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Meta-Analysis of Treatments for Platinum-Resistant Ovarian Cancer (PROC)

vs. Standard Chemotherapy

Based on Clinical trials

By Suchibrata

Background and Objective

This study aimed to conduct a meta-analysis, systematically integrating findings from multiple independent clinical trials. The goal was to derive more robust and generalizable conclusions about treatment efficacy for platinum-resistant ovarian cancer (PROC) than what could be inferred from individual studies alone.

We extracted and summarized key clinical endpoints - Overall Survival (OS), Progression-Free Survival (PFS), and Objective Response Rate (ORR) - from seven randomized phase III trials. These trials evaluated various investigational therapies compared to different single-agent chemotherapy regimens commonly used in PROC.

Methodology

Software Used - R

Models : Fixed Effect and Random Effects model.

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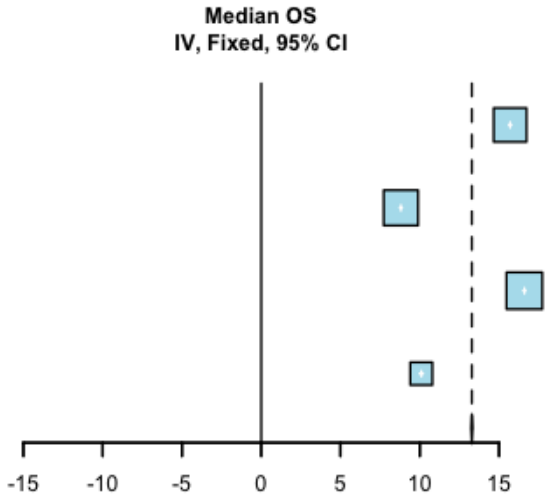
Forest plot for fixed effect model for overall survival

Study or Subgroup	Median OS	SE	Weight	Median OS IV, Fixed, 95% CI
Treatment = Avelumab+chemotherapy(PLD)				
JAVELIN Ovarian 200	15.7000	0.0394	26.8%	15.70 [15.62; 15.78]
Treatment = oral PXD+AUC2-carboplatin				
OVATURE	8.8100	0.0377	29.3%	8.81 [8.74; 8.88]
Treatment = bevacizumab+chemotherapy				
AURELIA	16.6000	0.0362	31.8%	16.60 [16.53; 16.67]
Treatment = nivolumab				
NINJA	10.1000	0.0587	12.1%	10.10 [9.98; 10.22]
Total (95% CI)			**100.0%**	**13.29 [13.25; 13.33]**



Heterogeneity: $Tau^2 = 15.3518$; $Chi^2 = 29151.20$, df = 3 (P = 0); $I^2 = 100.0\%$
Test for overall effect: Z = 650.75 (P = 0)
Test for overall effect: Z = 6.53 (P < 0.0001)
Test for subgroup differences: $Chi^2 = 29151.20$, df = 3 (P = 0)

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Interpretation

I^2 = 100%, chi-square p < 0.0001

→ Indicates extremely high heterogeneity across studies.

→ The differences in survival outcomes are not due to random variation.

→ Suggests the presence of true clinical or methodological differences between trials.

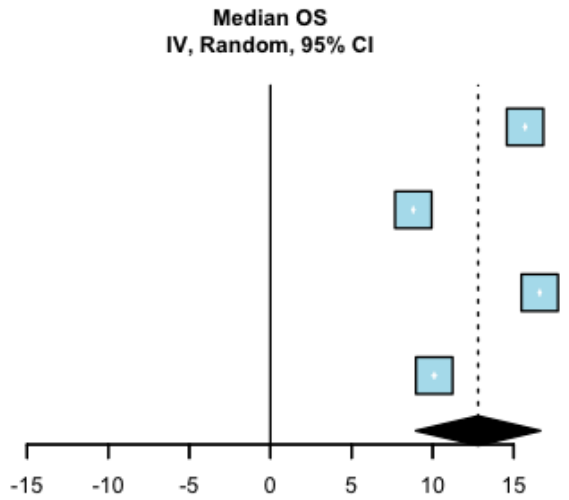
→ Fixed-effect model assumptions are likely violated — a random-effects model is more appropriate.

