Toetje
Hoe het lelijke eendje …….

Roy Lalisang

POST—ASCO

Oncologisch Netwerk
Zuidoost-Nederland

Pembrolizumab vs Platinum-Based Chemotherapy as First-Line Therapy for Advanced/Metastatic NSCLC With a PD-L1 TPS ≥1%: Open-Label, Phase 3 KEYNOTE-042 Study

Gilberto Lopes,[1] Yi-Long Wu,[2] Iveta Kudaba,[3] Dariusz M Kowalski,[4] Byoung Chul Cho,[5] Hande Z Turna,[6] Gilberto Castro, Jr,[7] Vichien Srimuninnimit,[8] Konstantin K. Laktionov,[9] Igor Bondarenko,[10] Karou Kubota,[11] Gregory M Lubiniecki,[12] Jin Zhang,[12] Debra Kush,[12] Tony Mok[13]

[1]Sylvester Comprehensive Cancer Center at the University of Miami, Miami, FL, USA; [2]Guangdong General Hospital and Guangdong Academy of Medical Sciences, Guandong, China; [3]Riga East Clinical University - Latvian Oncology Center, Riga, Latvia; [4]The Maria Sklodowska-Curie Memorial Cancer Centre and Institute of Oncology, Warsaw, Poland; [5]Yonsei Cancer Center, Seoul, South Korea; [6]Instanbul University Cerrahpasa Medical Faculty, Istanbul, Turkey; [7]Instituto do Câncer do Estado de São Paulo, São Paulo, Brazil; [8]Siriraj Hospital, Bangkok, Thailand; [9]NN Blokhin Russian Cancer Research Center, Moscow, Russia; [10]Dnipropetrovsk Medical Academy, Dnipro, Ukraine; [11]Nippon Medical School Hospital, Tokyo, Japan; [12]Merck & Co., Inc., Kenilworth, NJ, USA; [13]The Chinese University of Hong Kong, Shatin, Hong Kong PRC

PRESENTED AT: 2018 ASCO ANNUAL MEETING #ASCO18

PRESENTED BY: Gilberto Lopes

Pembrolizumab and PD-L1 for Metastatic NSCLC

- Monotherapy significantly improved OS vs docetaxel in metastatic NSCLC of PD-L1 tumor proportion score (TPS) ≥1% that progressed on or after platinum-containing chemotherapy[1a]
- Monotherapy significantly improved PFS and OS vs platinum-based chemotherapy in previously untreated metastatic NSCLC with PD-L1 TPS ≥50%[2b]
- Combination with platinum-based chemotherapy significantly improved OS over chemotherapy alone in untreated metastatic NSCLC, irrespective of PD-L1 expression[3,4b]
- Companion diagnostic: PD-L1 IHC 22C3 pharmDx assay (Agilent Technologies)
  - Used to assesses PD-L1 expression in formalin-fixed tumor samples
  - Expression measure: TPS, defined as the percentage of tumor cells with membranous PD-L1 staining

[a]Pts with sensitizing *EGFR* or *ALK* alteration must have also progressed on an appropriate TKI. [b]Pts with sensitizing *EGFR* or *ALK* alteration were excluded.

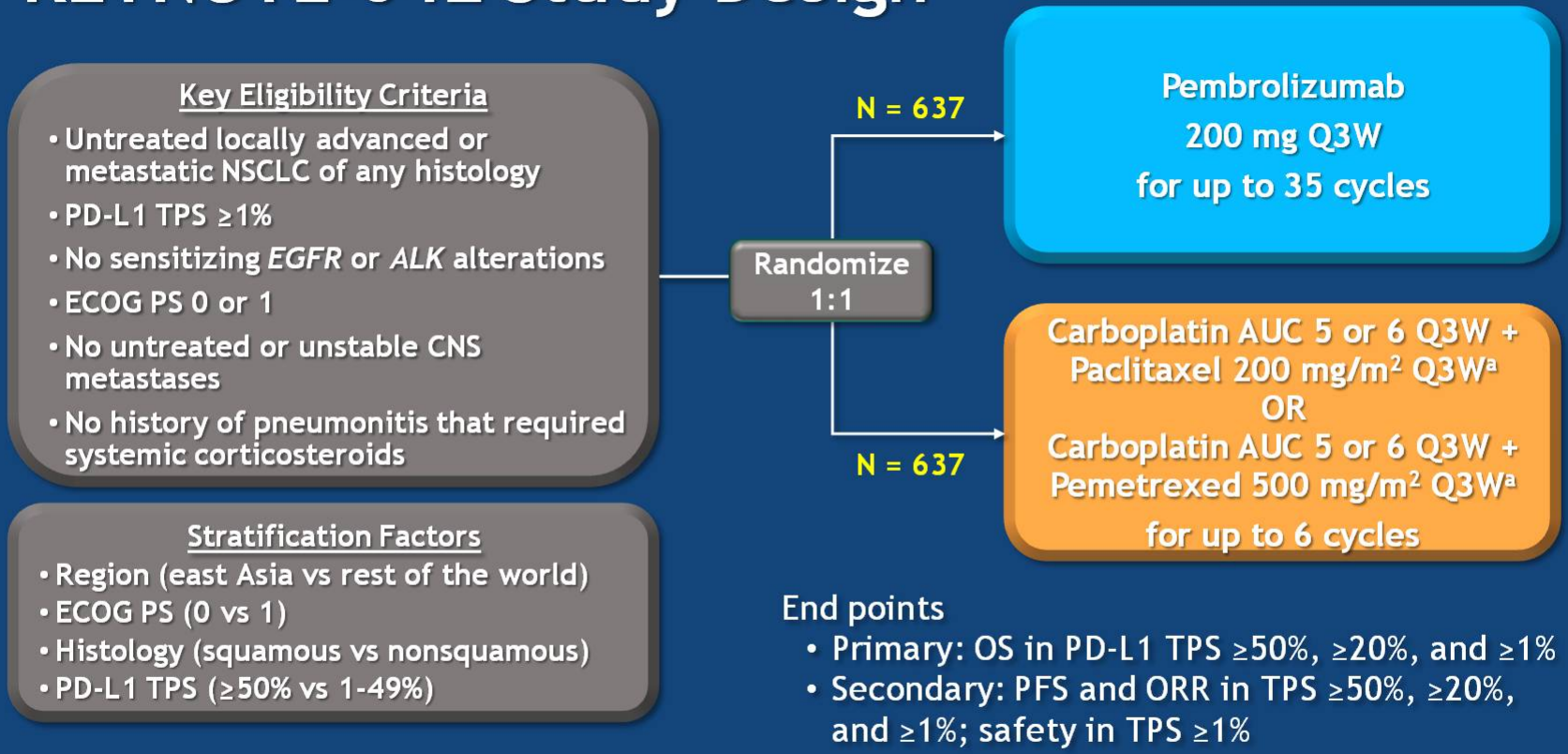
1. Herbst RS et al. *Lancet* 2016;387:1540-50. 2. Reck M et al. *N Engl J Med* 2016;375:1823-33.
3. Gandhi L et al. *N Engl J Med* 2018;378:2078-92. 4. Paz-Ares L et al. Presented at ASCO 2018; abstract 105.

