Weekly paclitaxel, pegylated liposomal doxorubicin or topotecan ± bevacizumab in platinum-resistant recurrent ovarian cancer: Analysis by chemotherapy cohort in the GCIG AURELIA randomised phase III trial

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Disclosures

- A Poveda, I Vergote: Roche (advisory boards)
- F Selle: Roche, PharmaMar (consultancy)
- F Hilpert, E Pujade-Lauraine: Roche (honoraria)
- A Bamias: Roche, GlaxoSmithKline (advisory boards)
- D Bollag: Roche (employee)
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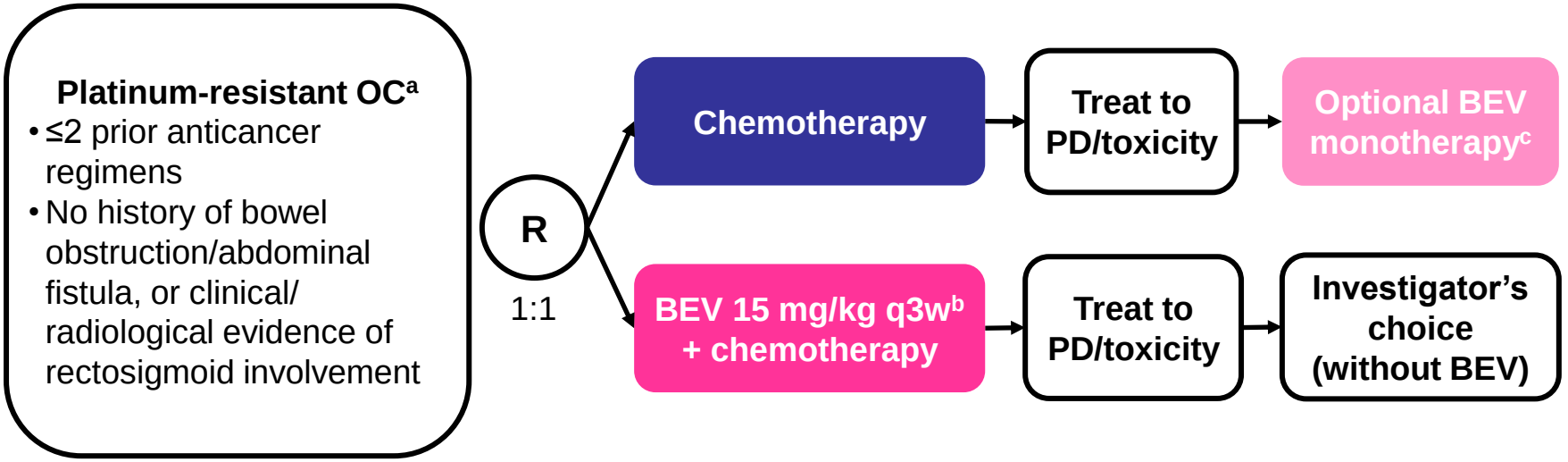
Background

- Ovarian cancer (OC) is a highly VEGF-driven disease
- Bevacizumab (BEV) significantly improves PFS when combined with CT and continued as a single agent in the:
  - Front-line setting (GOG-0218, ICON7)[1,2]
  - Platinum-sensitive recurrent setting (OCEANS)[3]
- The randomised phase III AURELIA trial demonstrated significantly improved PFS (primary endpoint) and ORR with the addition of BEV to CT in platinum-resistant OC[4]
  - PFS hazard ratio 0.48 (95% CI: 0.38–0.60; p<0.001)
  - Median PFS: 6.7 vs 3.4 months with chemotherapy alone
- We report an exploratory subgroup analysis according to CT cohort
  - CT was selected by the investigator before randomisation

CT = chemotherapy; ORR = overall response rate; PFS = progression-free survival; VEGF = vascular endothelial growth factor
1. Burger NEJM 2011; 2. Perren NEJM 2011; 3. Aghajanian JCO 2012; 4. Pujade-Lauraine ASCO 2012

AURELIA trial design



Stratification factors:

- Chemotherapy selected
- Prior anti-angiogenic therapy
- Treatment-free interval (<3 vs 3–6 months from previous platinum to subsequent PD)

Chemotherapy options (investigator's choice):

- Paclitaxel 80 mg/m^2 days 1, 8, 15, & 22 q4w
- Topotecan 4 mg/m^2 days 1, 8, & 15 q4w (or 1.25 mg/m^2, days 1–5 q3w)
- PLD 40 mg/m^2 day 1 q4w

PD = progressive disease; PLD = pegylated liposomal doxorubicin
[a]Epithelial ovarian, primary peritoneal or fallopian tube cancer
[b]Or 10 mg/kg q2w
[c]15 mg/kg q3w, permitted on clear evidence of progression

Statistical design

Primary objective: To compare PFS with CT alone vs BEV + CT according to RECIST v1.0

