DIAKOVERE
HENRIETTENSTIFT
Am Anfang ist der Mensch

Comprehensive Cancer Center Niedersachsen

Qualitätskonferenz zum Thema Zervixkarzinom
KKN, 15.6.2022

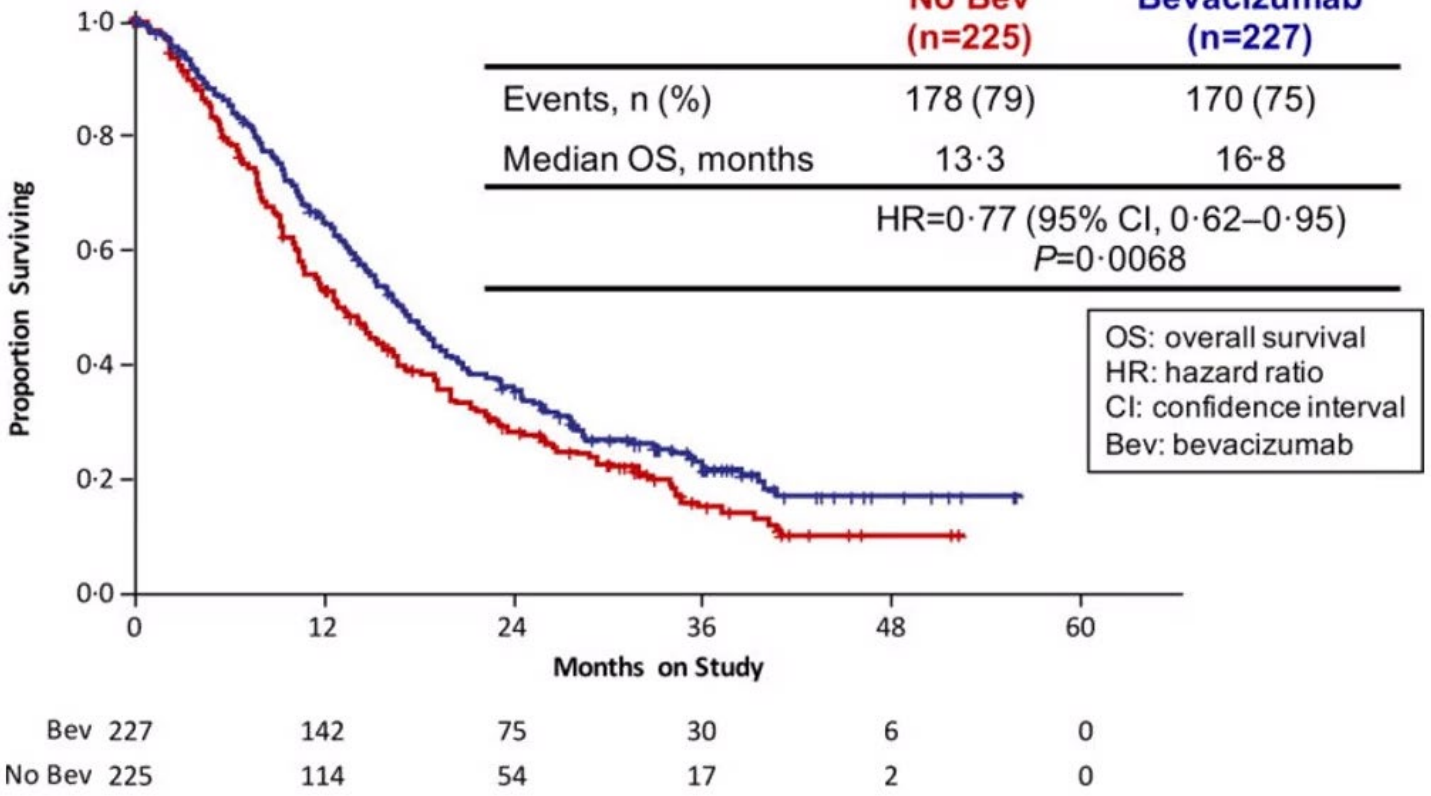
Therapieoptionen des fortgeschrittenen Zervixkarzinoms

W. Siggelkow

Diakovere Frauenklinik im Henriettenstift und Friederikenstift

Patient stage at initial presentation	Primary treatment
Stage IA, IB1-2, IIA	Surgery
Stage IB3, IIB, III, IVA	Chemoradiation
Stage IVB, recurrent, or metastatic	Platin/Paclitaxel + Bev*…
Secondline treatment	Monochemotherapie

Derzeitiger Standard in der fortgeschrittenen/metastasierten Situation des Zervixkarzinoms



GOG 240, Phase III-Studie

Cisplatin+ Topotecan/ Taxol

mit oder Ohne Bev.

OS-Benefit: 8.4 verus 7,1 Monate

18.8	Evidenzbasierte Empfehlung	Modifiziert 2021
Empfehlungsgrad B	Patientinnen mit metastasierten oder rediziviertem/persistierendem Zervixkarzinom sollten simultan Bevacizumab – unabhängig von einer Vorbehandlung mit einer Radio (-chemo) therapie – zur palliativen first-line Chemotherapie mit Cisplatin/Paclittaxel oder Topotecan/Paclitaxel erhalten.	
Level of Evidence 1+	Literatur: [446]	
	Konsens	

- **FDA approval 2014, EMA 2015**

Ansprechraten auf 2nd- line Therapien

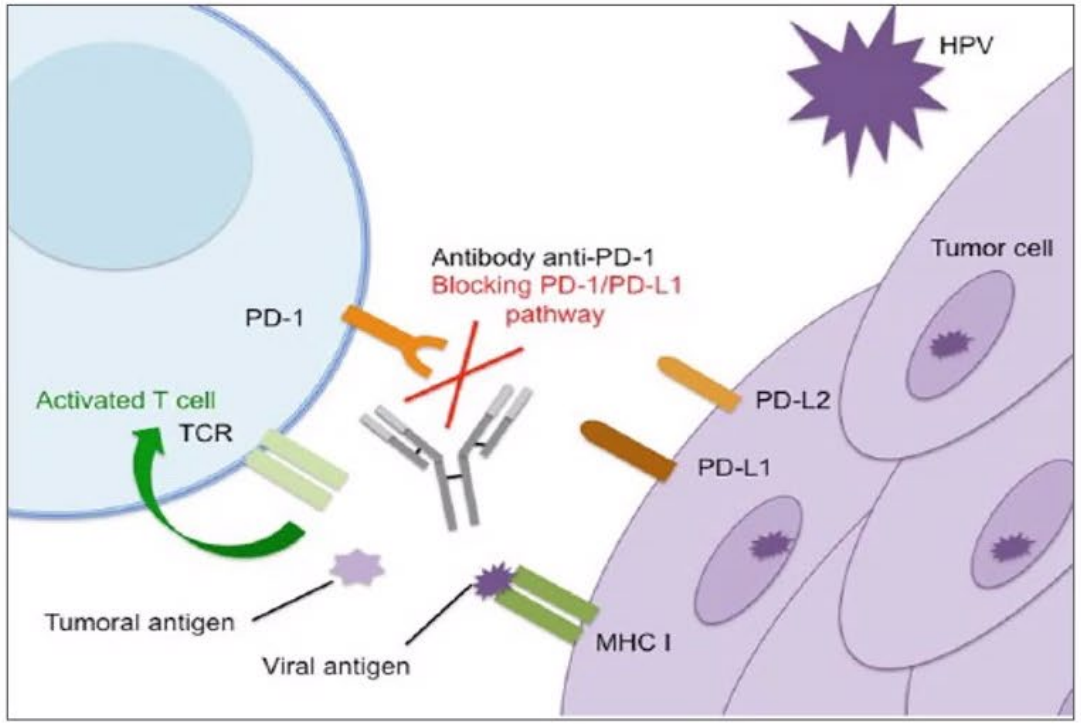
Table 4. Second-line therapy for metastatic cervical cancer

Agent	N	CR+PR (%)	PFS (months)	OS (months)
Bevacizumab [48]	46	11	3.4	7.3
Topotecan [62, 63]	94	13-19	2.1-2.4	6.4-6.6
Vinorelbine [64]	44	14	-	-
Gemcitabine [65]	22	5	2.1	6.5
Albumin-bound paclitaxel [66]	35	29	5.0	9.4
Docetaxel [67]	23	9	3.8	7.0
Pemetrexed [68, 69]	72	14-15	2.5-3.1	7.4-8.8
Irinotecan [70]	42	21	4.5	6.4
Sunitinib [71]	19	0	3.5	-
Erlotinib [72]	28	0	1.9	5.0
Lapatinib [73]	78	5	4.2	9.7
Pazopanib [73]	74	9	4.5	12.7
Pegylated liposomal doxorubicin [74]	27	11	3.2	8.9

Patient stage at initial presentation	Primary treatment
Stage IA, IB1-2, IIA	Surgery
Stage IB3, IIB, III, IVA	Chemoradiation
Stage IVB, recurrent, or metastatic	Platin/Paclitaxel + Bev*…
Secondline treatment	Monochemotherapie

Immunonkologie

Enttarnen des Tumors durch Blockade der Interaktion zwischen Immuncheckpoints der T-Zelle (PD-1/CTLA-4) und dem Tumor



- Präsentation viraler Antigene durch die Tumorzelle-

  Ausbildung einer spezifischen T-Zellantwort
- Hochregulation von PD-1/ PD-L 1 in HPV-assoziierten Dysplasien

  und Karzinomen

Enttarnewn, Nobelpreis

Pardoll DM, Nat Rev Cancer. 2012,
Iwai Y et al. Proc. Natl. Acad. Sci, 2002

KEYNOTE – 158 study

Multizentrische Phase II Studie zur Untersuchung von Pembolizumab in verschiedenen Tumorentitäten

Wichtige Einschlusskriterien

- Histologisch oder zytologisch gesicherter, fortgeschrittener solider Tumor, u.a.
  - Zervix-, Endometrium- oder Vulvakarzinom
  - Jeder Tumor mit MSI-H-Status
- Progression der Erkrankung unter bzw. Intoleranz gegenüber Standardtherapien.
- Tumormaterial zur weiteren Analyse
- Radiologisch messbare Erkrankung
- ECOG 0-1

Target Enrollment: 1350

Pembrolizumab 200 mg, iv, qw 3

Für max. 2 Jahre

Primärer Endpunkt: ORR

Sekundäre Endpunkte: DOR, PFS, OS

JCO, 2019

KEYNOTE – 158 study

Data cutoff 2018, medianes Follo-up von 10,2 Monaten

Total population	Overall[a] N = 98	PD-L1 Positive n = 82	PD-L1 Negative n = 15
ORR,[b] % (95% CI)	12.2 (6.5-20.4)	14.6 (7.8-24.2)	0 (0-21.8)
Best overall response, n (%)			
Complete response	3 (3.1)	3 (3.7)	0 (0.0)
Partial response	9 (9.2)	9 (11.0)	0 (0.0)
Stable disease	18 (18.4)	15 (18.3)	3 (20.0)
Progressive disease	55 (56.1)	44 (53.7)	10 (66.7)
Nonevaluable[c]	5 (5.1)	4 (4.9)	1 (6.7)
No assessment[d]	8 (8.2)	7 (8.5)	1 (6.7)
Patients with response	**n = 12**	**n = 12**	**n = 0**
Time to response, months, median (range)	2.1 (1.6 to 4.1)	2.1 (1.6 to 4.1)	—
Responders without subsequent disease progression, n (%)	6 (50.0)	6 (50.0)	—
Duration of response, months, median (range)	NR (3.7+ to 18.6+)	NR (3.7+ to 18.6+)	—

CI, confidence interval; NR, not reached.
[a]Includes 2 patients with unknown tumor PD-L1 expression level.
[b]At the time of analysis, all responses were confirmed.
[c]Patients for whom not all target lesions were captured on ≥1 postbaseline imaging assessment.
[d]Patients for whom no postbaseline tumor assessment was performed.

