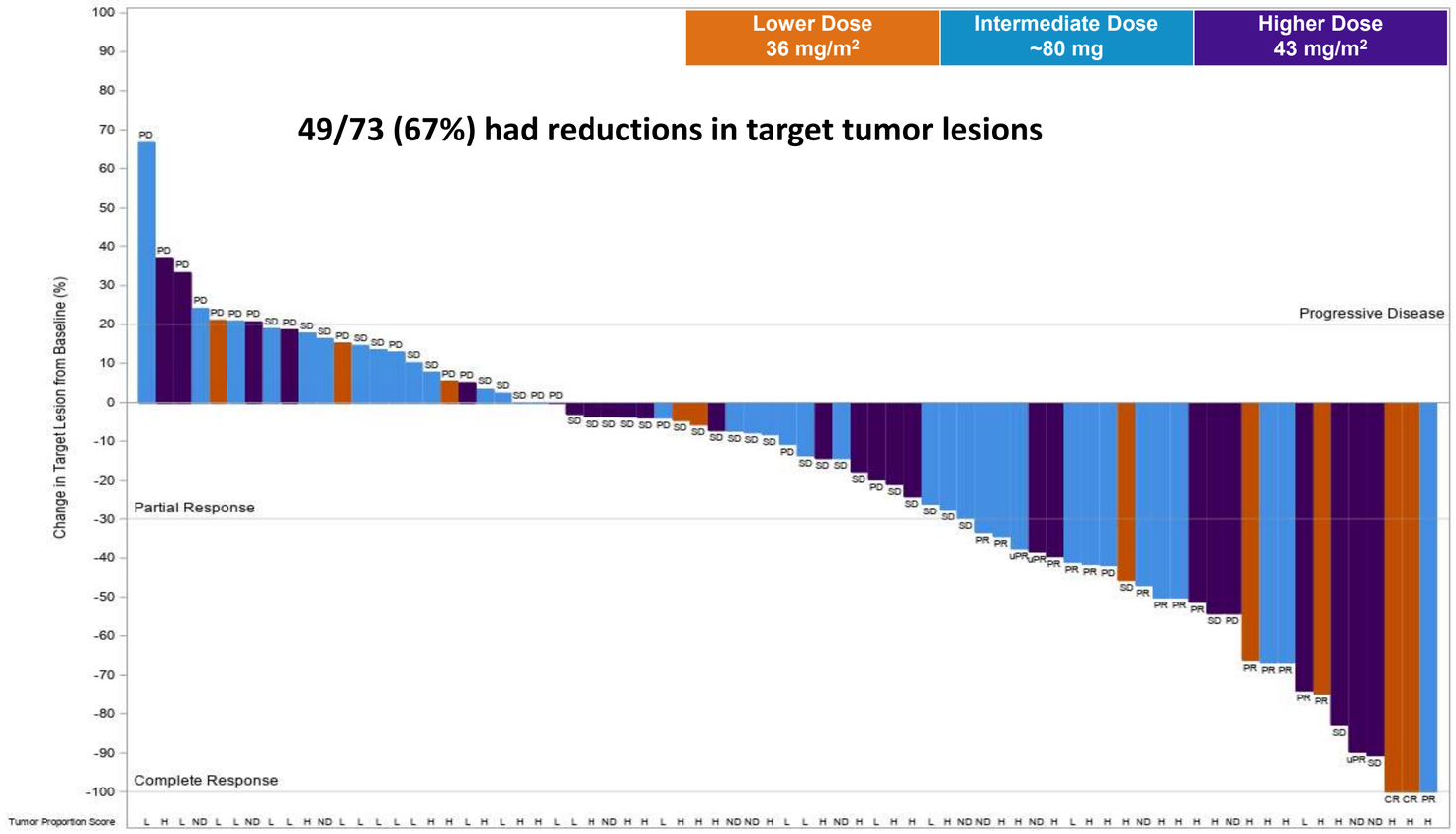


- **50% ORR** (30/60) for overall cohort
- **64% ORR** (21/33) in high FRα tumors
  - **59% ORR** (10/17) in PROC subset
  - **69% ORR** (11/16) in PSOC subset

