

Single-agent versus combination first-line chemotherapy in patients with advanced non-small-cell lung cancer (NSCLC) and a performance status (PS) of 2

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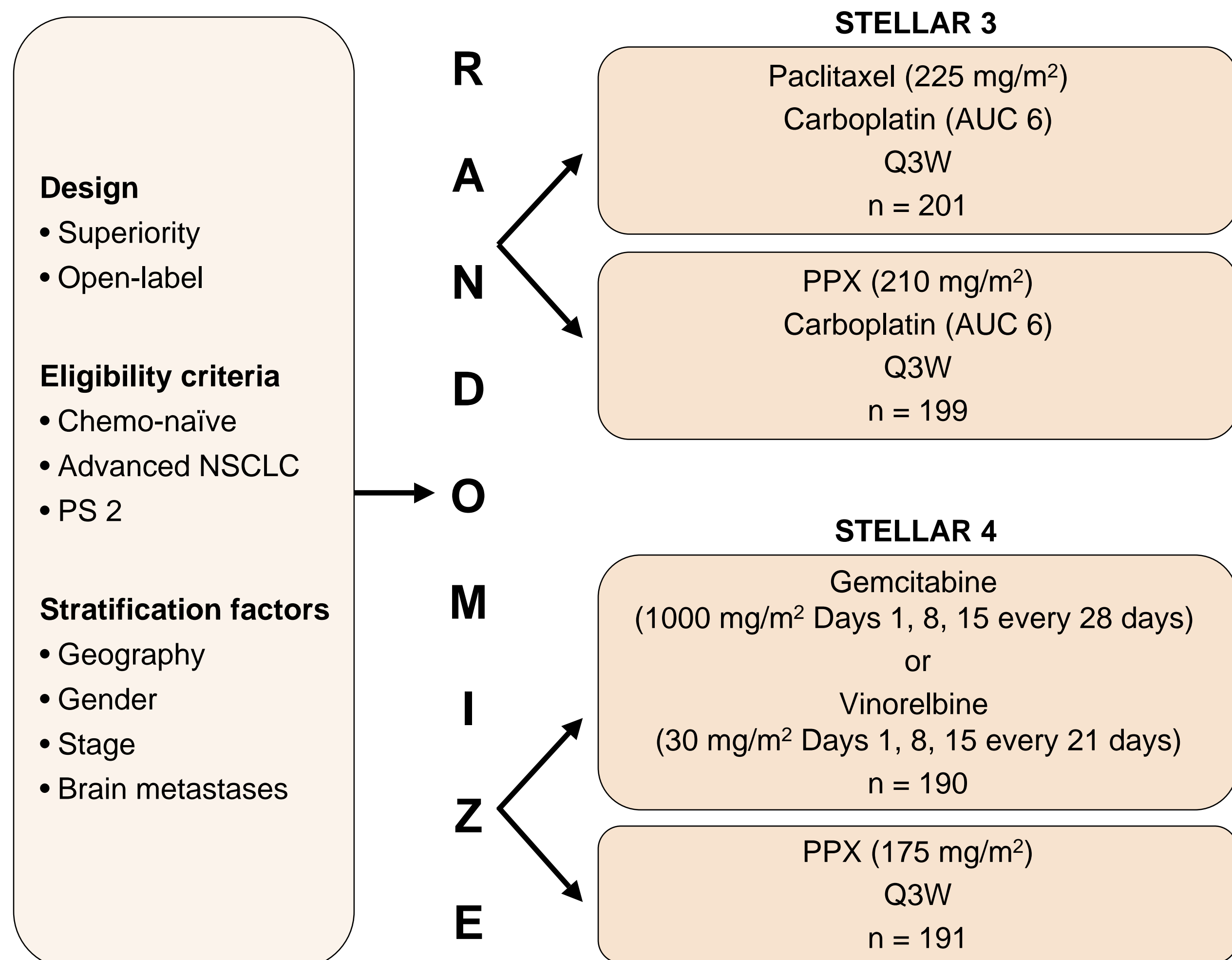
Background

- Impaired performance status in NSCLC is associated with poor prognosis and reduced tolerance for treatment-related toxicities.
- Current treatment guidelines agree that PS 2 patients with advanced NSCLC benefit from systemic chemotherapy; however, no consensus exists on specific treatment recommendations; i.e., single-agent versus combination chemotherapy.
- The available clinical data is limited to subset analysis of PS 2 patients enrolled in several randomized trials. Two recent phase III randomized trials in advanced NSCLC enrolled exclusively PS 2 patients and compared experimental treatment (paclitaxel poliglumex; PPX) to either combination chemotherapy (paclitaxel/carboplatin; P/C), or single agent chemotherapy (gemcitabine or vinorelbine; G or V).
- An exploratory comparison of survival between patients receiving single agent or combination chemotherapy was performed.