χ^2 = 29,151.20, degrees of freedom = 3, p < 0.0001 (Subgroup analysis)

→ Subgroup differences are highly significant. → Indicates that treatment type has a significant impact on overall survival (OS).

Forest plot for random effect model for overall survival

Study or Subgroup	Median OS	SE	Weight	Median OS IV, Random, 95% CI
Treatment = Avelumab+chemotherapy(PLD)				
JAVELIN Ovarian 200	15.7000	0.0394	25.0%	15.70 [15.62; 15.78]
Treatment = oral PXD+AUC2-carboplatin				
OVATURE	8.8100	0.0377	25.0%	8.81 [8.74; 8.88]
Treatment = bevacizumab+chemotherapy				
AURELIA	16.6000	0.0362	25.0%	16.60 [16.53; 16.67]
Treatment = nivolumab				
NINJA	10.1000	0.0587	25.0%	10.10 [9.98; 10.22]
Total (95% CI)			**100.0%**	**12.80 [8.96; 16.64]**



Heterogeneity: Tau^2 = 15.3518; Chi^2 = 29151.20, df = 3 (P = 0); I^2 = 100.0%
Test for overall effect: Z = 650.75 (P = 0)
Test for overall effect: Z = 6.53 (P < 0.0001)
Test for subgroup differences: Chi^2 = 29151.20, df = 3 (P = 0)

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Interpretation

I^2 = 100%, Tau^2 = 15.35, χ^2 p < 0.0001

→ Indicates extremely high heterogeneity across studies.

→ The magnitude of between-study variance (Tau^2 = 15.35) confirms that differences in OS are substantial and not due to chance.

→ Strongly suggests the presence of true clinical or methodological variability across trials.

→ A random-effects model is more appropriate in this context.

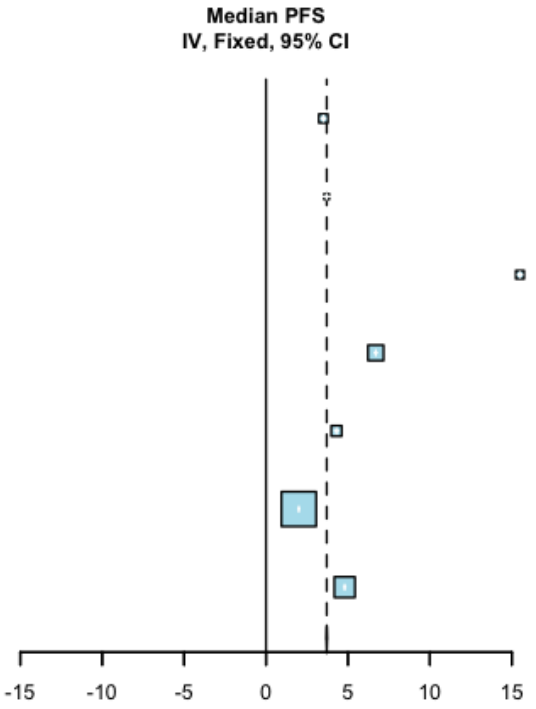
χ^2 = 29,151.20, degrees of freedom = 3, p < 0.0001 (Subgroup analysis)

→ Demonstrates that overall survival (OS) differs significantly across treatment types.

→ Indicates a strong subgroup effect, likely reflecting differences in treatment mechanisms or patient populations.

Forest plot for fixed effect model for progression free survival

Study or Subgroup	Median PFS	SE	Weight	Median PFS IV, Fixed, 95% CI
Treatment = lurbinectedin				
CORAIL	3.5000	0.0628	3.7%	3.50 [3.38; 3.62]
Treatment = Avelumab+PLD				
JAVELIN Ovarian 200	3.7000	0.1046	1.3%	3.70 [3.49; 3.91]
Treatment = oral PXD+AUC2-carboplatin				
OVATURE	15.5000	0.0679	3.2%	15.50 [15.37; 15.63]
Treatment = bevacizumab+chemotherapy				
AURELIA	6.7000	0.0362	11.2%	6.70 [6.63; 6.77]
Treatment = pertuzumab+chemotherapy				
PENELOPE	4.3000	0.0536	5.1%	4.30 [4.20; 4.40]
Treatment = nivolumab				
NINJA	2.0000	0.0162	55.7%	2.00 [1.97; 2.03]
Treatment = MIRV				
FORWARD I	4.8000	0.0273	19.7%	4.80 [4.75; 4.85]
Total (95% CI)			**100.0%**	**3.71 [3.68; 3.73]**



