Comprehensive Cancer Center
Tübingen-Stuttgart

5. Symposium für Hämatologie & Onkologie

Solide Tumoren

PD Dr. med. Dominik Schneidawind

22. Juli 2020

EBERHARD KARLS
UNIVERSITÄT
TÜBINGEN

Comprehensive
Cancer Center
Tübingen - Stuttgart

Offenlegung potenzieller Interessenkonflikte

1. Anstellungsverhältnis oder Führungsposition: keine
2. Beratungs- bzw. Gutachtertätigkeit: keine
3. Besitz von Geschäftsanteilen, Aktien oder Fonds: keine
4. Patent, Urheberrecht, Verkaufslizenz: keine
5. Honorare: keine
6. Finanzierung eigener wissenschaftlicher Untersuchungen: keine
7. Andere finanzielle Beziehungen: keine
8. Immaterielle Interessenkonflikte: keine

2020 ASCO ANNUAL MEETING

Pembrolizumab Plus Axitinib Versus Sunitinib as First-Line Therapy for Advanced Renal Cell Carcinoma: Updated Analysis of KEYNOTE-426

E. R. Plimack[1]; B. I. Rini[2]; V. Stus[3]; R. Gafanov[4]; T. Waddell[5]; D. Nosov[6]; F. Pouliot[7]; D. Soulières[8]; B. Melichar[9]; I. Vynnychenko[10]; S. J. Azevedo[11]; D. Borchiellini[12]; R. S. McDermott[13]; J. Bedke[14]; S. Tamada[15]; L. Yin[16]; M. Chen[16]; L. R. Molife[17]; M. B. Atkins[18]; T. Powles[19]

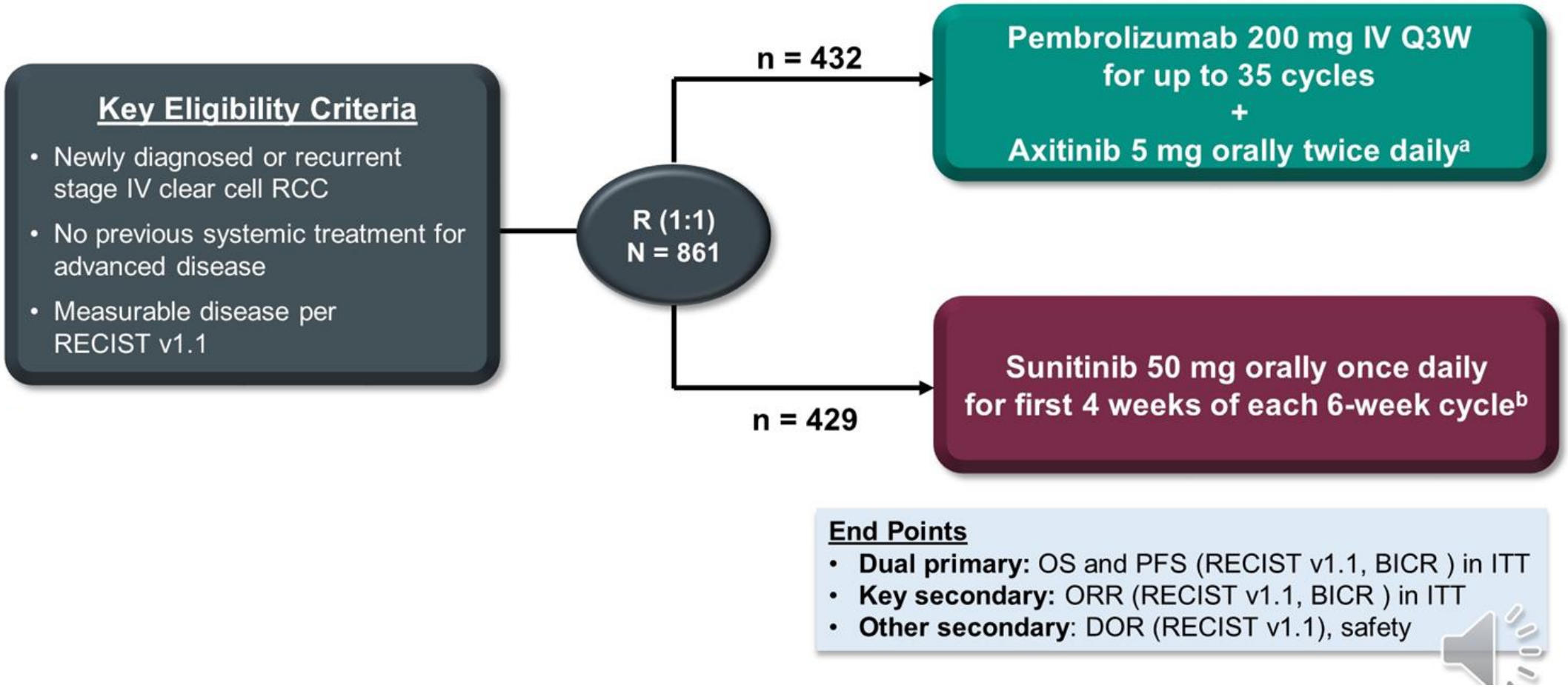
ORIGINAL ARTICLE

Pembrolizumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma

B.I. Rini, E.R. Plimack, V. Stus, R. Gafanov, R. Hawkins, D. Nosov, F. Pouliot, B. Alekseev, D. Soulières, B. Melichar, I. Vynnychenko, A. Kryzhanivska, I. Bondarenko, S.J. Azevedo, D. Borchiellini, C. Szczylik, M. Markus, R.S. McDermott, J. Bedke, S. Tartas, Y.-H. Chang, S. Tamada, Q. Shou, R.F. Perini, M. Chen, M.B. Atkins, and T. Powles, for the KEYNOTE-426 Investigators*