Secondary objectives: To compare

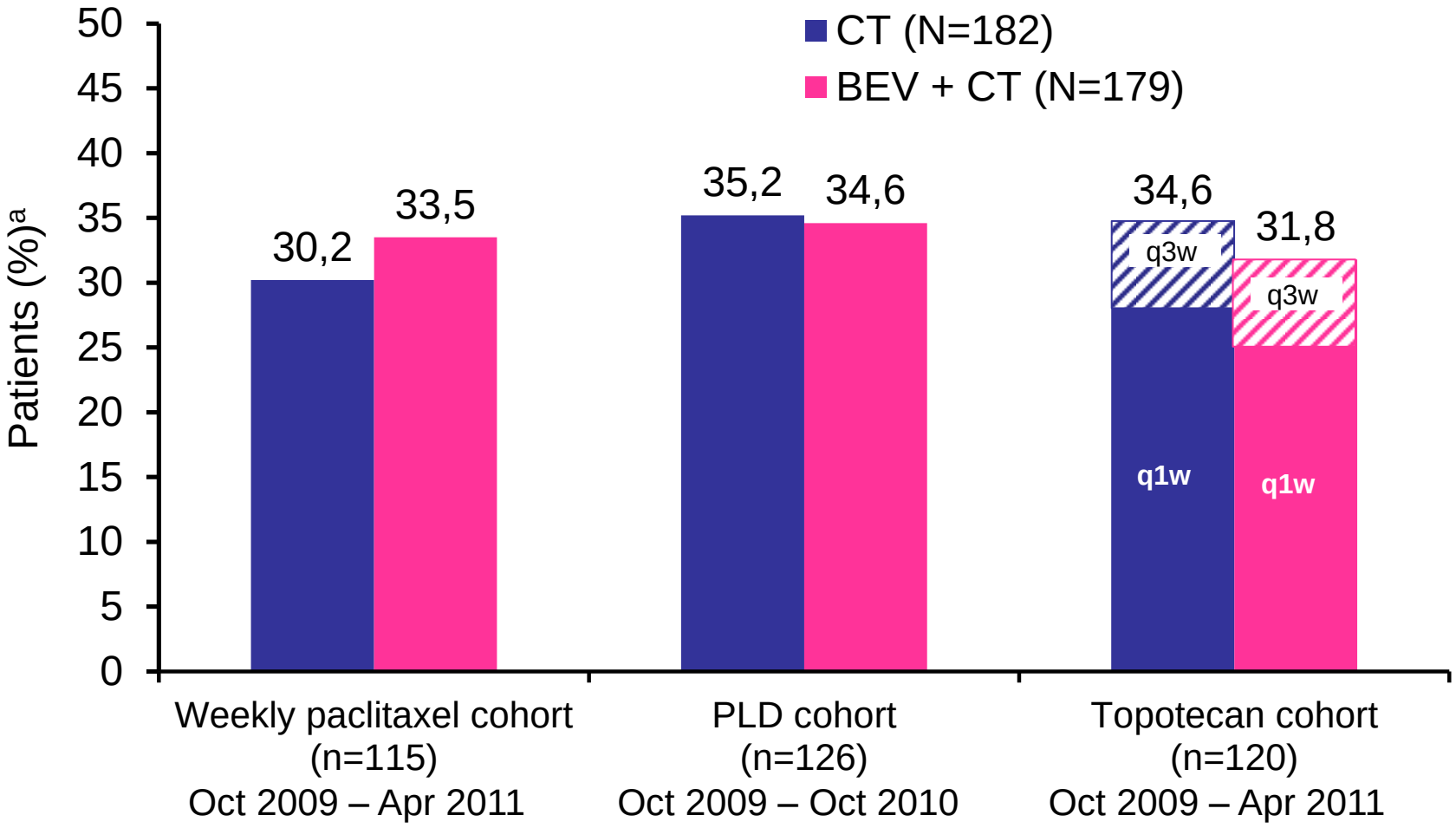
- Objective response rate (ORR) according to RECIST v1.0 and/or GCIG CA-125 criteria
- Overall survival
- Quality of life
- Safety and tolerability

Exploratory objectives: Including evaluation of safety and efficacy according to CT cohort (investigator's choice)

- CT choice was a stratification factor but patients were not randomised between the CT cohorts

RECIST = Response Evaluation Criteria in Solid Tumours

Investigator's choice of chemotherapy



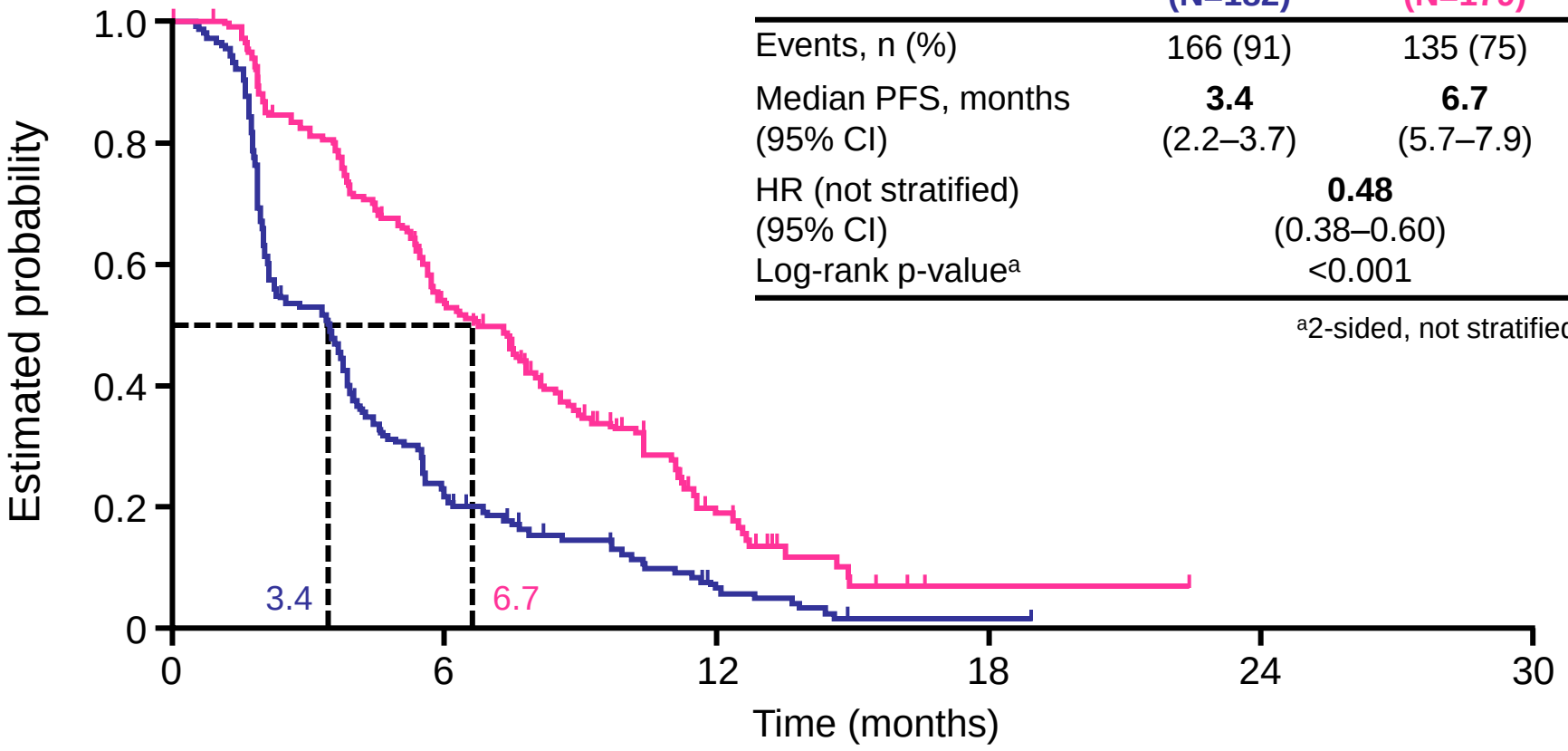
[a]*Percentages calculated per treatment arm*