JCO, 2019

KEYNOTE – 158 study

Nebenwirkungen

	N = 98	
	Any Grade	Grade 3-4
Any,[a] n (%)	64 (65.3)	12 (12.2)
Led to death, n (%)	0	0
Specific events, n (%)		
Hypothyroidism	10 (10.2)	0
Decreased appetite	9 (9.2)	0
Fatigue	9 (9.2)	0
Diarrhea	8 (8.2)	1 (1.0)
Aspartate aminotransferase increased	7 (7.1)	2 (2.0)
Asthenia	7 (7.1)	1 (1.0)
Pyrexia	7 (7.1)	1 (1.0)
Hyperthyroidism	7 (7.1)	0
Arthralgia	6 (6.1)	1 (1.0)
Nausea	6 (6.1)	0
Pruritus	6 (6.1)	0
Rash	6 (6.1)	0
Vomiting	6 (6.1)	0
Abdominal pain	5 (5.1)	0
Alanine aminotransferase increased	3 (3.1)	3 (3.1)

[a]Four patients (4.1%) discontinued pembrolizumab because of treatment-related AEs.

	N = 98	
	Any Grade	Grade 3-4
Any, n (%)	25 (25.5)	5 (5.1)
Led to death, n (%)	0	0
Specific events, n (%)		
Hypothyroidism	11 (11.2)	0
Hyperthyroidism	9 (9.2)	0
Infusion reactions	3 (3.1)	0
Colitis	2 (2.0)	0
Hepatitis	2 (2.0)	2 (2.0)
Severe skin reactions	2 (2.0)	2 (2.0)
Adrenal insufficiency	1 (1.0)	1 (1.0)
Myositis	1 (1.0)	0
Pneumonitis	1 (1.0)	0
Uveitis	1 (1.0)	0

[a]Events were based on a list of terms specified at the time of analysis and were included regardless of attribution to study treatment or immune relatedness by the investigator. Related terms were included.

Pembrolizumab FDA approved 2nd line

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U.S. FOOD & DRUG ADMINISTRATION

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FDA approves pembrolizumab for advanced cervical cancer with disease progression during or after chemotherapy

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Hematology/Oncology (Cancer) Approvals & Safety Notifications

Drug Information Soundcast in Clinical Oncology (D.I.S.C.O.)

Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book)

On June 12, 2018, the Food and Drug Administration approved pembrolizumab (Keytruda, Merck and Co. Inc.) for patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumors express PD-L1 (CPS ≥1) as determined by an FDA-approved test.

Pembrolizumab was investigated in 98 patients with recurrent or metastatic cervical cancer enrolled in a single cohort of KEYNOTE 158 (NCT02628067), a multicenter, non-randomized, open-label, multi-cohort trial. Patients were treated with pembrolizumab intravenously at a dose of 200 mg every 3 weeks until unacceptable toxicity or documented disease progression. Among the 98 patients, approval was based on 77 (79%) patients who had tumors that expressed PD-L1 with a CPS ≥1 and who had received at least one line of chemotherapy for metastatic disease. PD-L1 status was determined using the PD-L1 IHC 22C3 pharmDx Kit.

Content current as of:
06/13/2018

FDA-approval

Juni 2018

rec./met. Zervixkarzinom

2nd line

CPS≥ 1

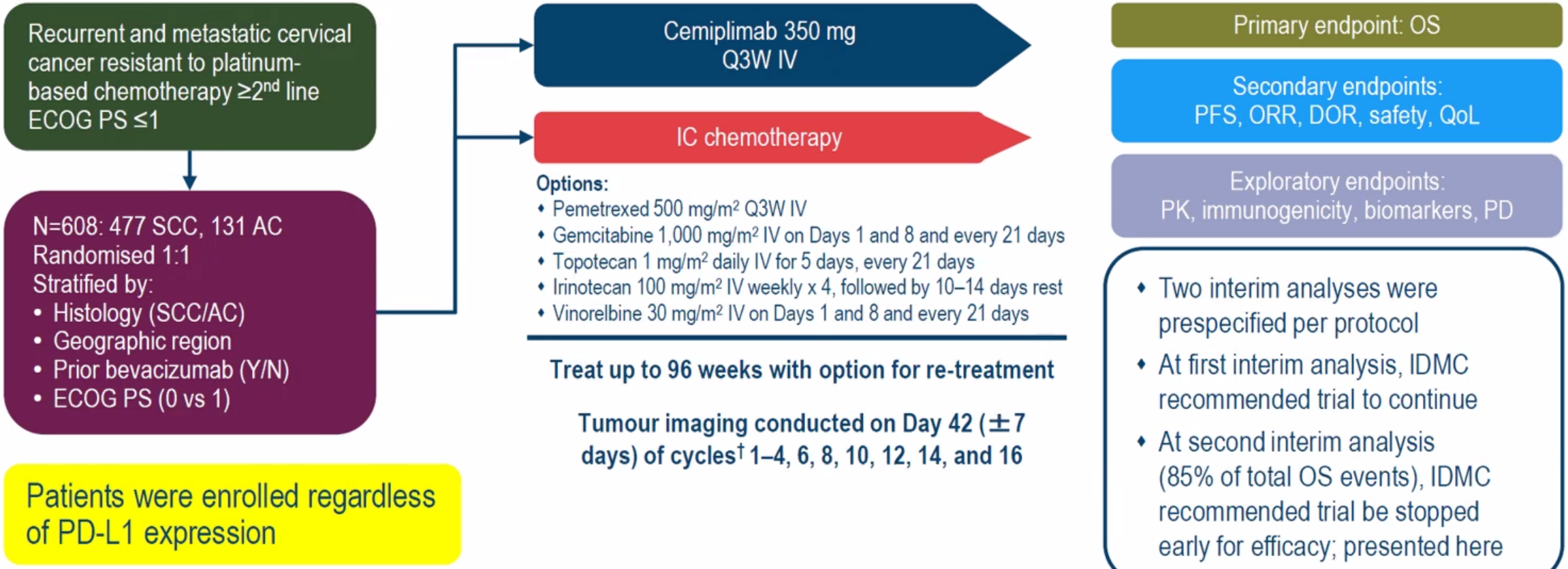
Highlights ESMO 2021 (virtual plenary)

Target: PD-1 receptor

EMPOWER-CERVICAL 1/GOG-3016/ENGOT-CX9: RESULTS OF PHASE 3 TRIAL OF CEMIPLIMAB VS INVESTIGATOR'S CHOICE (IC) CHEMOTHERAPY (CHEMO) IN RECURRENT/METASTATIC (R/M) CERVICAL CARCINOMA

Krishnansu S Tewari,* Bradley J Monk,* Ignace Vergote, Austin Miller, Andreia Cristina de Melo, Hee Seung Kim, Yong Man Kim, Alla Lisyanskaya, Vanessa Samouëlian, Domenica Lorusso, Fernanda Damian, Chih-Long Chang, Evgeniy A Gotovkin, Shunji Takahashi, Daniella Ramone, Joanna Pikiel, Beata Maćkowiak-Matejczyk, Eva Maria Guerra, Nicoletta Colombo, Yulia Makarova, Jingjin Li, Shaheda Jamil, Vladimir Jankovic, Chieh-I Chen, Frank Seebach, David M Weinreich, George D Yancopoulos, Israel Lowy, Melissa Mathias, Matthew G Fury, and Ana Oaknin

EMPOWER-Cervical 1/GOG-3016/ENGOT-cx9: Interim analysis of phase III trial of cemiplimab vs investigator's choice (IC) chemotherapy (chemo) in recurrent/metastatic (R/M) cervical carcinoma



*Performed according to ENGOT Model C.[1] †To account for differences in drug administration schedules, one cycle is defined as 6 weeks.

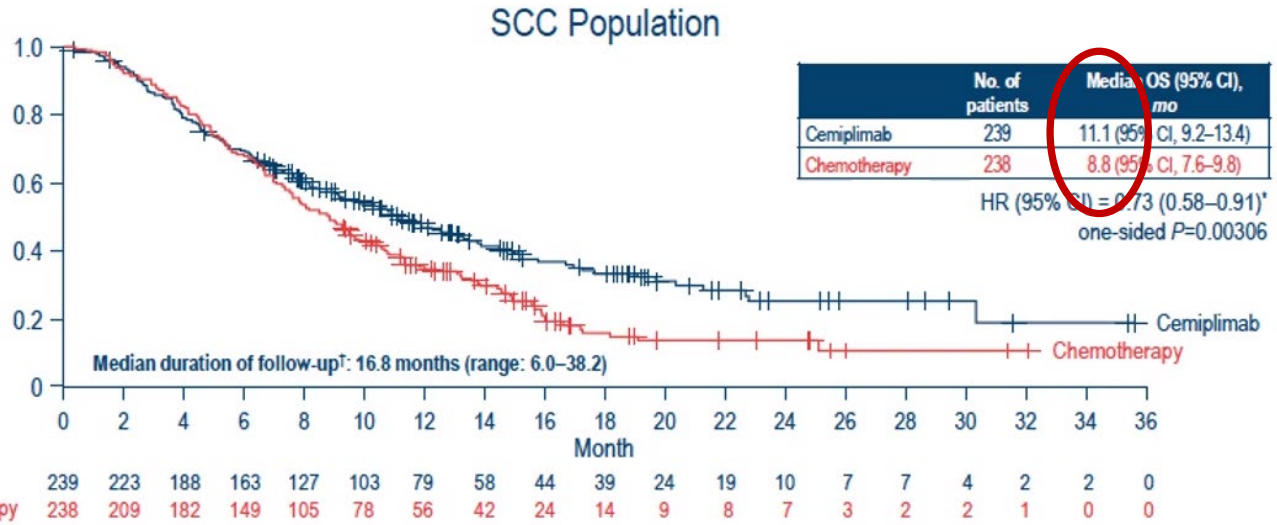
AC, adenocarcinoma or adenosquamous carcinoma; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IC, investigator's choice; IDMC, Independent Data Monitoring Committee; IV, intravenously; ORR, objective response rate; OS, overall survival; PD, pharmacodynamics; PD-L1, programmed cell death ligand 1; PFS, progression-free survival; PK, pharmacokinetics; Q3W, every 3 weeks; QoL, quality of life; SCC, squamous cell carcinoma.