First-Line Pembrolizumab Monotherapy

- KEYNOTE-024: pembrolizumab monotherapy vs platinum-based chemotherapy for metastatic NSCLC with PD-L1 TPS ≥50% and no sensitizing *EGFR* or *ALK* alterations[1]
  - Pembrolizumab provided superior PFS (primary end point) and OS (key secondary end point)
  - Pembrolizumab had a better safety profile
- Unmet need: more effective and tolerable first-line therapy for metastatic NSCLC
- **Objective of KEYNOTE-042 (NCT02228094): investigate role of first-line pembrolizumab in patients with PD-L1 expression (TPS ≥1%)**

1. Reck M et al. *N Engl J Med* 2016;375:1823-33.

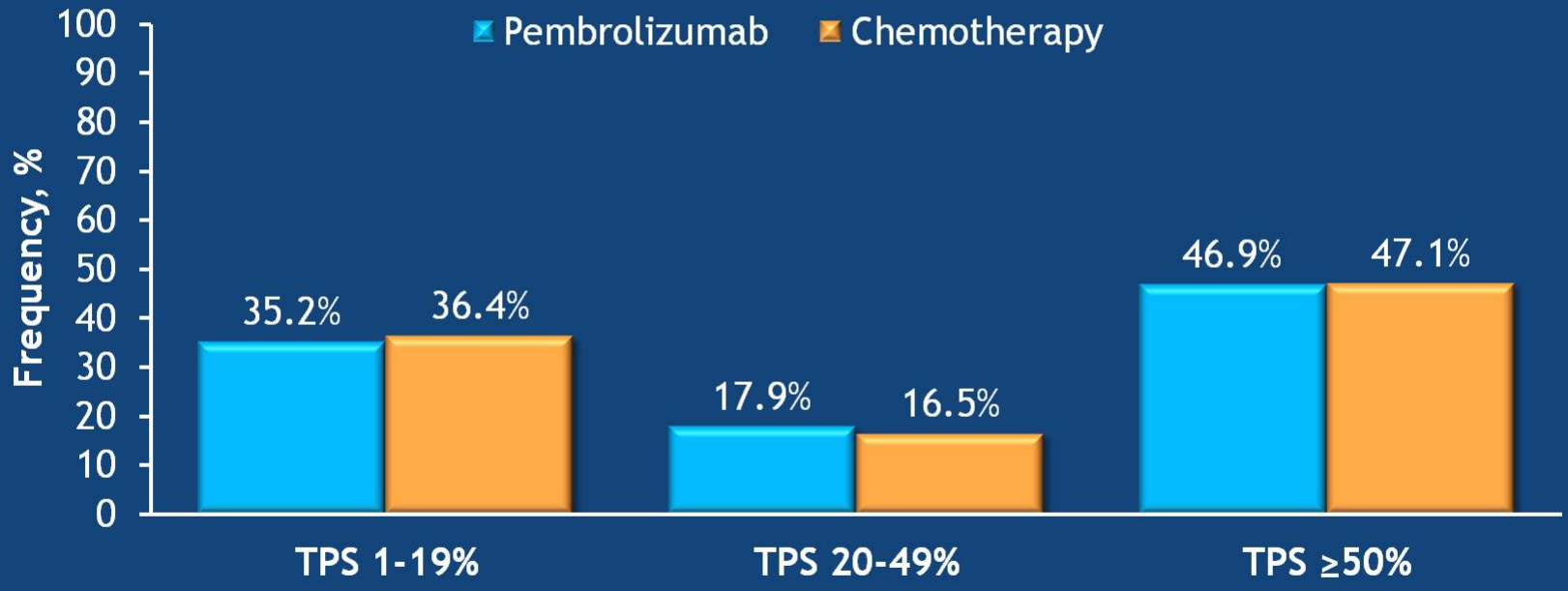
KEYNOTE-042 Study Design



End points
- Primary: OS in PD-L1 TPS ≥50%, ≥20%, and ≥1%
- Secondary: PFS and ORR in TPS ≥50%, ≥20%, and ≥1%; safety in TPS ≥1%

[a]Pemetrexed maintenance therapy was optional but strongly encouraged for patients with nonsquamous histology.