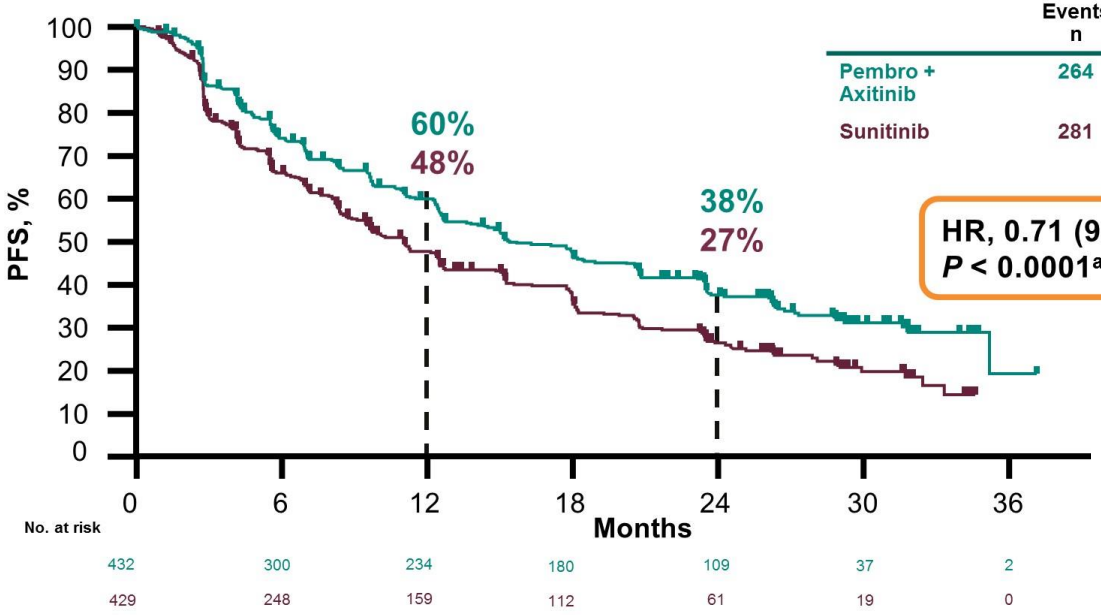
ABSTRACT

J Clin Oncol 37, 2019 (suppl; abstr 4500)



J Clin Oncol 37, 2019 (suppl; abstr 4500)

PFS in the ITT Population



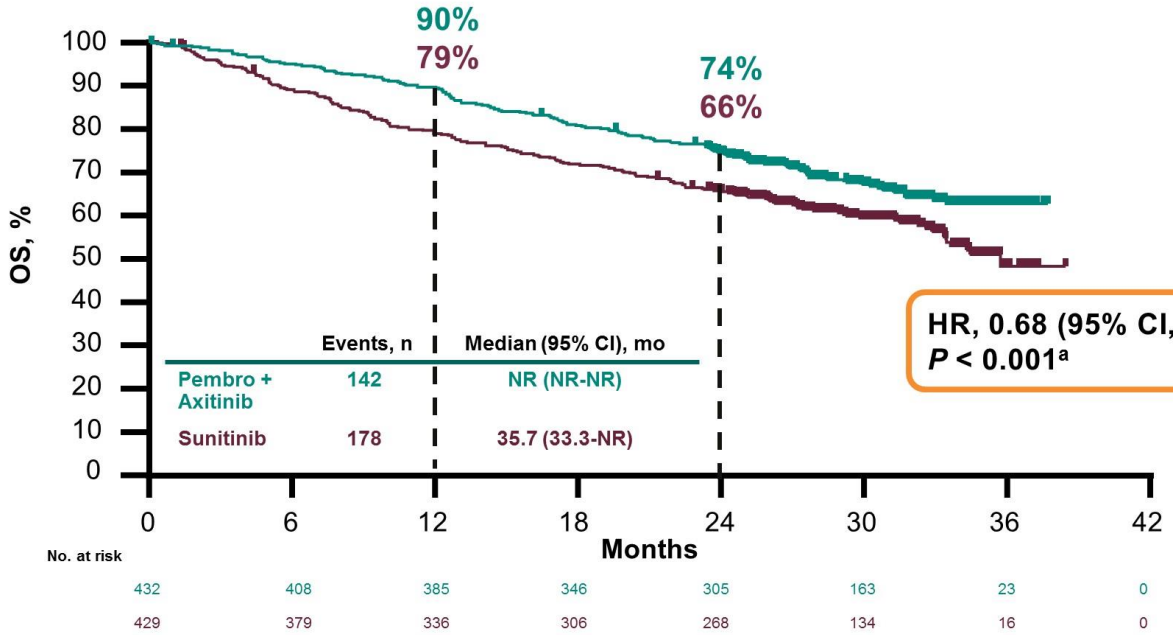
	Events, n	Median (95% CI), mo
Pembro + Axitinib	264	15.4 (12.7-18.9)
Sunitinib	281	11.1 (9.1-12.5)

HR, 0.71 (95% CI, 0.60-0.84)
***P* < 0.0001[a]**

[a]Because superiority of pembrolizumab + axitinib was shown at the first interim analysis, no alpha was allocated to PFS; only nominal *P* values are reported. Da

	Pembro + Axitinib n = 432	Sunitinib n = 429
Best response, n (%)		
CR	38 (8.8)	13 (3.0)
PR	222 (51.4)	158 (36.8)
SD	100 (23.1)	150 (35.0)
PD	49 (11.3)	74 (17.2)
NE[b]	16 (3.7)	28 (6.5)
NA[c]	7 (1.6)	6 (1.4)
Duration of response, median (range), mo	23.5 (1.4+ to 34.5+)	15.9 (2.3 to 31.8+)

