Relacorilant + Nab-paclitaxel vs Nab-paclitaxel in Platinum-Resistant Ovarian Cancer: Pharmacokinetics and Pharmacokinetic/Pharmacodynamic Exposure-Response

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SUMMARY AND CONCLUSIONS

- *ROSELLA is a positive phase 3 study for relacorilant and nab-paclitaxel in patients with platinum-resistant ovarian cancer that met both dual primary endpoints of progression-free survival (PFS; hazard ratio [HR], 0.70; P=0.0076) and overall survival (HR, 0.65; P=0.0004; see ESGO presentation MO1-3)*
- **Exposure-response analyses of Study-552 and ROSELLA identified no relationships between PFS and nab-paclitaxel or relacorilant exposures**
- **Similar nab-paclitaxel exposures were observed following nab-paclitaxel 80 mg/m^2 in combination with relacorilant vs nab-paclitaxel 100 mg/m^2 monotherapy, and no relationships were identified between nab-paclitaxel exposures and commonly reported adverse events (AEs)**
- **No association was observed between relacorilant exposures and the probability of AEs, except for all-grade anemia**

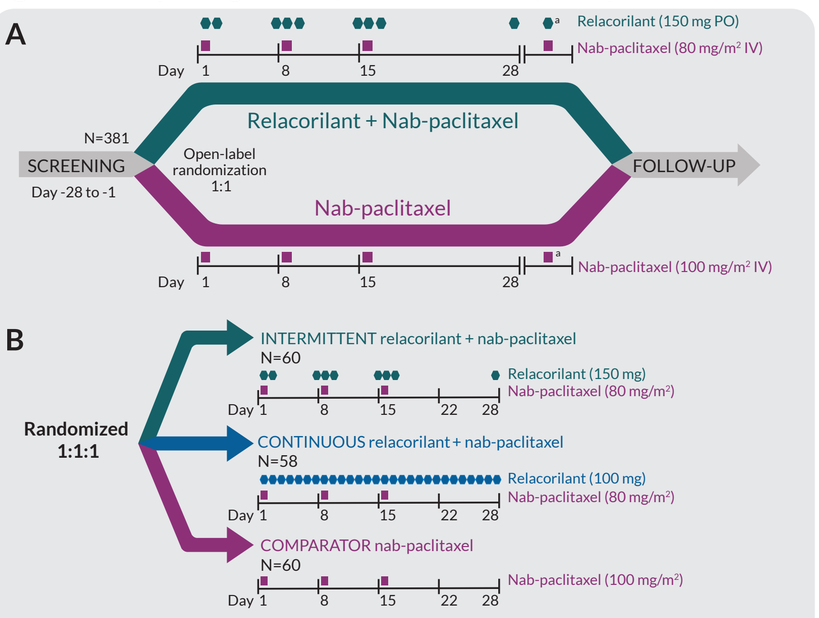
BACKGROUND AND OBJECTIVE

- Relacorilant is a novel, selective glucocorticoid receptor (GR) antagonist that restores the sensitivity of ovarian cancers to cytotoxic chemotherapy[1–4]
  - Ovarian cancers express the GR, and glucocorticoids suppress chemotherapy-induced apoptosis of tumors and the antitumor immune response[1,5–9]
- In the phase 3 ROSELLA and phase 2 Study-552 trials, adding relacorilant to nab-paclitaxel improved PFS and overall survival in patients with platinum-resistant ovarian cancer[6,10]
- Previous clinical trials have demonstrated that increasing weekly nab-paclitaxel dose and plasma exposure does not improve efficacy in patients with breast or non–small cell lung cancers[11–14]
- This pharmacokinetic/pharmacodynamic (PK/PD) exposure-response (ER) analysis evaluated relationships between nab-paclitaxel PK vs PFS and safety endpoints in Study-552 and between relacorilant PK vs PFS and safety endpoints in Study-552 and ROSELLA

METHODS

- The study designs for ROSELLA and Study-552 are given in **Figure 1**
  - Prophylactic granulocyte-colony stimulating factor treatment was required in treatment arms containing relacorilant in Study-552