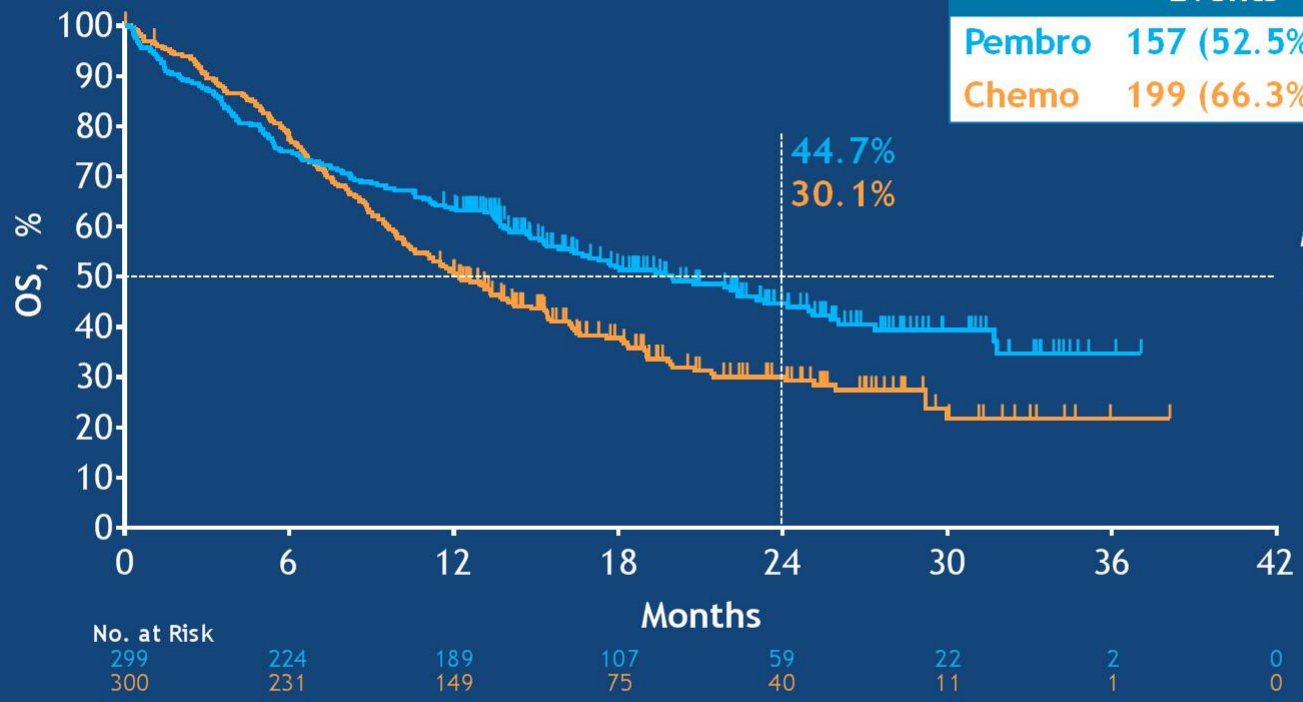
Frequency of PD-L1 TPS Categories: TPS ≥1% Population



Data cutoff date: Feb 26, 2018.

Overall Survival: TPS ≥50%

	Events	HR (95% CI)	*P*
Pembro	157 (52.5%)	0.69 (0.56-0.85)	0.0003
Chemo	199 (66.3%)		