OS in the ITT Population

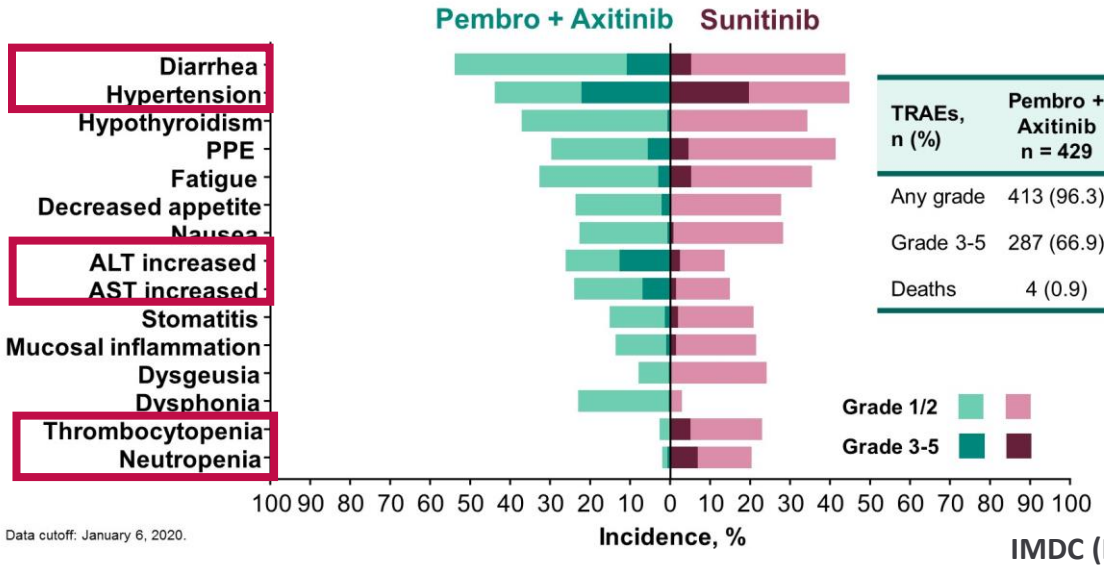


	Events, n	Median (95% CI), mo
Pembro + Axitinib	142	NR (NR-NR)
Sunitinib	178	35.7 (33.3-NR)

HR, 0.68 (95% CI, 0.55-0.85)
***P* < 0.001[a]**

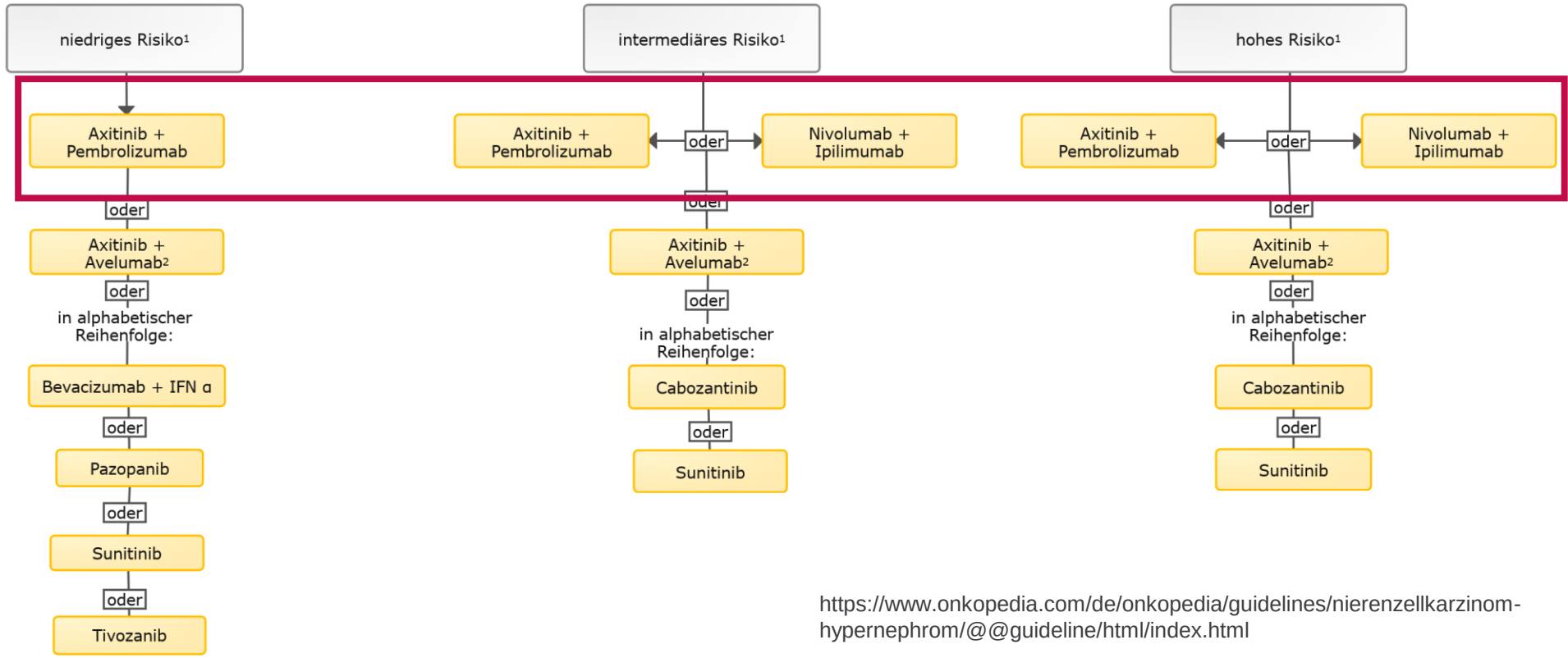
[a]Because superiority of pembrolizumab + axitinib was shown at the first interim analysis, no alpha was allocated to OS; only nominal *P* values are reported. Data cutoff: January 6, 2020.