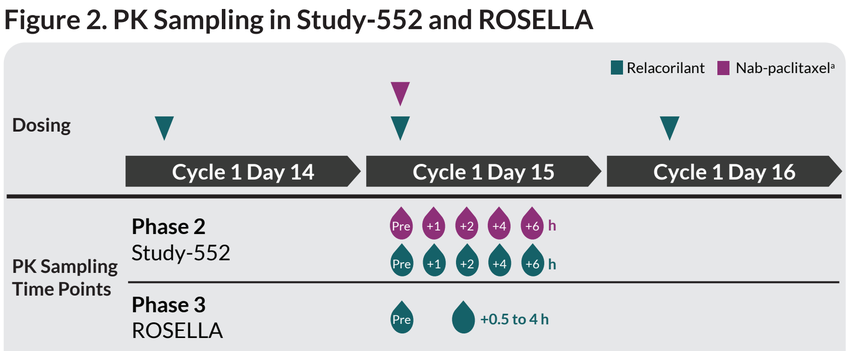
Figure 1. Study Designs for A) ROSELLA and B) Study-552



The data cutoff date for the ROSELLA analysis was February 24, 2025. [a]Ongoing cycles.
IV, intravenous; PO, by mouth.

- Because relacorilant inhibits CYP3A4 (a pathway of elimination for nab-paclitaxel), the nab-paclitaxel dose in combination with relacorilant was reduced to 80 mg/m² in both studies to provide similar plasma exposures as nab-paclitaxel 100 mg/m^2 monotherapy
- Intensive PK sampling was used in Study-552, allowing PK parameters to be determined by noncompartmental analysis, and sparse sampling in ROSELLA, where PK parameters were determined by population PK modeling (**Figure 2**)
  - Plasma concentrations were measured using validated liquid chromatography-tandem mass spectrometry assays
  - Nab-paclitaxel area under the curve (AUC_{0-6}) and maximum concentration (C_{max}) were calculated using noncompartmental analysis (Study-552)
  - Relacorilant AUC_{0-24} and C_{max} were calculated using noncompartmental analysis (Study-552) and population PK modeling (ROSELLA)

Figure 2. PK Sampling in Study-552 and ROSELLA



[a]Bioanalysis included the analyte, paclitaxel, following administration of nab-paclitaxel in patients with PROC.
h, hours; PK, pharmacokinetic; PROC, platinum-resistant ovarian cancer.

PK/PD Exposure-Response Analyses for Efficacy

- Nab-paclitaxel exposures were pooled across Study-552 dosing arms to provide the most robust dataset and most sensitive method for identifying exposure-driven trends and to evaluate whether response is associated with a potential increase in nab-paclitaxel AUC/C_{max}
- PFS was defined as the time from the date of randomization to the date of first documented progressive disease by Response Evaluation Criteria in Solid Tumors v1.1 or death from any cause

PK/PD Exposure-Response Analyses for Safety

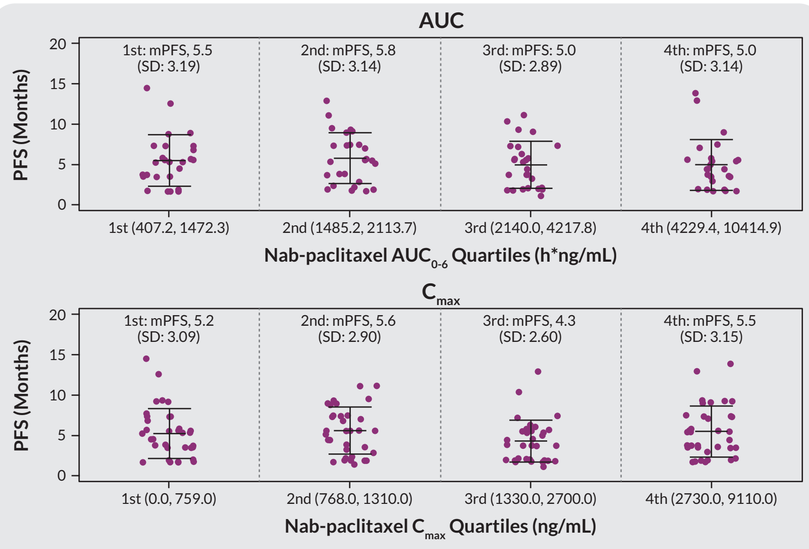
- Event endpoints were the commonly reported AEs across both studies, including peripheral neuropathy, neutropenia, anemia, skin and subcutaneous tissue disorders, and gastrointestinal (GI) disorders
  - An "event" was defined as ≥1 occurrence of any treatment-emergent AE preferred term of the specific AE. "No event" was defined as the absence of the specific AE during the entire study
- For nab-paclitaxel, scatter plotting analyses were performed for all-grade AEs
- For relacorilant, logistic regression analyses were performed to assess whether increasing exposure was associated with a higher probability of experiencing an all-grade AE
  - The logistic regression model included the continuous, log-transformed relacorilant PK parameter (AUC_{0-24} and C_{max}) as the single independent variable
  - Analyses for grade ≥3 AEs were performed for neutropenia and anemia as sufficient events allowed for meaningful analyses

