KEYNOTE-021

KEYNOTE-021

Primary Endpoint: Achieved an Objective Response

アメリカ、台湾２７施設

非小細胞肺癌患者

All comer(腺癌、扁平上皮癌)

化学療法未治療の非小細胞肺癌患者
（１次治療）
- EGFR遺伝子変異　陰性
- ALK融合遺伝子　陰性
- PD-L１高発現
(TPS≧1%, 1%<TPS)

R

Pembrolizumab

CBDCA(AUC=5)+Pem(500mg/m2)
（Non-Sq Pem維持療法許容）
Up to 4 cycles

CBDCA(AUC=5)+Pem(500mg/m2)
（Non-Sq Pem維持療法許容）
Up to 4 cycles

Achieved OR
30/60
18/63

※化学療法群の後治療では、クロスオーバーでPembrolizumab使用が79/97例であったにも関わらず、OSにおいて一次での使用が成績良かった。１次治療で化学療法より優先してPembrolizumaを使用することとなる。

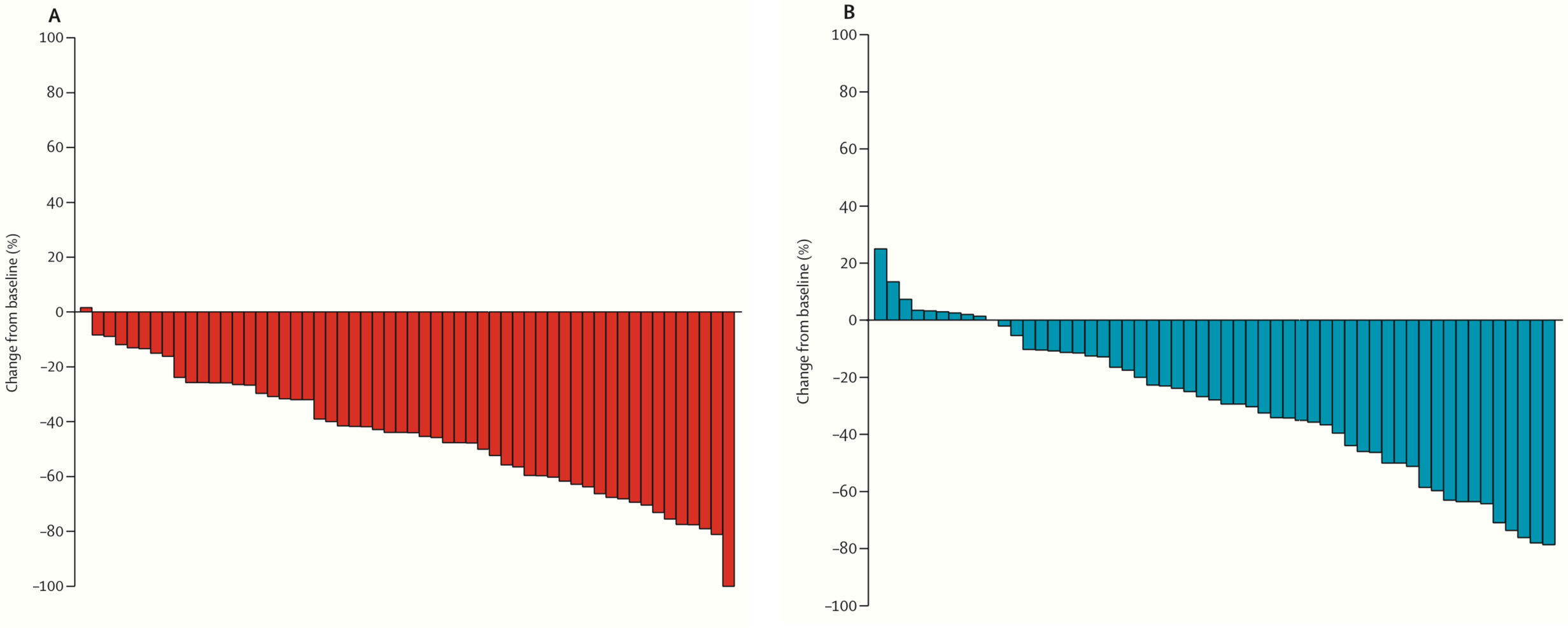
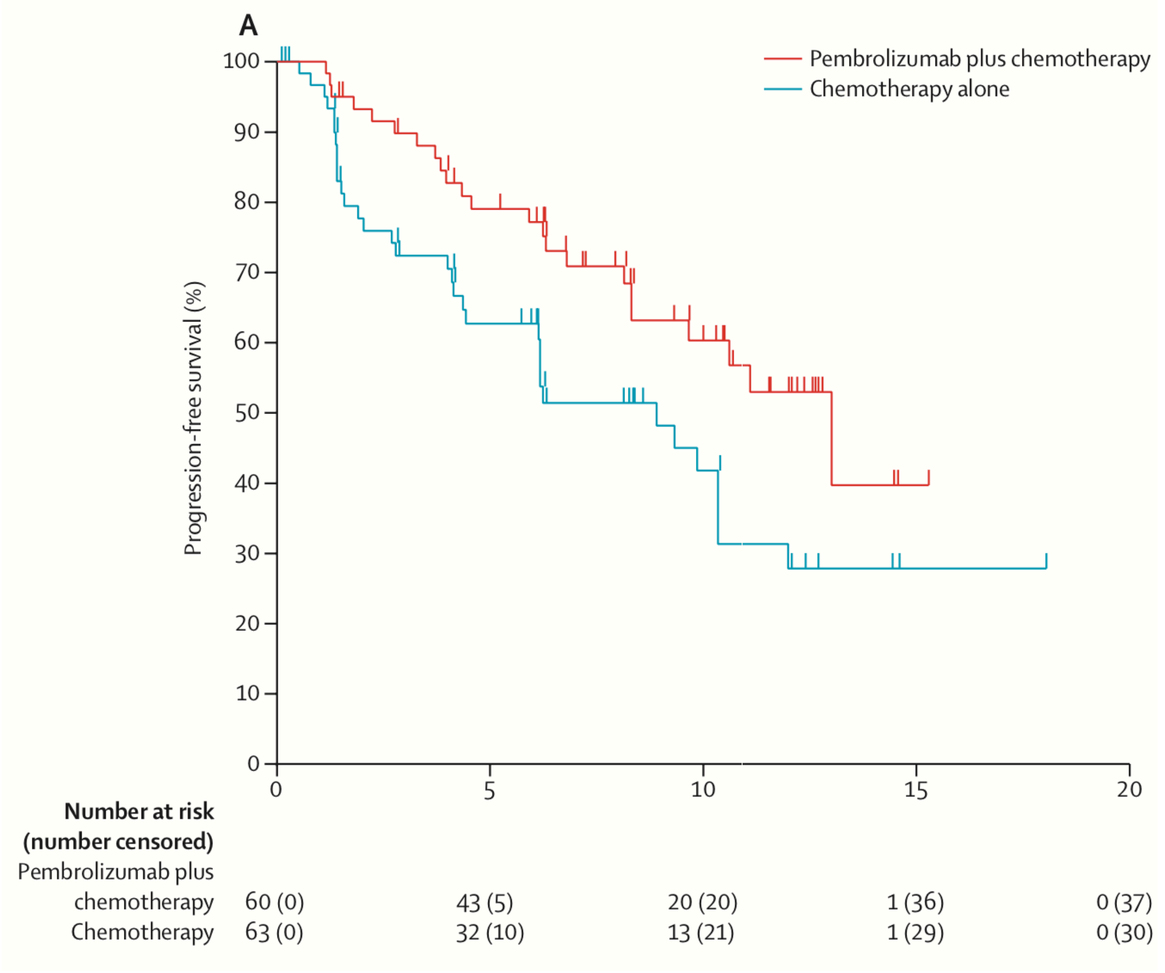


Figure 2: **Best percentage change from baseline in tumour size in the pembrolizumab plus chemotherapy group (n=56; A) and the chemotherapy alone group (n=55; B)**

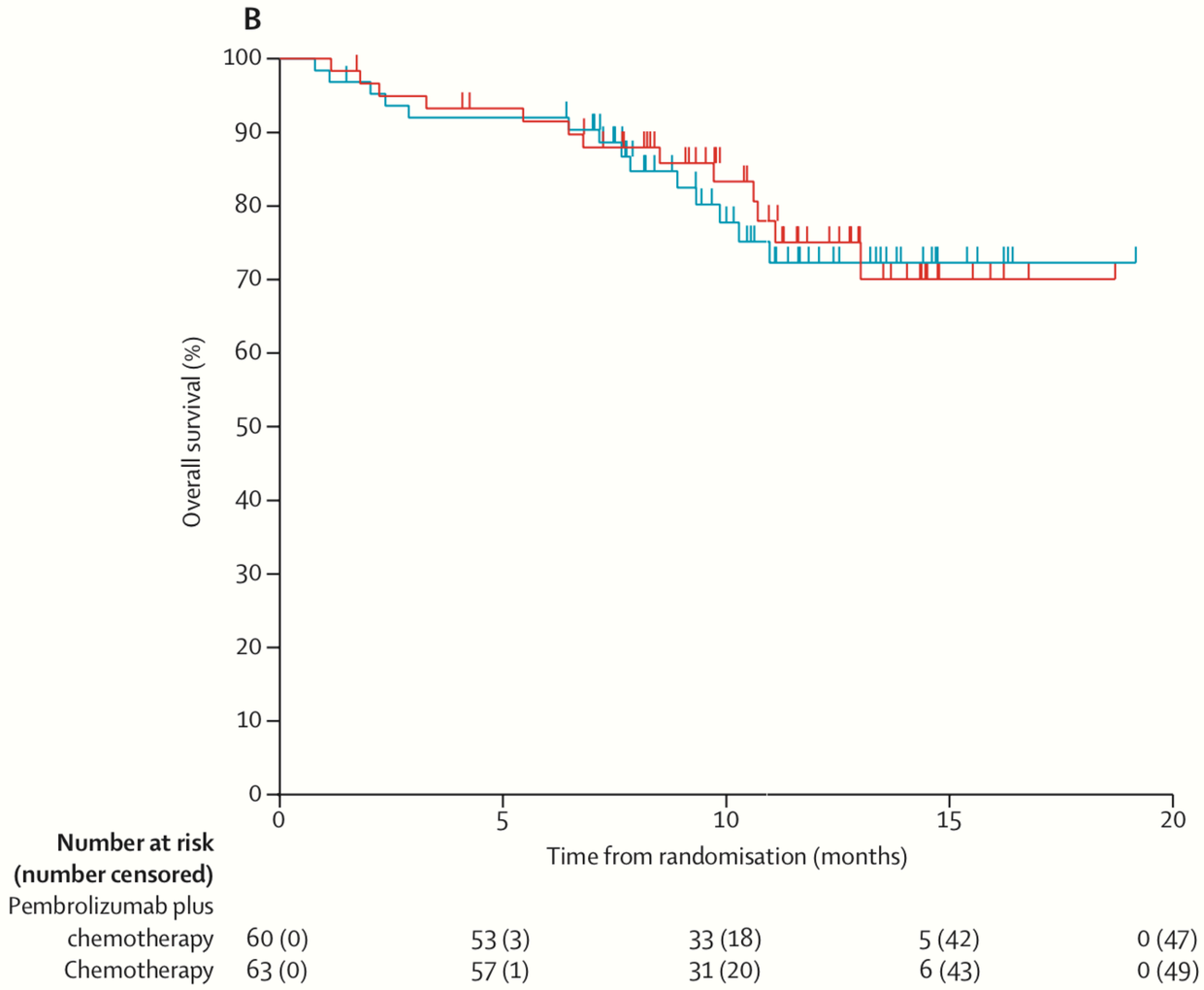
Tumour size was defined as the sum of the longest diameters of target lesions. Evaluable patients were those who had both measurable disease per Response Evaluation Criteria In Solid Tumors version 1.1 by masked, independent central radiology review at baseline and at least one post-baseline radiological assessment.