1. Vergote I et al. *Int J Gynecol Cancer.* 2019;0:1–4.

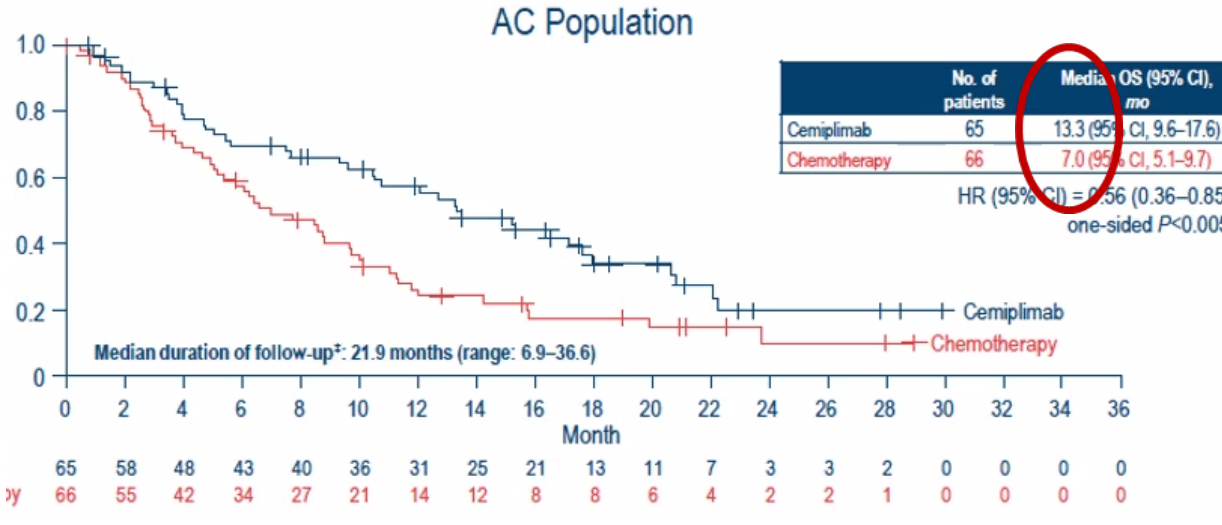
Data cutoff date: 4 Jan 2021

Gesamtüberleben

+2,3 Monate



+6,3 Monate



27-30% Risiko-Reduktion für Tod in der Cemiplimab-Kohorte

Objective response rate

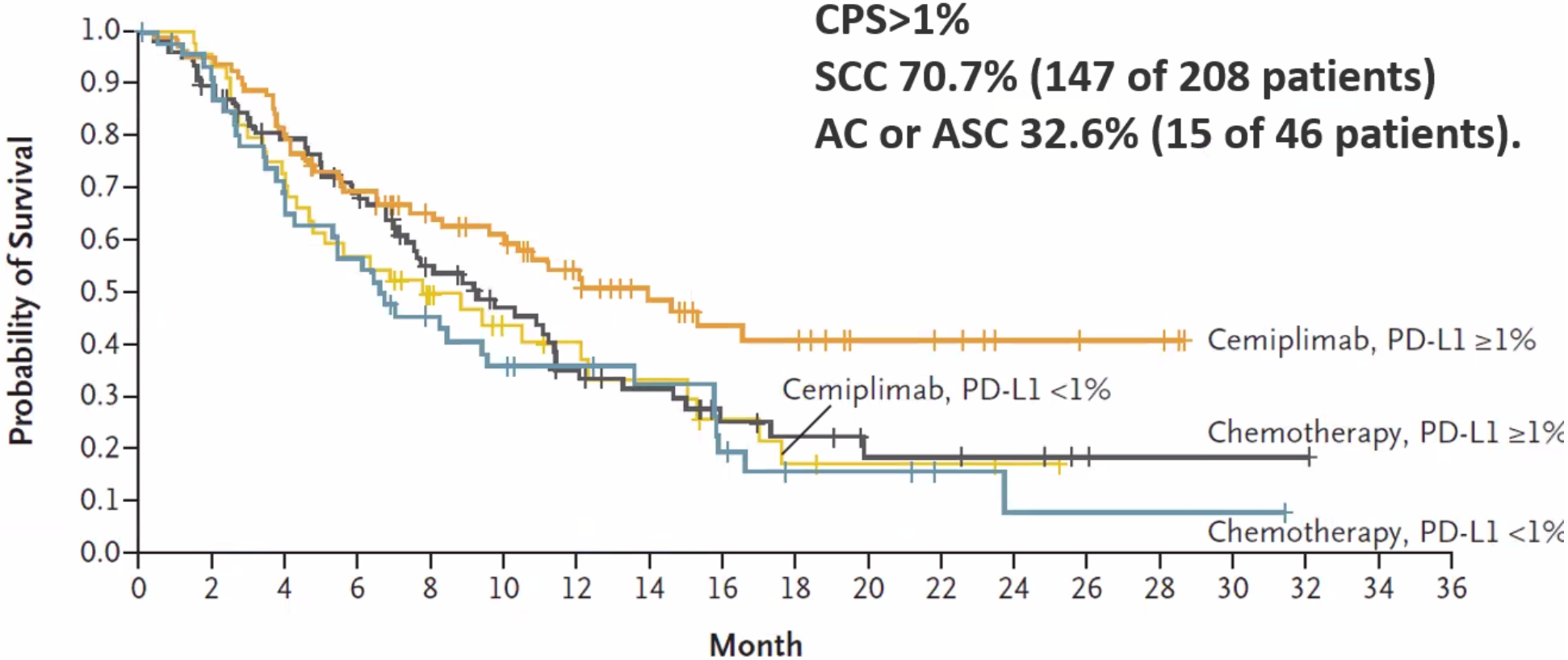
By investigator assessment	Overall population	
	Cemiplimab (n=304)	Chemotherapy (n=304)
Response		
Objective response rate (ORR:CR+PR)	50 (16.4)	19 (6.3)
95% CI for ORR[a]	(12.5, 21.1)	(3.8, 9.6)
Best overall tumour response, n (%)		
Complete response (CR)[b]	10 (3.3)	3 (1.0)
Partial response (PR)[b]	40 (13.2)	16 (5.3)
Stable disease (SD)[c]	125 (41.1)	148 (48.7)
Progressive disease (PD)	105 (34.5)	88 (28.9)
Not evaluable (NE)	24 (7.9)	49 (16.1)
Stratified CMH test one-sided *P*-value[d]	0.00004	
Odds ratio (95% CI)[d]	2.984 (1.707, 5.215)	
KM estimated median DOR, months (95% CI)[e]	16.4 (12.4, NE)	6.9 (5.1, 7.7)
Median observed time to response, months (range)	2.7 (1.2–11.4)	1.6 (1.2–9.0)

- ORR of SCC population
  - Cemiplimab: 17.6% (95% CI: 13.0–23.0)
  - Chemotherapy: 6.7% (95% CI: 3.9–10.7)
- ORR of AC population
  - Cemiplimab: 12.3% (95% CI: 5.5–22.8)
  - Chemotherapy: 4.5% (95% CI: 0.9–12.7)

[a]Clopper-Person exact confidence interval (CI); [b]CR/PR must be confirmed by repeated assessments no less than 4 weeks apart; [c]SD criteria must be met at least once for a minimum duration of 4 weeks after first dose date; [d]One-sided *P*-value and odds ratio using geographic region and histology stratified Cochran-Mantel-Haenszel (CMH) test. Due to the low response rate in the chemotherapy arm, the results from CMH test should be interpreted with caution; [e]Based on patients with confirmed CR or PR.
AC, adenocarcinoma or adenosquamous carcinoma; DOR, duration of response; KM, Kaplan-Meier; SCC, squamous cell carcinoma.

Overall Survival According to PD-L1 Expression Status in the Overall Trial Population (N=254)

CPS>1%
SCC 70.7% (147 of 208 patients)
AC or ASC 32.6% (15 of 46 patients).



No. at Risk																			
Cemiplimab, PD-L1 ≥1%	82	78	65	55	45	39	30	22	16	15	10	9	4	3	3	0	0	0	0
Cemiplimab, PD-L1 <1%	44	41	30	25	18	13	11	9	6	4	3	3	1	0	0	0	0	0	0
Chemotherapy, PD-L1 ≥1%	80	69	58	50	36	28	20	16	10	8	5	5	4	2	1	1	1	0	0

Checkpoint-basierte Kombinationsbehandlungen

Pembrolizumab plus Chemotherapy versus Placebo plus Chemotherapy for Persistent, Recurrent, or Metastatic Cervical Cancer: Randomized, Double-Blind, Phase 3 KEYNOTE-826 Study

Nicoletta Colombo,[1] Coraline Dubot,[2] Domenica Lorusso,[3] Valeria Caceres,[4] Kosei Hasegawa,[5] Ronnie Shapira-Frommer,[6] Krishnansu S. Tewari,[7] Pamela Salman,[8] Edwin Hoyos Usta,[9] Eduardo Yañez,[10] Mahmut Gümüş,[11] Mivael Olivera Hurtado de Mendoza,[12] Vanessa Samouëlian,[13] Vincent Castonguay,[14] Alexander Arkhipov,[15] Sarper Toker,[16] Kan Li,[16] Stephen M. Keefe,[16] Bradley J. Monk,[17] on behalf of the KEYNOTE-826 Investigators

[1]University of Milan-Bicocca and European Institute of Oncology (IEO) IRCCS, Milan, Italy; [2]Institut Curie Saint-Cloud, Saint-Cloud, France, Group d'Investigateurs Nationaux pour l'Etude des Cancers Ovariens (GINECO); [3]Fondazione Policlinico Universitario A Gemelli IRCCS and Catholic University of Sacred Heart, Rome, Italy; [4]Instituto de Oncología Angel H. Roffo, Buenos Aires, Argentina; [5]Saitama Medical University International Medical Center, Hidaka, Saitama, Japan; [6]Ella Lemelbaum Institute for Immuno-Oncology, Sheba Medical Center, Ramat Gan, Israel; [7]University of California, Irvine, Orange, CA, USA; [8]Oncovida Cancer Center, Providencia, Chile; [9]IMAT Oncomedica S.A., Monteria, Colombia; [10]Universidad de la Frontera, Temuco, Chile; [11]Istanbul Medeniyet University Hospital, Istanbul, Turkey; [12]Instituto Nacional de Enfermedades Neoplásicas, INEN, Lima, Perú; [13]Centre Hospitalier de l'Université de Montréal (CHUM), Centre de Recherche de l'Université de Montréal (CRCHUM), Université de Montréal, Montréal, QC, Canada; [14]Centre Hospitalier Universitaire de Québec, Université Laval, Québec City, QC, Canada; [15]Medical Rehabilitation Center under the Ministry of Health of Russian Federation, Moscow, Russia; [16]Merck & Co., Inc., Kenilworth, NJ, USA; [17]Arizona Oncology (US Oncology Network), University of Arizona College of Medicine, Creighton University School of Medicine, Phoenix, AZ, USA

KEYNOTE-826: Randomized, Double-Blind, Phase 3 Study

Key Eligibility Criteria

- Persistent, recurrent, or metastatic cervical cancer not amenable to curative treatment
- No prior systemic chemotherapy (prior radiotherapy and chemoradiotherapy permitted)
- ECOG PS 0 or 1