J Clin Oncol 37, 2019 (suppl; abstr 4500)



TRAEs, n (%)	Pembro + Axitinib n = 429	Sunitinib n = 425
Any grade	413 (96.3)	415 (97.6)
Grade 3-5	287 (66.9)	265 (62.4)
Deaths	4 (0.9)	6 (1.4)

IMDC (International Metastatic RCC Database Consortium) Score



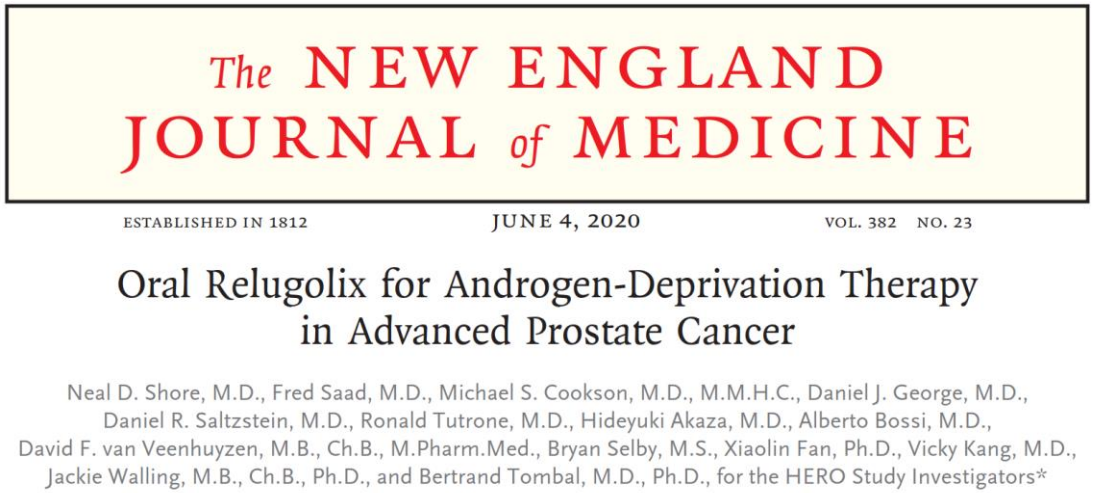
https://www.onkopedia.com/de/onkopedia/guidelines/nierenzellkarzinom-hypernephrom/@@guideline/html/index.html

J Clin Oncol 37, 2019 (suppl; abstr 4500)

2020 ASCO ANNUAL MEETING

HERO Phase 3 Trial: Relugolix, an Oral GnRH Receptor Antagonist, versus Leuprolide Acetate for Advanced Prostate Cancer

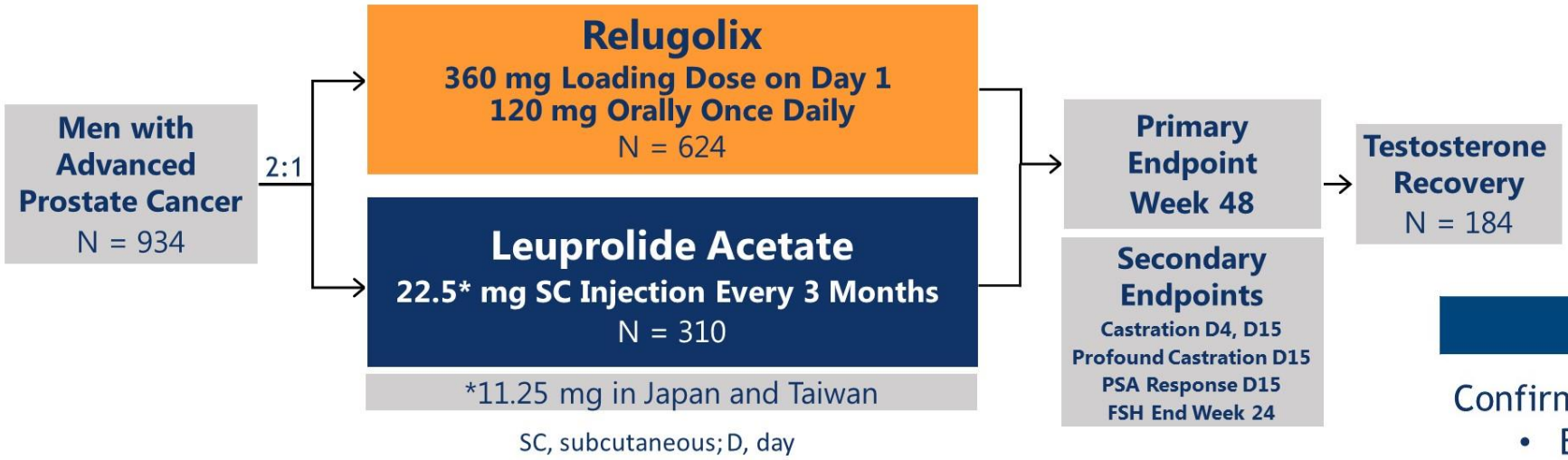
Neal D. Shore,[1] Fred Saad,[2] Michael S. Cookson,[3] Daniel J. George,[4] Daniel R. Saltzstein,[5] Ronald Tutrone,[6] Hideyuki Akaza,[7] Alberto Bossi,[8] David F. van Veenhuyzen,[9] Bryan Selby,[9] Xiaolin Fan,[9] Vicky Kang,[9] Jackie Walling,[9] Bertrand Tombal,[10] for the HERO Study Investigators



J Clin Oncol 38: 2020 (suppl; abstr 5602)

Phase 3 HERO Study Design

- A multinational phase 3 randomized, open-label, parallel group study to evaluate the safety and efficacy of relugolix in men with advanced prostate cancer
- **Primary Endpoint**: Sustained castration through 48 weeks (< 50 ng/dL)



