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Supplementary information

New standards and new constraints redefine treatment sequencing in platinum-resistant ovarian cancer

In the format provided by the authors and unedited

Supplementary Fig. 1 | Three regimens in platinum-resistant ovarian cancer: trial-level comparison (A)

Trial / regimen	KEYNOTE-B96[4] Pembro + weekly paclitaxel ± bevacizumab	ROSELLA[5] Relacorilant + nab-paclitaxel	MIRASOL[3] Mirvetuximab soravtansine
Mechanism added to taxane	PD-1 checkpoint blockade ± VEGF inhibition (bevacizumab in ~73%)	Selective glucocorticoid receptor antagonism Restores chemosensitivity	FRα-directed antibody–drug conjugate (DM4 payload; monotherapy, no chemo partner)
Patients randomized (*n*) Prior systemic lines	643 overall; 466 in CPS ≥1 1–2 prior lines	381 1–3 prior lines	453 1–3 prior lines
Biomarker requirement	**PD-L1 CPS ≥1 for label/benefit** All-comers enrolled; benefit clearest CPS ≥1	**None** Biomarker-unselected	**FRα-high (PS2+ ≥75%, ≥2+ staining)** ~32% of patients screened were eligible
Prior therapies	Platinum-based (1–2 lines) Prior bevacizumab not required (36% prior Bevacizumab), 37% prior PARP-i	Platinum + bevacizumab (both required) 61% prior PARP-i; 43% 2 prior PROC lines	Platinum-based (1–3 lines) 62% prior bevacizumab; 55% prior PARP-I, 46% 2 prior PROC lines
Median PFS (months) Hazard ratio	8.4 vs 7.6 (CPS ≥1); 8.3 vs 6.4 (overall) HR 0.72 (CPS ≥1); 0.71 (overall) by BICR	6.54 vs 5.52 (BICR) HR 0.70 (0.54–0.91); p=0.0076	5.62 vs 3.98 HR 0.65 (sensitivity 0.72 by BICR); p<0.001
Median OS (months) Hazard ratio (95% CI)	**18.2 vs 14.0 (CPS ≥1)** HR 0.76 (final analysis)	**16.0 vs 11.9 (updated final)** HR 0.65 (0.51–0.83); p=0.0004	**16.46 vs 12.75** HR 0.67 (0.50–0.89); p=0.005
ORR (investigator)	53.0% vs 46.6% (CPS ≥1) 50.4% vs 41.1% (overall); DOR 10.4 vs 8.1 mo	36.9% vs 30.1% Clinical benefit rate 51.1% vs 38.9% at 24 wk	42.3% vs 15.9% CR 5.3% vs 0%; DOR 6.8 vs 4.5 mo
Distinctive toxicity	Immune-related AEs	↑ Gr ≥3 neutropenia (44 vs 25%), anaemia (18 vs 8%), fatigue (9 vs 2%)	Ocular: blurred vision 41%, keratopathy 32%
Patient-reported outcomes	Reported separately QLQ-OV28/C30 collected in primary publication	Not yet reported in detail QLQ-OV28/C30 collected	HRQoL maintained vs chemo Attitude, fatigue, global health status-QoL nominally favored MIRV

A practical decision frame (B)

A single patient might be eligible for one, two or all three regimens depending on biomarkers and prior therapy.

2nd-line, PD-L1 CPS ≥1, FRα-high, no prior bevacizumab

All three are biologically eligible.
— Pembro + paclitaxel ± bev: largest OS signal (18.2 mo)
— Relacorilant + nab-paclitaxel: needs prior bev (not had)
— Mirvetuximab: avoids taxane re-exposure

Decision drivers
cumulative neuropathy risk, ocular toxicity tolerance, access to bevacizumab, need for visible response

3rd-line, post-bev, post-PARPi, FRα-low or unknown

Pembro regimen often inaccessible (prior lines, label); mirvetuximab excluded by biomarker.
— Relacorilant + nab-paclitaxel: the patient most directly represented in ROSELLA

Decision drivers
marrow reserve, prior taxane-free interval, tolerance for combination toxicity

2nd–3rd line, FRα-high, prior taxane and bevacizumab

Mirvetuximab uniquely offers a non-taxane backbone with maintained HRQoL.
— Mirvetuximab: monotherapy ADC, no chemo partner
— Relacorilant + nab-paclitaxel: another taxane line

Decision drivers
existing neuropathy, ocular care, access, patient preference for monotherapy

ADC, antibody–drug conjugate; AEs adverse events; bev, bevacizumab; BICR, blinded independent central review; chemo, chemotherapy; CR, complete response; CPS, combined positive score; DOR, duration of response; FRα, folate receptor α; GR, grade; HR, hazard ratio; HRQoL, health-related quality of life; MIRV, mirvetuximab soravtansine; PARP-I, poly(ADP-ribose) polymerase inhibitor; pembro, pembrolizumab; PROC, platinum-resistant ovarian cancer;

All cross-trial comparisons are descriptive: no head-to-head trial exists, populations are nested but non-identical, and control arms differ.