Stratification Factors

- Metastatic disease at diagnosis (yes vs no)
- PD-L1 CPS (<1 vs 1 to <10 vs ≥10)
- Planned bevacizumab use (yes vs no)

R
1:1

Pembrolizumab 200 mg IV Q3W
for up to 35 cycles
+
Paclitaxel + Cisplatin or Carboplatin IV Q3W
for up to 6 cycles[a]
±
Bevacizumab 15 mg/kg IV Q3W

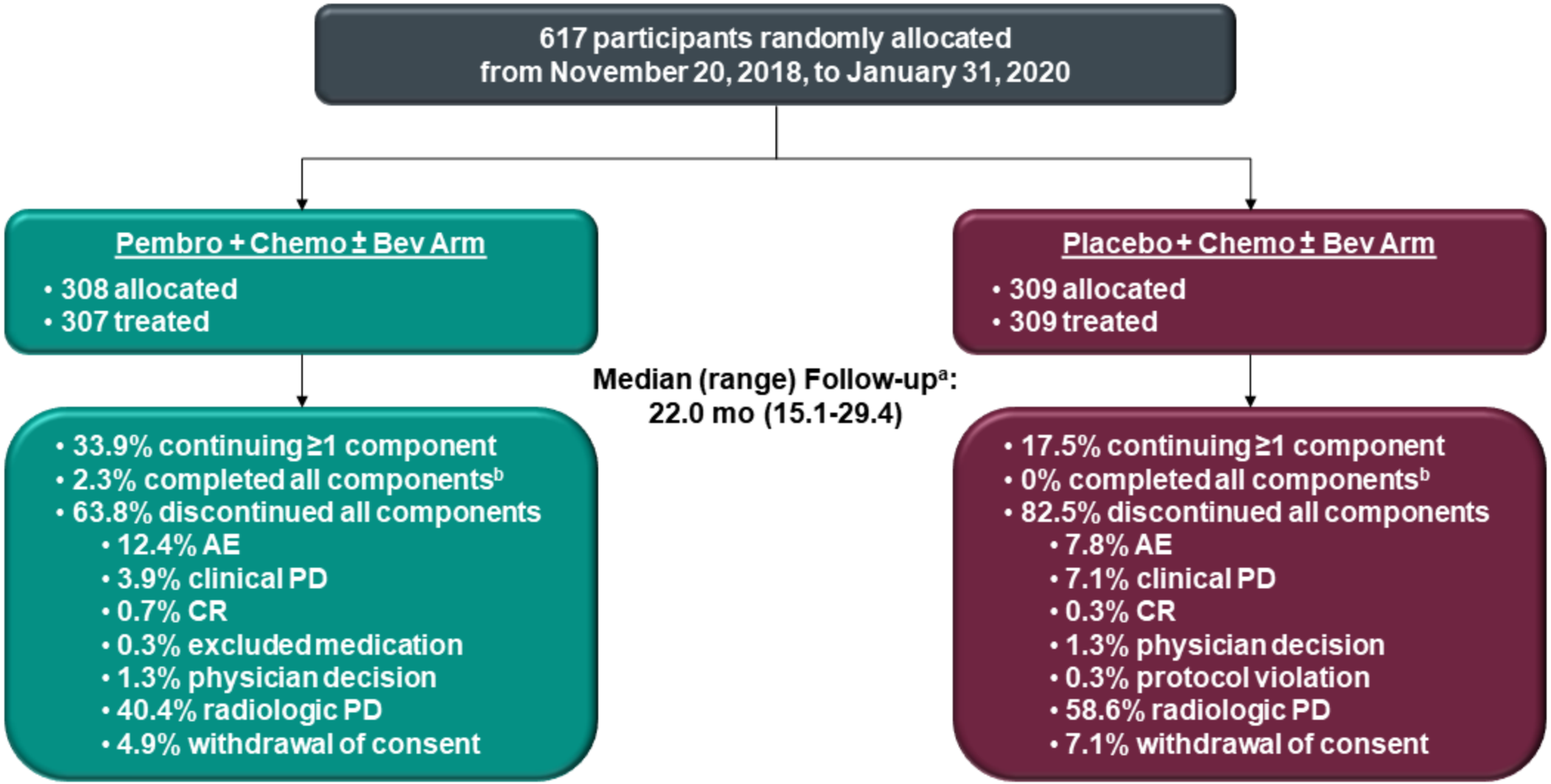
Placebo IV Q3W
for up to 35 cycles
+
Paclitaxel + Cisplatin or Carboplatin IV Q3W
for up to 6 cycles[a]
±
Bevacizumab 15 mg/kg IV Q3W

End Points

- **Dual primary:** OS and PFS per RECIST v1.1 by investigator
- **Secondary:** ORR, DOR, 12-mo PFS, and safety
- **Exploratory:** PROs assessed per EuroQol EQ-5D-5L VAS

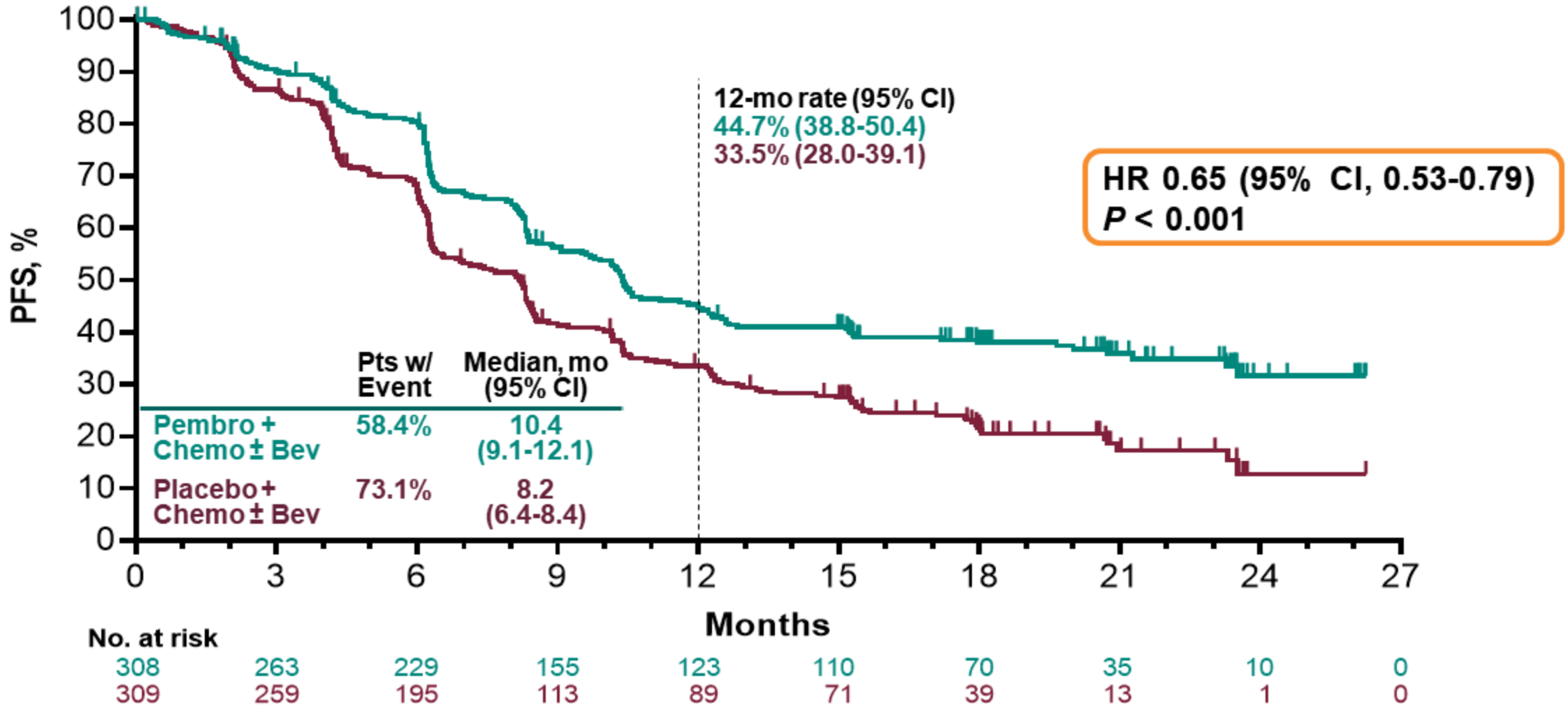
[a]Paclitaxel: 175 mg/m^2. Cisplatin: cisplatin 50 mg/m^2. Carboplatin: AUC 5 mg/mL/min. The 6-cycle limit was introduced with protocol amendment 2, although participants with ongoing clinical benefit who were tolerating chemotherapy could continue beyond 6 cycles after sponsor consultation.
CPS, combined positive score (number of PD-L1–staining cells [tumor cells, lymphocytes, macrophages] divided by the total number of viable tumor cells, multiplied by 100); PROs, patient-reported outcomes; VAS, visual analog scale. KEYNOTE-826 ClinicalTrials.gov identifier, NCT03635567.

Treatment Disposition, All-Comer Population



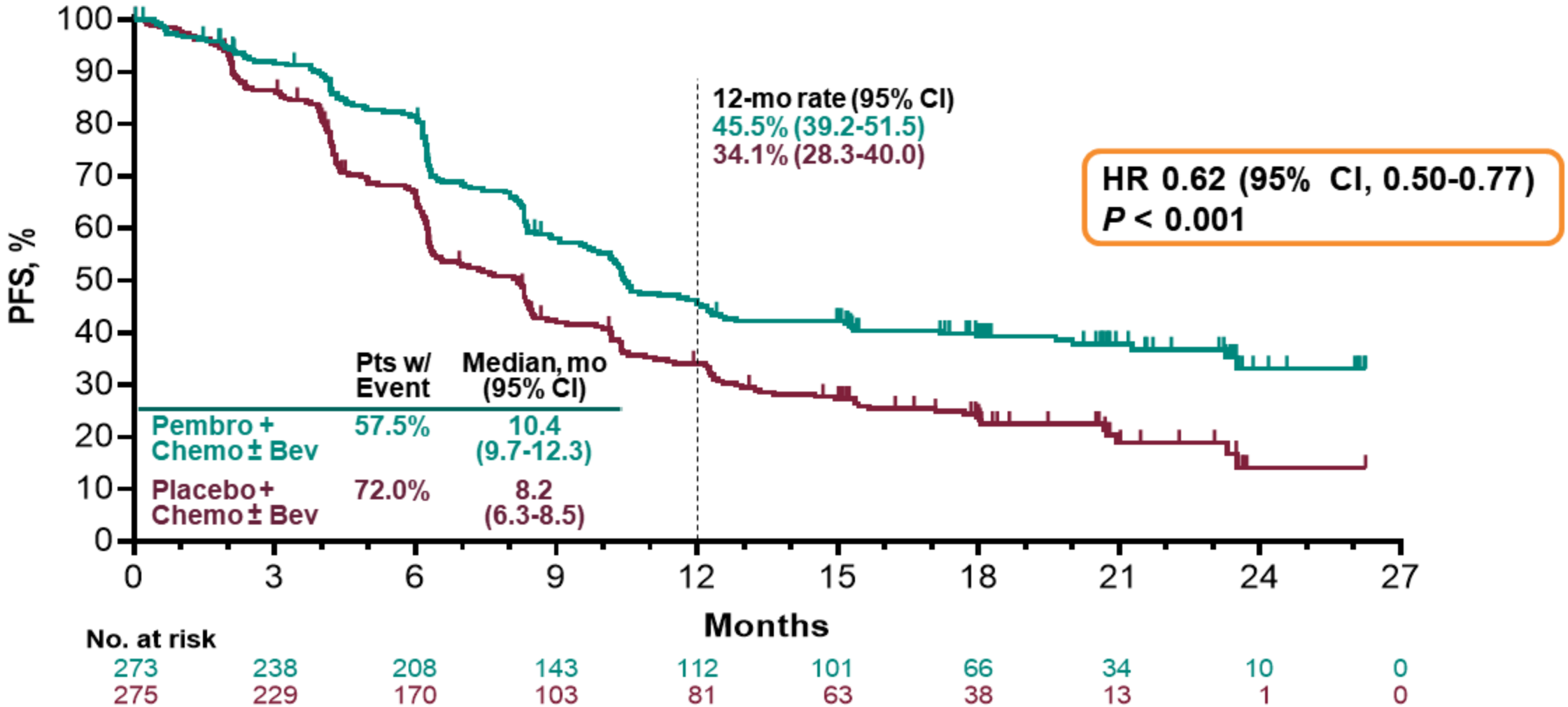
[a]Defined as the time from randomization to the data cutoff date of May 3, 2021.
[a]Includes participants who received bevacizumab and discontinued at cycle 35 or earlier.