Methods

- Two recent trials (STELLAR 3 and 4) were large, phase III, open-label, randomized trials of PPX in combination with carboplatin (C) versus paclitaxel (P)/C and single-agent PPX versus vinorelbine (V) or gemcitabine (G) respectively, for first-line treatment of PS 2 patients with advanced NSCLC.^{1,2}
- An exploratory comparison of the control arms was performed to evaluate the degree of benefit and amount of added toxicity associated with combination versus single agent chemotherapy.
- The study design for STELLAR 3 and STELLAR 4 is summarized in Figure 1.

Figure 1: STELLAR Trials Design



- Demographic risk factors (Table 1) were similar for the two trials and consistent with those expected for a PS 2 population. For STELLAR 3 and 4 respectively:
 - 73% and 80% of the patients had more than two co-morbid conditions
 - 40% and 35% had >5% weight loss
 - nearly half had extra-thoracic metastases.
- Time to progression was improved with combination chemotherapy compared to single agent (Table 2).
- Although survival for patients receiving P/C was improved, this trend did not reach statistical significance (Figure 2A). One-year survival rates (Table 2) did not show a statistically significant difference (31% versus 26%; P = .112).
- In both trials, patients receiving PPX had similar overall survival compared with patients on the control arms.
- When considering all PS 2 patients enrolled in STELLAR 3 and STELLAR 4 (N = 781), patients receiving single agent treatment had similar survival to patients receiving combination chemotherapy (Figure 2B; HR = 0.86; P = .071).
- The frequency of serious adverse events was 40% in the combination-study and 35% in the single agent-study. The frequency of drug-related serious adverse events was 21% in the combination-study and 5% in the single agent-study.

Table 1: STELLAR Patient Demographics

		STELLAR 3 (P/C)	STELLAR 4 (G or V)
Number patients on control arm		201	190
Sex	Male	156 (78%)	134 (71%)
	Female	45 (22%)	56 (30%)
Race	Caucasian	188 (94%)	170 (90%)
	Other	13 (6%)	20 (11%)
Age	Mean	61.5	62.8
	Median (range)	63.0 (36–89)	64 (30–90)
	<50	26 (13%)	19 (10%)
	50–59	58 (29%)	44 (23%)
	60–69	69 (34%)	83 (44%)
	>70	48 (24%)	44 (23%)
	>80	5 (3%)	9 (4.7%)
Geographic location	US	45 (22%)	24 (13%)
	Western Europe or Canada	27 (13%)	25 (13%)
	Others	129 (64%)	141 (74%)
Stage	IIIA	0	2 (<1%)
	IIIB	55 (27%)	59 (31%)
	IV	146 (73%)	129 (68%)
Brain metastases		15 (7%)	6 (3%)
>5% Weight loss		80 (40%)	66 (35%)
Extrathoracic metastases		87 (43%)	84 (44%)
Prior radiation		46 (23%)	39 (21%)
>2 Co-morbid conditions		147 (73%)	152 (80%)
Ever smoker		171 (85%)	156 (82%)

Results

Figure 2A: Overall survival STELLAR 3 and STELLAR 4 (control arms)