Carboplatin and pemetrexed with or without pembrolizumab for advanced, non-squamous non-small-cell lung cancer: a randomised, phase 2 cohort of the open-label KEYNOTE-021 study

KEYNOTE-021 (PD1/PDL1-71)



Number at risk (number censored)					
Pembrolizumab plus chemotherapy	60 (0)	43 (5)	20 (20)	1 (36)	0 (37)
Chemotherapy	63 (0)	32 (10)	13 (21)	1 (29)	0 (30)



Number at risk (number censored)					
Pembrolizumab plus chemotherapy	60 (0)	53 (3)	33 (18)	5 (42)	0 (47)
Chemotherapy	63 (0)	57 (1)	31 (20)	6 (43)	0 (49)

KEYNOTE-021 G (NCT02039674): Phase 2, Open-label, Randomized Study[1]

Key Eligibility Criteria

- Untreated stage IIIB or IV nonsquamous NSCLC
- No activating *EGFR* mutation or *ALK* translocation
- Biopsy sample for PD-L1 assessment[a]
- ECOG PS 0-1
- No untreated brain metastases
- No ILD or pneumonitis requiring systemic steroids

R (1:1)[a]
N = 123

- **Pembrolizumab** 200 mg IV Q3W (2 years) + Carboplatin AUC 5 mg/mL/min + Pemetrexed 500 mg/m² Q3W (4 cycles)
- **Carboplatin AUC 5 mg/mL/min + Pemetrexed 500 mg/m² Q3W (4 cycles)**

Pemetrexed 500 mg/m² Q3W permitted as maintenance therapy

END POINTS

Primary: ORR (RECIST v1.1, per blinded, independent central review)

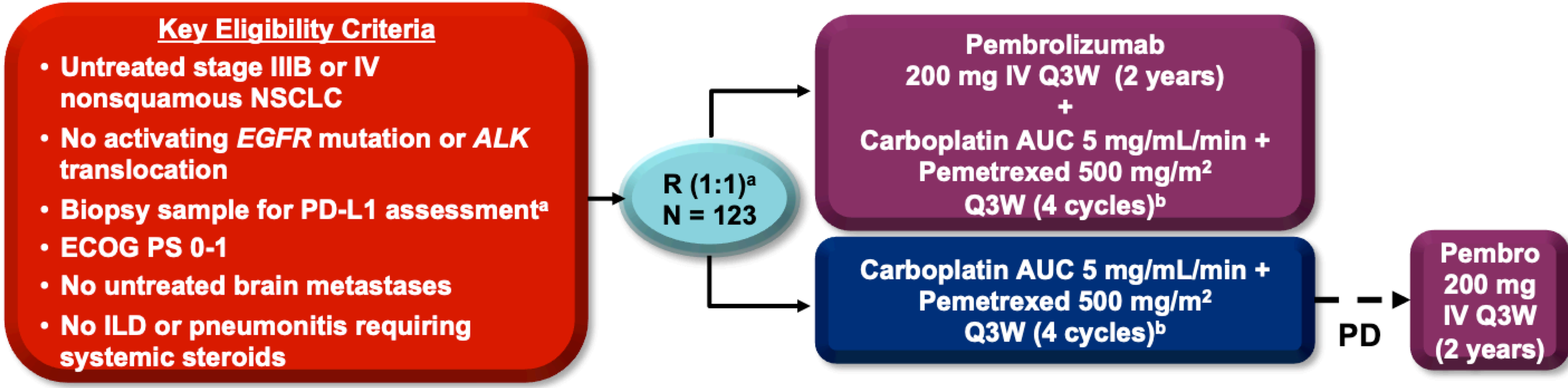
Key secondary: PFS

Other secondary: OS, safety, relationship between antitumor activity and PD-L1 TPS

[a]Randomization was stratified by PD-L1 TPS <1% vs ≥1%.

1. Langer CJ et al. Lancet Oncol 2016; dx.doi.org/10.1016/S1470-2045(16)30498-3.

KEYNOTE-021 G (NCT02039674): Phase 2, Open-label, Randomized Study[1]



END POINTS

Primary: ORR (RECIST v1.1, per blinded, independent central review)

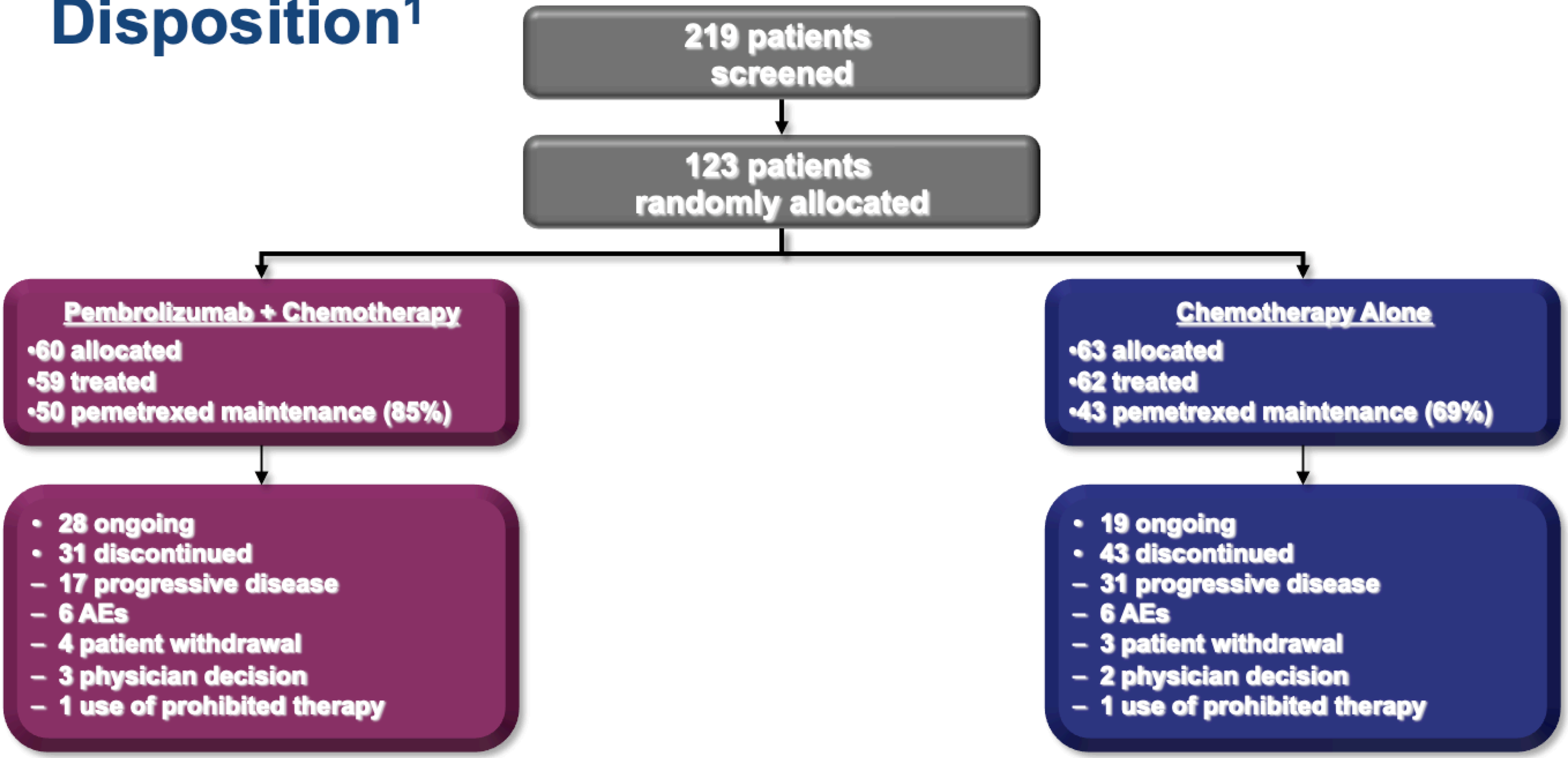
Key secondary: PFS

Other secondary: OS, safety, relationship between antitumor activity and PD-L1 TPS

[a]Randomization was stratified by PD-L1 TPS <1% vs ≥1%.

1. Langer CJ et al. Lancet Oncol 2016; dx.doi.org/10.1016/S1470-2045(16)30498-3.

Disposition[1]