PFS: All-Comer Population



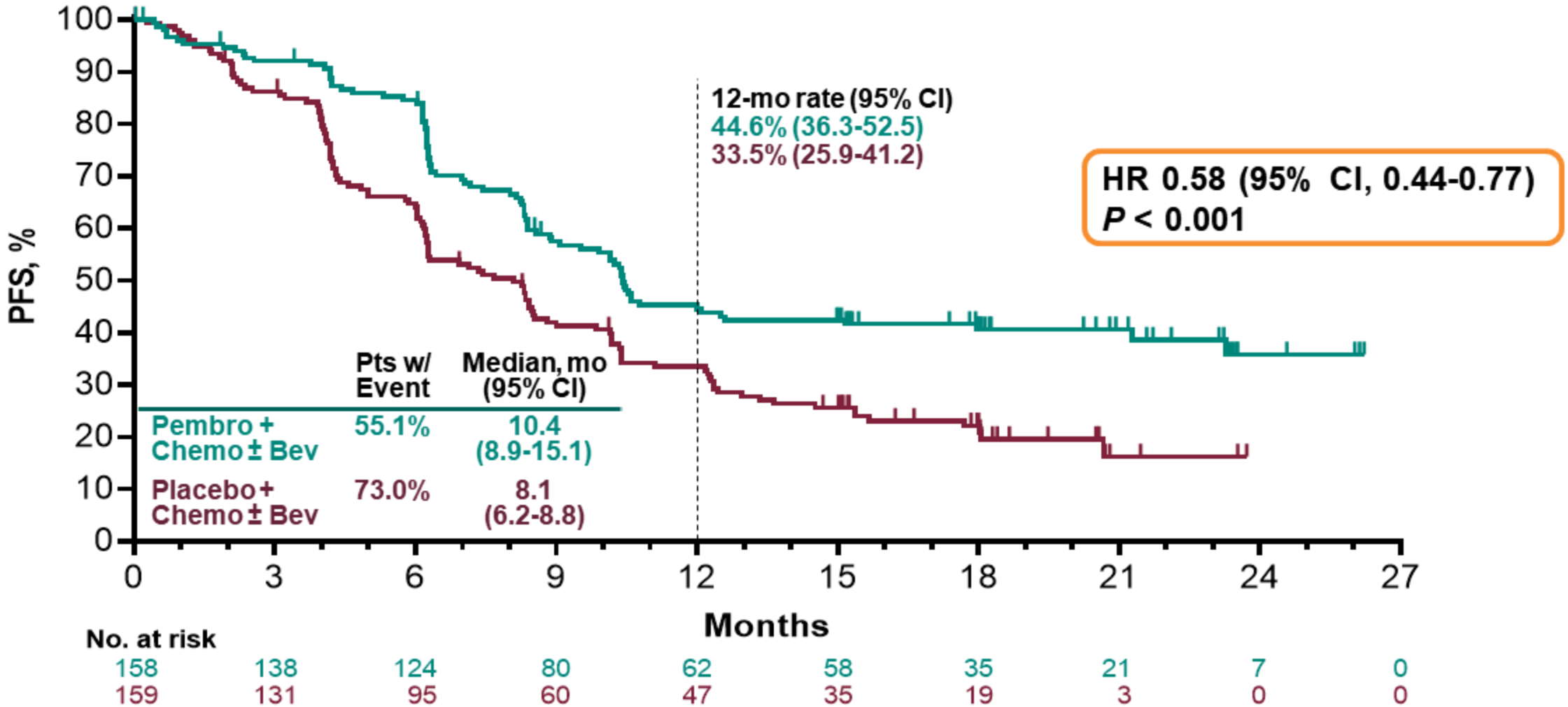
Response assessed per RECIST v1.1 by investigator review.
Data cutoff date: May 3, 2021.

PFS: PD-L1 CPS ≥1 Population



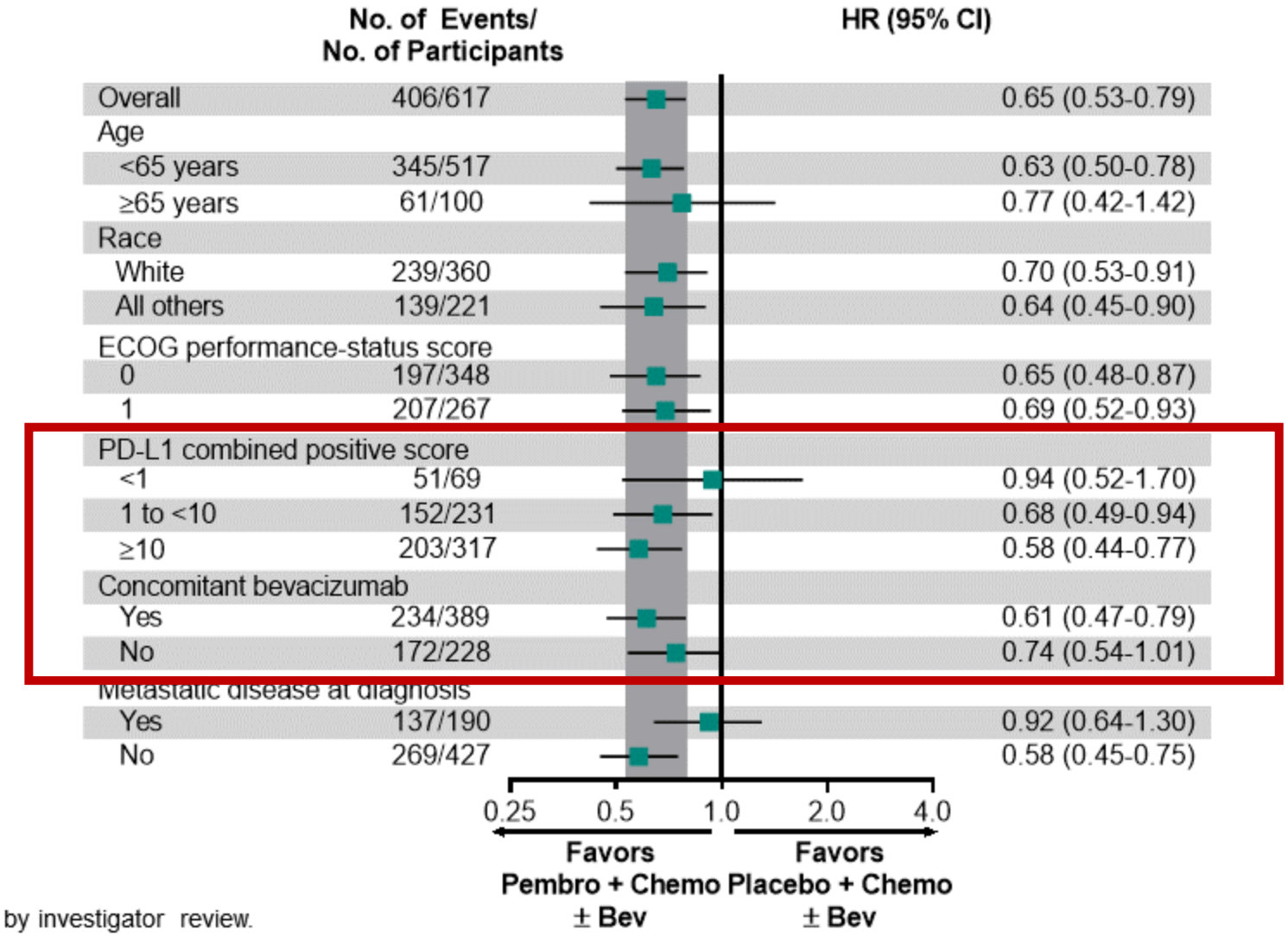
Response assessed per RECIST v1.1 by investigator review.
Data cutoff date: May 3, 2021.

PFS: PD-L1 CPS ≥10 Population



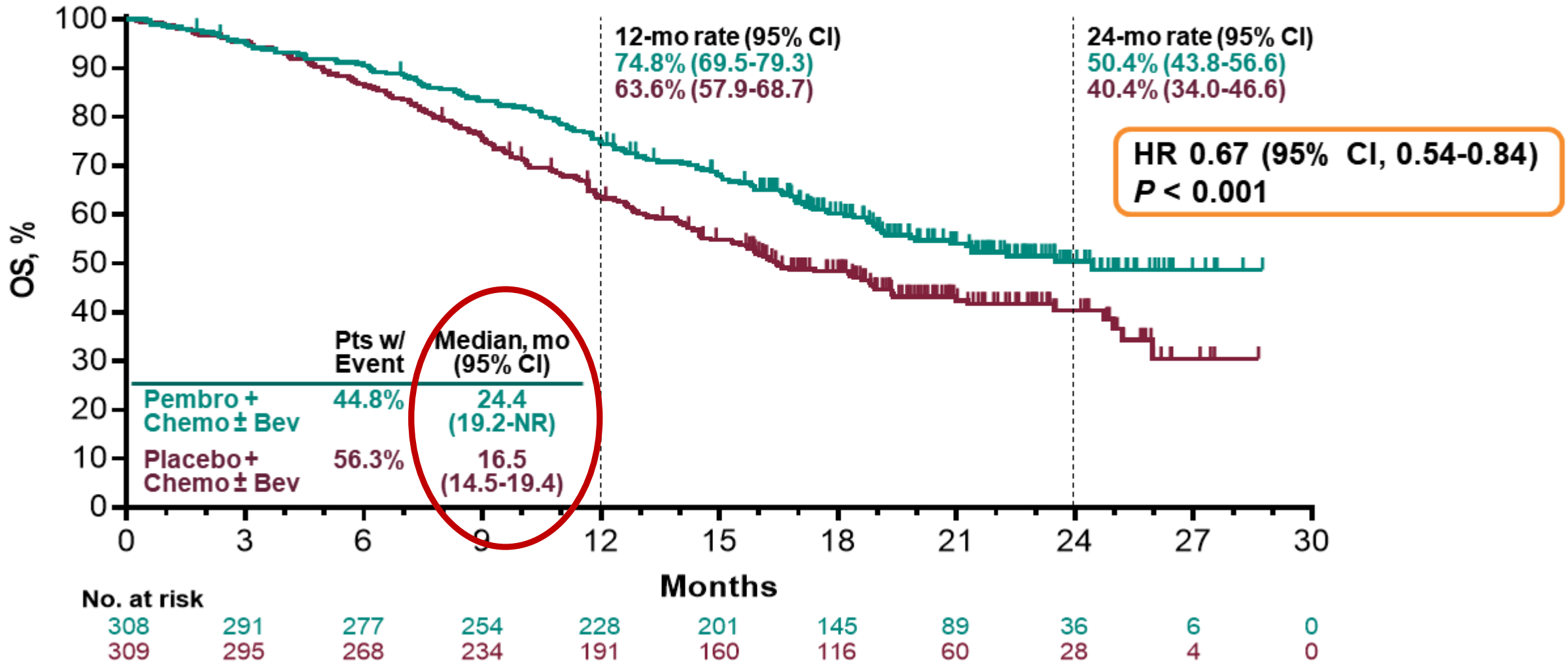
Response assessed per RECIST v1.1 by investigator review.
Data cutoff date: May 3, 2021.