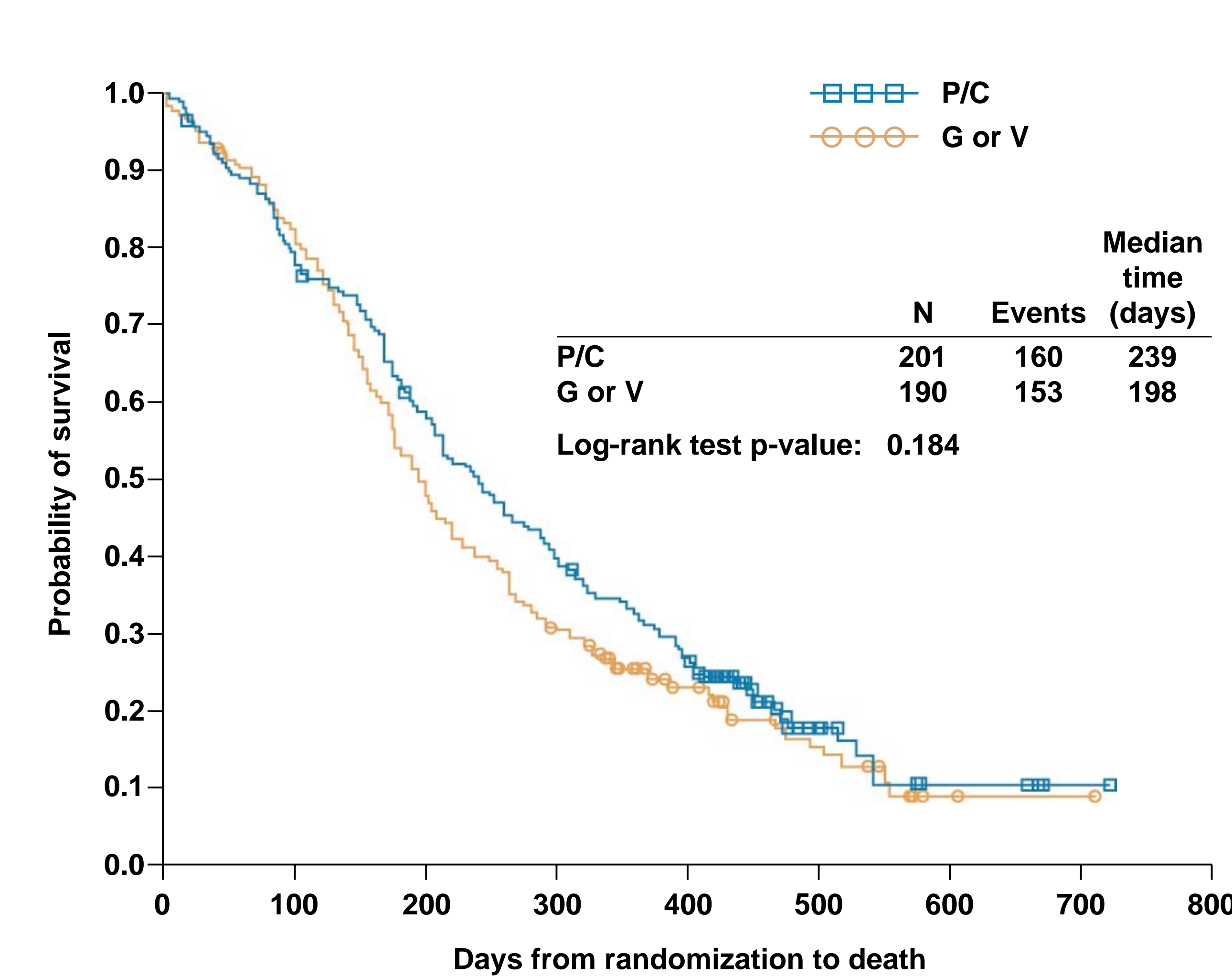


Table 2: Efficacy Results

	STELLAR 3 (P/C) n = 201	STELLAR 4 (G or V) n = 190	HR	P-value
Median overall survival (mos)	8.0	6.6	0.86	.184
Time to progression (mos)	4.6	3.5	0.69	<.001
12-month survival (%)	31	26		NS
24-month survival (%)	11	10		NS

Table 3A: Hematologic Adverse Events

	STELLAR 3 (P/C) n = 198		STELLAR 4 (G or V) n = 187	
	All grades	Grade 3–4	All grades	Grade 3–4
Neutropenia	27%	16%	14%	8%
Febrile neutropenia	3%	3%	<1%	<1%
Anemia	25%	7%	36%	9%
Thrombocytopenia	14%	8%	9%	<1%

Figure 2B: Overall survival STELLAR 3 (combination) and STELLAR 4 (single-agent) (control and experimental arms)