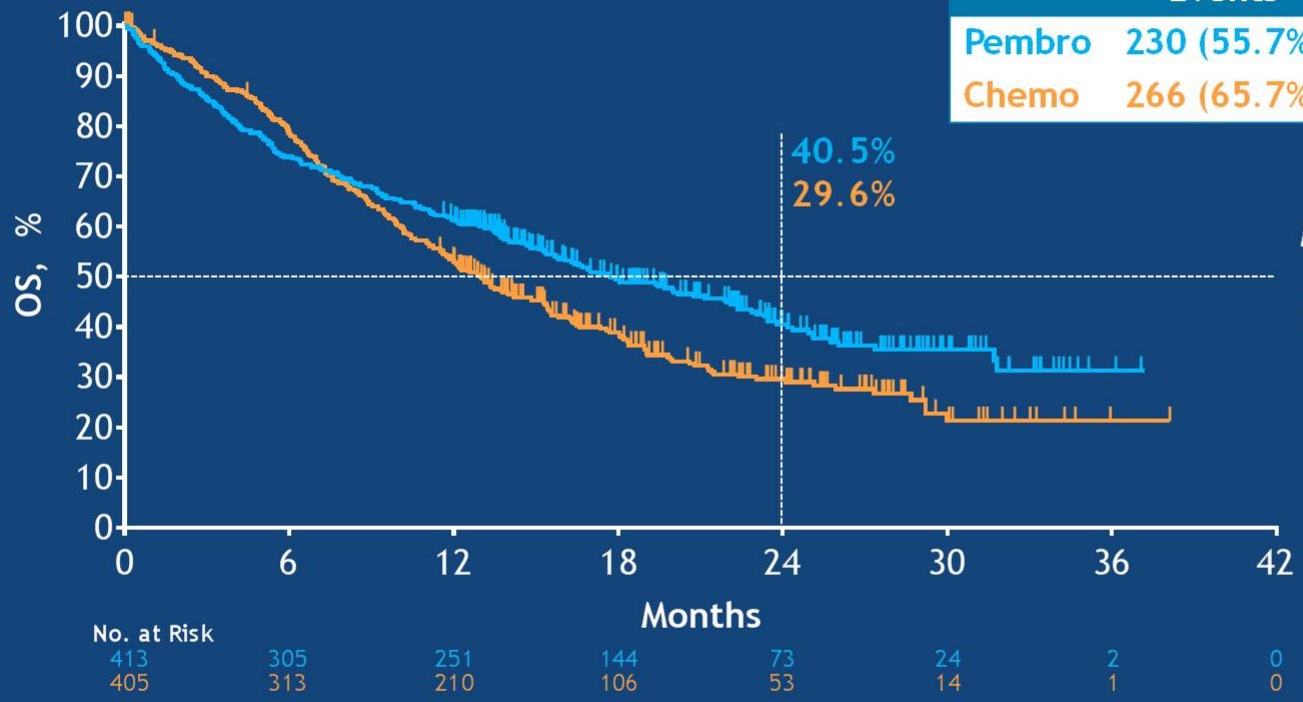


Median (95% CI)
20.0 mo (15.4-24.9)
12.2 mo (10.4-14.2)

Data cutoff date: Feb 26, 2018.

Overall Survival: TPS ≥20%

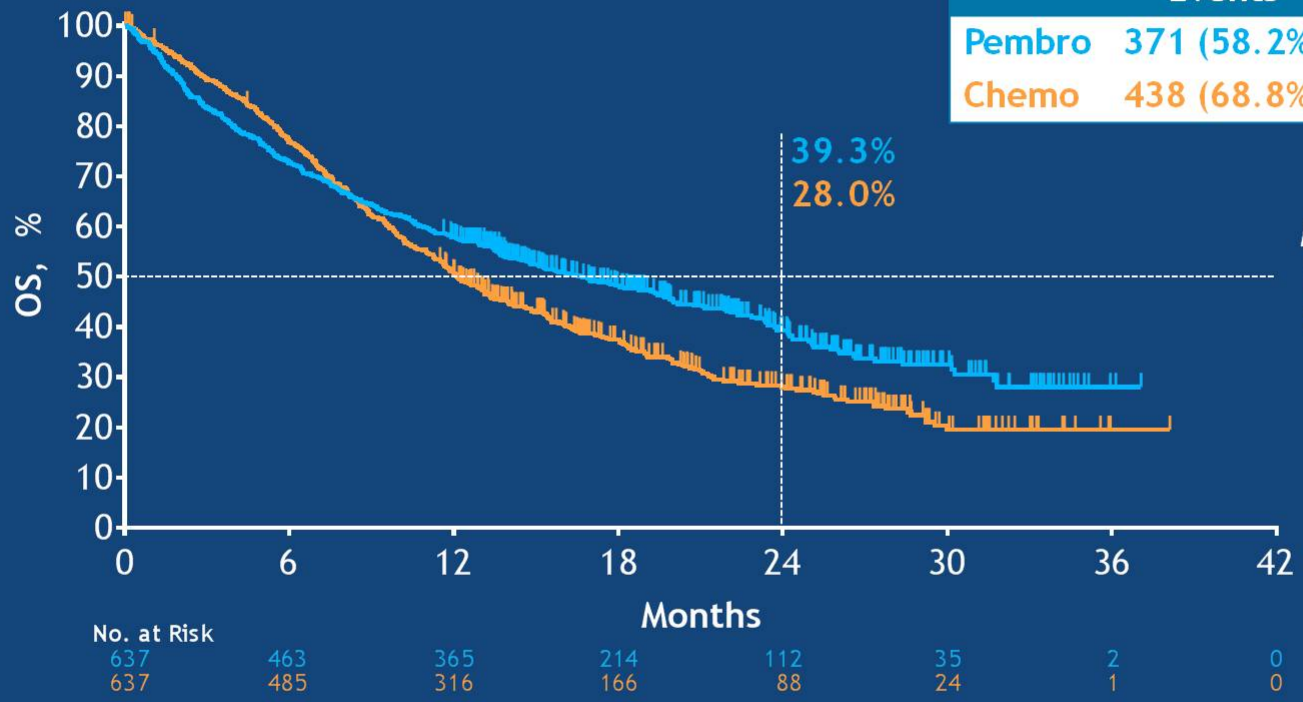
	Events	HR (95% CI)	*P*
Pembro	230 (55.7%)	0.77 (0.64-0.92)	0.0020
Chemo	266 (65.7%)		



Median (95% CI)
17.7 mo (15.3-22.1)
13.0 mo (11.6-15.3)