PFS: Protocol-Specified Subgroups, All-Comer Population



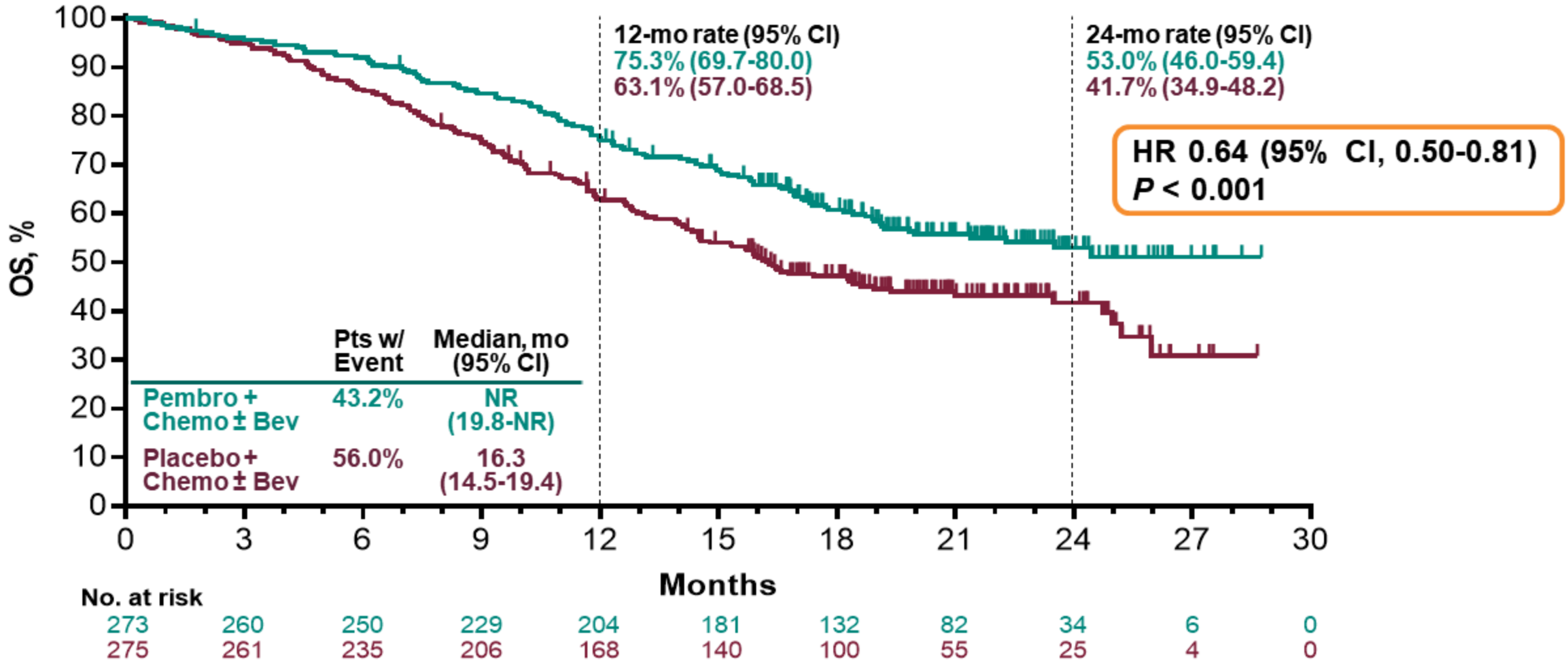
Response assessed per RECIST v1.1 by investigator review.
Data cutoff date: May 3, 2021.

OS: All-Comer Population



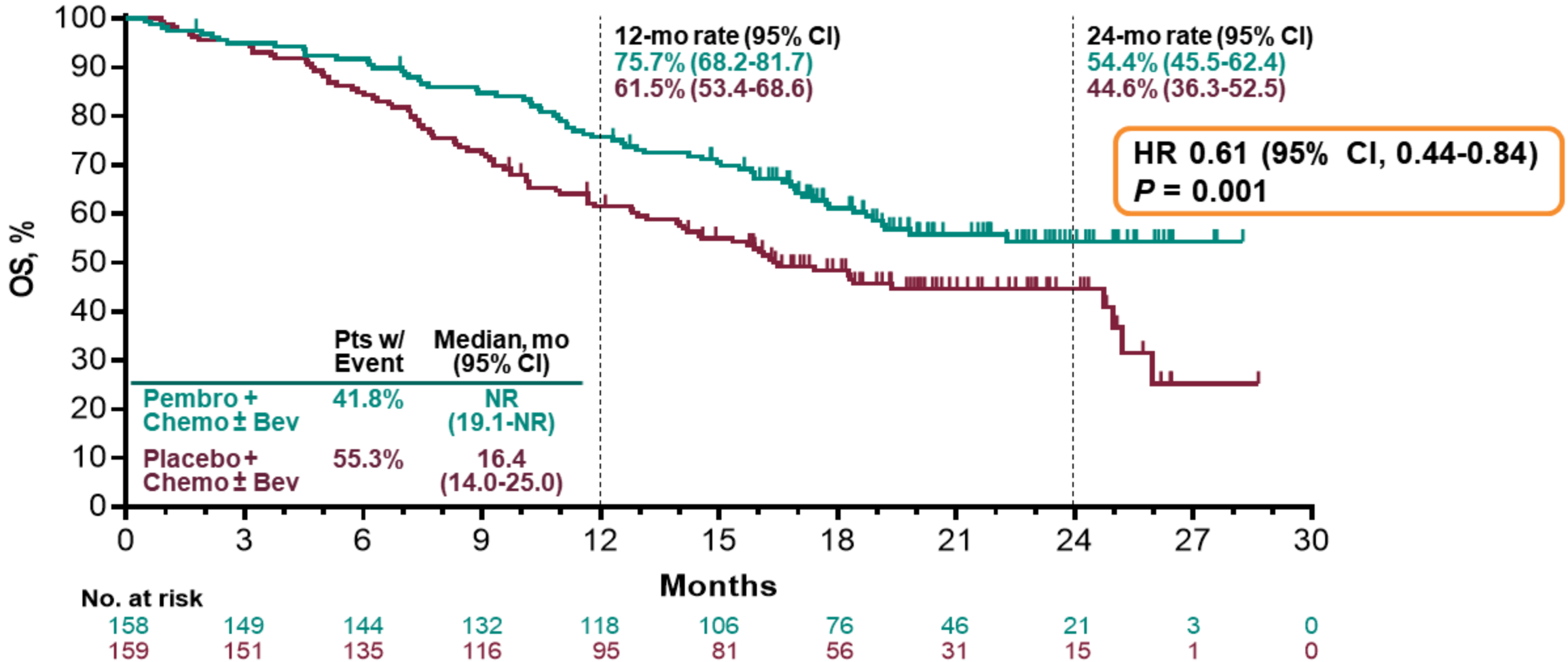
Data cutoff date: May 3, 2021.

OS: PD-L1 CPS ≥1 Population



Data cutoff date: May 3, 2021.

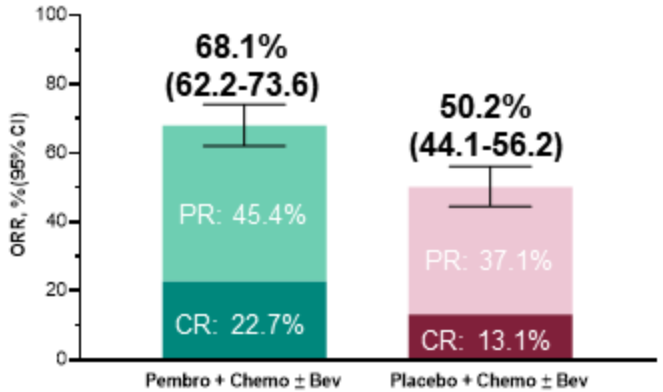
OS: PD-L1 CPS ≥10 Population

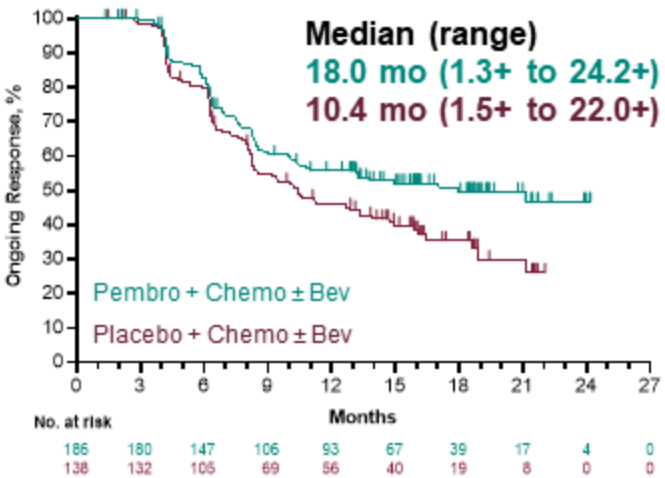


Data cutoff date: May 3, 2021.