1. Langer CJ et al. *Lancet Oncol* 2016; dx.doi.org/10.1016/S1470-2045(16)30498-3.
Data cutoff date: August 8, 2016.

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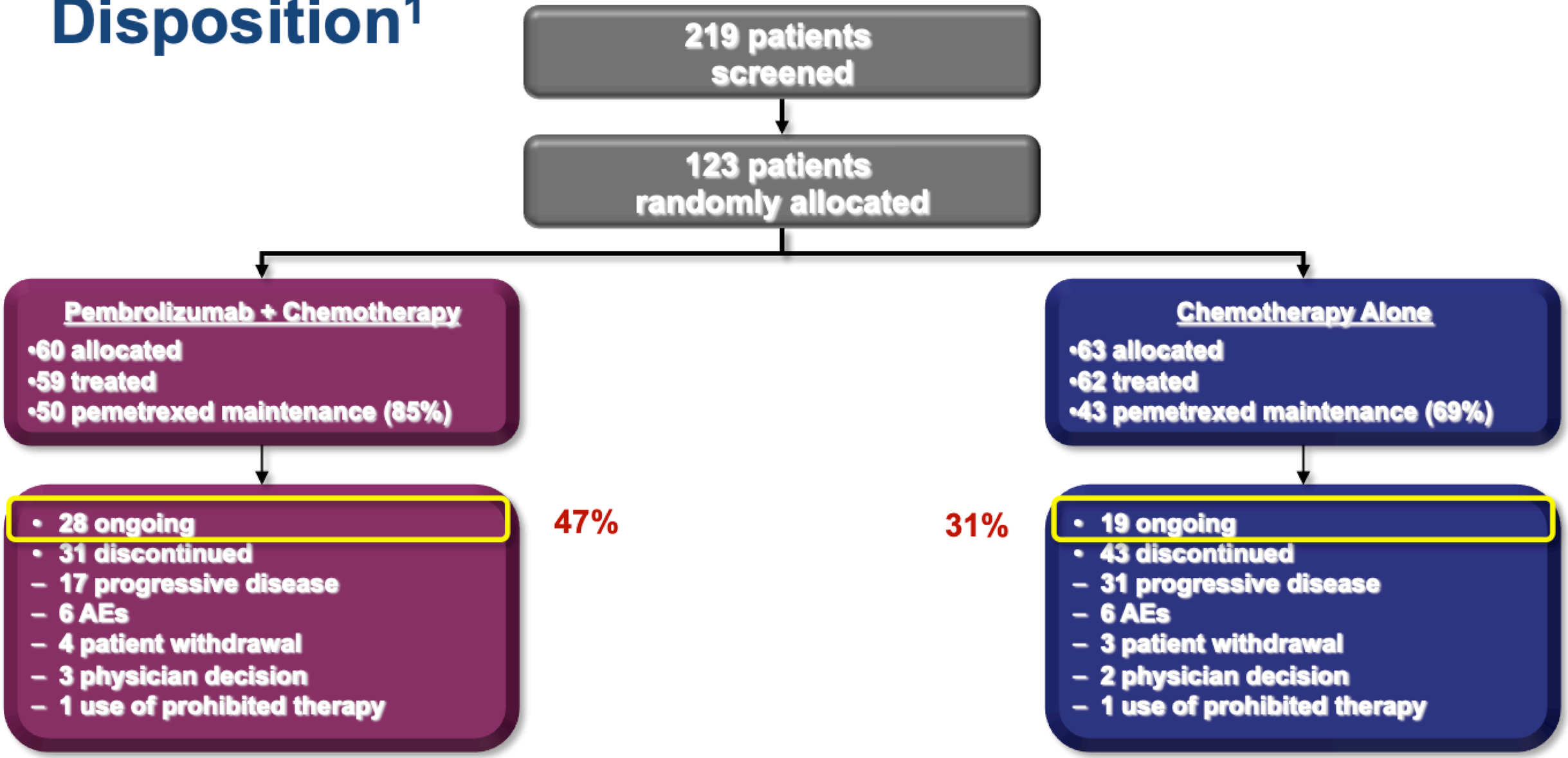

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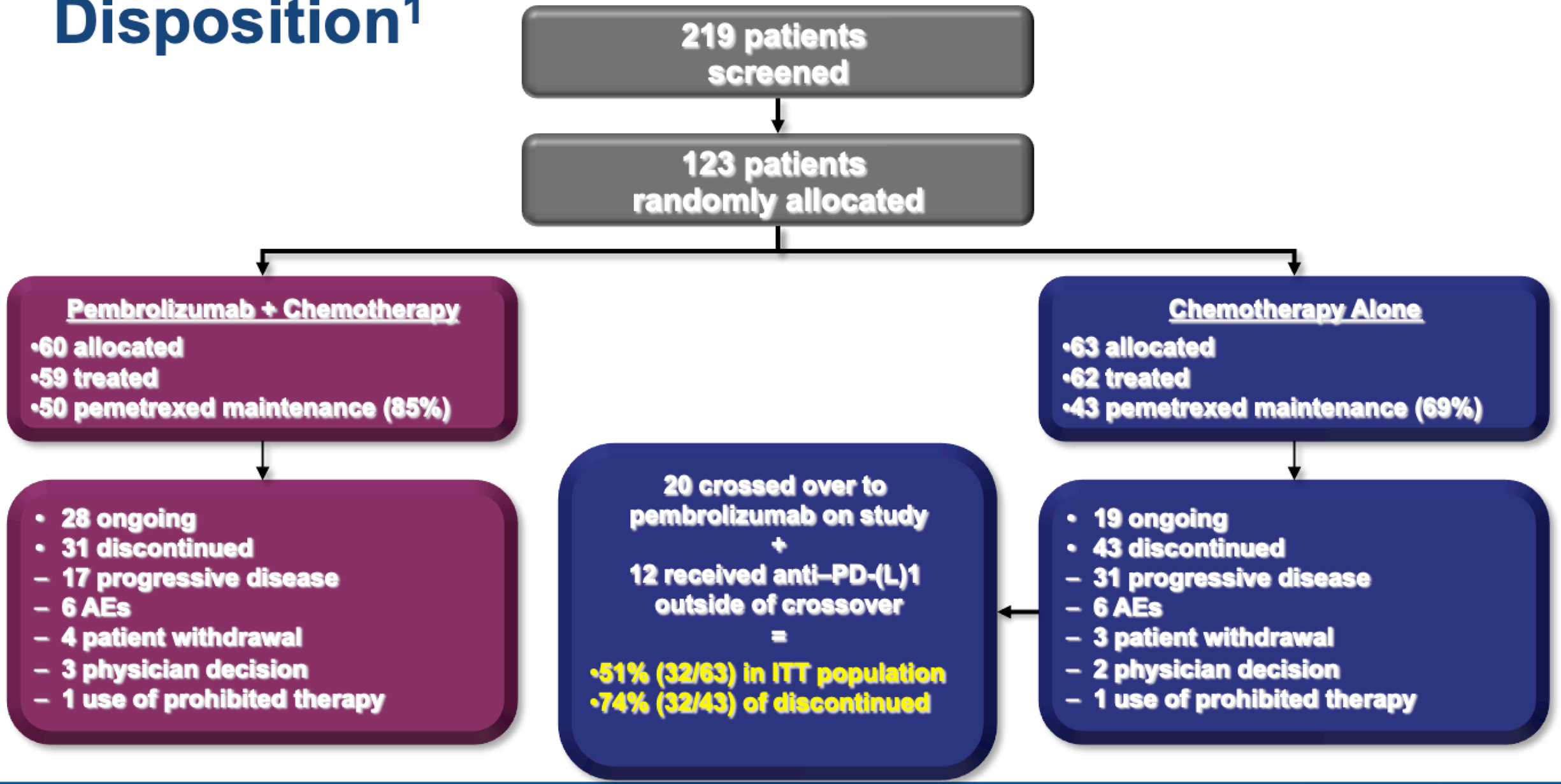

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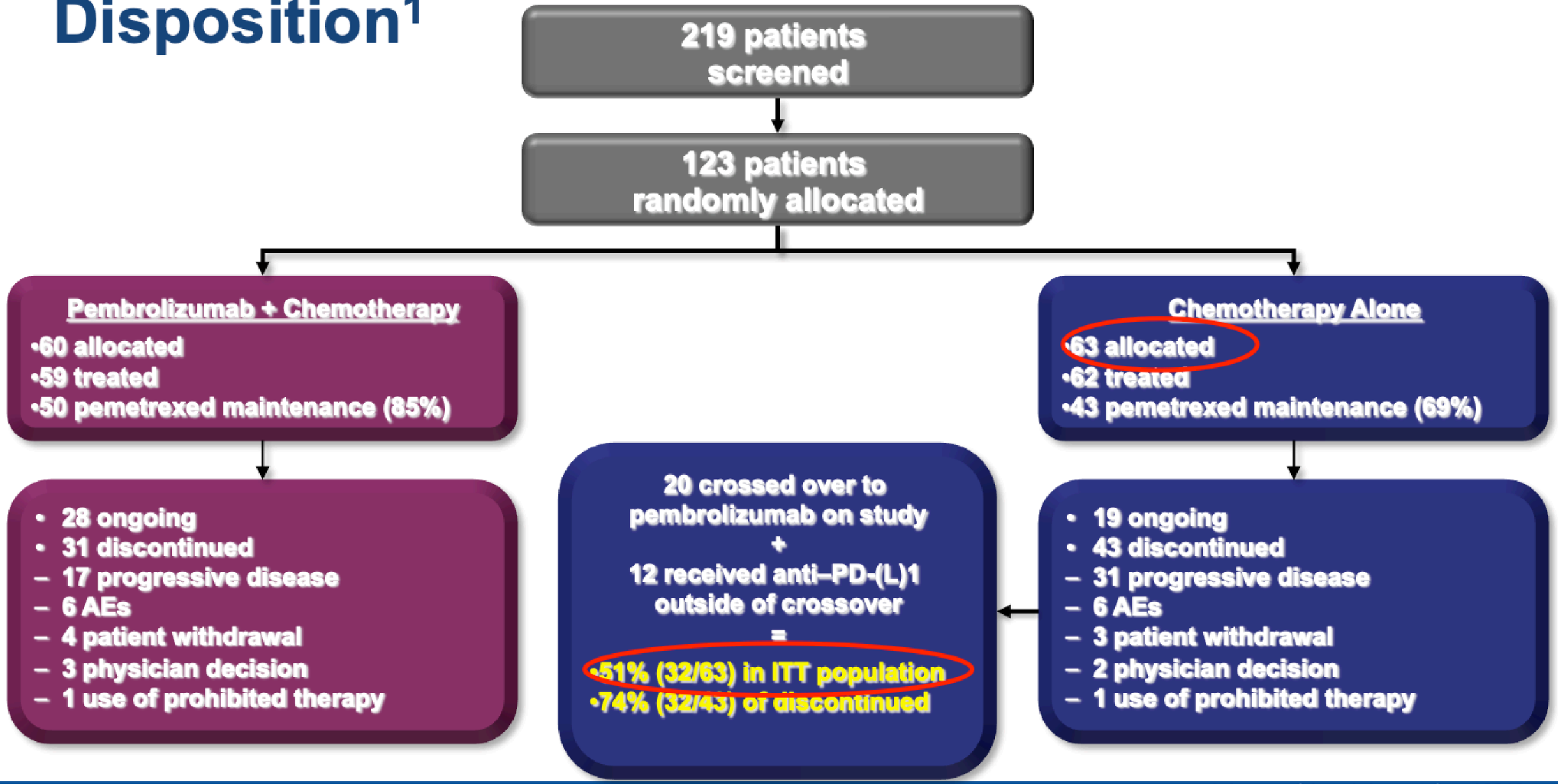
Disposition[1]