Overall Survival: TPS ≥1%

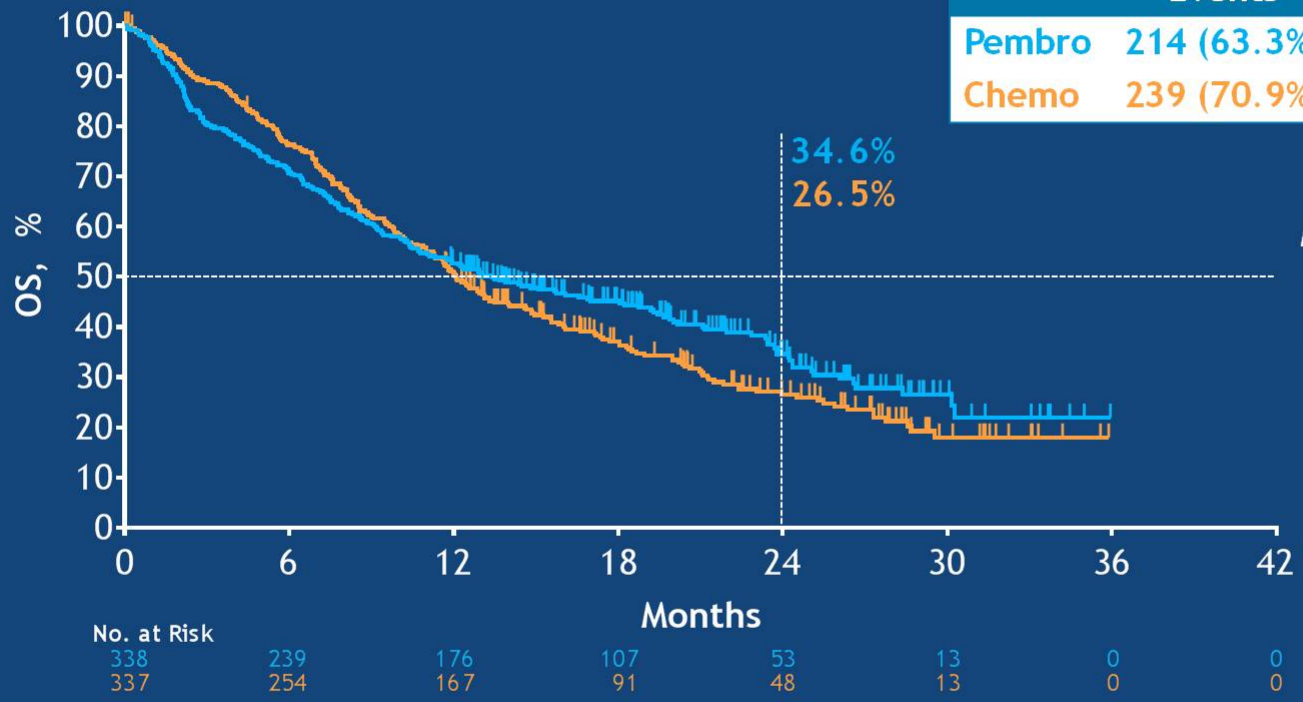
	Events	HR (95% CI)	*P*
Pembro	371 (58.2%)	0.81 (0.71-0.93)	0.0018
Chemo	438 (68.8%)		



Median (95% CI)
16.7 mo (13.9-19.7)
12.1 mo (11.3-13.3)

Overall Survival: TPS ≥1-49% (Exploratory Analysis[a])

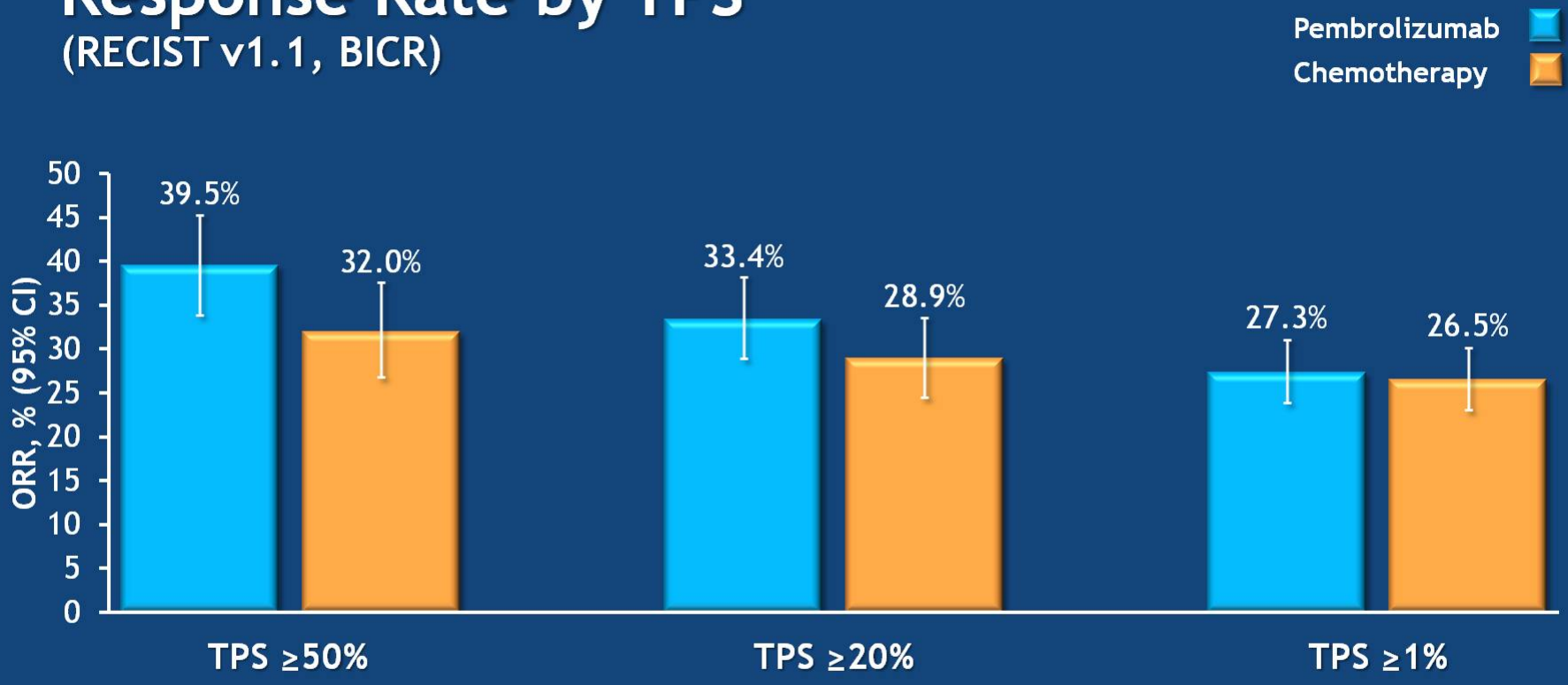
	Events	HR (95% CI)
Pembro	214 (63.3%)	0.92 (0.77-1.11)
Chemo	239 (70.9%)	