Baseline characteristics: Generally balanced between arms, some differences between cohorts

Characteristic, %	Weekly paclitaxel		PLD		Topotecan	
	CT (N=55)	BEV + CT (N=60)	CT (N=64)	BEV + CT (N=62)	CT (N=63)	BEV + CT (N=57)
Median age, years	60	60	62	63.5	61	60
(range)	(25–80)	(25–79)	(32–77)	(39–78)	(35–84)	(26–80)
Age ≥65 years	25	42	34	48	43	26
Histology at diagnosis[a]						
Serous/adenocarcinoma	87	88	77	85	87	88
Clear cell	6	3	9	2	5	2
FIGO stage III/IV	87	87	81	90	89	96
Grade at diagnosis						
1	5	12	6	2	3	4
2	31	30	22	24	27	35
3	45	52	63	58	63	47
Missing	18	7	9	16	6	14
2 prior chemotherapy regimens	51	55	33	26	46	40
PFI <3 months[b]	27	27	20	27	25	26
ECOG PS						
0	49	63	59	55	54	61
1	40	30	34	32	40	35
2	7	3	6	13	5	4

PFI = platinum-free interval. [a]Multiple answers possible. [b]From last platinum to subsequent PD

Progression-free survival: Overall population



	CT (N=182)	BEV + CT (N=179)
Events, n (%)	166 (91)	135 (75)
Median PFS, months (95% CI)	**3.4** (2.2–3.7)	**6.7** (5.7–7.9)
HR (not stratified) (95% CI)	**0.48** (0.38–0.60)	
Log-rank p-value[a]	<0.001	

[a]2-sided, not stratified

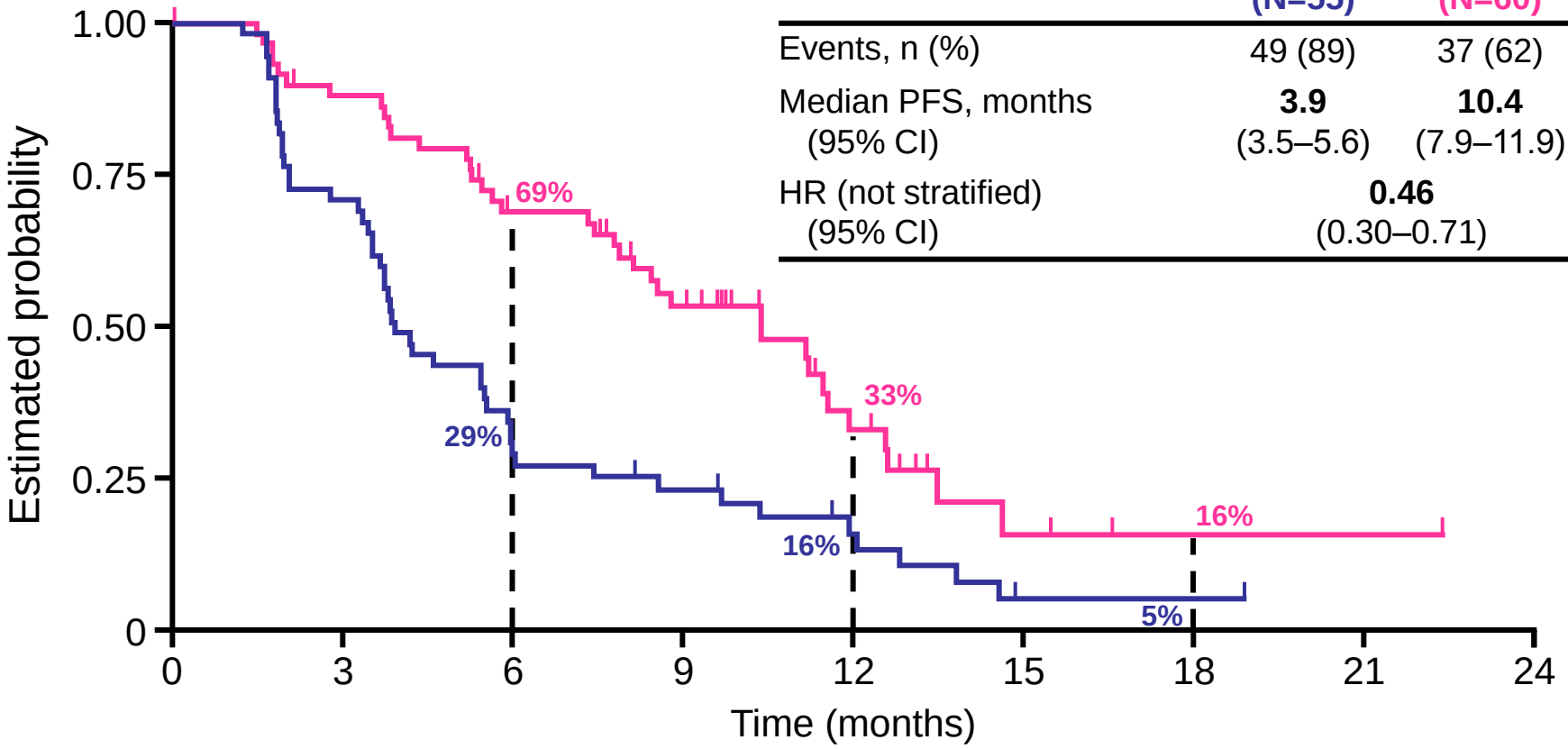
No. at risk:

CT	182	93	37	20	8	1	1	0	0
BEV + CT	179	140	88	49	18	4	1	1	0

Median duration of follow-up: 13.9 months (CT arm) vs 13.0 months (BEV + CT arm)

PFS: Cohort treated with paclitaxel

	CT (N=55)	BEV + CT (N=60)
Events, n (%)	49 (89)	37 (62)
Median PFS, months (95% CI)	**3.9** (3.5–5.6)	**10.4** (7.9–11.9)
HR (not stratified) (95% CI)	**0.46** (0.30–0.71)	



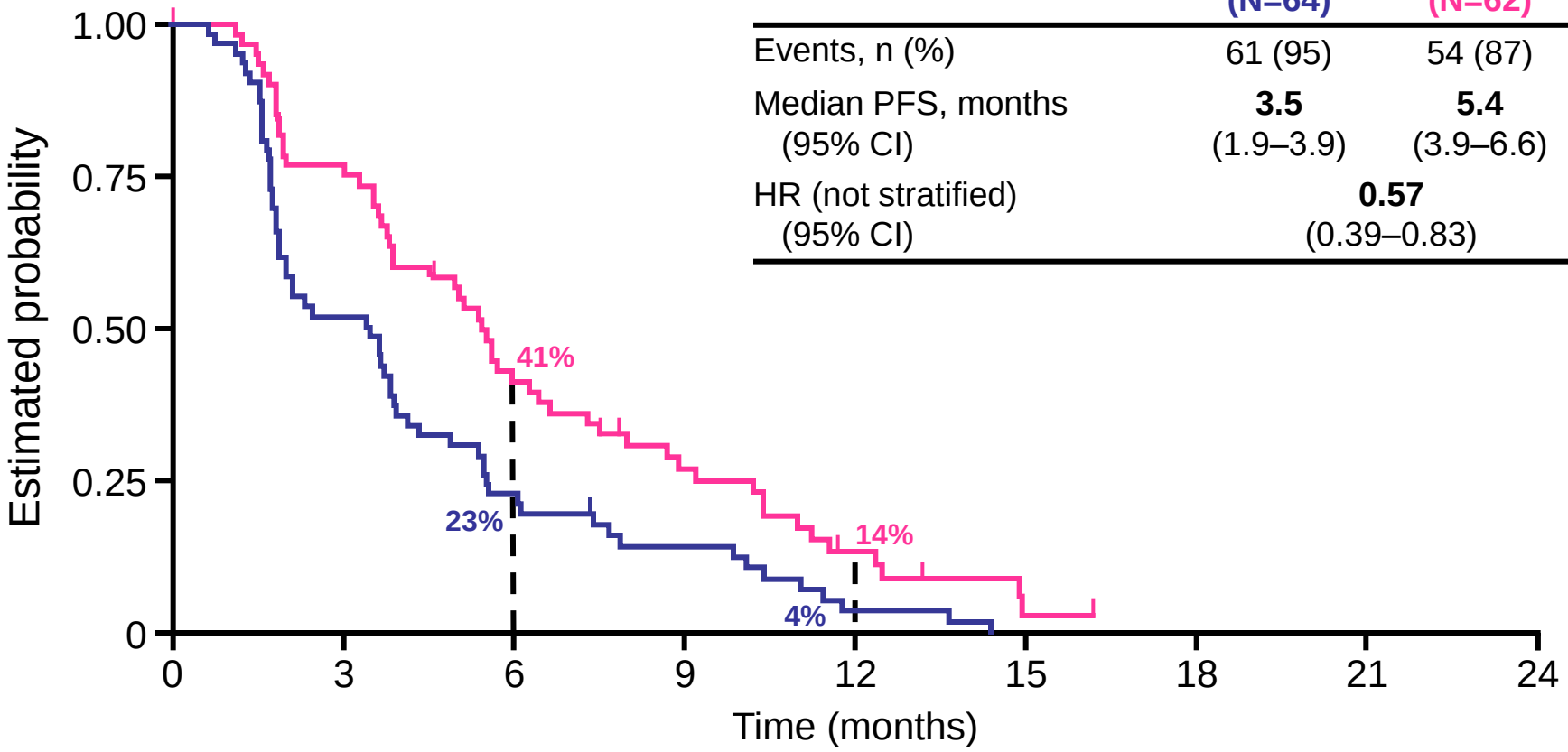
No. at risk:

CT	55	39	16	11	6	1	1	0	0
BEV + CT	60	51	38	27	11	3	1	1	0

Median duration of follow-up: 12.7 months (CT arm) vs 12.8 months (BEV + CT arm)

PFS: Cohort treated with PLD

	CT (N=64)	BEV + CT (N=62)
Events, n (%)	61 (95)	54 (87)
Median PFS, months (95% CI)	**3.5** (1.9–3.9)	**5.4** (3.9–6.6)
HR (not stratified) (95% CI)	**0.57** (0.39–0.83)	

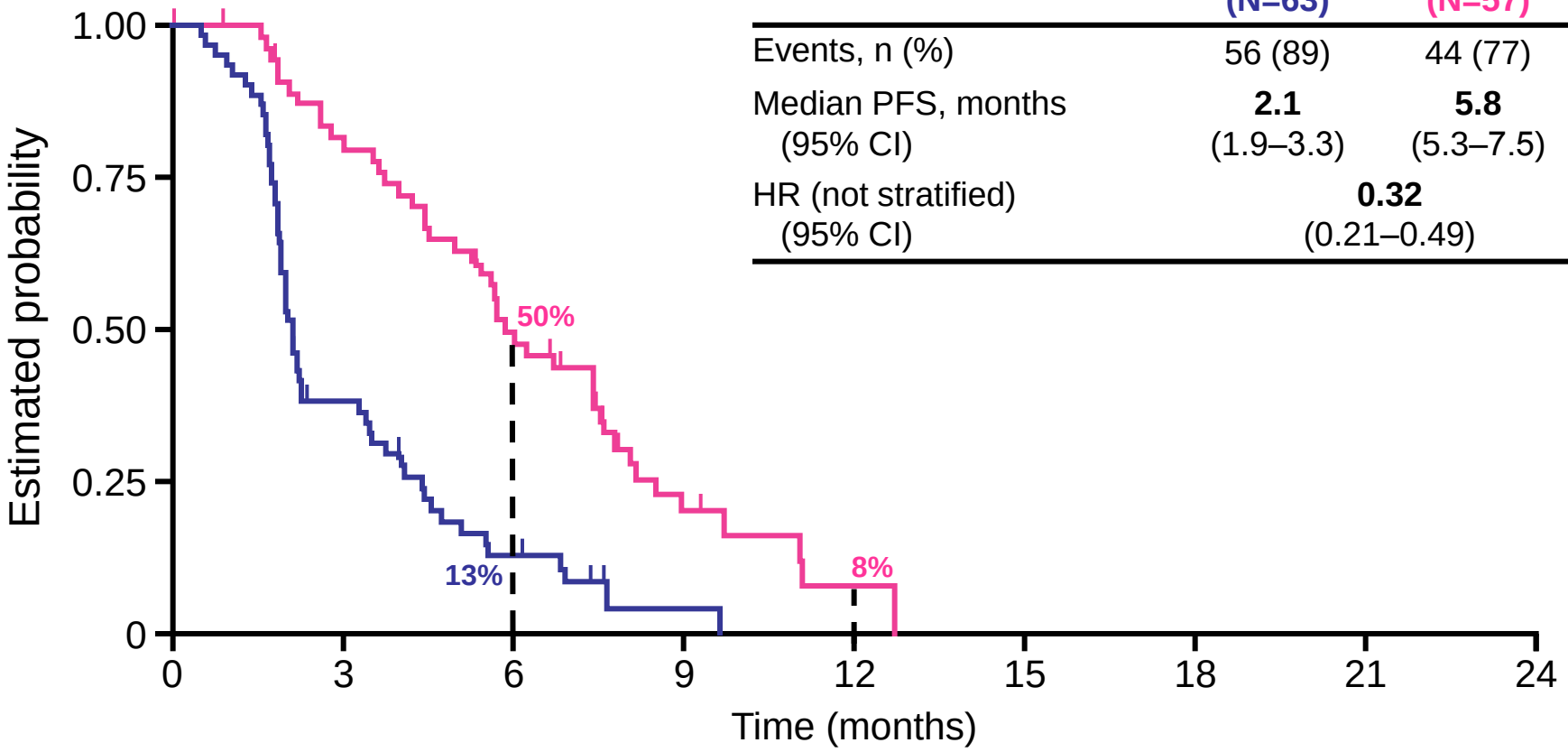


No. at risk:

CT	64	32	14	8	2	0	0	0	0
BEV + CT	62	46	24	14	6	1	0	0	0

Median duration of follow-up: 15.8 months (CT arm) vs 16.7 months (BEV + CT arm)