1. Langer CJ et al. *Lancet Oncol* 2016; dx.doi.org/10.1016/S1470-2045(16)30498-3.
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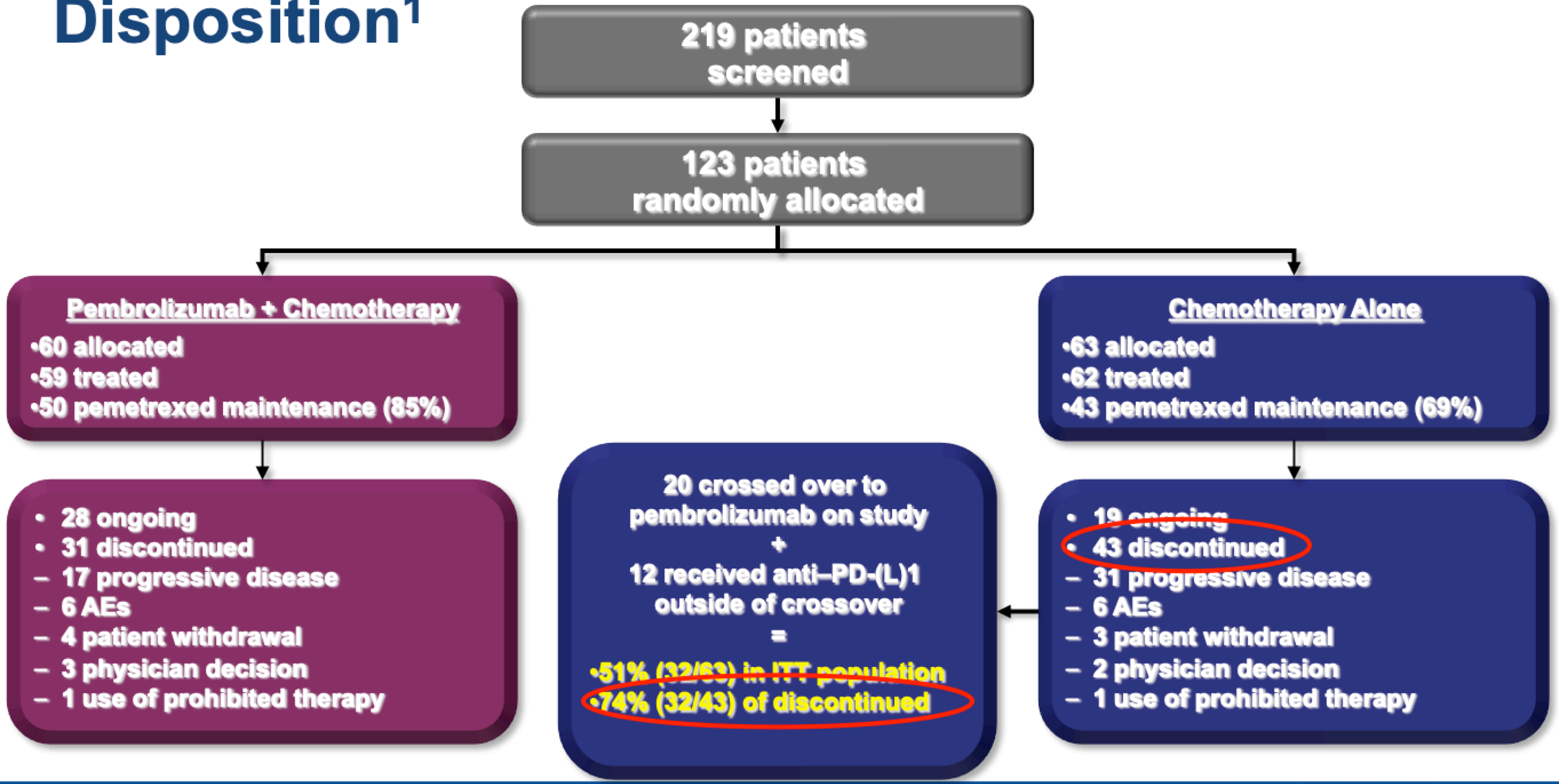
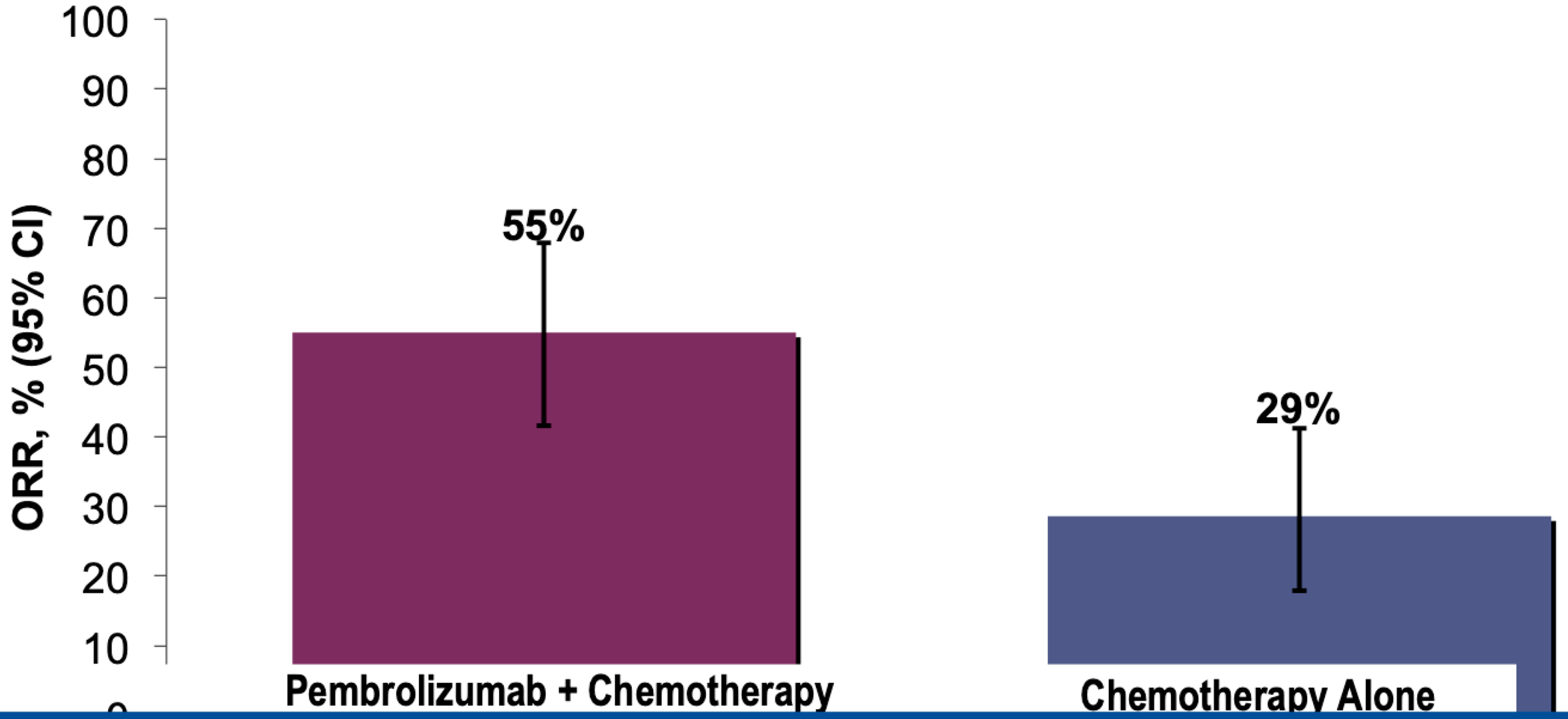


1. Langer CJ et al. *Lancet Oncol* 2016; dx.doi.org/10.1016/S1470-2045(16)30498-3.
Data cutoff date: August 8, 2016.

Confirmed Objective Response Rate[1]
(RECIST v1.1 by Blinded, Independent Central Review)



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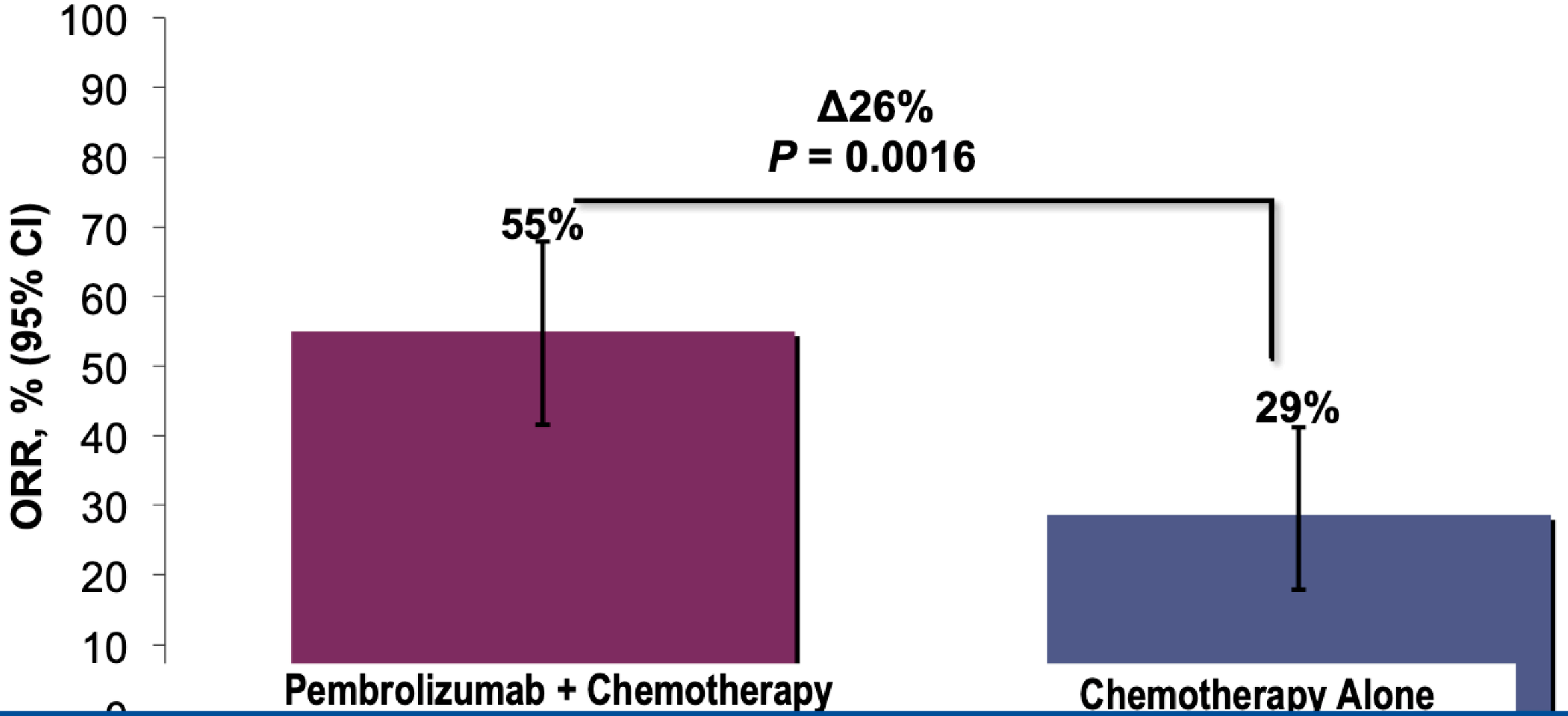