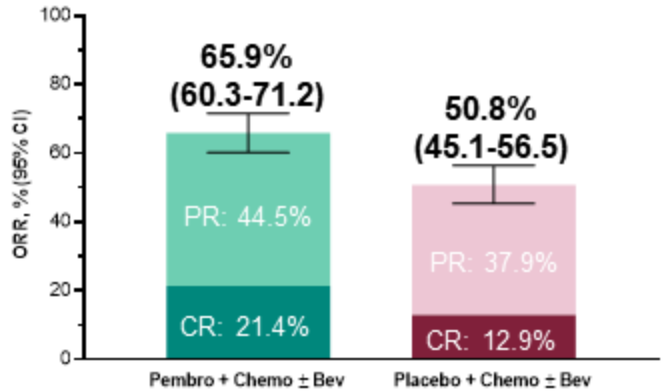
ORR and DOR: All Analysis Populations

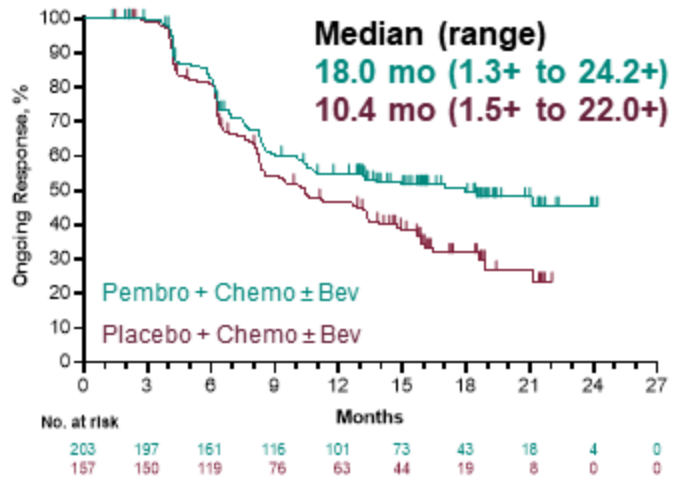
PD-L1 CPS ≥1



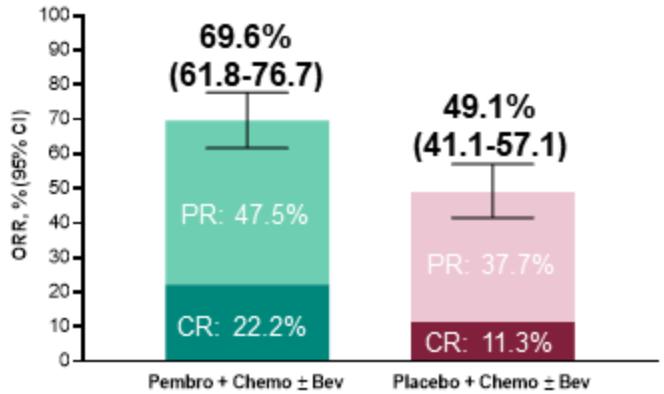


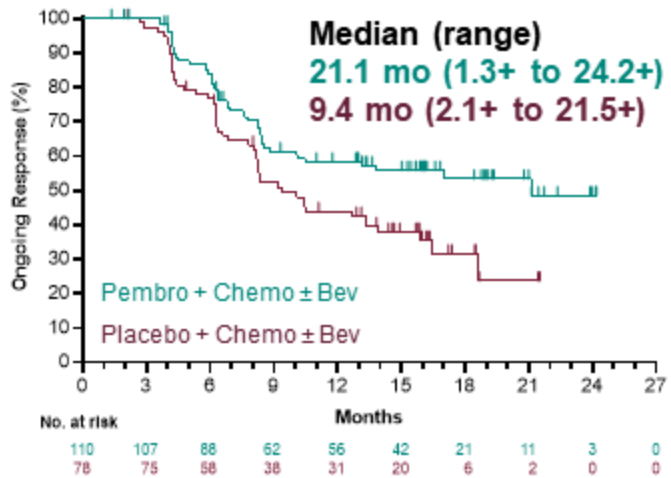
All-Comer





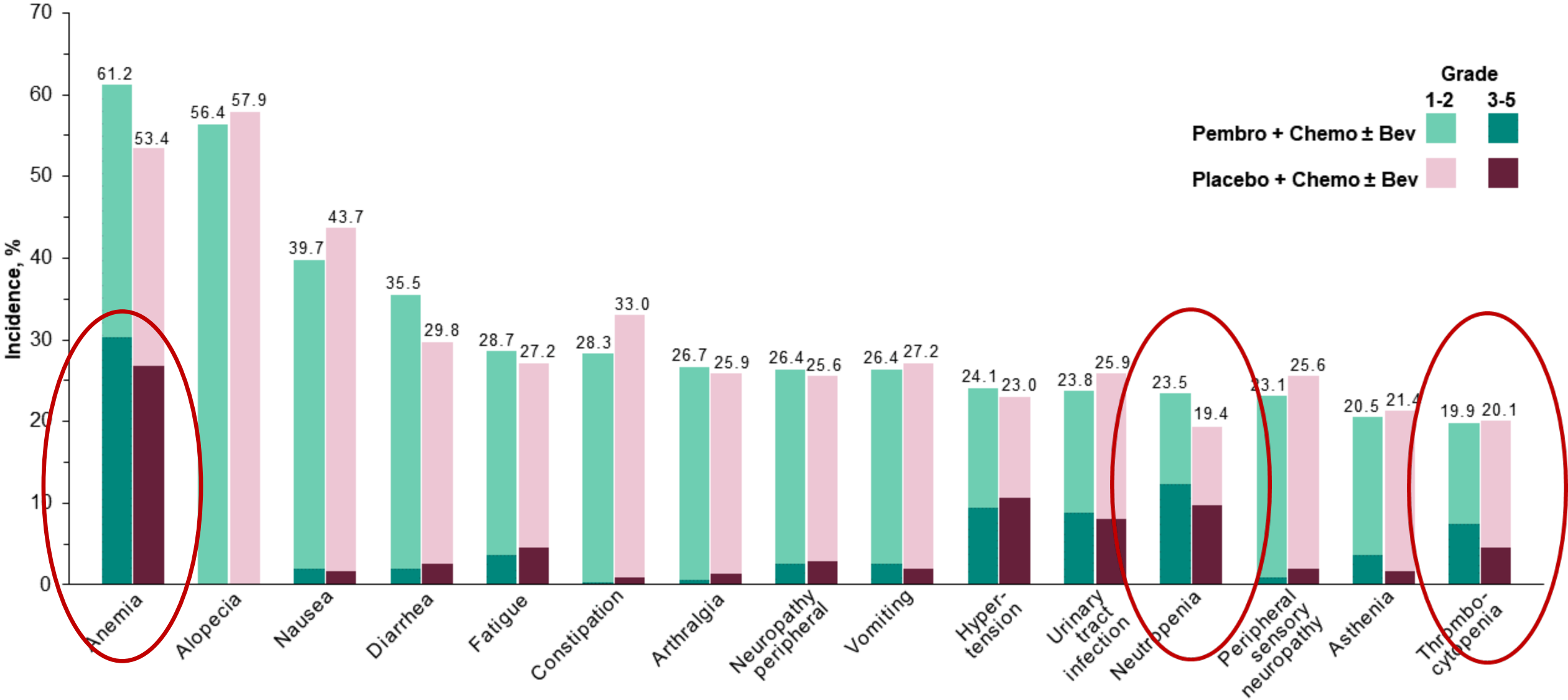
PD-L1 CPS ≥10





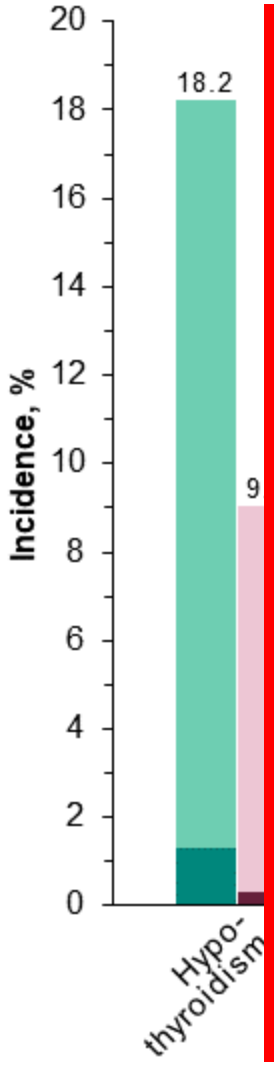
Response assessed per RECIST v1.1 by investigator review.
Data cutoff date: May 3, 2021.

All-Cause AEs, Incidence ≥20% in Either Arm



Data cutoff date: May 3, 2021.

Immune-Mediated AEs, Incidence ≥2 Patients in Either Arm



28.4.2022:

Keytruda ist in Kombination mit Chemotherapie mit oder ohne Bevacizumab zur Behandlung des persistierenden, rezidivierenden oder metastasierenden Zervixkarzinoms mit PD L1-exprimierenden Tumoren (CPS ≥ 1) bei Erwachsenen zugelassen.

ORIGINAL ARTICLE

Pembrolizumab for Persistent, Recurrent, or Metastatic Cervical Cancer

Nicoletta Colombo, M.D., Ph.D., Coraline Dubot, M.D., Domenica Lorusso, M.D., Ph.D., Valeria Caceres, M.D., Ph.D., Kosei Hasegawa, M.D., Ph.D., Ronnie Shapira-Frommer, M.D., Krishnansu S. Tewari, M.D., Pamela Salman, M.D., Edwin Hoyos Usta, M.D., Eduardo Yañez, M.D., Mahmut Gümüş, M.D., Mivael Olivera Hurtado de Mendoza, M.D., Vanessa Samouëlian, M.D., Ph.D., Vincent Castonguay, M.D., Alexander Arkhipov, M.D., Ph.D., Sarper Toker, M.D., M.B.A., Kan Li, Ph.D., Stephen M. Keefe, M.D., and Bradley J. Monk, M.D., for the KEYNOTE-826 Investigators*

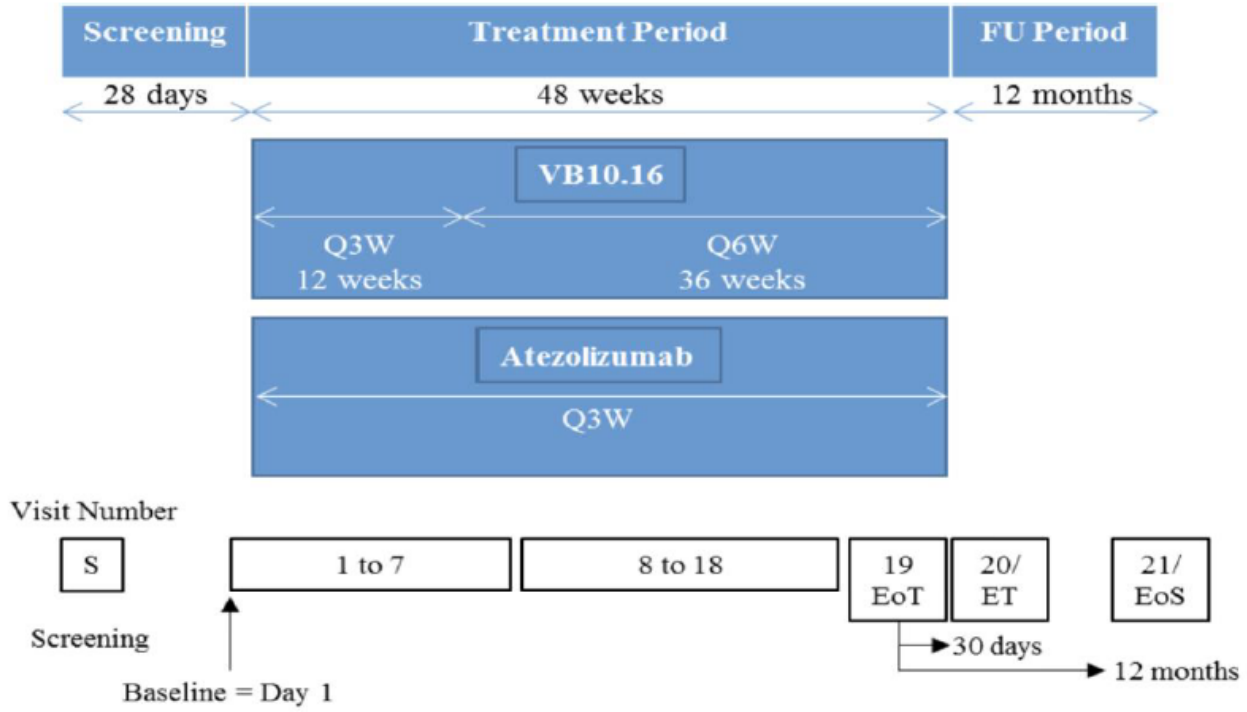
[a]Events were considered regardless of attribu s listed.
Data cutoff date: May 3, 2021.