Median (95% CI)
13.4 mo (10.7-18.2)
12.1 mo (11.0-14.0)

[a]No alpha allocated to this comparison.

Response Rate by TPS
(RECIST v1.1, BICR)

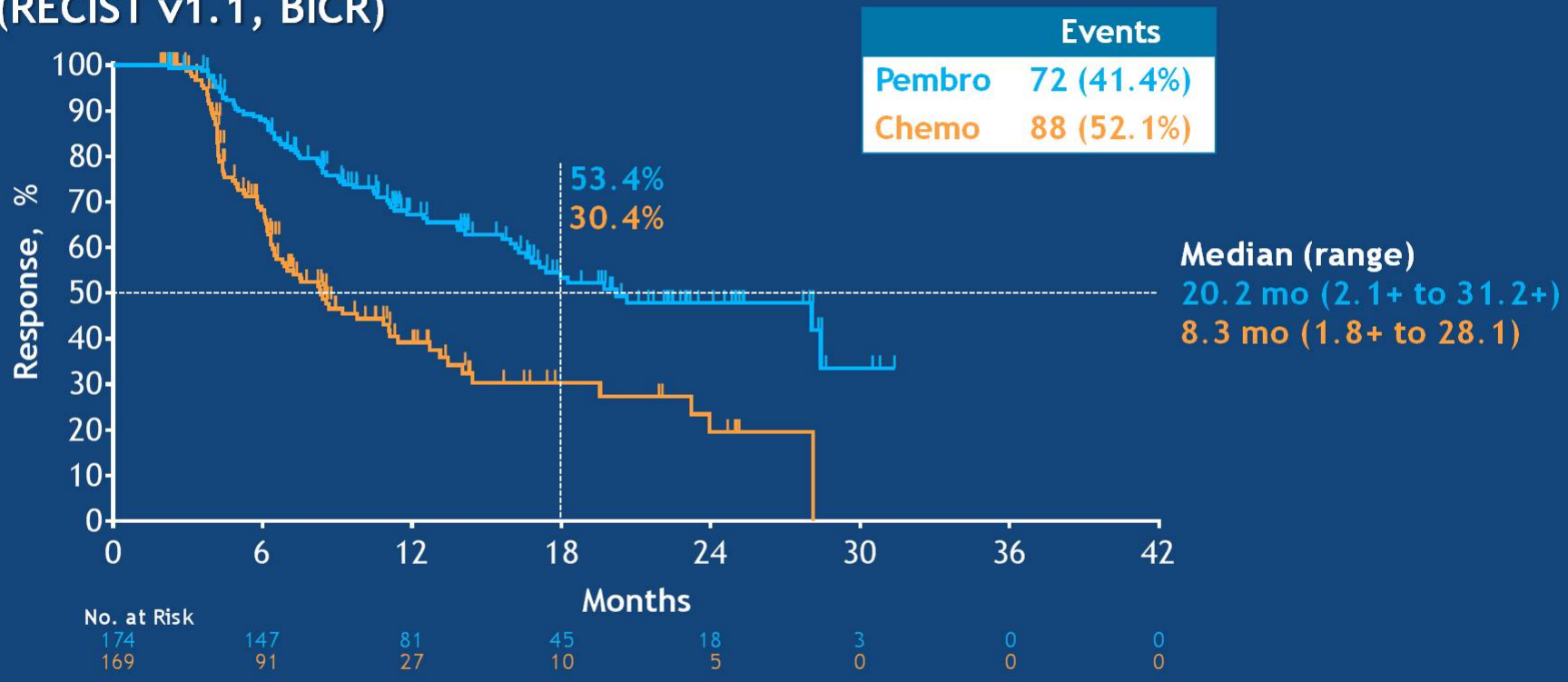


ORR for TPS 1-49%: 16.6% (95% CI 12.8-21.0) for pembro vs 21.7% (95% CI 17.4-26.4).
CR in pembro arm: 0 with TPS ≥50%, 2 with TPS ≥20%, 3 with TPS ≥1%; CR in chemo arm: 0 with TPS ≥50%, 1 with TPS ≥20%, 3 with TPS ≥1%.

Data cutoff date: Feb 26, 2018.

Duration of Response: TPS ≥1%

(RECIST v1.1, BICR)



Median DOR for pembro vs chemo: 20.2 mo vs 10.8 mo for TPS ≥50%, 20.2 mo vs 8.3 mo for TPS ≥20%, and 17.4 mo vs 8.2 mo for TPS 1-49%.