1. Langer CJ et al. *Lancet Oncol* 2016; dx.doi.org/10.1016/S1470-2045(16)30498-3.
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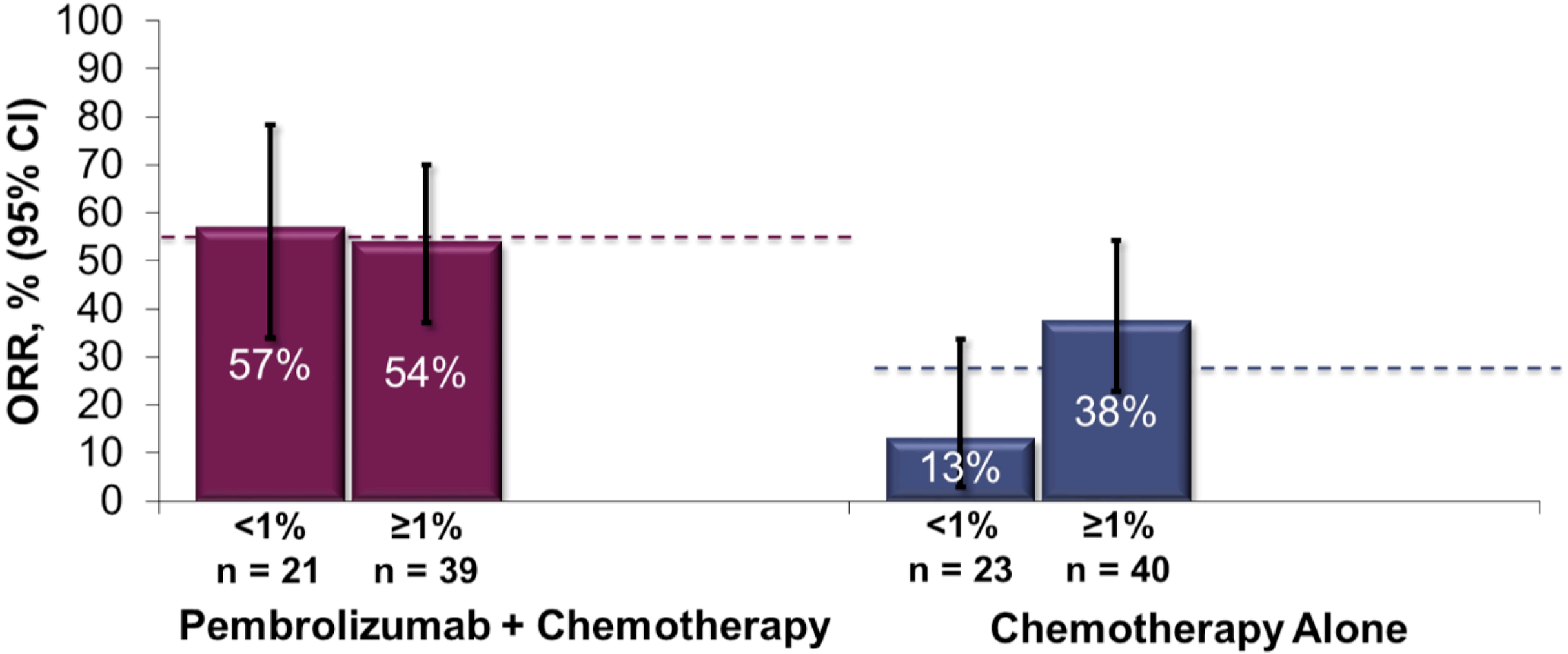
Objective Response Rate by PD-L1 Status[1]
(RECIST v1.1 by Blinded, Independent Central Review)

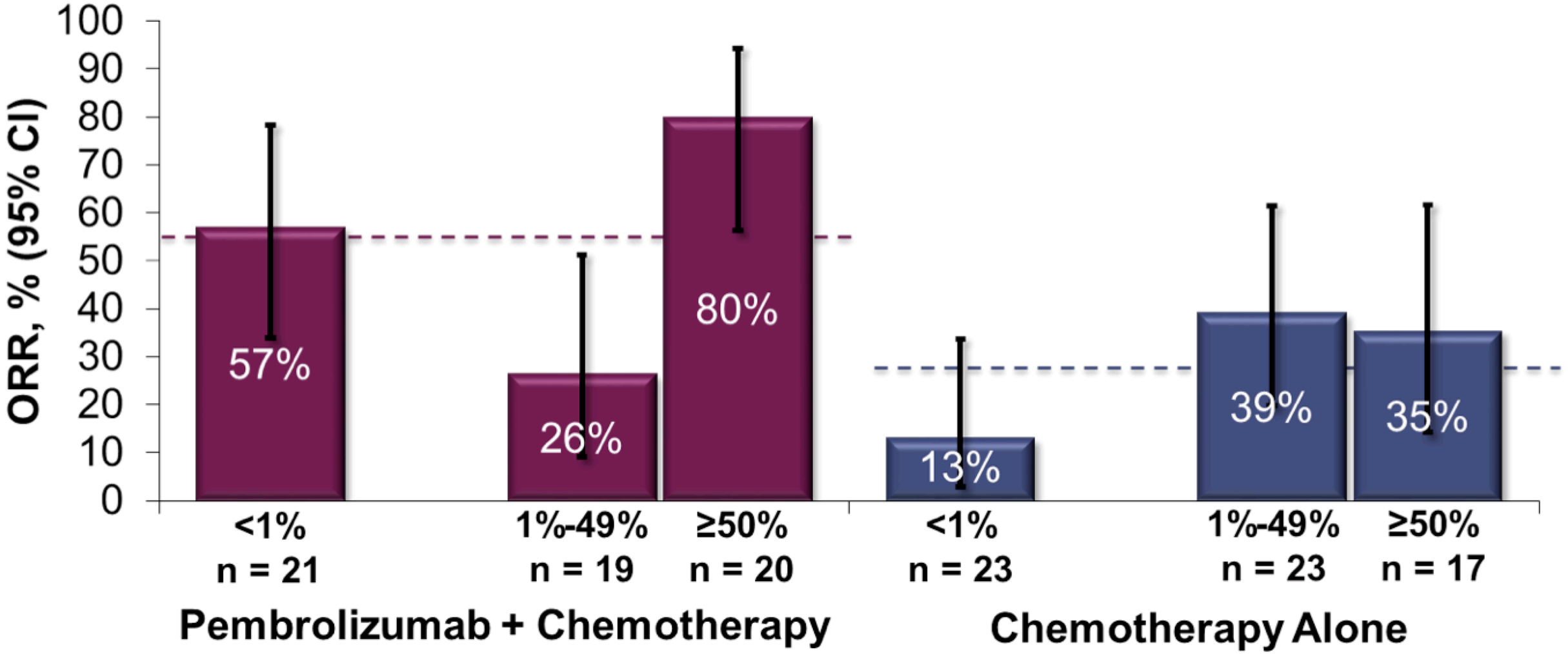


Horizontal dotted lines represent the ORR in the total population.

1. Langer CJ et al. *Lancet Oncol* 2016; dx.doi.org/10.1016/S1470-2045(16)30498-3.

Data cutoff date: August 8, 2016.

Objective Response Rate by PD-L1 Status[1]
(RECIST v1.1 by Blinded, Independent Central Review)

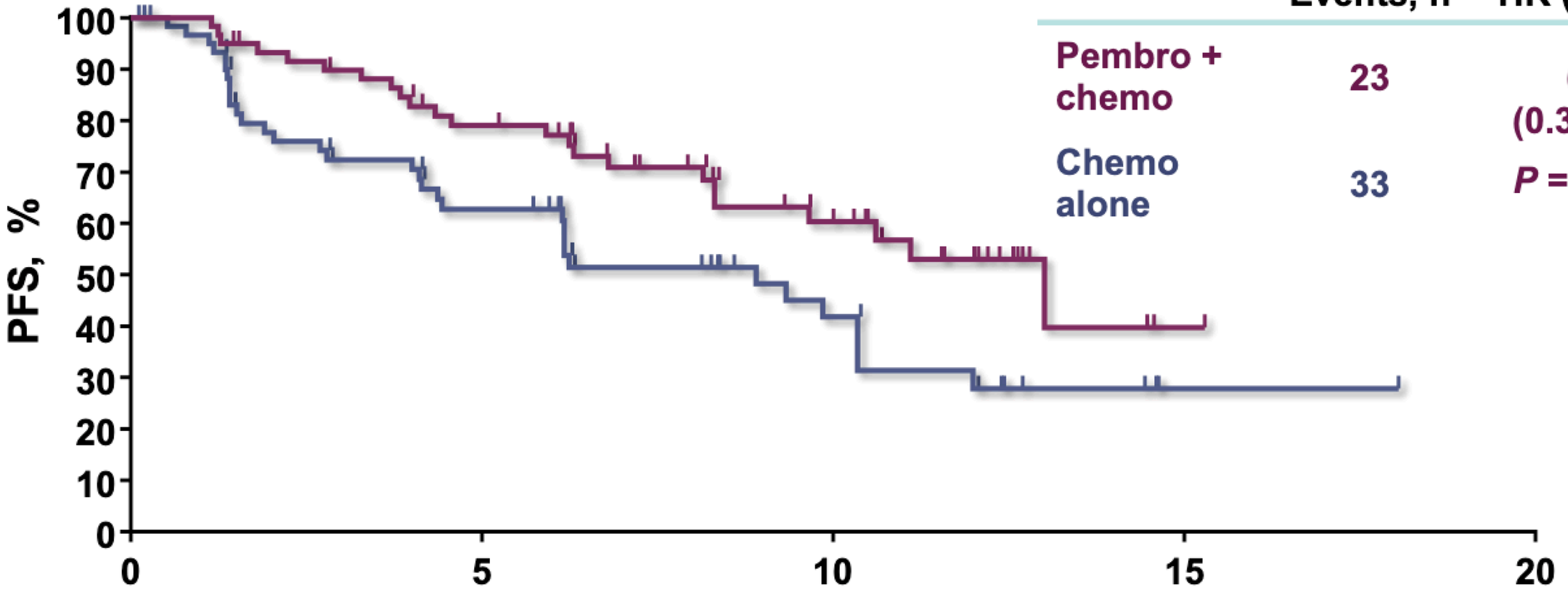


Horizontal dotted lines represent the ORR in the total population.

1. Langer CJ et al. *Lancet Oncol* 2016; dx.doi.org/10.1016/S1470-2045(16)30498-3.

Data cutoff date: August 8, 2016.