O'Malley et al. ASCO 2021, IGCS 2021

Antibody Drug Conjugates: Upifitamab in PROC – UPLIFT Cohort

Maximum % Change from Baseline in Target Lesions in Evaluable Patients with Ovarian Cancer (n=73*)



Best Response in Evaluable Patients with Ovarian Cancer (n=75**)

	NaPi2b High (TPS≥75)	NaPi2b Low (TPS<75)	Not Yet Determined NaPi2b	All Patients
N	**38**	**23**	**14**	**75**
CR	2 (5)	0	0	2 (3)
PR	11 (29)	2 (9)	2 (14)	15 (20)
uPR	1 (3)	0	2 (14)	3 (4)
SD	19 (50)	8 (35)	7 (50)	34 (45)
PD	5 (13)	13 (57)	3 (21)	21 (28)
Confirmed ORR	**13 (34)**	**2 (9)**	**2 (14)**	**17 (23)**
DCR	**33 (87)**	**10 (43)**	**11 (79)**	**54 (72)**

Median Duration of Response in NaPi2b High: ~5 months

CR, complete response; DCR, disease control rate; PR, partial response; H, high NaPi2b expression; L, low NaPi2b expression; ND, NaPi2b expression not yet determined or tissue not available; ORR, overall response rate; uPR, unconfirmed PR.
*2 pts in waterfall plot excluded as post-baseline tumor measurement shows "Not Measurable", yet "PD" was assigned by Investigator in the response dataset. **22 patients were not evaluable by RECIST 1.1: 10 deaths (4 disease progression, 2 pneumonitis, 2 sepsis, 1 viral pneumonia, 1 unknown); 5 patient withdrawals; 1 enrolled in hospice; 1 clinical progression; 4 discontinued treatment; 1 had not yet reached first scan.
Data cut June 10, 2021.

UP-NEXT/GOG-3049: Phase 3 Study of UpRi Monotherapy Maintenance vs Placebo in Platinum-Sensitive Recurrent OC

Key Enrollment Criteria:

- Platinum-sensitive recurrence, following platinum induction
- NaPi2b high biomarker selection by TPS≥75
- 2–4 prior platinum-based regimes (including induction)
- Prior PARPi therapy allowed, but only required for BRCAmut
- SD in addition to CR/PR as best response following platinum induction

Primary Endpoint:

- PFS

Informed by FDA Feedback and CHMP Scientific Advice
Plans to Initiate in 2022

Shared with permission

BRCAmut, breast cancer gene mutated; CR, complete response; OC, ovarian cancer; PARPi, poly (ADP-ribose) polymerase inhibitor; PFS, progression-free survival; PR, partial response; SD, stable disease.

Upifitamab rilsodotin is an investigational agent not approved for use in any country.

