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Avutometinib and Defactinib in Recurrent Low-Grade Serous Ovarian Cancer: A Phase 2 Study in Japanese Patients (RAMP201J)

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Disclosure

X	No, nothing to disclose
	Yes, please specify:

Phase 2 RAMP 201J: Study Design and Patient Baseline Characteristics

Study Design

Objective: To evaluate the efficacy, pharmacokinetics, and safety of avutometinib + defactinib in Japanese patients with recurrent LGSOC

Key eligibility criteria
- Confirmed LGSOC diagnosis
- Recurrent disease after prior platinum therapy
- Documented *KRAS* status (ie, *KRAS* mt or wt)
- Measurable disease per RECIST v1.1

Safety run-in (n=6)
- Avutometinib 3.2 mg PO BIW + defactinib 200 mg PO BID 3 weeks on, 1 week off for 1 full cycle (28 days)

No dose-limiting toxicities occurred among 6 patients enrolled and reviewed to confirm safety dose

Treatment phase (N=16)[a]
- Avutometinib 3.2 mg PO BIW 3 weeks on, 1 week off + defactinib 200 mg PO BID 3 weeks on, 1 week off

Pharmacokinetic assessment comparing Japanese to Western patients to ensure exposure equivalency[b]

Primary endpoint of the final analysis: ORR by BICR

Study status: Ongoing

The data cutoff date for this ad hoc interim analysis of investigator-assessed response was May 29, 2026

Patient Baseline Characteristics and Disposition

Characteristic	All patients (N=16)
Age, median (range), y	47 (23–72)
ECOG PS, n (%) 0 1	 14 (88) 2 (13)
KRAS status, n (%) *KRAS* mt *KRAS* wt	 7 (44) 9 (56)
Time since last recurrence, median (range), mo	3.8 (1–21)
Number of prior lines of therapy, n (%) 1, 2, or 3 ≥4	 3 (19) each 7 (44)
Prior therapy, n (%)[c] Platinum Bevacizumab PARP inhibitor therapy Hormonal therapy	 16 (100) 10 (63) 6 (38) 5 (31)

At the time of data cutoff:
- Median (range) duration of follow-up was 12.4 (5.4-18.1) mo
- 11 (69%) patients were on treatment at data cutoff, and 5 (31%)[d] patients discontinued treatment

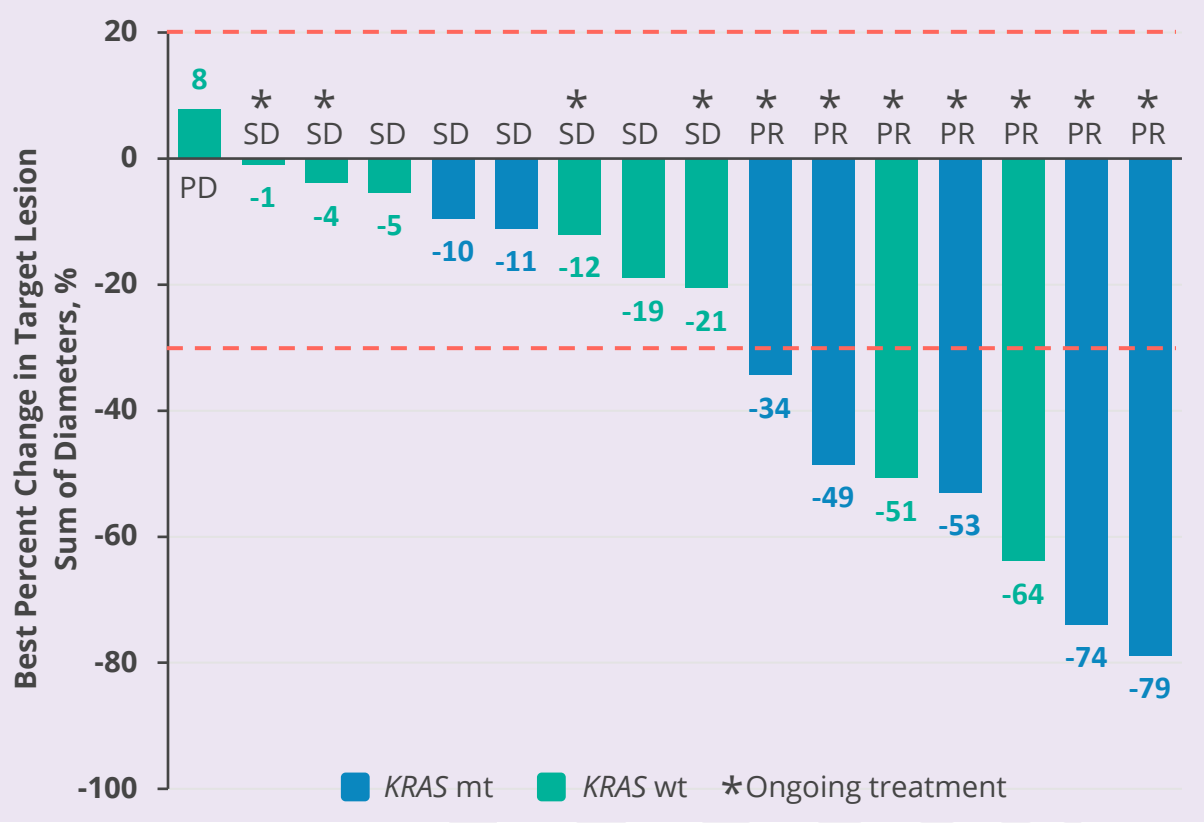
[a]Includes 6 patients from the safety run-in. [b]Includes all patients (N=16). [c]Medications used as prior therapies are consistent with the Japanese health insurance system. MEK inhibitors were not approved for LGSOC treatment in Japan at the time of study enrollment. [d]Primary reasons for discontinuation were clinical progression (n=3 [19%]), radiographic progression (RECIST 1.1; n=1 [6%]), and other reason (n=1 [6%]).