Heterogeneity: Tau^2 = 20.3765; Chi^2 = 49778.80, df = 6 (P = 0); I^2 = 100.0%
Test for overall effect: Z = 305.90 (P = 0)
Test for overall effect: Z = 3.39 (P = 0.0007)
Test for subgroup differences: Chi^2 = 49778.80, df = 6 (P = 0)

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Interpretation

I^2 = 100%, χ^2 p < 0.0001

→ Indicates extreme heterogeneity — the studies are likely estimating different treatment effects.

→ Fixed-effect model assumptions are invalid in this context due to non-random variation across studies.

→ Strongly supports the use of a random-effects model.

χ^2 = 49,778.80, degrees of freedom = 6, p < 0.0001 (Subgroup analysis)

→ Confirms statistically significant differences in progression-free survival (PFS) across treatment groups.

→ Suggests that treatment type meaningfully influences PFS outcomes. Pooled Median PFS = 3.71 months [95% CI: 3.68–3.73]

→ The narrow confidence interval is misleading due to extreme heterogeneity (I^2 = 100%).

→ Interpretation of this pooled estimate should be cautious, as it may oversimplify true between-study variability.

Forest plot for random effect model for progression free survival

Study or Subgroup	Median PFS	SE	Weight	Median PFS IV, Random, 95% CI
Treatment = lurbinectedin				
CORAIL	3.5000	0.0628	14.3%	3.50 [3.38; 3.62]
Treatment = Avelumab+PLD				
JAVELIN Ovarian 200	3.7000	0.1046	14.3%	3.70 [3.49; 3.91]
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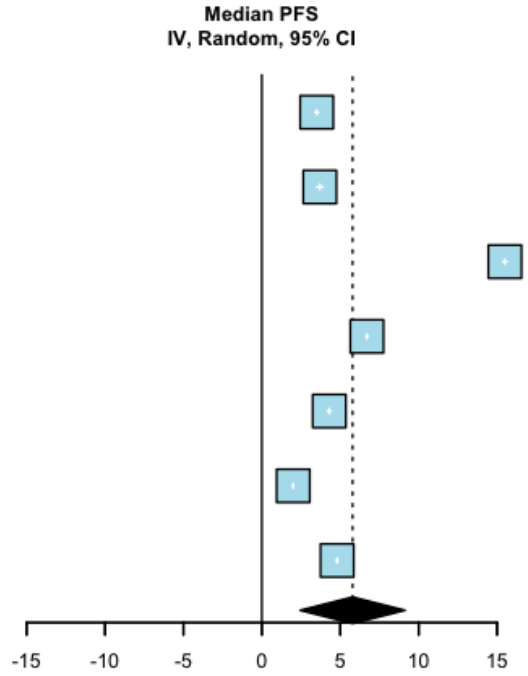
Treatment = MIRV				
FORWARD I	4.8000	0.0273	14.3%	4.80 [4.75; 4.85]
Total (95% CI)			**100.0%**	**5.79 [2.44; 9.13]**



Heterogeneity: $Tau^2 = 20.3765$; $Chi^2 = 49778.80$, df = 6 (P = 0); $I^2 = 100.0\%$
Test for overall effect: Z = 305.90 (P = 0)
Test for overall effect: Z = 3.39 (P = 0.0007)
Test for subgroup differences: $Chi^2 = 49778.80$, df = 6 (P = 0)

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Interpretation

I^2 = 100%, Tau^2 = 20.38, χ^2 p < 0.0001

→ Indicates extremely high heterogeneity across studies.

→ Suggests that trials likely differ in design, patient populations, or treatment efficacy.

→ The pooled estimate should be interpreted with caution, as studies are not estimating a single common effect.