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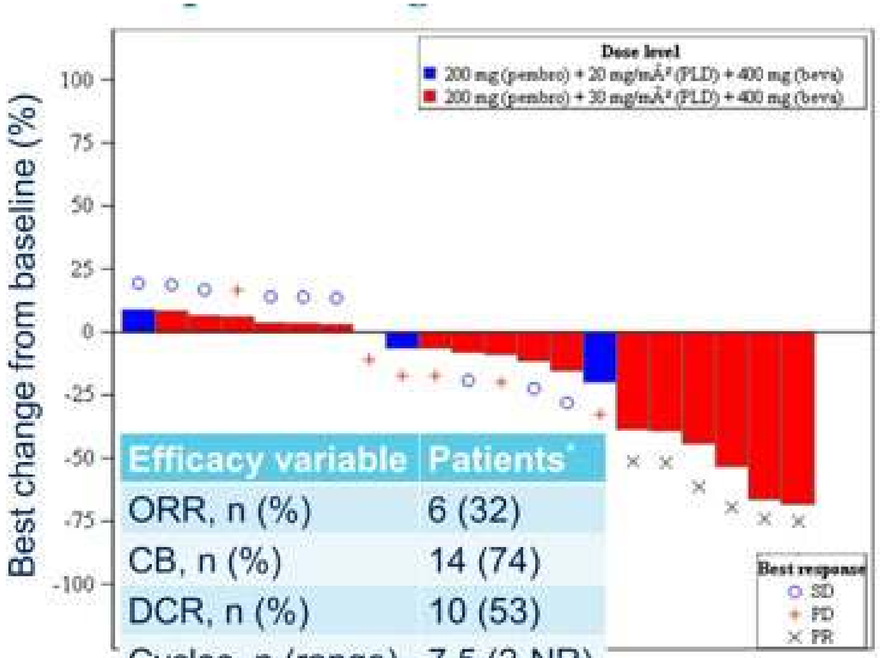
Immunotherapy Combinations

Pembrolizumab, PLD, Bevacizumab

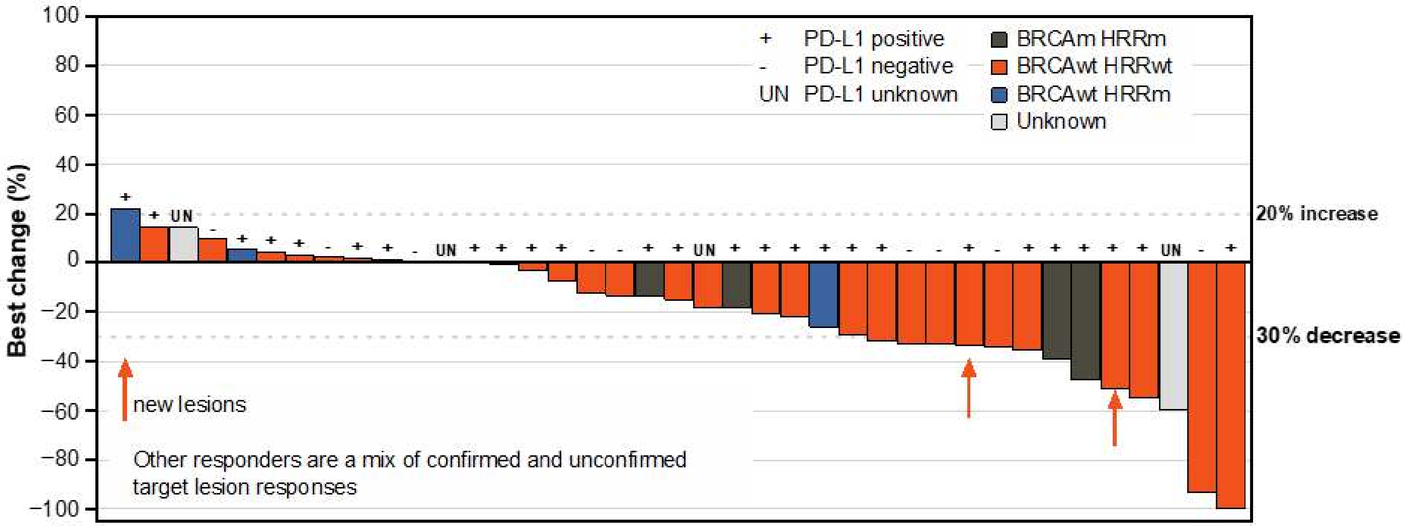


Efficacy variable	Patients*
ORR, n (%)	6 (32)
CB, n (%)	14 (74)
DCR, n (%)	10 (53)
Cycles, n (range)	7.5 (2-NR)

*treated at MTD (n=19)

Patient

OPAL
Niraparib + Dostarlimab + Bevacizumab



ORR 17.9% (8.7-31.3)

Ghiringhelli et al. ASCO 2021; Liu et al. Society of Gynecologic Oncology Annual Meeting 2021