PFS: Cohort treated with topotecan



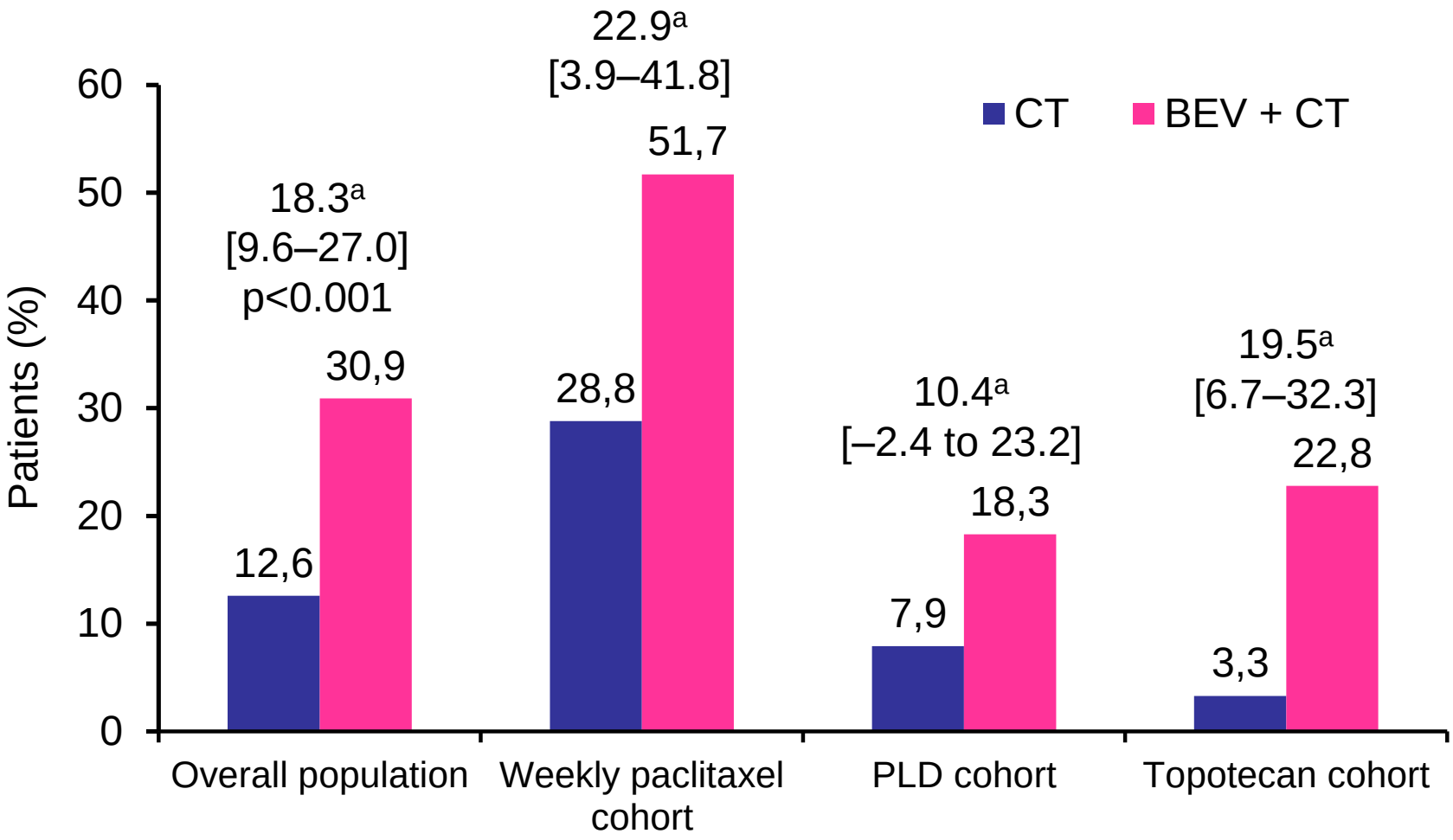
	CT (N=63)	BEV + CT (N=57)
Events, n (%)	56 (89)	44 (77)
Median PFS, months (95% CI)	**2.1** (1.9–3.3)	**5.8** (5.3–7.5)
HR (not stratified) (95% CI)	**0.32** (0.21–0.49)	

No. at risk:

CT	63	22	7	1	0	0	0	0	0
BEV + CT	57	43	26	8	1	0	0	0	0

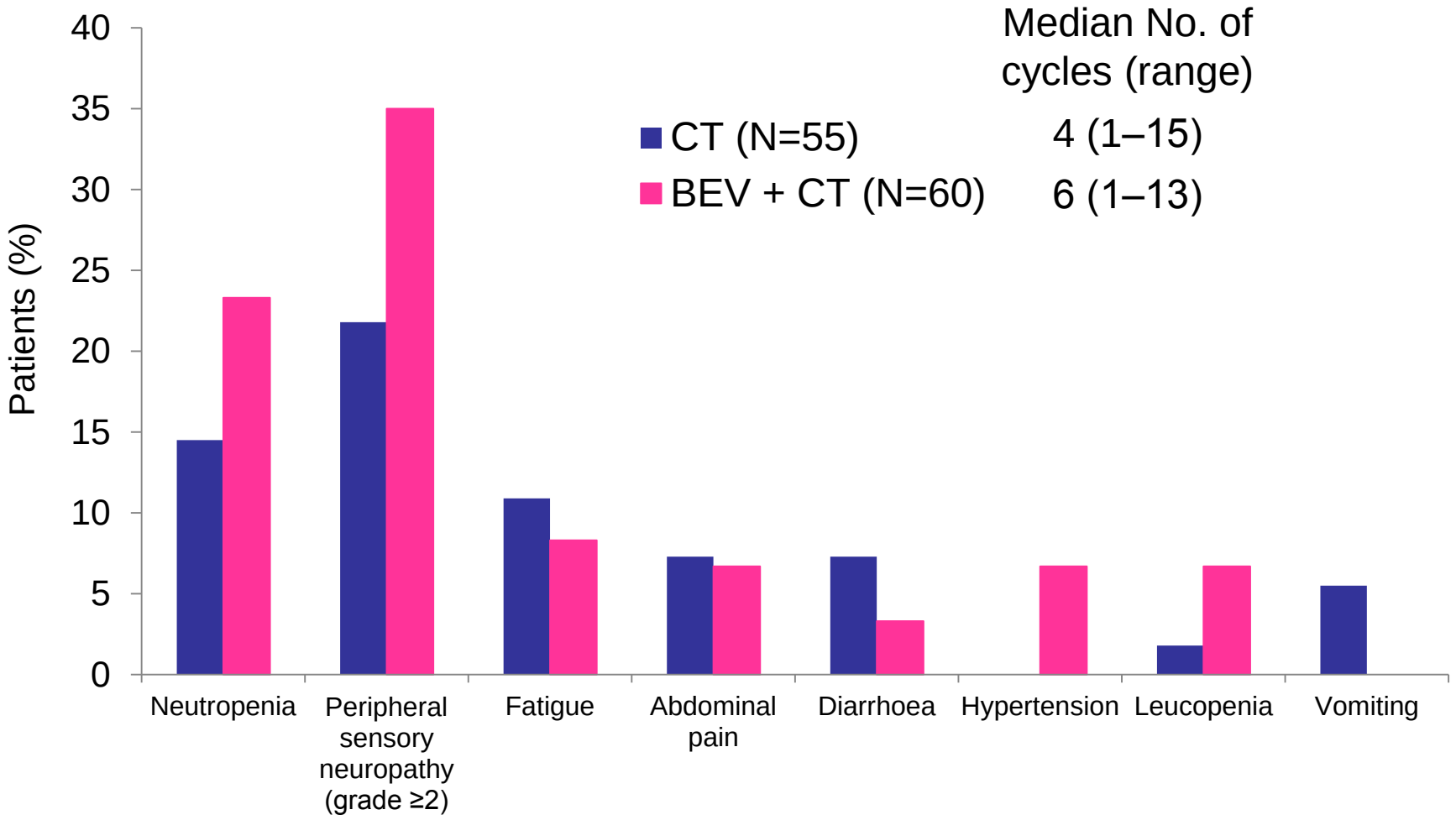
Median duration of follow-up: 9.0 months (CT arm) vs 10.5 months (BEV + CT arm)

Summary of best overall response rates (RECIST, CA-125 criteria or both)



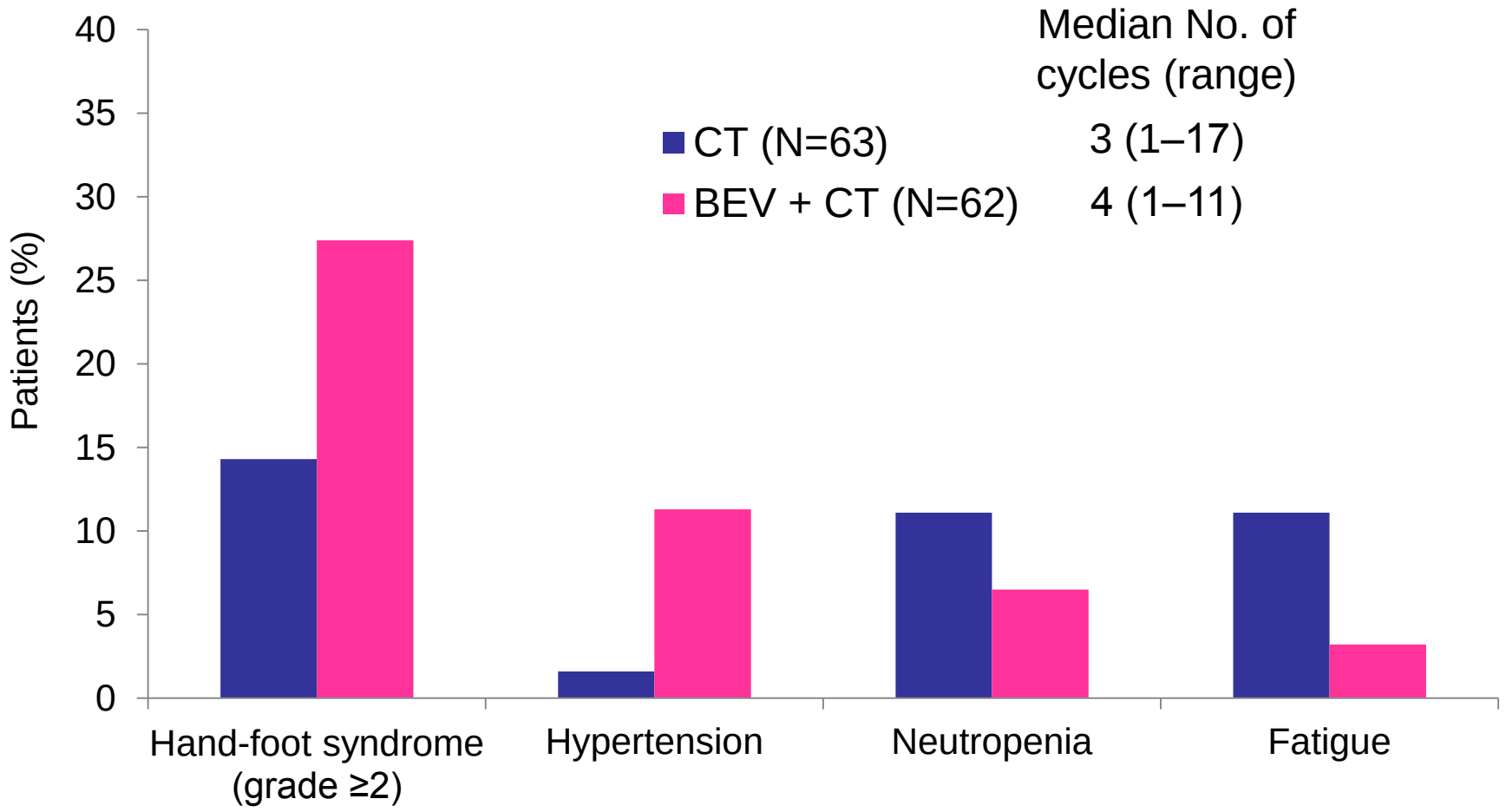
[a]*Difference in overall response rate; 95% CI with Hauck–Anderson continuity correction*