χ^2 = 49,778.80, degrees of freedom = 6, p < 0.0001 (Subgroup analysis)

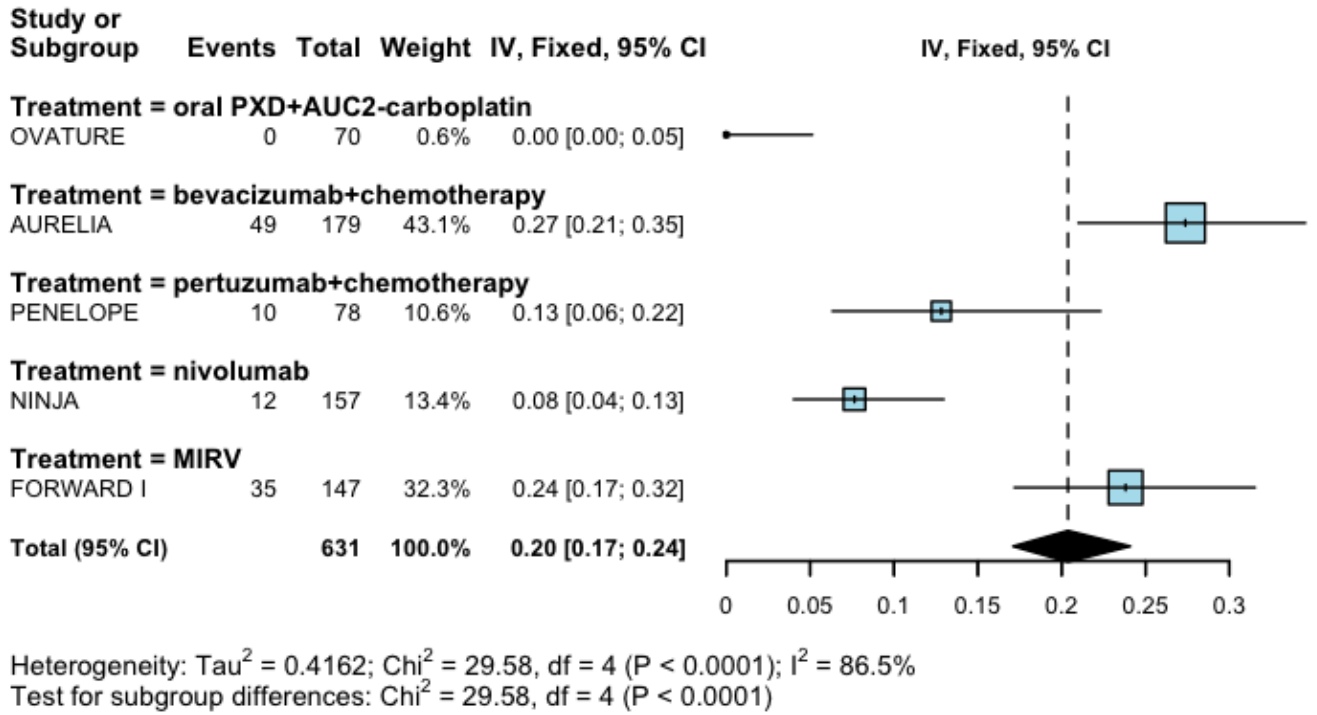
→ Confirms statistically significant variation in PFS outcomes across treatment groups.

→ Strongly supports the presence of treatment-dependent differences in progression-free survival. Pooled Median PFS = 5.79 months [95% CI: 2.44–9.13]

→ The wide confidence interval reflects substantial uncertainty and between-study variability.

→ Highlights the importance of considering study-level factors when interpreting pooled results.

Forest plot for fixed effect model for Objective Response Rate



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Interpretation

I^2 = 86.5%, χ^2 p < 0.0001

→ Indicates high heterogeneity across studies.

→ The assumption of a common treatment effect (fixed-effect model) is not valid.

→ Suggests substantial variability in response rates due to differences in study design, population, or interventions.