RESULTS

PK/PD Exposure-Response Analyses for Efficacy

- No ER trends were observed between PFS and nab-paclitaxel AUC or C_{max} (**Figures 3 and 4**)
- Similar nab-paclitaxel exposures were observed following nab-paclitaxel 80 mg/m² in combination with relacorilant vs nab-paclitaxel 100 mg/m² monotherapy

Figure 3. No Association Between Nab-paclitaxel PK and PFS in Study-552: Scatterplot Analysis

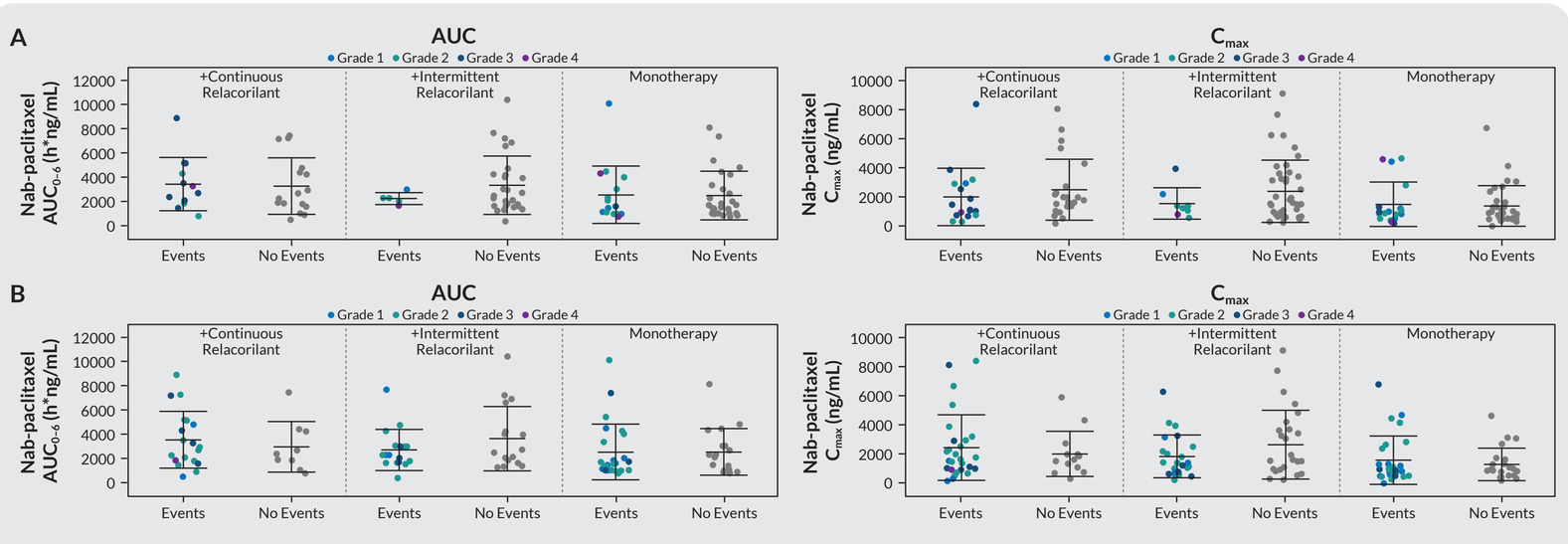


Error bars: mean ± SD. AUC, area under the curve; C_{max}, maximum plasma concentration; mPFS, mean progression-free survival; SD, standard deviation.