Progression-free Survival[1]
(RECIST v1.1 by Blinded, Independent Central Review)



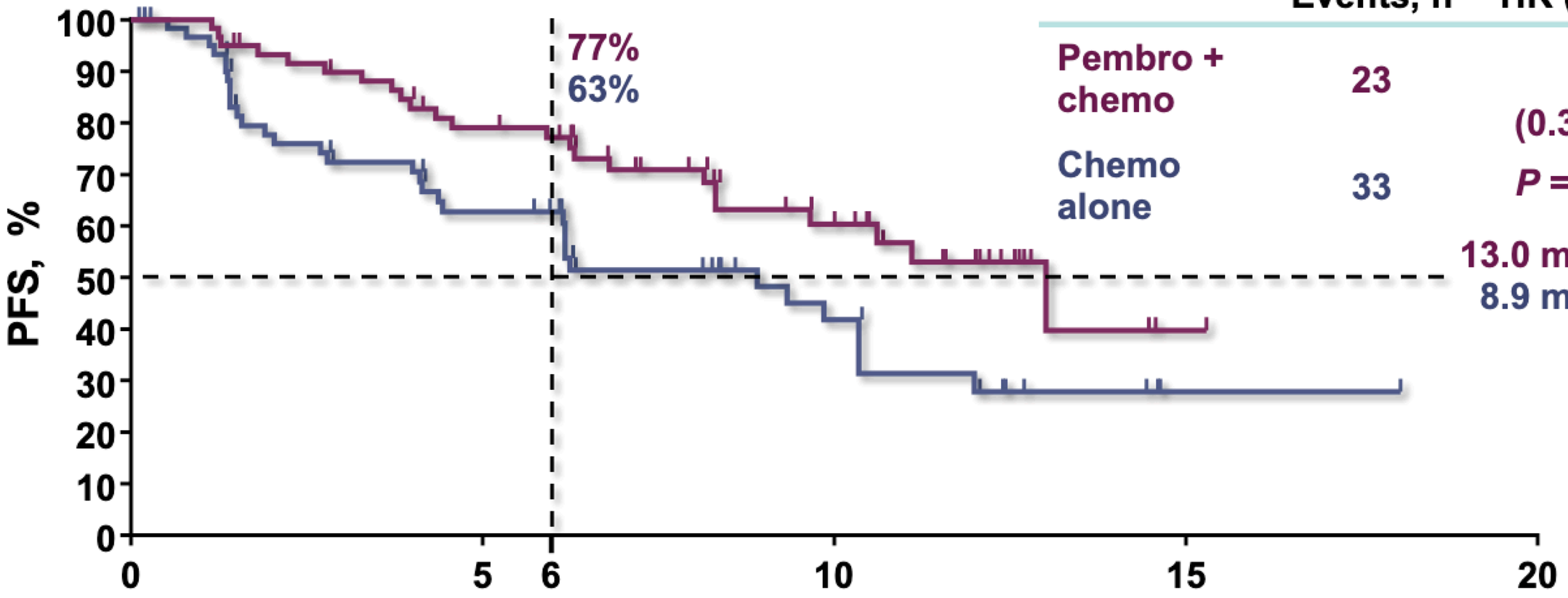
No. at risk

60	43	20	1	0
63	32	13	1	0

Adapted from *The Lancet Oncology*, Langer,CJ., et. al.,17(11) "Carboplatin and pemetrexed with or without pembrolizumab for advanced, non-squamous non-small-cell lung cancer: a randomised, phase 2 cohort of the open-label KEYNOTE-021 study," 1497-1508. 1. Langer CJ et al. *Lancet Oncol* 2016; dx.doi.org/10.1016/S1470-2045(16)30498-3. Data cutoff date: August 8, 2016.

Progression-free Survival[1]

(RECIST v1.1 by Blinded, Independent Central Review)



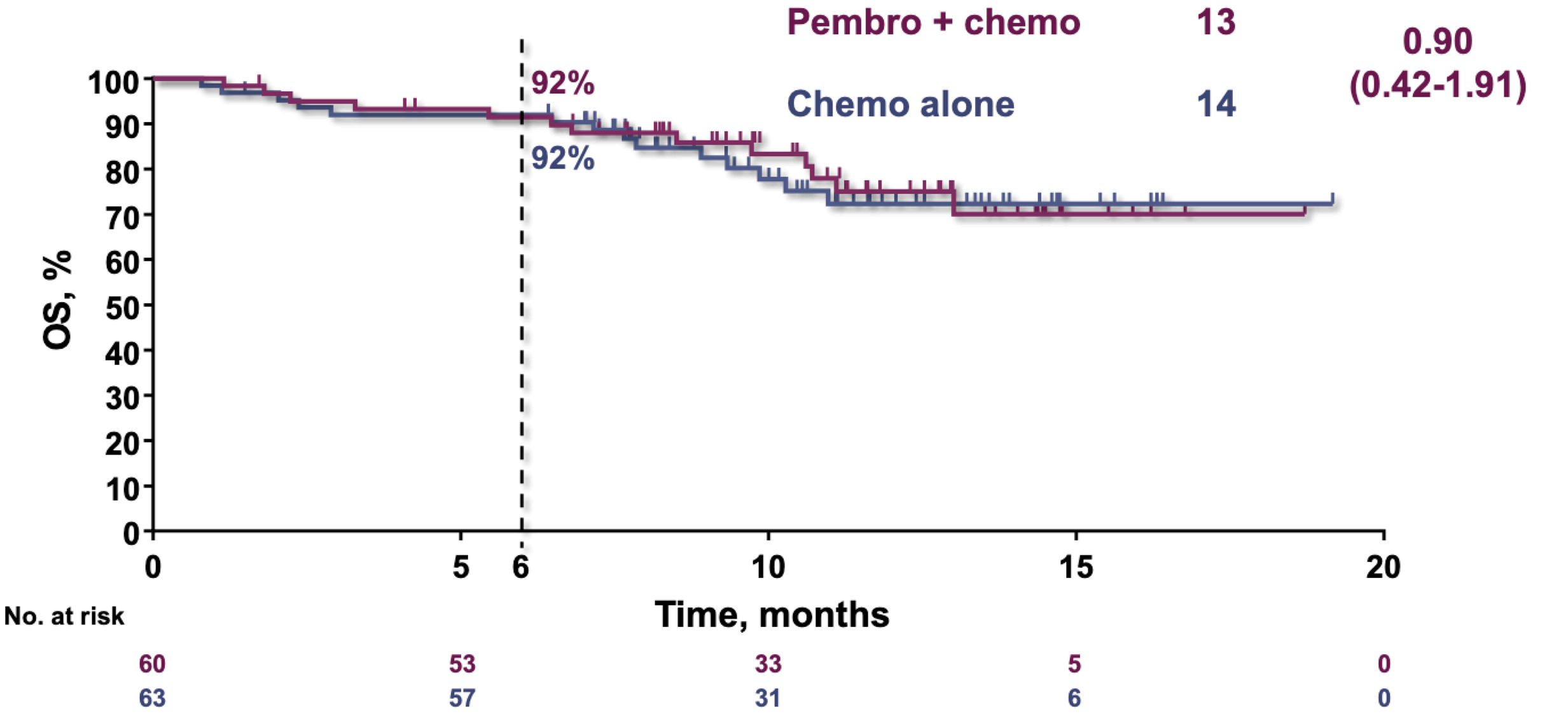
	Events, n	HR (95% CI)
Pembro + chemo	23	0.53 (0.31-0.91)
Chemo alone	33	*P* = 0.0102
		13.0 mo
		8.9 mo

No. at risk

60	43	20	1	0
63	32	13	1	0

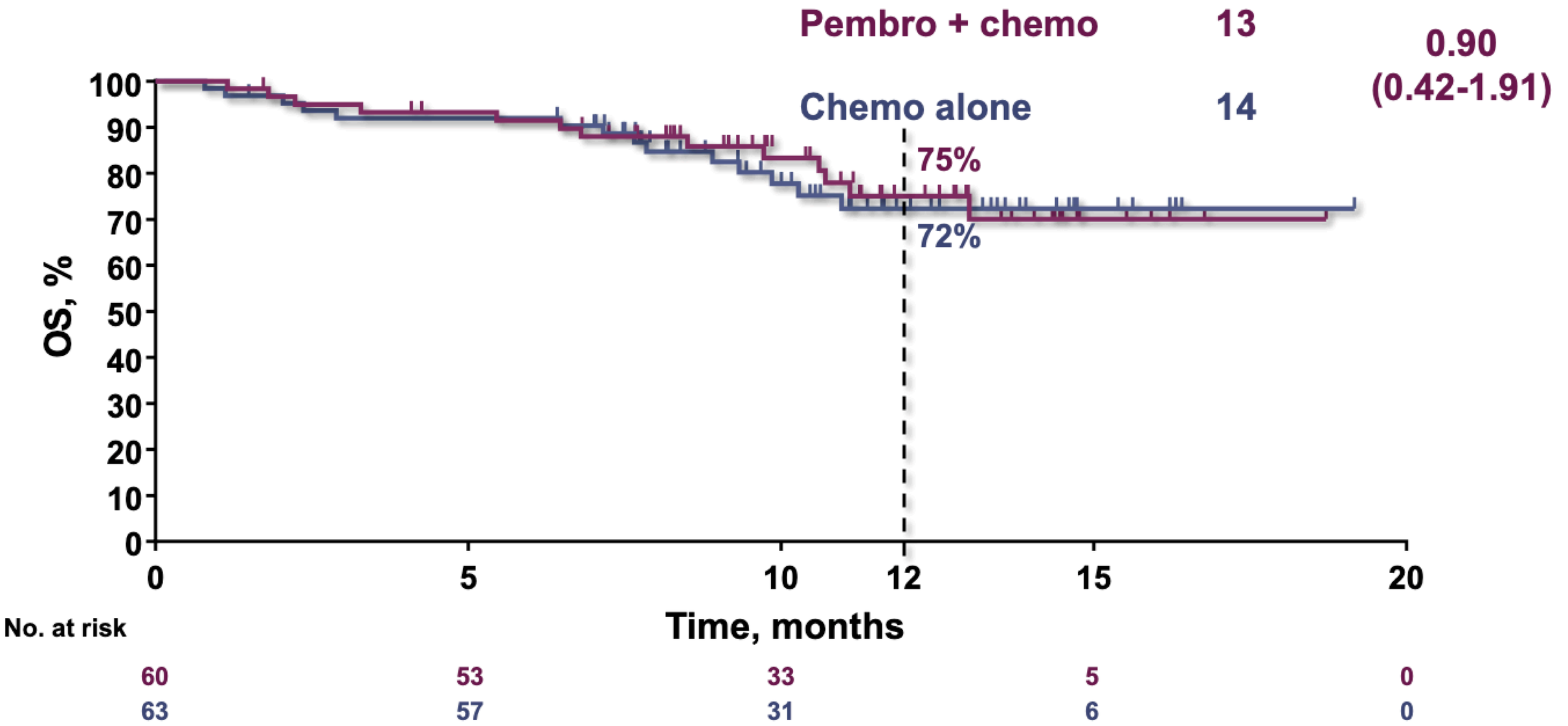
Adapted from *The Lancet Oncology*, Langer,CJ., et. al.,17(11) "Carboplatin and pemetrexed with or without pembrolizumab for advanced, non-squamous non-small-cell lung cancer: a randomised, phase 2 cohort of the open-label KEYNOTE-021 study," 1497-1508. 1. Langer CJ et al. *Lancet Oncol* 2016; dx.doi.org/10.1016/S1470-2045(16)30498-3. Data cutoff date: August 8, 2016.