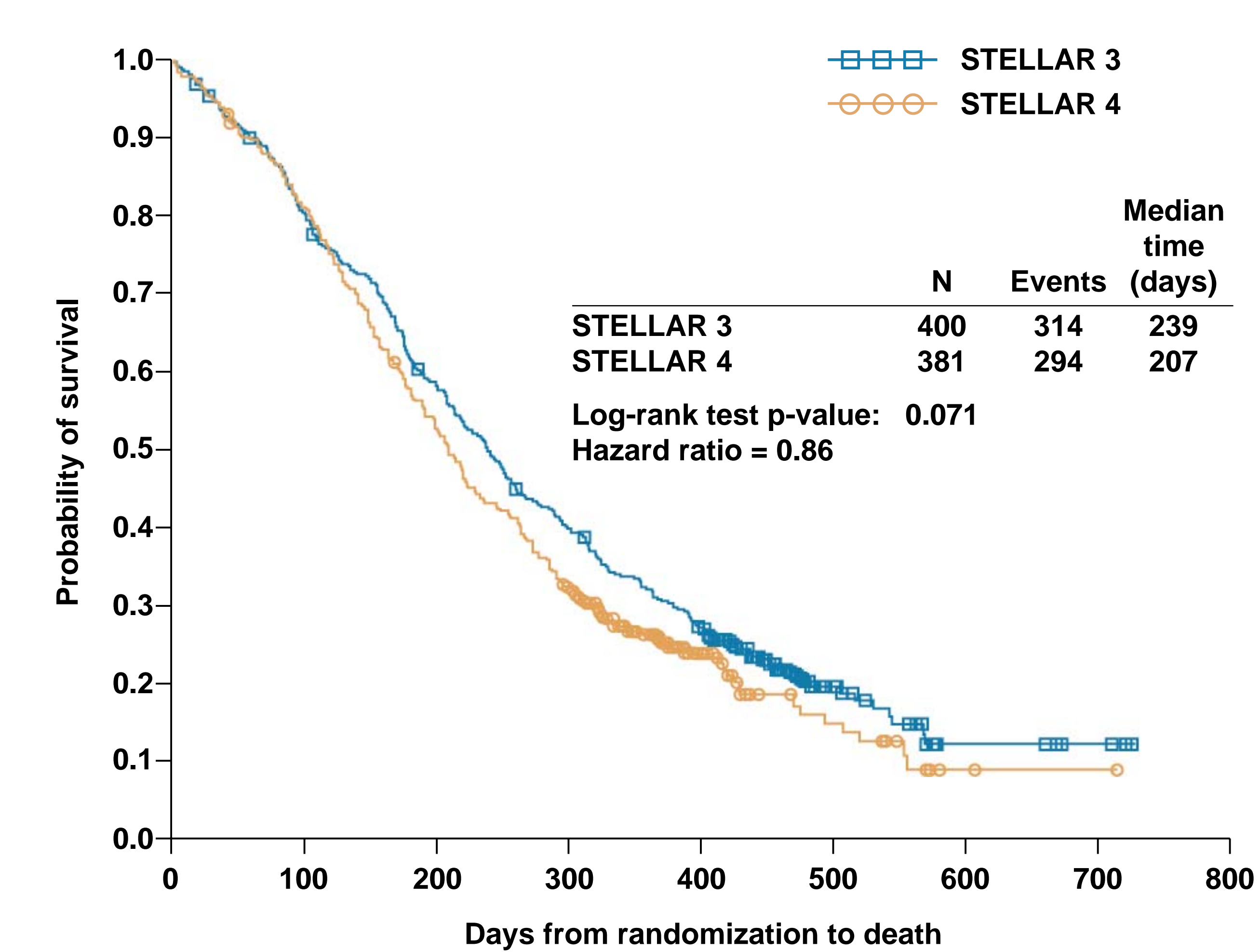


Table 3B: Non-hematologic Adverse Events

	STELLAR 3 (P/C) n = 198		STELLAR 4 (G or V) n = 187	
	All grades	Grade 3–4	All grades	Grade 3–4
Neuropathy	59%	10%	5%	0%
Nausea	38%	5%	29%	1%
Vomiting	21%	2%	17%	2%
Diarrhea	19%	4%	6%	0%
Dyspnea	17%	9%	30%	17%
Fatigue	17%	5%	25%	9%

Conclusion

- PS 2 patients receiving single agent chemotherapy have a similar outcome compared to patients receiving combination chemotherapy.
- Serious treatment-related toxicities are less frequent with single agent therapy.
- Based on the currently available evidence, the use of single-agent therapy seems reasonable in PS 2 patients.

References

- J Clin Oncol. 2005, 23(16S):7011.
- Eur J Cancer. 2005, S3(2):324.