BICR, blinded independent central review; BID, twice daily; BIW, twice weekly; ECOG PS, Eastern Cooperative Oncology Group performance status; *KRAS*, Kirsten rat sarcoma virus; LGSOC, low-grade serous ovarian cancer; MEK, mitogen-activated extracellular signal-regulated kinase; mt, mutant; ORR, objective response rate; PARP, poly(ADP-ribose) polymerase; PO, orally; RECIST v1.1, Response Evaluation Criteria in Solid Tumors - Version 1.1; wt, wild-type.

ORR and Best Percent Change in Target Lesions and Response (by Investigator Assessment)

Response rates, n (%)	*KRAS* mt (n=7)	*KRAS* wt (n=9)	All patients (N=16)
Confirmed ORR	**5 (71)**	**2 (22)**	**7 (44)**
CR	0	0	0
PR	5 (71)	2 (22)	7 (44)
SD[a]	2 (29)	6 (67)	8 (50)
PD	0	1 (11)	1 (6)
DCR	7 (100)	8 (89)	15 (94)

- 44% (7/16) of patients had confirmed ORR
- 94% (15/16) of patients had a decrease in target lesions

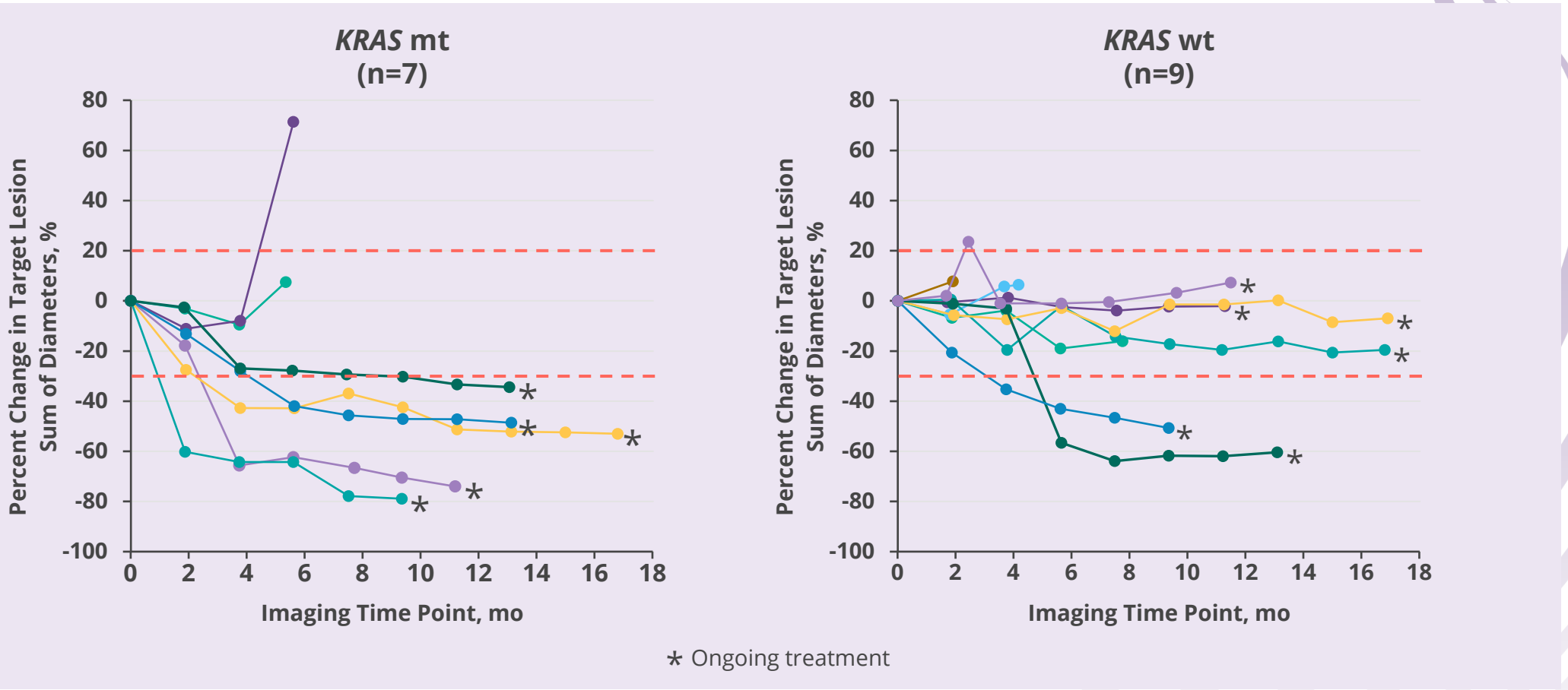


Data cutoff date of May 29, 2026. Orange dashed lines indicate thresholds for ≥20% increase and ≥30% decrease.