Overall Survival[1]



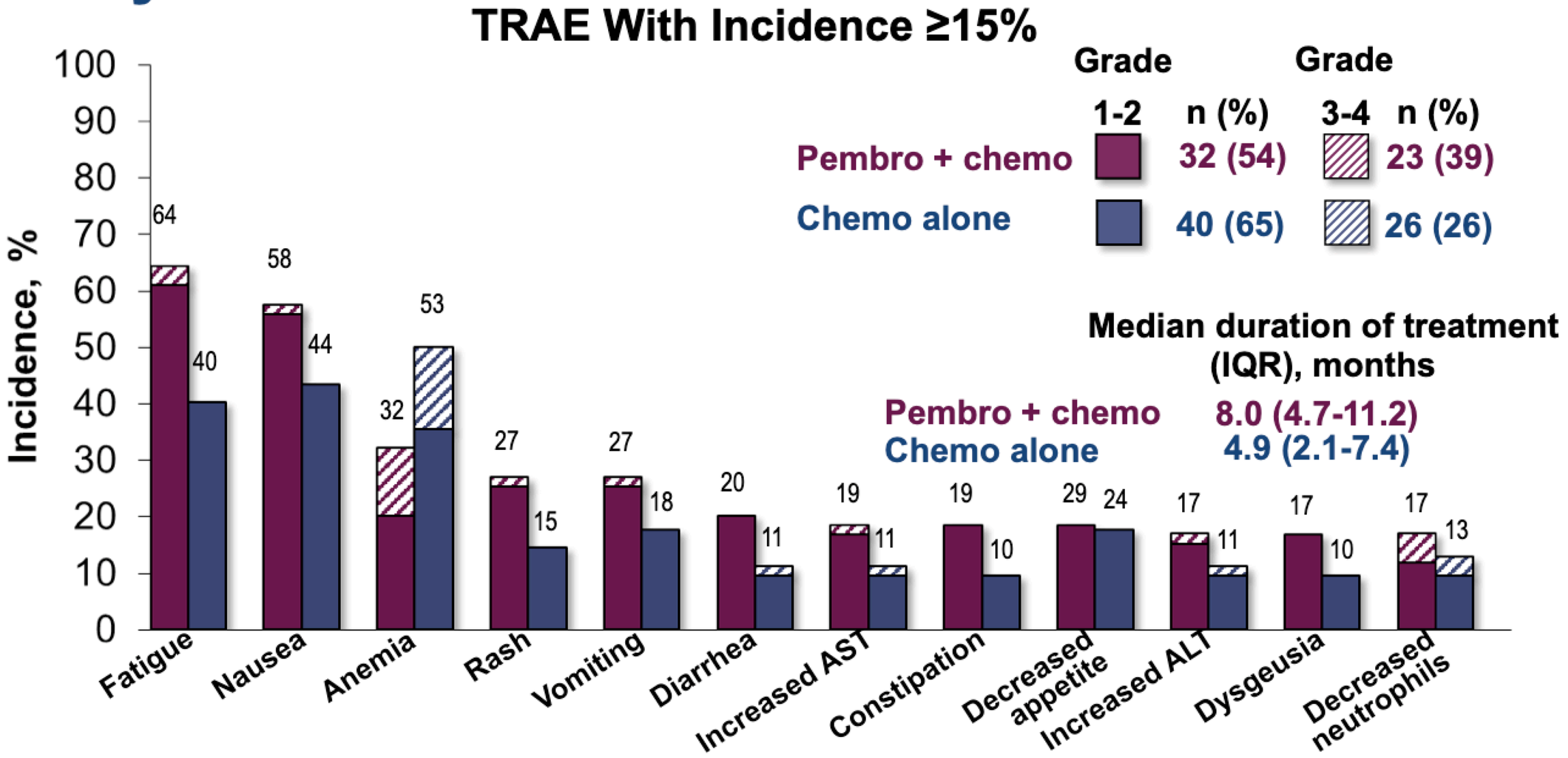
Adapted from *The Lancet Oncology*, Langer,CJ., et. al.,17(11) "Carboplatin and pemetrexed with or without pembrolizumab for advanced, non-squamous non-small-cell lung cancer: a randomised, phase 2 cohort of the open-label KEYNOTE-021 study," 1497-1508. ©2016 with permission from Elsevier. 1. Langer CJ et al. *Lancet Oncol* 2016; dx.doi.org/10.1016/S1470-2045(16)30498-3. Data cutoff date: August 8, 2016.

Overall Survival[1]



Adapted from *The Lancet Oncology*, Langer,CJ., et. al.,17(11) "Carboplatin and pemetrexed with or without pembrolizumab for advanced, non-squamous non-small-cell lung cancer: a randomised, phase 2 cohort of the open-label KEYNOTE-021 study," 1497-1508. ©2016 with permission from Elsevier. 1. Langer CJ et al. *Lancet Oncol* 2016; dx.doi.org/10.1016/S1470-2045(16)30498-3. Data cutoff date: August 8, 2016.

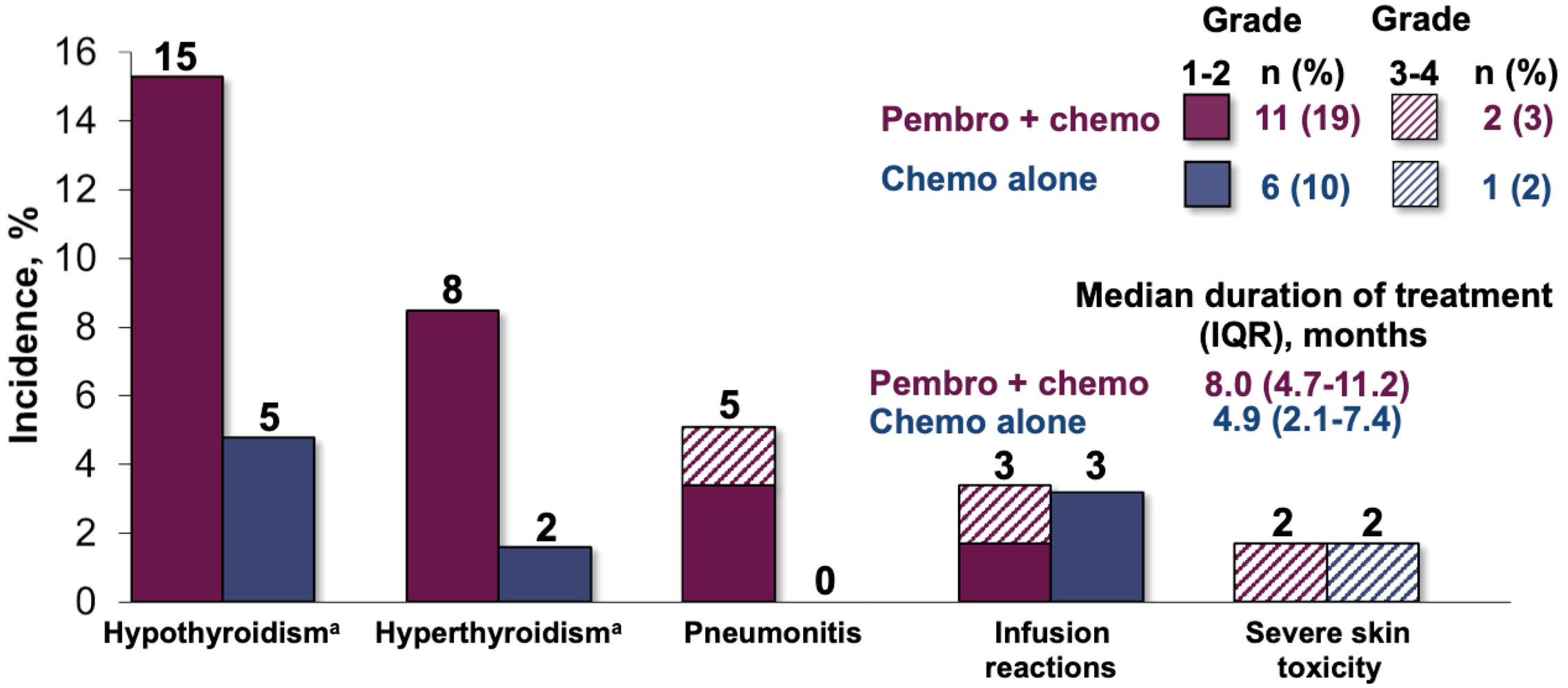
Safety[1]



1. Langer CJ et al. *Lancet Oncol* 2016; dx.doi.org/10.1016/S1470-2045(16)30498-3. Data cutoff date: August 8, 2016.

Safety[1]

AEs With Possible Immune Etiology



1. Langer CJ et al. *Lancet Oncol* 2016; dx.doi.org/10.1016/S1470-2045(16)30498-3. Data cutoff date: August 8, 2016.

Conclusions

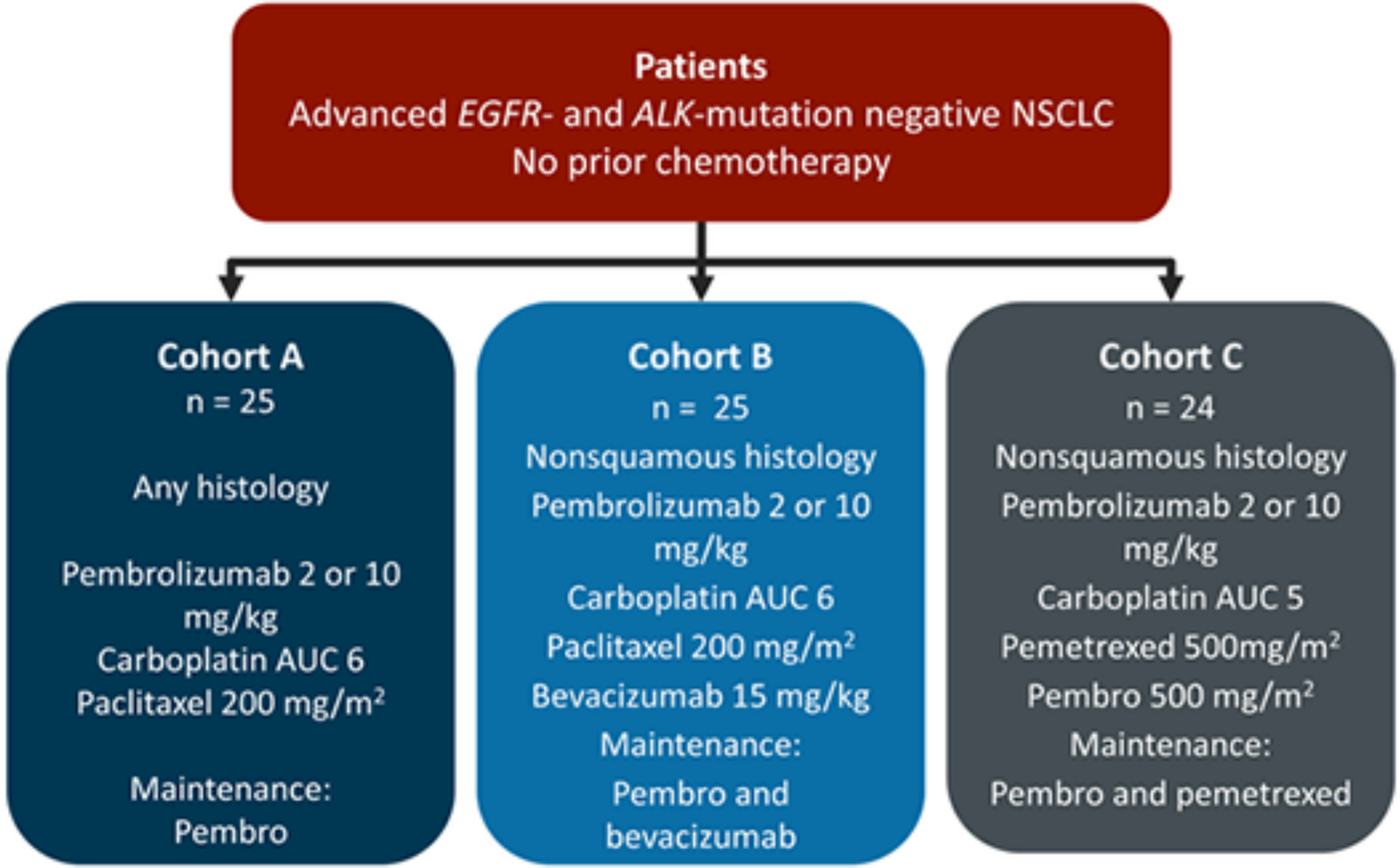
- Pembrolizumab in combination with carboplatin + pemetrexed appears superior to carboplatin + pemetrexed alone as first-line therapy for advanced nonsquamous NSCLC[1]
  - ORR nearly doubled by adding pembrolizumab to chemotherapy: 55% vs 29%
  - Risk of progression or death nearly halved: HR of 0.53 for PFS; median PFS for pembrolizumab + chemotherapy exceeds 1 year
  - Similar OS between arms: 92% survival at 6 months
- Pembrolizumab in combination with carboplatin + pemetrexed is tolerable and has a manageable safety profile
- Pembrolizumab in combination with carboplatin and pemetrexed could be an effective treatment option for patients with chemotherapy-naive, advanced nonsquamous NSCLC