SC, subcutaneous; D, day

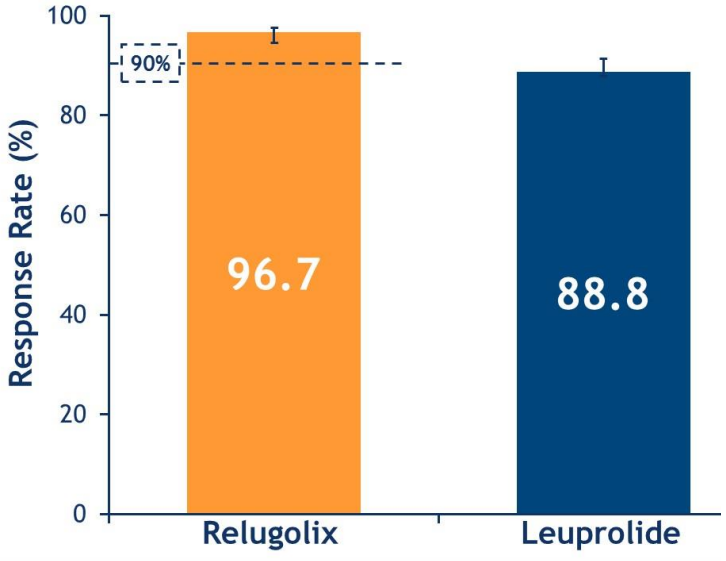
Inclusion
Confirmed advanced prostate cancer • Biochemical or clinical relapse • Metastatic disease • Advanced localized disease
Requiring ≥ 1 year of ADT
Serum testosterone ≥ 150 ng/dL
Serum PSA > 2.0 ng/mL
ECOG Score 0/1

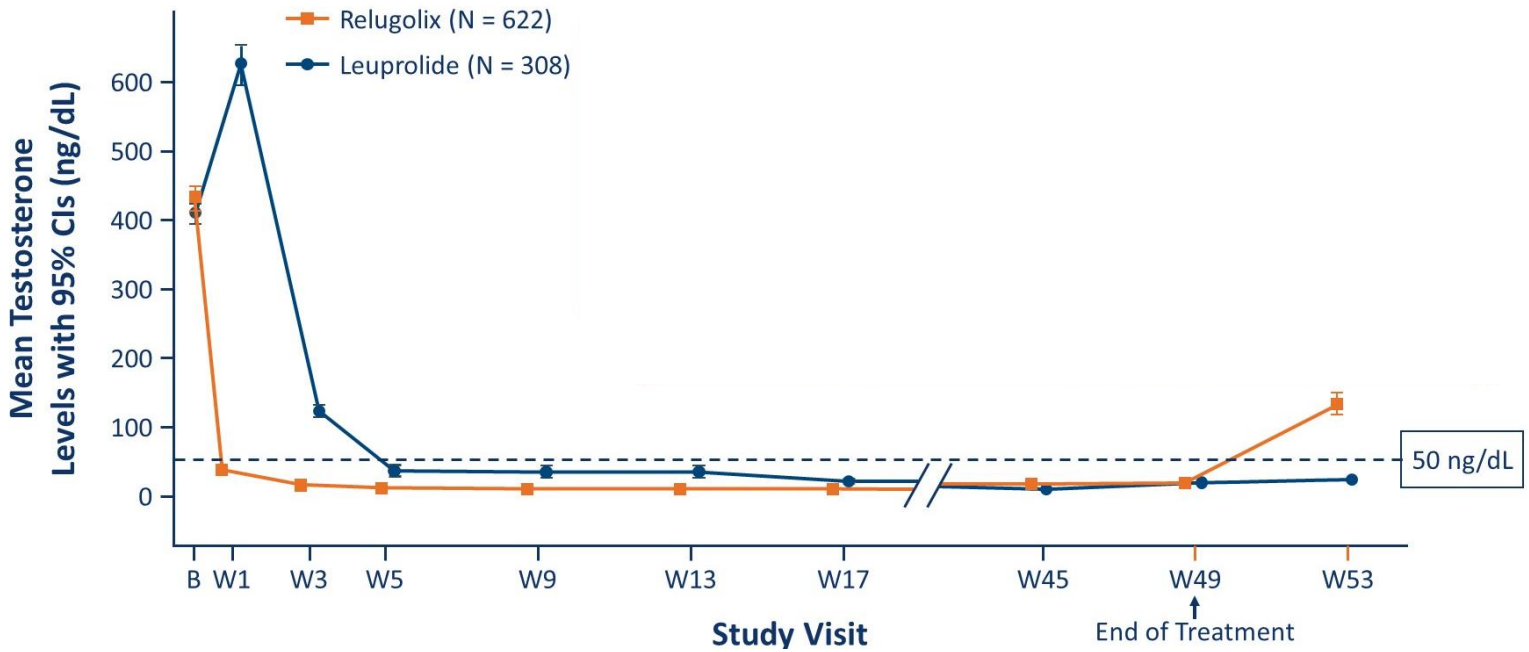
J Clin Oncol 38: 2020 (suppl; abstr 5602)