Most common[a] grade ≥3 AEs: Paclitaxel cohort



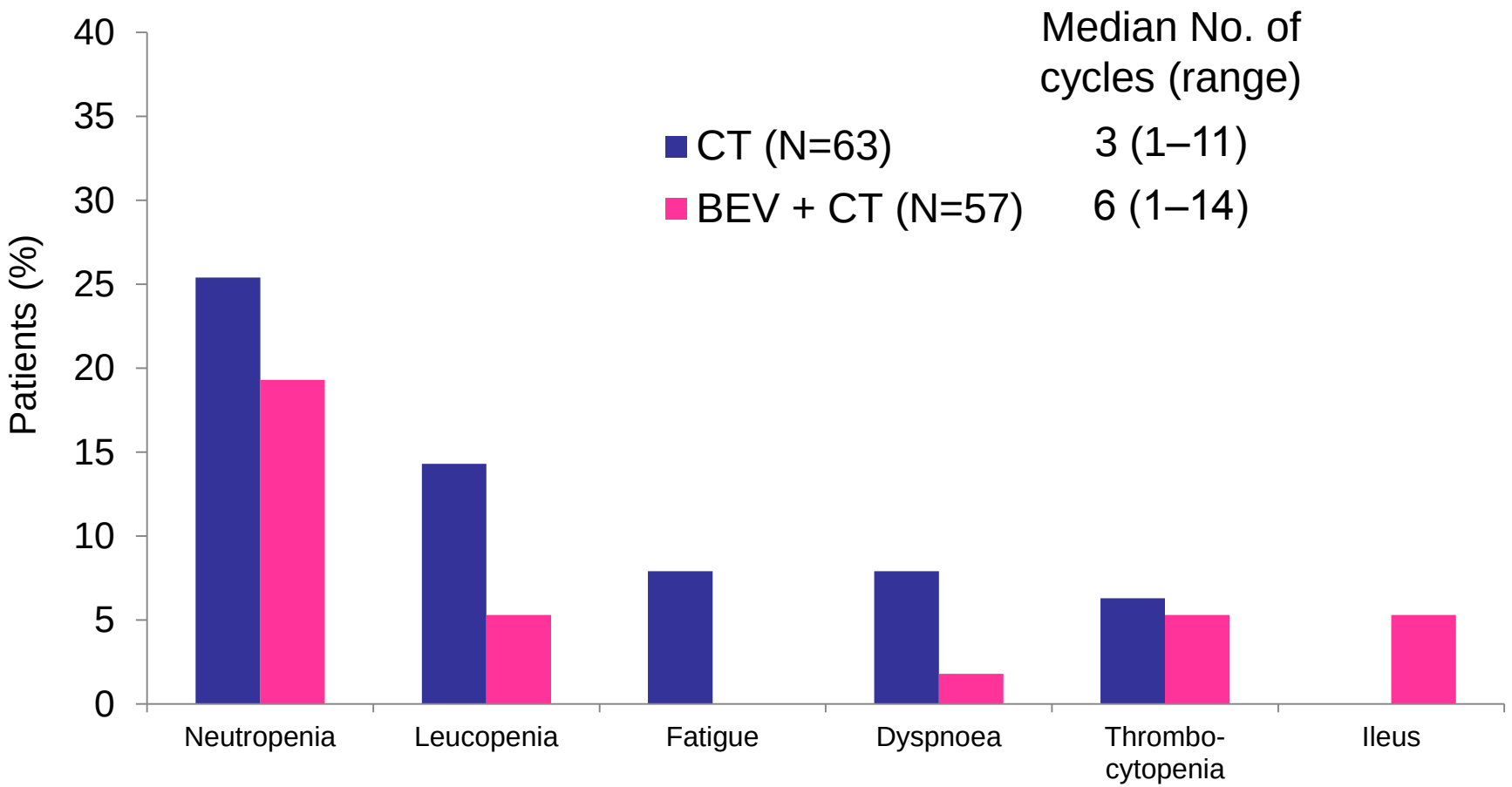
[a]*In >5% of patients in either treatment arm*

Most common[a] grade ≥3 AEs: PLD cohort



[a]*In >5% of patients in either treatment arm*

Most common[a] grade ≥3 AEs: Topotecan cohort



[a]*In >5% of patients in either treatment arm*

Conclusions

- The effect of BEV on PFS within the individual CT cohorts is consistent with results in the overall population, demonstrating benefit with the addition of BEV to CT for platinum-resistant recurrent OC
- The BEV safety profile is consistent with previous experience
  - Numerical increases in the overall incidences of peripheral sensory neuropathy (paclitaxel) and hand-foot syndrome (PLD) may be explained by longer duration of CT exposure associated with prolonged PFS
  - Overall, no indication that BEV exacerbates CT-related AEs
- BEV combined with CT should be considered a new standard option in platinum-resistant OC