PK/PD Exposure-Response Analyses for Safety

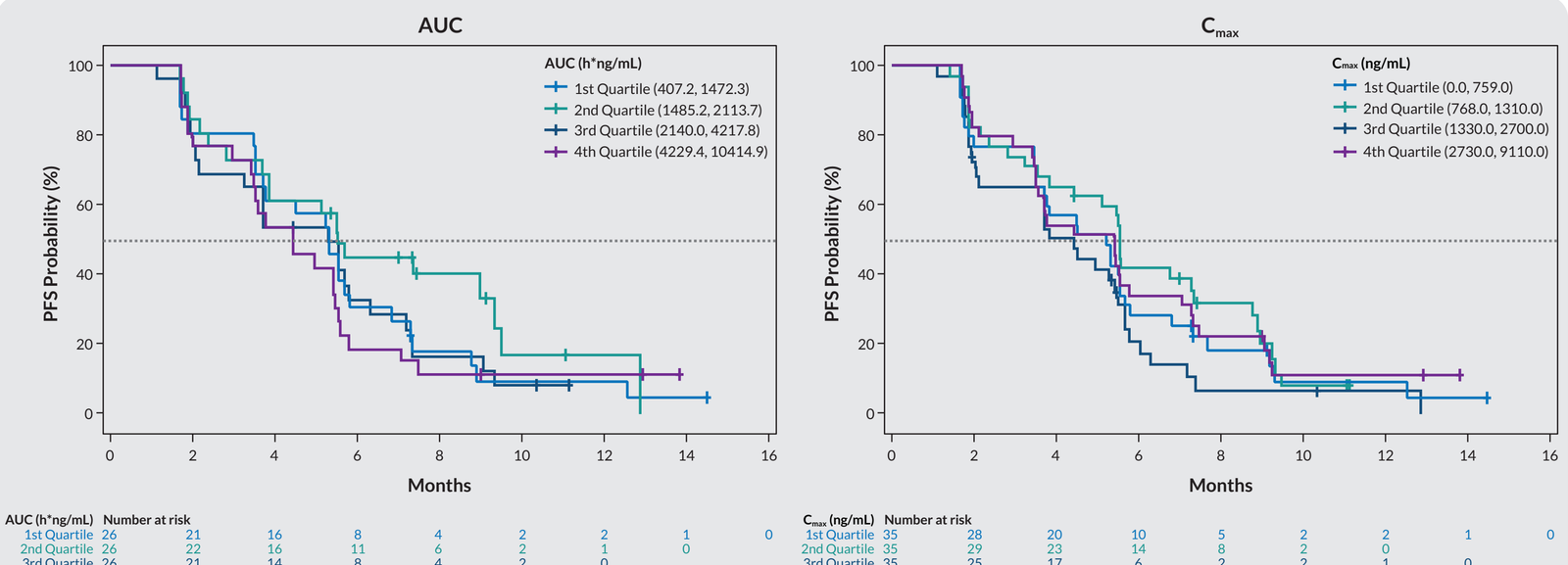
- The range of nab-paclitaxel plasma exposures (AUC and C_{max}) observed were similar between patients with the occurrence of a specific AE and no event reported
- No ER trends were observed between nab-paclitaxel exposure and occurrence of neutropenia or anemia (**Figure 6**), which are well-characterized risks of nab-paclitaxel. There were also no ER trends between nab-paclitaxel exposure and the occurrence of peripheral neuropathy, skin and subcutaneous tissue disorders, and GI disorders

Figure 6. No Association Between Nab-paclitaxel PK and A) Neutropenia or B) Anemia in Study-552: Scatterplot Analysis



Error bars: mean ± SD.
AUC, area under the curve; C_{max}, maximum plasma concentration; SD, standard deviation.