Primary Endpoint – Sustained Castration

Key Secondary Endpoint – Noninferiority to Leuprolide

HERO





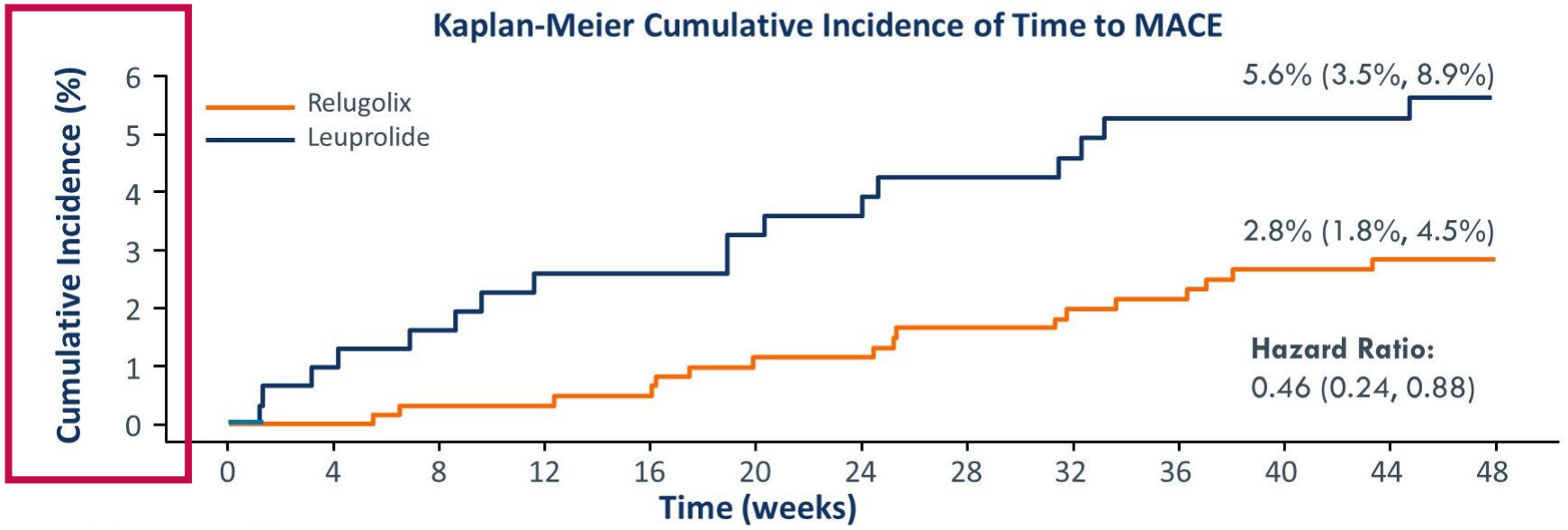
J Clin Oncol 38: 2020 (suppl; abstr 5602)

Summary of Adverse Events

	Relugolix (N = 622)	Leuprolide (N = 308)
Any Adverse Event	92.9%	93.5%
Related to study drug	73.6%	68.8%
Any ≥ Grade 3	18.0%	20.5%
≥ Grade 3 related to study drug	3.4%	2.6%
Fatal Adverse Events	1.1%	2.9%

HERO

54% Reduction in Risk of Major Adverse Cardiovascular Events (MACE)



J Clin Oncol 38: 2020 (suppl; abstr 5602)

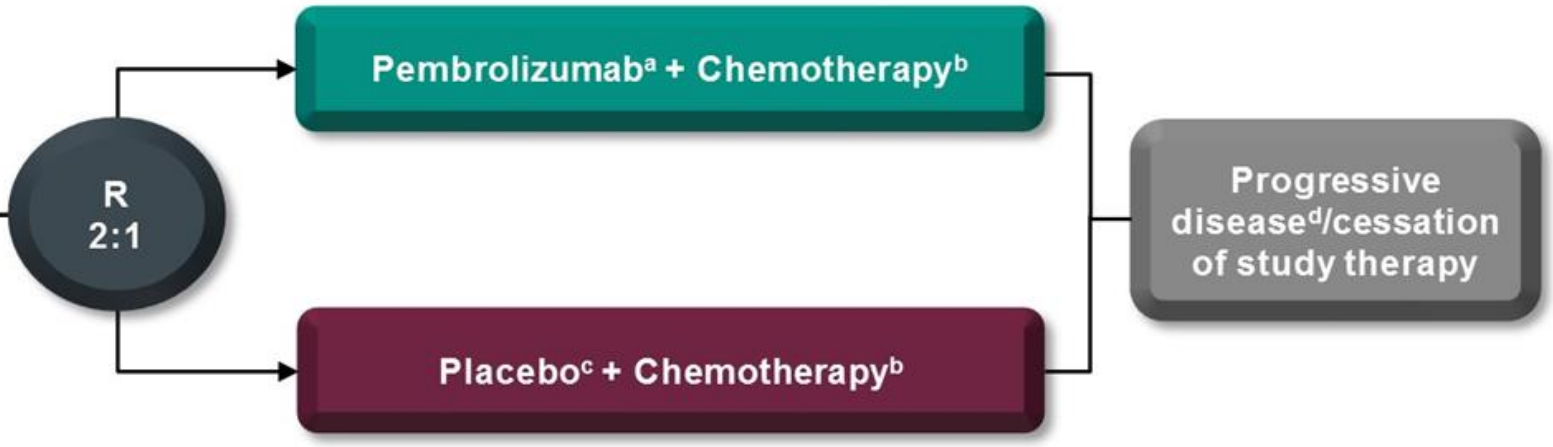
KEYNOTE-355: Randomized, Double-Blind, Phase 3 Study of Pembrolizumab + Chemotherapy versus Placebo + Chemotherapy for Previously Untreated Locally Recurrent Inoperable or Metastatic Triple-Negative Breast Cancer

Javier Cortes[1], David W. Cescon[2], Hope S. Rugo[3], Zbigniew Nowecki[4], Seock-Ah Im[5], Mastura Md Yusof[6], Carlos Gallardo[7], Oleg Lipatov[8], Carlos H. Barrios[9], Esther Holgado[1], Hiroji Iwata[10], Norikazu Masuda[11], Marco Torregroza Otero[12], Erhan Gokmen[13], Sherene Loi[14], Zifang Guo[15], Jing Zhao[15], Gursel Aktan[15], Vassiliki Karantza[15], Peter Schmid[16]

J Clin Oncol 38: 2020 (suppl; abstr 1000)

KEYNOTE-355 Study Design (NCT02819518)