GOG Highlight Reel Strategies in PROC

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Strategies in PROC: Targeting Replication Stress/PARPi Resistance

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Response in Specific Treatment Groups

BRCAmut

Response Category	Adavosertib Alone (n=15)	Adavosertib and Olaparib (n=16)
Best Overall Response, n (%)		
Partial Response	3 (20)	3 (19)
Stable Disease	10 (67)	12 (75)
Progressive Disease	2 (13)	1 (6)
Objective Response Rate	20%	19%
95% CI	4 – 48	4 – 46
Duration of Response (95% CI)	5.6 (5.5 – NR)	6.4 (5.6 – NR)
Stable Disease > 4 months	7 (47%)	10 (62%)
Clinical Benefit Rate (95% CI)	67% (33 – 88)	81% (54 – 96)
Duration of Clinical Benefit (95% CI)	5.6 (4.6 – 8.1)	5.6 (3.7 – NR)

GOG Highlight Reel

Strategies in PROC: Targeting Replication Stress/PARPi Resistance

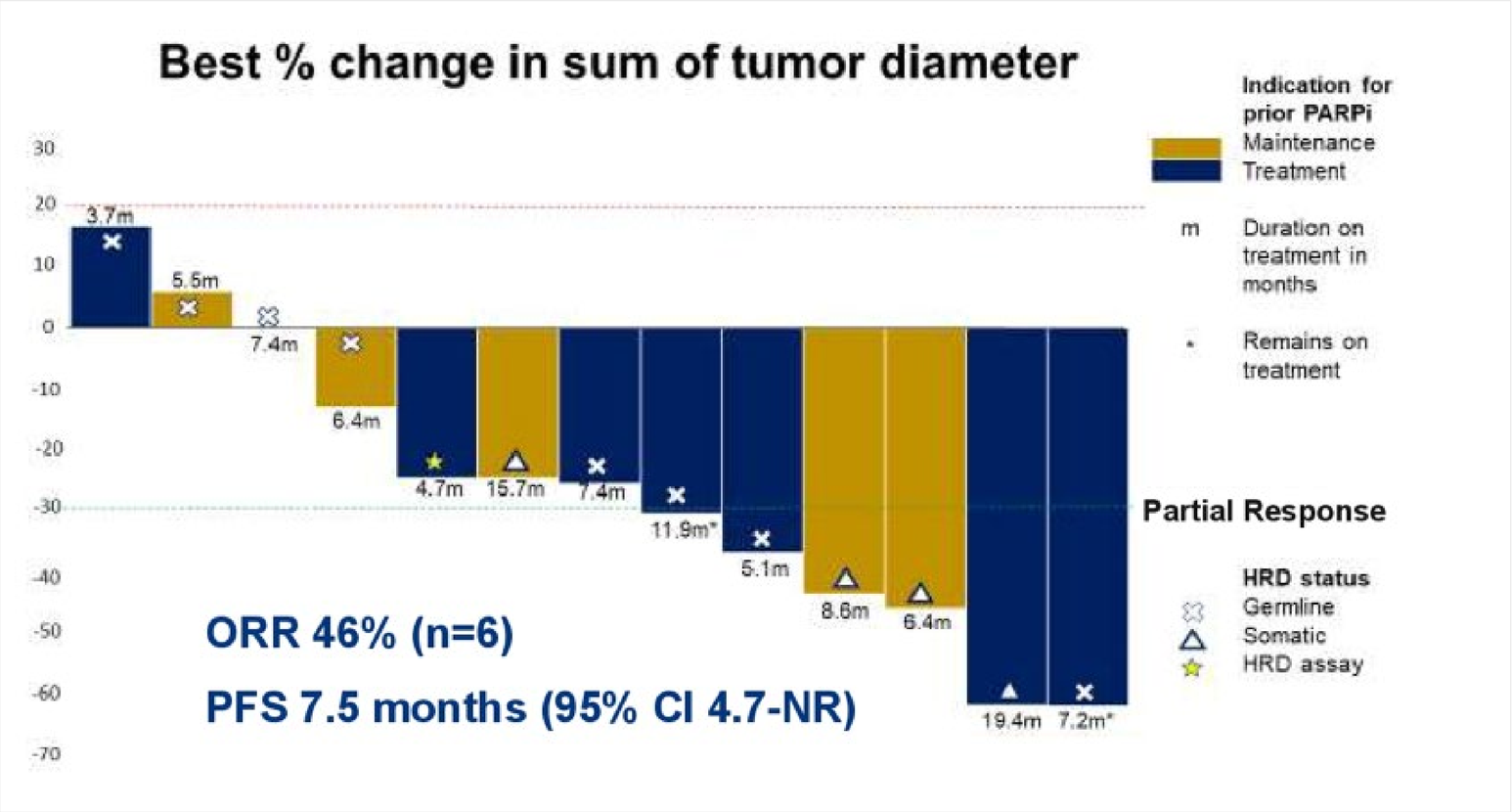
Response in Specific Treatment Groups

*BRCA*wt

Response Category	Adavosertib Alone (n=16)	Adavosertib and Olaparib (n=18)
Best Overall Response, n (%)		
Partial Response	5 (31)	7 (39)
Stable Disease	10 (63)	10 (56)
Progressive Disease	1 (6)	1 (6)
Objective Response Rate	31%	39%
95% CI	11 – 59	17 – 64
Duration of Response (95% CI)	4.1 (2.8 – NR)	8.7 (2.8 – NR)
Stable Disease > 4 months	6 (38%)	10 (56%)
Clinical Benefit Rate (95% CI)	69% (41 – 89)	94% (73 – 100)
Duration of Clinical Benefit (95% CI)	4.1 (2.8 – 7.4)	8.4 (3.1 – 10.1)

Clinical Activity of Ceralasertib + Olaparib in Patients with PARP Resistance

- 13 subjects
- BRCA/HRD
  - Germline *BRCAmut* 69% (n=9)
  - Somatic *BRCAmut* 23% (n=3)
  - Positive HRD score 8% (n=1)
- Prior PARPi
  - 1st line maintenance 8% (n=1)
  - 2nd line maintenance 38% (n=5)
  - Treatment 54% (n=7)