Zulassung Cemiplimab in Deutschland?

HPV als Target für Therapien?

Vaccinbody C-02

Multi-Centre, open-label Phase IIa Trial of the Combination of VB10.16 and Atezolizumab in Patients with Advanced or Recurrent, Non-resectable HPV16-Positive Cervical Cancer



11 intramuscular (i.m.) vaccinations for up to 48 weeks from first vaccination. 5 vaccinations of 3 mg VB10.16 during the first 12 weeks, followed by vaccination every 6 weeks for up to 48 weeks + Atezolizumab (1200 mg) i.v. infusion every 3 weeks

Einschlusskriterien (Auswahl):

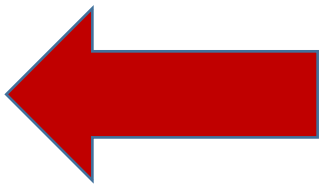
- persistent, recurrent, or metastatic non-resectable squamous cell carcinoma, adeno-squamous carcinoma, or adenocarcinoma of the cervix, not eligible for treatment with systemic CTX, radiotherapy or other standard-of-care anticancer treatment.
- HPV16 positive tumour. Provision of an archival tumour tissue sample not older than 2 years or new biopsy for analysing HPV16 status .
- a biopsy for PD L1 assessment at screening and measurable disease as assessed by the local site radiology as per RECIST 1.1.

Ausschlusskriterien (Auswahl)

- prior treatment with CD137, anti-PD-1, or anti-PD-L1 therapeutic antibody or other immune checkpoint targeting agents
- concomitant or prior malignant disease, brain metastases, known or suspected autoimmune disease

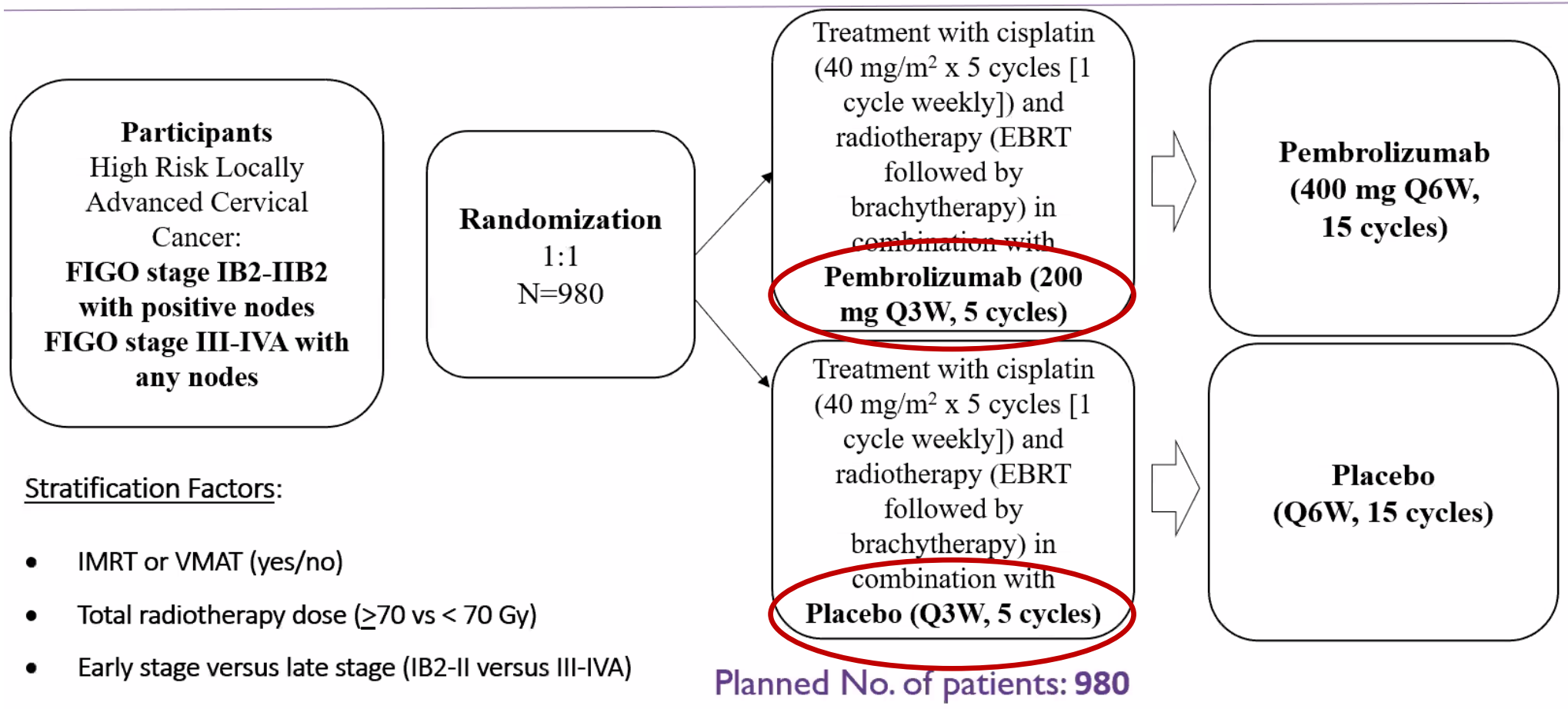
Neue Ansätze in der Primärsituation?

Patient stage at initial presentation	Primary treatment
Stage IA, IB1-2, IIA	Surgery
Stage IB3, IIB, III, IVA	Chemoradiation
Stage IVB, recurrent, or metastatic	Platin/Paclitaxel + Bev*…
Secondline treatment	Monochemotherapie



MSD-MK3475-A18 ENGOT-Cx11

Randomized, phase III, double-blinded study of chemoradiation with or without Pembrolizumab for the treatment of high – risk, locally advanced cervical cancer



Stratification Factors:

- IMRT or VMAT (yes/no)
- Total radiotherapy dose (≥70 vs < 70 Gy)
- Early stage versus late stage (IB2-II versus III-IVA)

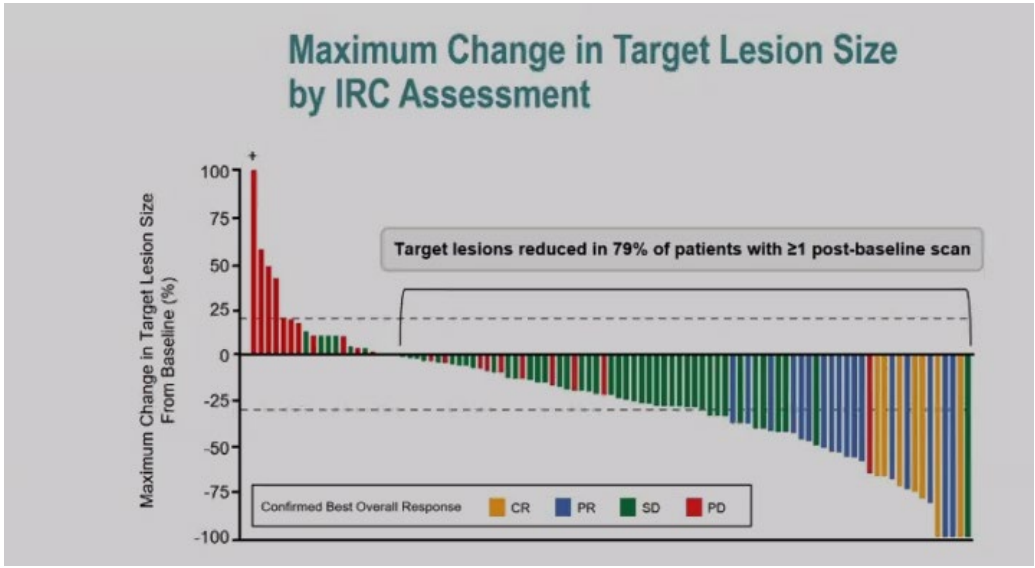
Planned No. of patients: **980**

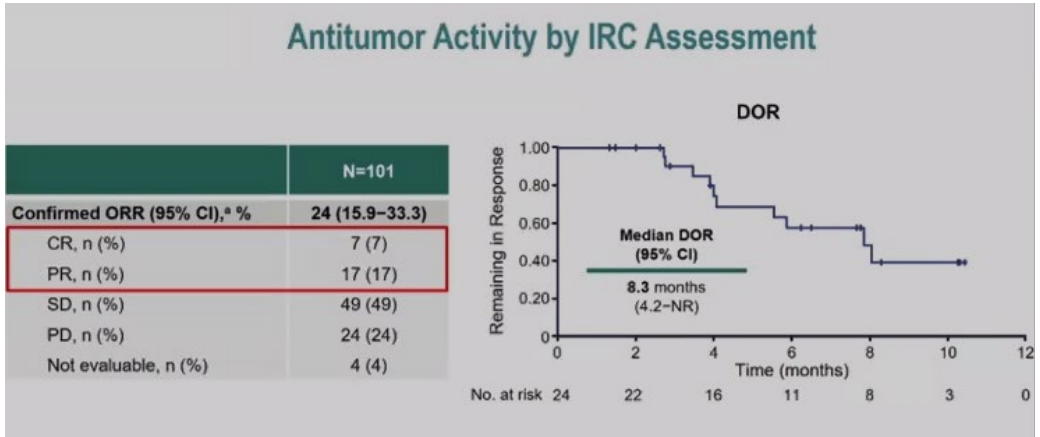
Phase III
Primärer Endpunkt:
PFS/ OS
1:1 Rando

FDA grants accelerated approval to

tisotumab vedotin for r/m Cervival Cancer

- Antibody-drug conjugate (ADC)
- Multiple anti-Tumoreffekte
- September 2021 von der FDA für die 2nd und 3rd line zugelassen
- Phase II Studie mit 101 Pat., Study ongoing,
- planned nr. of patients: 482
- Tisotumab vs Mono CXT investigators Choice





Zusammenfassung

- Zulassung von neuen Substanzen in der Kombination - und Mono-Therapie
- Mehr Optionen in den späteren Therapielinien durch „upcoming substances“
- r/m Zervix-Karzinom kann in eine „chronische Therapie“ überführt werden
- Stellenwert der Chemotherapie rückläufig?