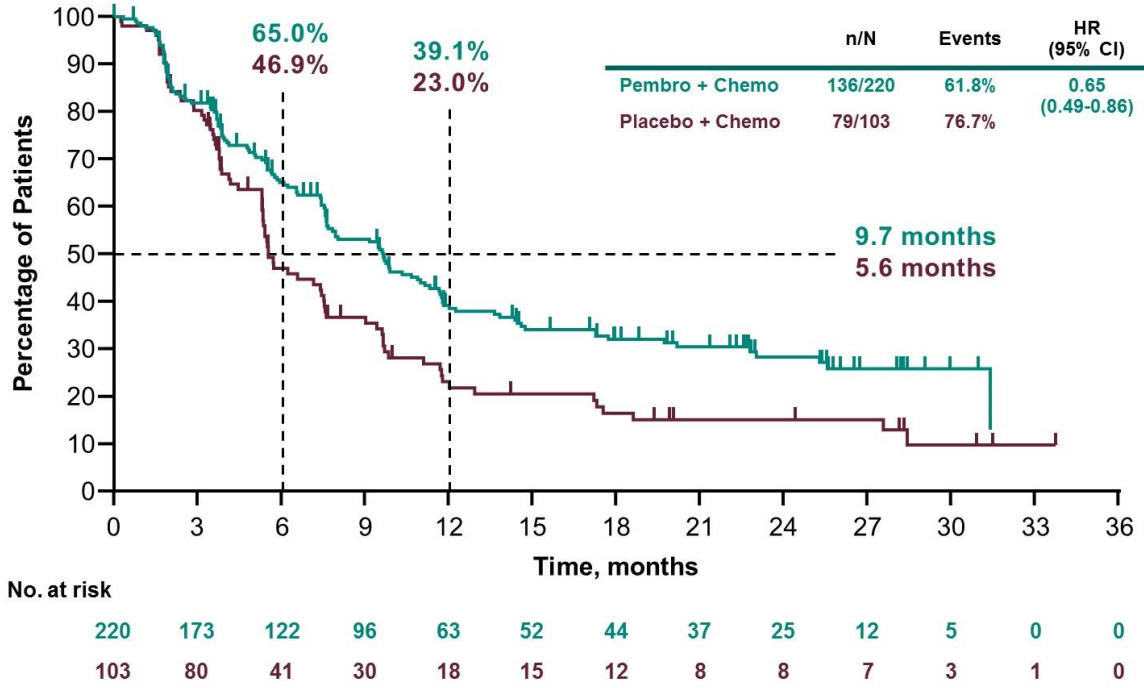
Key Eligibility Criteria
- Age ≥18 years
- Central determination of TNBC and PD-L1 expression
- Previously untreated locally recurrent inoperable or metastatic TNBC
- Completion of treatment with curative intent ≥6 months prior to first disease recurrence
- ECOG performance status 0 or 1
- Life expectancy ≥12 weeks from randomization
- Adequate organ function
- No systemic steroids
- No active CNS metastases
- No active autoimmune disease



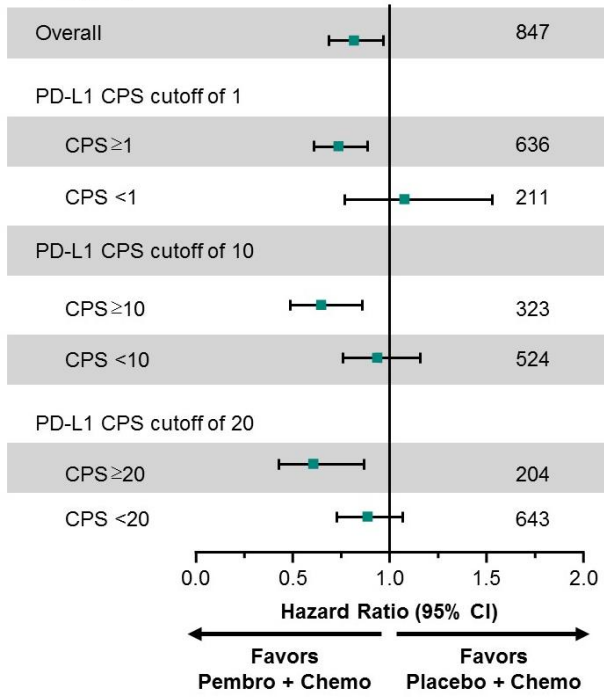
Stratification Factors:
- Chemotherapy on study (taxane vs gemcitabine/carboplatin)
- PD-L1 tumor expression (CPS ≥1 vs CPS <1)
- Prior treatment with same class chemotherapy in the neoadjuvant or adjuvant setting (yes vs no)

J Clin Oncol 38: 2020 (suppl; abstr 1000)

Progression-Free Survival: PD-L1 CPS ≥10



	n/N	Events	HR (95% CI)	P-value (one-sided)
Pembro + Chemo	136/220	61.8%	0.65 (0.49-0.86)	0.0012[a]
Placebo + Chemo	79/103	76.7%		