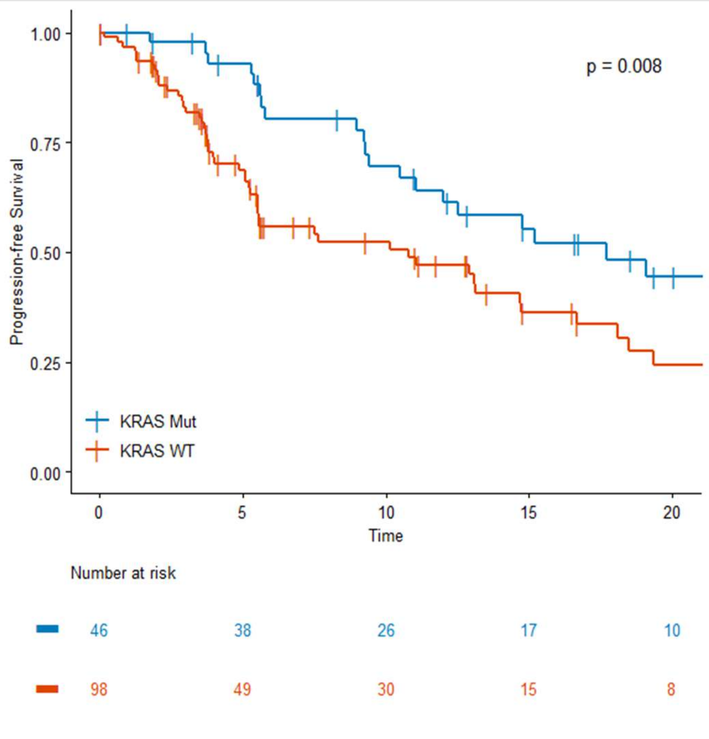


Wethington et al. ASCO 2021

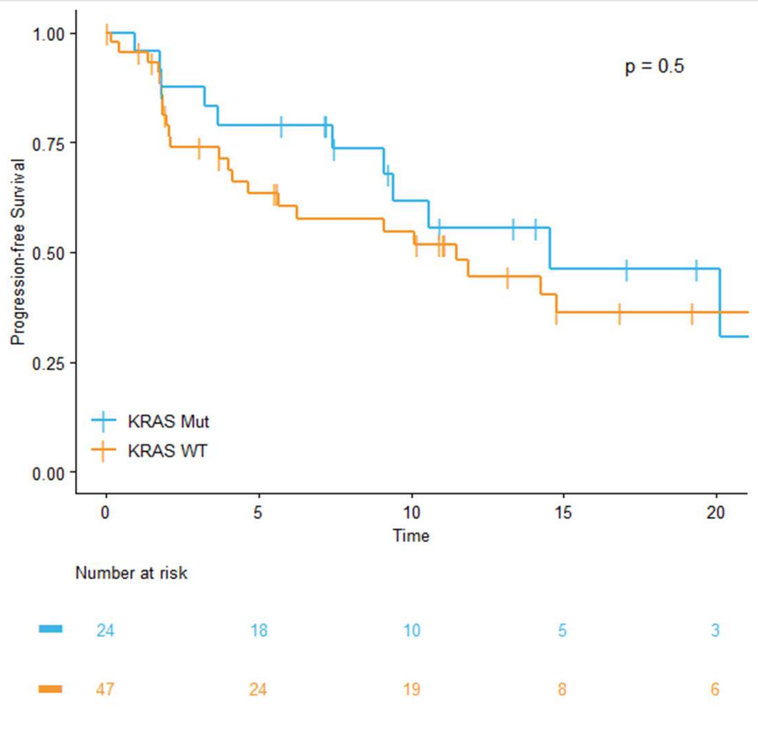
Updates in Low Grade Serous Ovarian Cancer: MILO