Figure 4. No Association Between Nab-paclitaxel PK and PFS in Study-552: Kaplan-Meier Curves



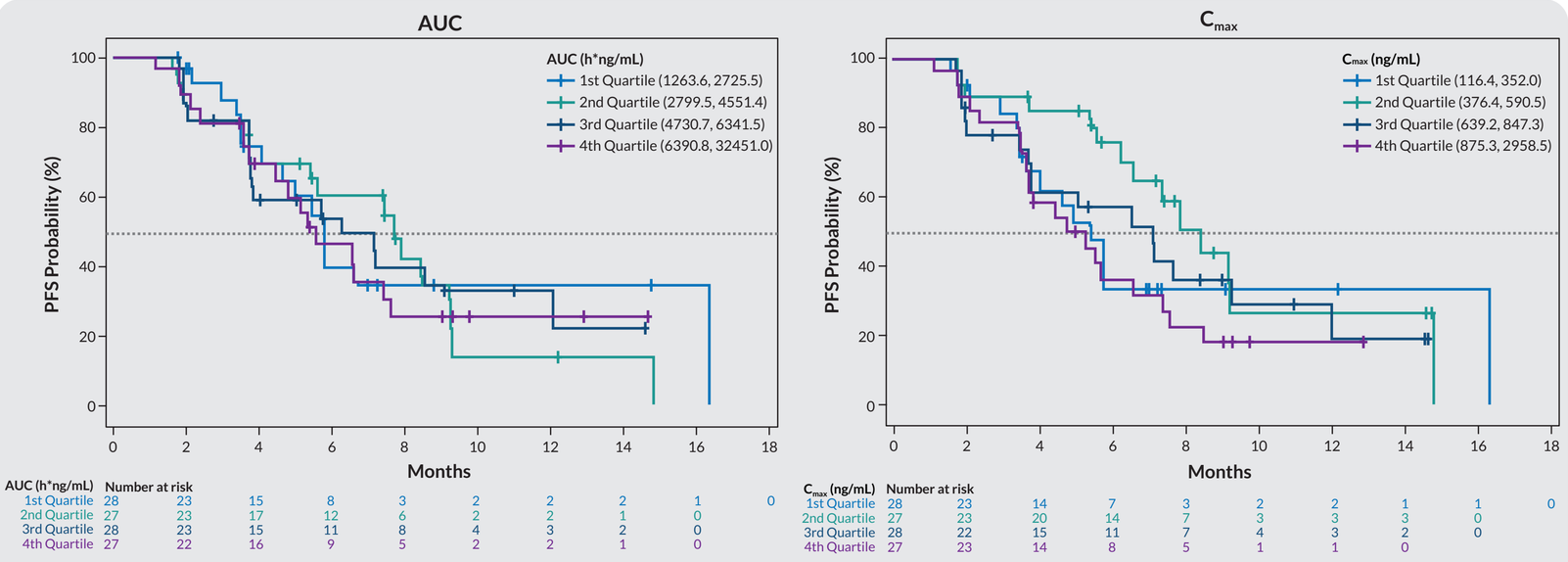
AUC (h*ng/mL)	Number at risk								
1st Quartile	26	21	16	8	4	2	2	1	0
2nd Quartile	26	22	16	11	6	2	1	0	
3rd Quartile	26	21	14	8	4	2	0		
4th Quartile	26	20	14	5	3	2	2	0	

Cmax (ng/mL)	Number at risk								
1st Quartile	35	28	20	10	5	2	2	1	0
2nd Quartile	35	29	23	14	8	2	0		
3rd Quartile	35	25	17	6	2	2	1	0	
4th Quartile	35	29	19	12	7	2	2	0	

AUC, area under the curve; C_{max}, maximum plasma concentration; PFS, progression-free survival.

- No ER trends were observed between relacorilant PK and PFS in ROSELLA or Study-552 (**Figure 5** presents results from ROSELLA)

Figure 5. No Association Between Relacorilant PK and PFS in ROSELLA: Kaplan-Meier Curves



AUC (h*ng/mL)	Number at risk								
1st Quartile	28	23	15	8	3	2	2	2	1	0
2nd Quartile	27	23	17	12	6	2	2	1	0
3rd Quartile	28	23	15	11	8	4	3	2	0
4th Quartile	27	22	16	9	5	2	2	1	0

Cmax (ng/mL)	Number at risk								
1st Quartile	28	23	14	7	3	2	2	1	1	0
2nd Quartile	27	23	20	14	7	3	3	3	0	
3rd Quartile	28	22	15	11	7	4	3	2	0	
4th Quartile	27	23	14	8	5	1	1	0		

AUC, area under the curve; C_{max}, maximum plasma concentration; PFS, progression-free survival.