[a]Includes SD, unconfirmed PR, and unconfirmed CR.

BID, twice daily; BIW, twice weekly; CR, complete response; DCR, disease control rate; *KRAS*, Kirsten rat sarcoma virus; mt, mutant; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease; wt, wild-type.

Disease Control in Avutometinib + Defactinib in Patients With *KRAS* mt and *KRAS* wt LGSOC



Prolonged disease control was observed in patients with *KRAS* mt and *KRAS* wt LGSOC

Data cutoff date of May 29, 2026. All patients received ≥1 postbaseline assessment; therefore, the mITT and efficacy evaluable populations are the same. Orange dashed lines indicate thresholds for ≥20% increase and ≥30% decrease.

KRAS, Kirsten rat sarcoma virus; LGSOC, low-grade serous ovarian cancer; mITT, modified intent-to-treat; mt, mutant; wt, wild-type.

Safety Profile and Conclusions

Safety Profile

TRAEs,[a] n (%)	All patients (N=16)	
Preferred term	**All grades**	**Grade 3[b]**
Any TRAE	16 (100)	9 (56)
TRAEs (≥25% of patients)		
Nonlaboratory AEs		
Peripheral edema	9 (56)	0
Stomatitis	9 (56)	0
Diarrhea	8 (50)	0
Nausea	8 (50)	0
Rash	8 (50)	3 (19)
Malaise	7 (44)	2 (13)
Paronychia	6 (38)	0
Vision blurred	5 (31)	0
Rash maculopapular	5 (31)	1 (6)
Acne	4 (25)	0
Dermatitis acneiform	4 (25)	1 (6)
Dry eye	4 (25)	0
Laboratory-related AEs		
Increased CPK	15 (94)	3 (19)
Increased ALT	5 (31)	2 (13)
Increased blood bilirubin	5 (31)	0

- AEs were managed with dose interruptions (n=15 [93%])[c] or reductions (n=5 [31%])[d]
- No discontinuations due to AEs and no grade 4 or 5 TRAEs; 3 deaths due to PD

RAMP 201J Summary

- Avutometinib + defactinib demonstrated promising preliminary efficacy in Japanese patients with recurrent LGSOC
  - ORR: overall, 44%; *KRAS* mt, 71%; *KRAS* wt, 22%
  - DCR: overall, 94%; *KRAS* mt, 100%; *KRAS* wt; 89%
- The combination was generally well tolerated with no new safety signals and no discontinuations due to AEs
- The pharmacokinetic profiles of both avutometinib and defactinib in patients with recurrent LGSOC were similar between Japanese and Western patients[e]

Avutometinib + defactinib demonstrated promising efficacy, similar pharmacokinetics, and a manageable safety profile in Japanese patients with recurrent LGSOC, consistent with results from RAMP 201

The phase 3 study, RAMP 301 (NCT06072781), is ongoing and enrolling in Japan

Data cutoff date of May 29, 2026.

[a]Most common AEs (preferred term) considered by the investigator to be related to study drug (either avutometinib or defactinib). [b]Other grade 3 events included back pain, neck pain, anemia, hypoalbuminemia, and pyogenic granuloma (n=1 each). [c]Most common were rash and increased blood CPK (n=4 [25%] each). [d]Most common were rash (n=2 [13%]) and malaise, anemia, and increased ALT (n=1 [6%] each). [e]Data not shown. See QR code on next slide.

AE, adverse event; ALT, alanine aminotransferase; BID, twice daily; BIW, twice weekly; CPK, creatine phosphokinase; DCR, disease control rate; *KRAS*, Kirsten rat sarcoma virus; LGSOC, low-grade serous ovarian cancer; mt, mutant; ORR, objective response rate; PD, progressive disease; TRAE, treatment-related adverse event; wt, wild-type.

Acknowledgments

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This study is sponsored by Verastem Oncology.

For more information, please use this QR code to access an oral presentation presented at JSGO 2026.

JSGO, Japan Society of Gynecologic Oncology.

Kaneda M, et al. A phase 2 trial of the combination therapy of avutometinib and defactinib in Japanese patients with recurrent low-grade serous ovarian cancer. Paper presented orally at: 68th Annual Meeting of Japan Society of Gynecologic Oncology; July 17–19, 2026; Sapporo, Japan.