PFS Kaplan-Meier Plot by KRAS Mutation

Binimetinib (MEK162) Treatment



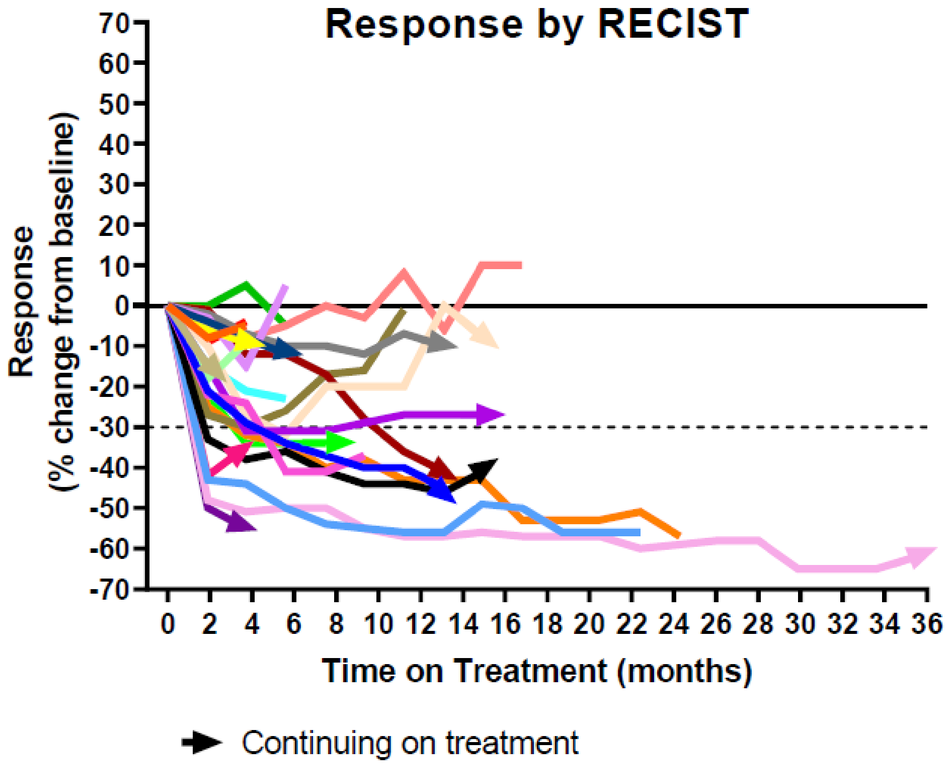
PCC Treatment

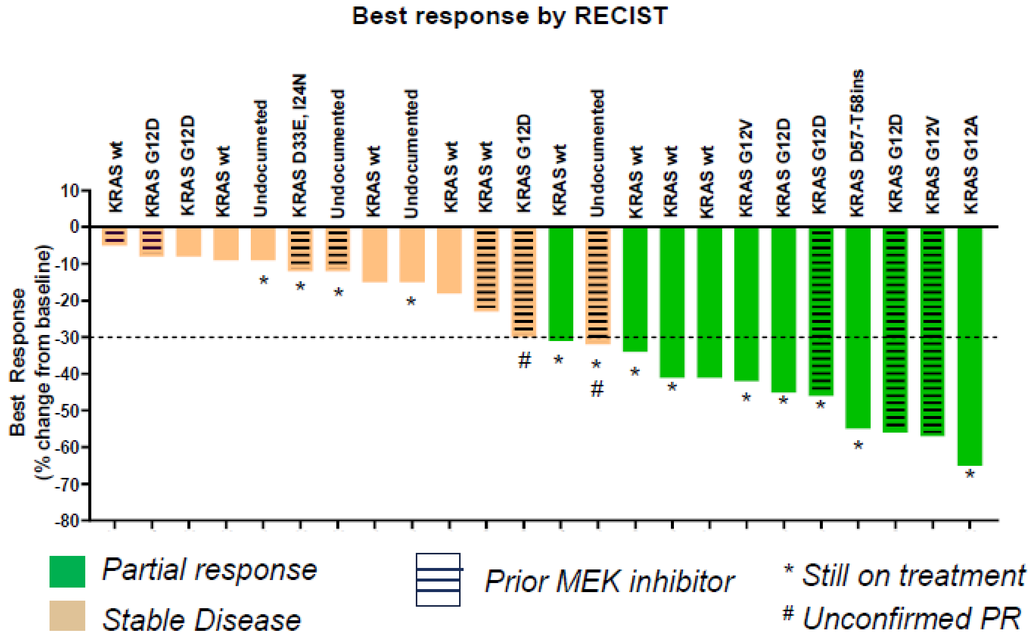


Binimetinib Treatment Group		
	N(%)	Median PFS months (95% CI)
All Patients	144	12.9 (9.4, 18.1)
KRAS mutation	46 (32%)	17.7 (12, NA)
KRAS WT	98 (68%)	10.8 (5.6, 16.7)
PCC Treatment Group		
All Patients	71	11.9 (9.1, 24.6)
KRAS mutation	24 (34%)	14.6 (9.4,NA)
KRAS WT	47 (66%)	11.5 (5.7, 26.6)

Grisham et al. ASCO 2021

Updates in Low Grade Serous Ovarian Cancer: FRAME – VS-6776 + Defactinib





- Overall response rate (ORR) = 46% (11/24)
- KRAS mutant ORR = 64% (7/11)
  - *KRAS* wild-type ORR = 44% (4/9)
  - *KRAS* status undetermined (3 SD; 1 unconfirmed PR)
- Responses in patients previously treated with MEKi
- Median PFS 23 months (95% CI 10.6-NR) across all LGSOC

Banerjee et al. ESMO 2021