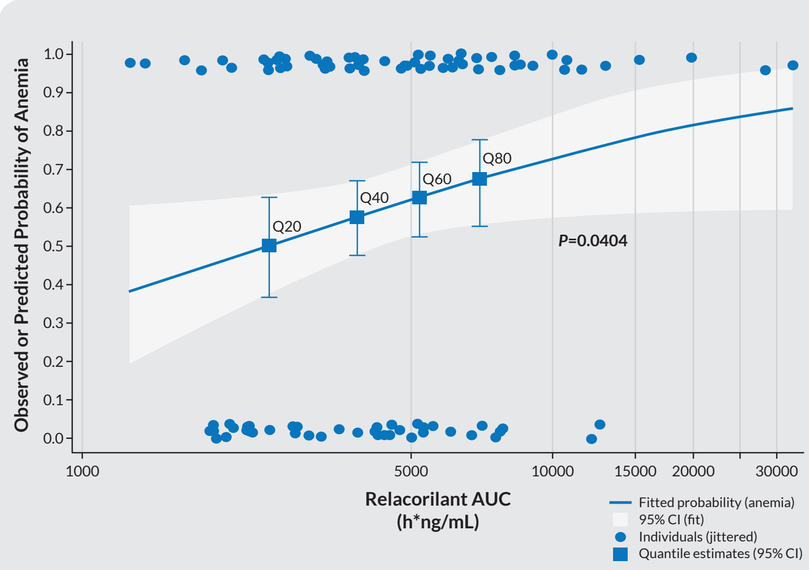
- Logistic regression analyses identified no association between relacorilant PK and the probability of occurrence of neutropenia, peripheral neuropathy, skin and subcutaneous tissue disorders, and GI disorders (**Table 1**)
- Increasing relacorilant AUC was associated with a statistically significant increase in the probability of observing an occurrence of anemia and may reflect an additive effect or synergy (**Table 1 and Figure 7**)
- No relationship was observed between increasing probability of grade ≥3 anemia with increasing relacorilant exposures (AUC and C_{max})

Table 1. Logistic Regression Analysis for the Association Between Relacorilant PK and Safety Events in the ROSELLA Study

Adverse Event	Logistic Regression Analyses	*P* Values	
		AUC	C_{max}
Peripheral neuropathy	All-grade	0.2454	0.3469
Skin and subcutaneous tissue disorders	All-grade	0.5358	0.9281
GI disorders	All-grade	0.2200	0.2122
Neutropenia	All-grade	0.1616	0.4274
	Grade ≥3	0.1062	0.4956
Anemia	All-grade	0.0404	0.1278
	Grade ≥3	0.4369	0.9832

AUC, area under the curve; C_{max}, maximum plasma concentration; GI, gastrointestinal.

Figure 7. Association Between Relacorilant AUC and All-Grade Anemia in the ROSELLA Study



AUC, area under the curve; CI, confidence interval; Q, quantile.

References

1. Greenstein AE, Hunt HJ. *Oncotarget*. 2021;12(13):1243–1255. **2.** Stringer-Reasor EM, et al. *Gynecol Oncol*. 2015;138(3):656–662. **3.** Munster PN, et al. *Clin Cancer Res*. 2022;28(15):3214–3224. **4.** Greenstein AE, Hunt HJ. *Int Immunopharmacol*. 2023;120:110312. **5.** Veneris JT, et al. *Gynecol Oncol*. 2017;146(1):153–160. **6.** Colombo N, et al. *J Clin Oncol*. 2023;41(30):4779–4789. **7.** Melhem A, et al. *Clin Cancer Res*. 2009;15(9):3196–3204. **8.** Chen L, et al. *Inflammopharmacol*. 2018;26:1331–1338. **9.** Block TS, et al. *Cancer Manag Res*. 2017;9:65–72. **10.** Olawaiye AB, et al. *Lancet*. 2025; 405(10496):2205–2216. **11.** Gradishar WJ, et al. *J Clin Oncol*. 2009;27(22):3611–3619. **12.** Nyman DW, et al. *J Clin Oncol*. 2005;23(31):7785–7793. **13.** Biganzoli L, et al. *Breast Cancer Res*. 2020;22(1):83. **14.** Takeuchi S, et al. *Cancer Med*. 2023;12(8):9133–9143.

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Presenter Disclosure

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