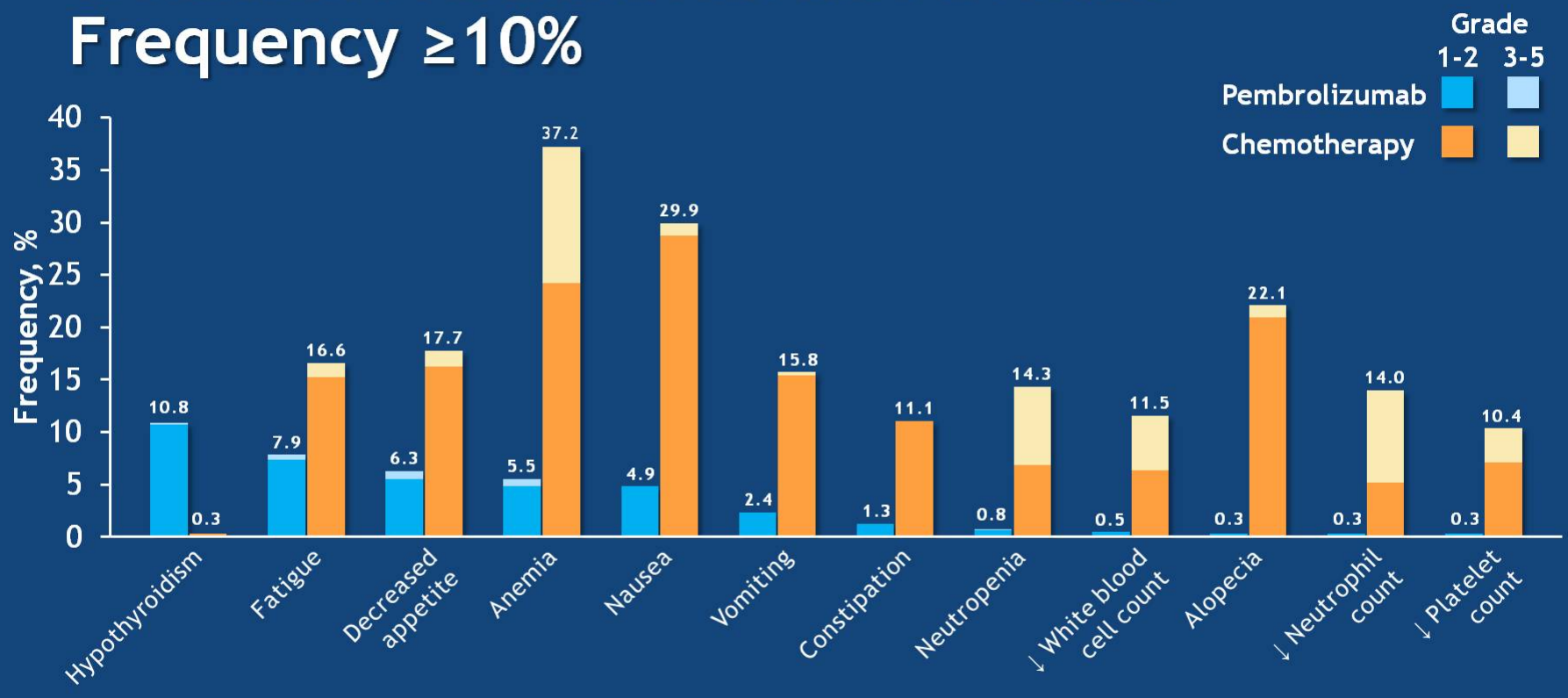
Summary of Exposure and Adverse Events: All Treated Patients

	Pembrolizumab (N = 636)	Chemotherapy (N = 615)
No. of doses, median (range)	9 (1-36)	6 (1-42)
Treatment-related AEs	399 (62.7%)	553 (89.9%)
Grade 3-5	113 (17.8%)	252 (41.0%)
Led to death	13 (2.0%)	14 (2.3%)
Led to discontinuation	57 (9.0%)	58 (9.4%)
Immune mediated AEs and infusion reactions[a]	177 (27.8%)	44 (7.2%)
Grade 3-5	51 (8.0%)	9 (1.5%)
Led to death	1 (0.2%)[b]	0