1. Langer CJ et al. *Lancet Oncol* 2016; dx.doi.org/10.1016/S1470-2045(16)30498-3.

KEYNOTE-021 (PD1/PDL1-71)

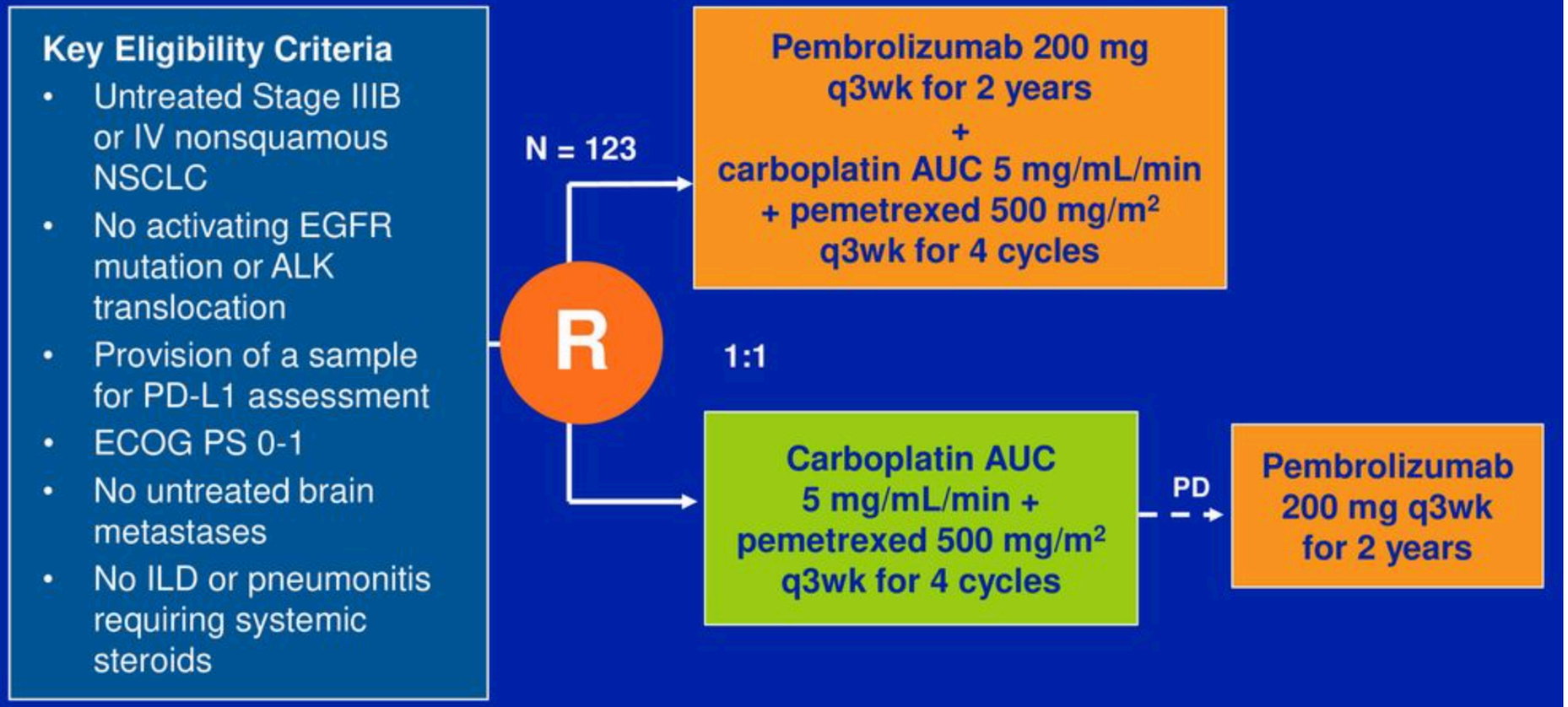
ESMO2017 in Spain

KEYNOTE-021 Design



Gadgeel SM, et al. *J Clin Oncol*. 2016;34(suppl).

KEYNOTE-021 Cohort G



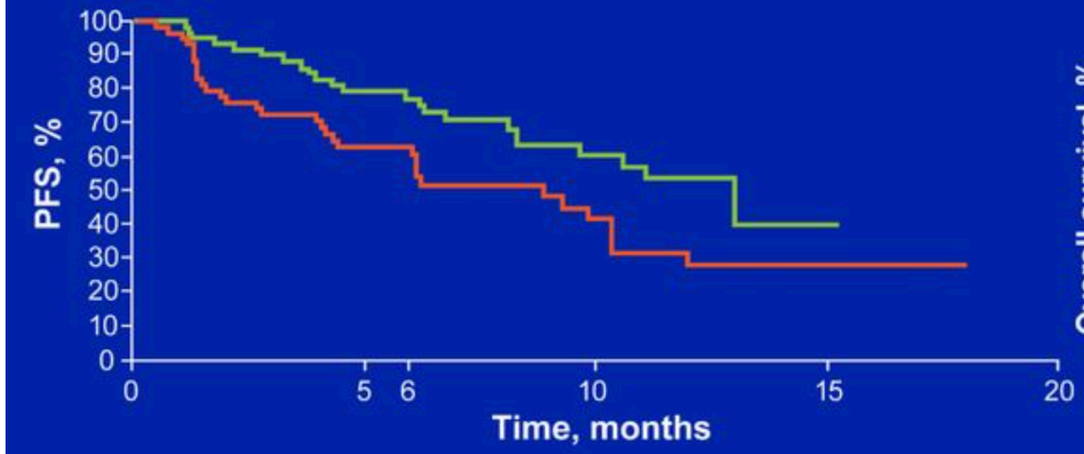
Endpoints

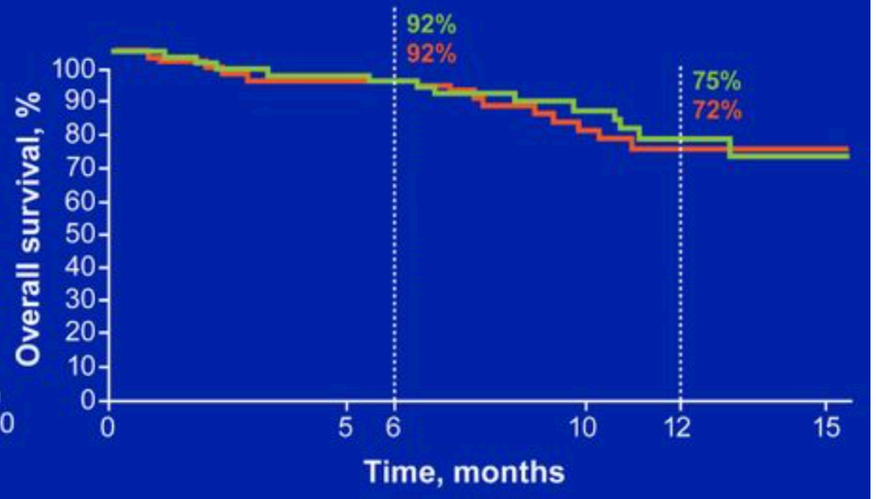
Primary: ORR (RECIST v1.1 per blinded, independent central review)

Key secondary: PFS

Langer C et al. *Lancet Oncol* 2016;17(11):1497-1508, *Proc ESMO* 2016;Abstract LBA46_PR.

KEYNOTE-021: Survival data





	Events, n	Median	HR (95% CI)
Pembro + chemo (n = 60)	23	13.0 mo	0.53 (0.31-0.91)
Chemo alone (n = 63)	33	8.9 mo	*p* = 0.0102

	Events, n	HR (95% CI)
Pembro + chemo	13	0.90 (0.42-0.91)
Chemo alone	14	

- **Median PFS improved by 4.1 months**
- No difference in OS
  - Estimated rate of OS @ 12 months: 75% (combo) vs 72% (CT)
- In chemotherapy arm, crossover is 51% to anti-PD-1/PD-L1 therapies (pembrolizumab and others)

Langer C et al. *Lancet Oncol* 2016;17(11):1497-1508, *Proc ESMO* 2016;Abstract LBA46_PR.

KEYNOTE-021: Select Adverse Events

	Pembrolizumab + Carbo/Pemetrexed (n = 59)		Carbo/Pemetrexed (n = 62)	
AEs	**Grade 1-2**	**Grade ≥3**	**Grade 1-2**	**Grade ≥3**
Fatigue	61%	3%	40%	0
Anemia	20%	12%	39%	15%
Decreased neutrophil count	12%	5%	10%	3%
Decreased lymphocyte count	5%	3%	3%	2%
Thrombocytopenia	2%	4%	3%	3%
Hypothyroidism	15%	0	5%	0
Hyperthyroidism	8%	0	2%	0
Pneumonitis	3%	2%	0	0

Langer CJ et al. Lancet Oncol 2016;17(11):1497-1508.