χ^2 = 29.58, degrees of freedom = 4, p < 0.0001 (Subgroup analysis)

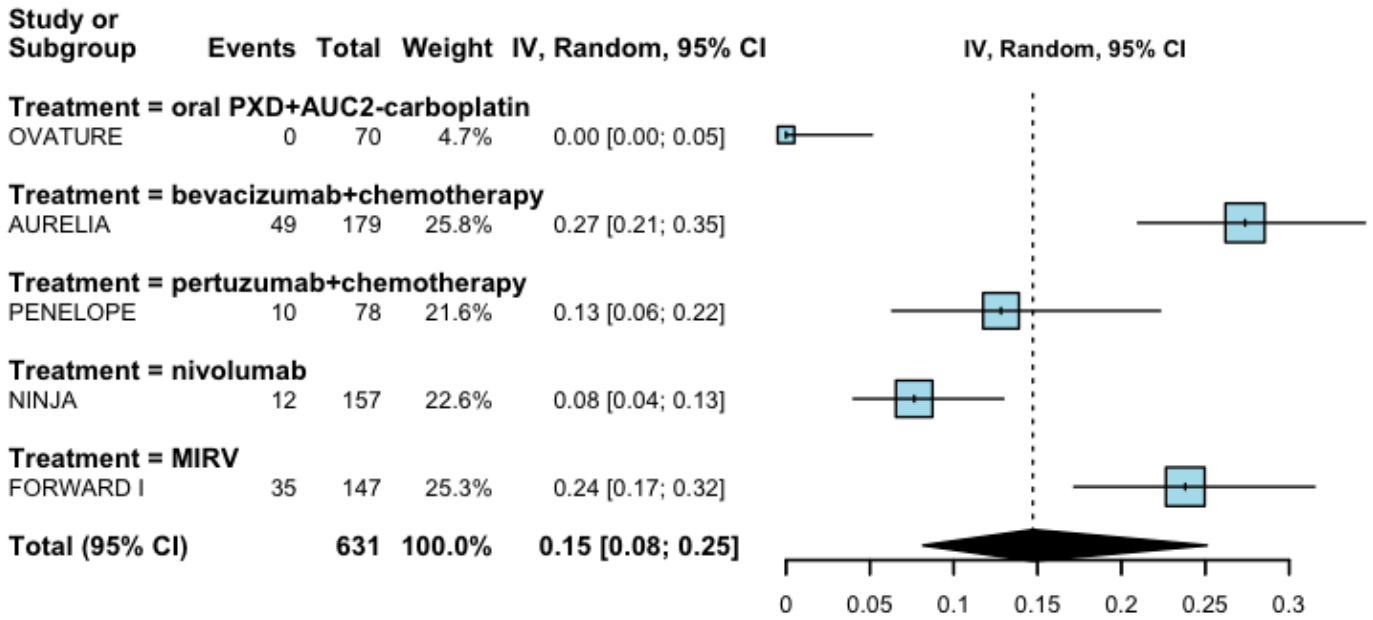
→ Confirms that objective response rates (ORR) vary significantly across treatment types.

→ Points to meaningful differences in efficacy between therapies. Fixed-Effect Pooled ORR = 20% [95% CI: 17% to 24%]

→ Indicates a moderate overall response rate across all included studies. → However, due to high heterogeneity (I^2 = 86.5%), this pooled estimate may be misleading.

→ A random-effects model would provide a more reliable and generalizable estimate.

Forest plot for Random Effect model for Objective Response Rate



Heterogeneity: $Tau^2 = 0.4162$; $Chi^2 = 29.58$, df = 4 ($P < 0.0001$); $I^2 = 86.5\%$
Test for subgroup differences: $Chi^2 = 29.58$, df = 4 ($P < 0.0001$)

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Interpretation

I^2 = 86.5%, Tau^2 = 0.42, χ^2 p < 0.0001

→ Indicates substantial heterogeneity in objective response rates across studies.

→ Suggests real differences in treatment efficacy, study populations, or trial design.

→ Justifies the use of a random-effects model to account for this variability and provide a more generalizable estimate.

χ^2 = 29.58, degrees of freedom = 4, p < 0.0001 (Subgroup analysis)

→ Demonstrates statistically significant differences in ORR between treatment types.

→ Confirms that treatment selection meaningfully impacts response outcomes in platinum-resistant ovarian cancer.

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