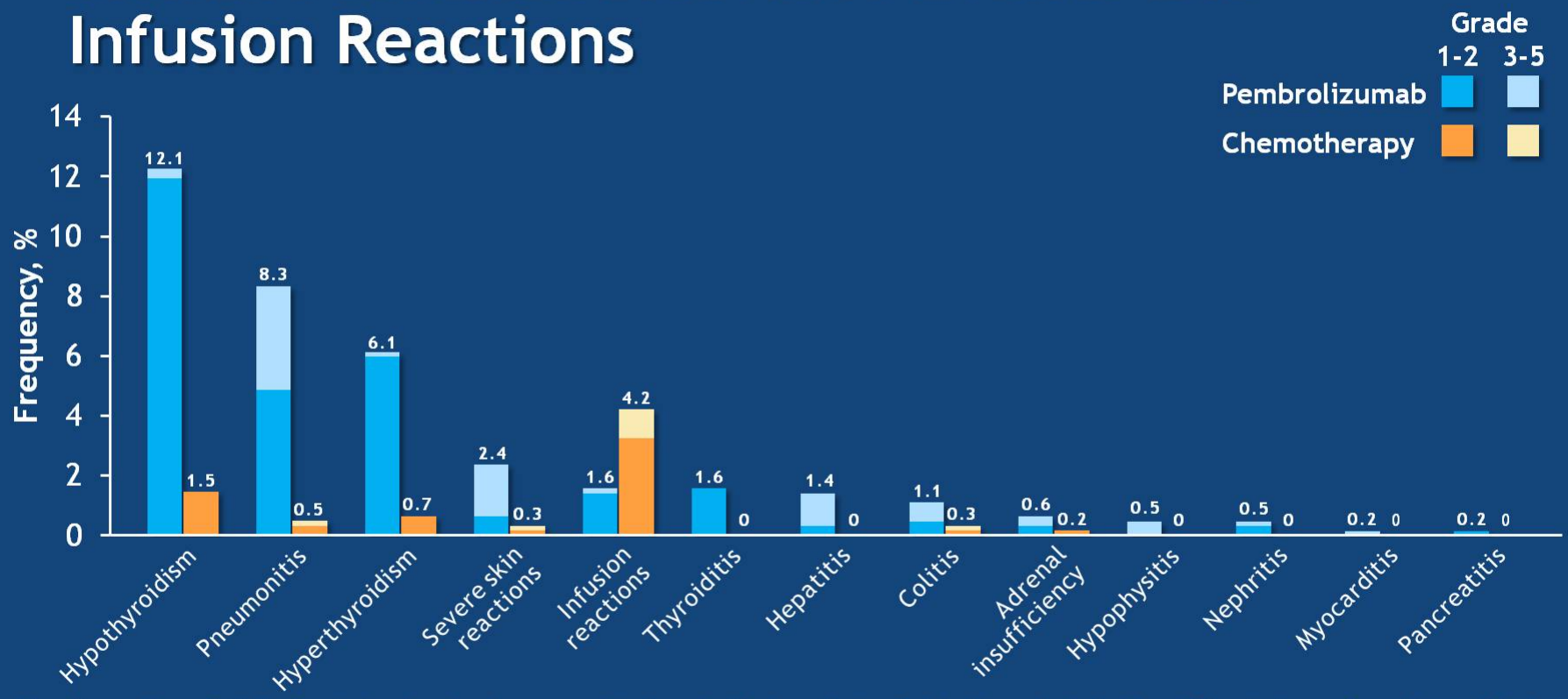
[a]Based on a list of terms specified by the sponsor and considered regardless of attribution to treatment or immune relatedness by the investigator.
[b]Pneumonitis.

Data cutoff date: Feb 26, 2018.

Treatment-Related Adverse Events: Frequency ≥10%



Immune-Mediated Adverse Events and Infusion Reactions



Considered regardless of attribution to treatment or immune relatedness by the investigator. Related terms included in addition to the preferred terms listed.

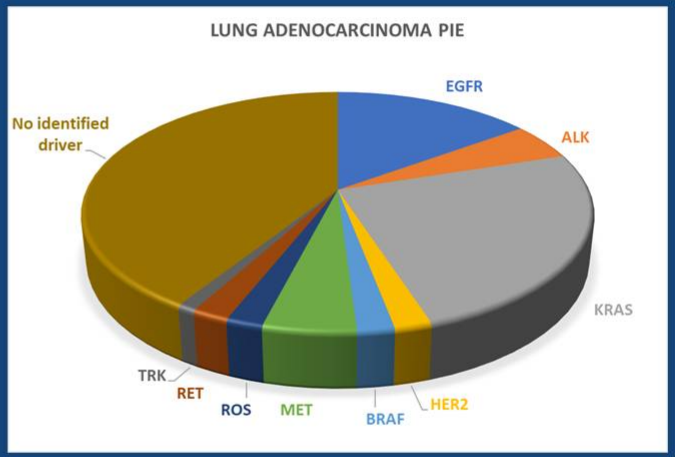
Data cutoff date: Feb 26, 2018.

Summary and Conclusions

- Pembrolizumab significantly improved OS over platinum-based chemotherapy as first-line therapy for advanced/metastatic NSCLC with PD-L1 TPS ≥50%, ≥20%, and ≥1%
  - HR (95% CI) of 0.69 (0.56-0.85), 0.77 (0.64-0.92), and 0.81 (0.71-0.93), respectively
  - Greater magnitude of benefit for pembrolizumab at higher levels of PD-L1 expression is consistent with previous studies of pembrolizumab monotherapy in metastatic NSCLC
  - In an exploratory analysis of TPS 1-49% population, HR (95% CI) was 0.92 (0.77-1.11)
- No significant PFS benefit for pembrolizumab at this analysis
  - Based on recommendation of external data monitoring committee, study is continuing to evaluate PFS based on additional follow-up
- Duration of response longer in patients treated with pembrolizumab than chemotherapy at all levels of PD-L1 expression

Non-Small Cell Lung Cancer is a lump term—but targeted therapy has taught us that all all cannot be lumped together

"lump"



"individualized slices of pie"

… een mooie zwaan werd

- 2001 NSCLC vs SCLC
  - Platinum/Cyclo vs EP vs CAV

- 2018
  - Biomarkers: PDL1%, EGFR, ALK, Tumor mutational burden%
  - Middelen: platinum, docetaxel, pembroluzimab, nivolumab, ipilumimab, pemetrexed, atezolizumab, alectinib, erlotinib, gefitinib, bevacizumab, …..

POST–ASCO

Oncologisch Netwerk Zuidoost-Nederland