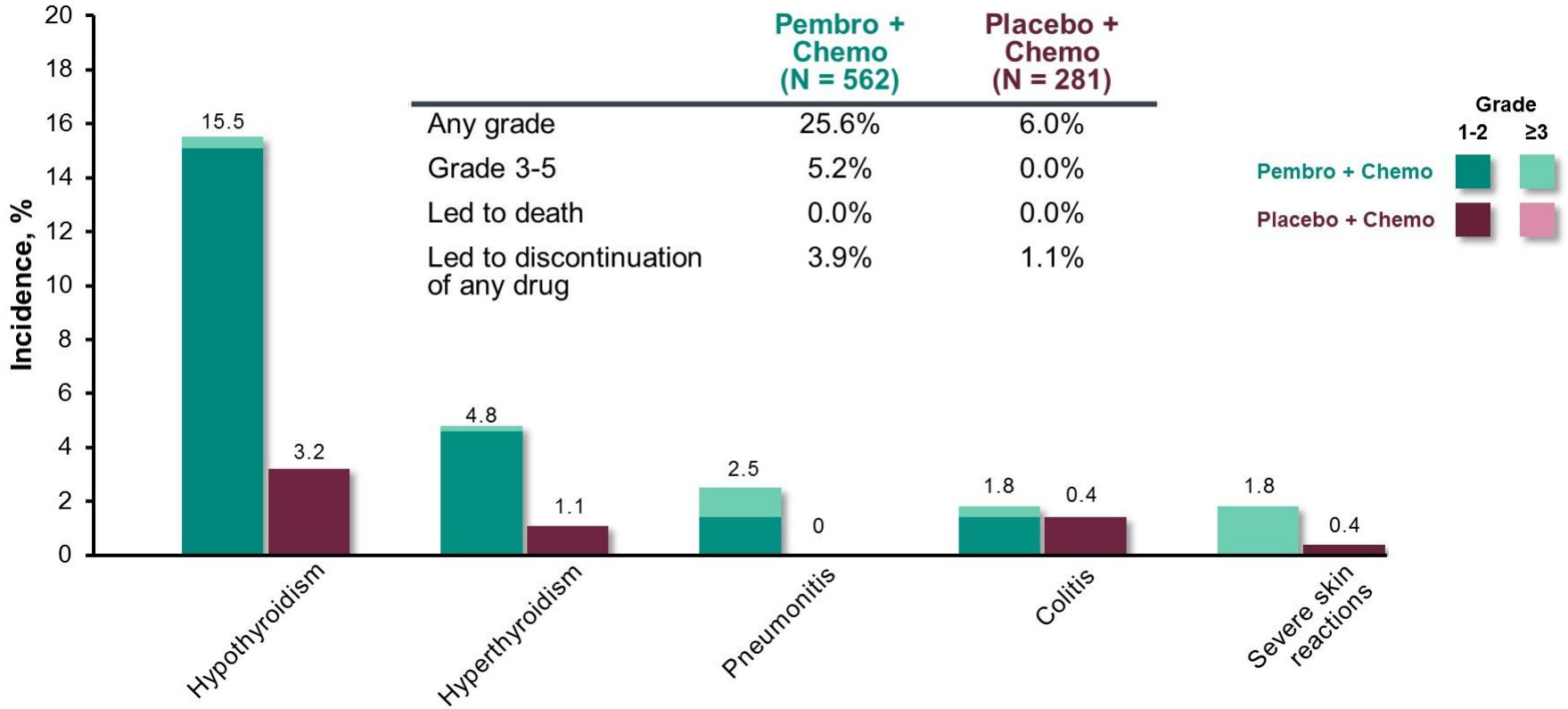


Subgroup	N	Median PFS (mo) Pembro + Chemo	Median PFS (mo) Placebo + Chemo	Hazard Ratio for Progression or Death (95% CI)
Overall	847	7.5	5.6	0.82 (0.69 to 0.97)
PD-L1 CPS cutoff of 1				
CPS ≥1	636	7.6	5.6	0.74 (0.61 to 0.89)
CPS <1	211	6.3	6.2	1.08 (0.77 to 1.53)
PD-L1 CPS cutoff of 10				
CPS ≥10	323	9.7	5.6	0.65 (0.49 to 0.86)
CPS <10	524	5.8	5.7	0.94 (0.76 to 1.16)
PD-L1 CPS cutoff of 20				
CPS ≥20	204	9.5	5.4	0.61 (0.43 to 0.87)
CPS <20	643	6.6	5.8	0.89 (0.73 to 1.07)

J Clin Oncol 38: 2020 (suppl; abstr 1000)

All Treatment-Related	Pembro + Chemo (N = 562)	Placebo + Chemo (N = 281)
Any grade	96.3%	95.0%
Grade 3-5	68.1%	66.9%
Led to death	0.4%[a]	0.0%
Led to discontinuation of any drug	18.1%	11.0%

Immune-Mediated AEs



	Pembro + Chemo (N = 562)	Placebo + Chemo (N = 281)
Any grade	25.6%	6.0%
Grade 3-5	5.2%	0.0%
Led to death	0.0%	0.0%
Led to discontinuation of any drug	3.9%	1.1%

J Clin Oncol 38: 2020 (suppl; abstr 1000)

KEYNOTE-048: Progression After the Next Line of Therapy Following Pembrolizumab or Pembrolizumab Plus Chemotherapy vs EXTREME as First-Line Therapy for Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma

Kevin Harrington,[1] Danny Rischin,[2] Richard Greil,[3] Denis Soulieres,[4] Makoto Tahara,[5] Gilberto Castro,[6] Amanda Psyrri,[7] Neus Baste,[8] Prakash C. Neupane,[9] Åse Bratland,[10] Thorsten Fuereder,[11] Brett G. M. Hughes,[12] Ricard Mesia Sr.,[13] Nuttapong Ngamphaiboon,[14] Tamara Rordorf,[15] Wan Zamaniah Wan Ishak,[16] Yayan Zhang,[17] Burak Gumuscu,[17] Ramona F. Swaby,[17] Barbara Burtness[18]

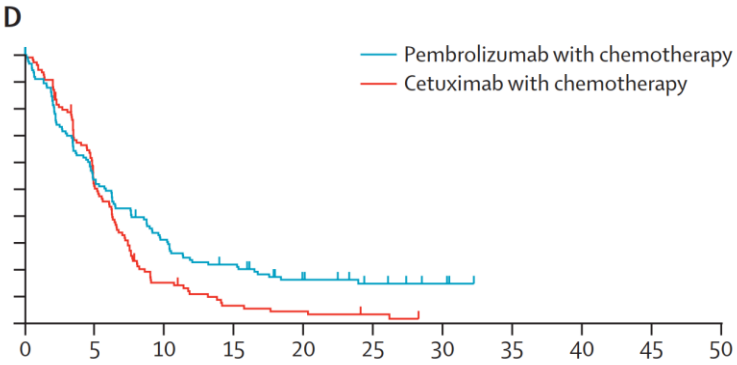
J Clin Oncol 38: 2020 (suppl; abstr 6505)

Pembrolizumab alone or with chemotherapy versus cetuximab with chemotherapy for recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-048): a randomised, open-label, phase 3 study

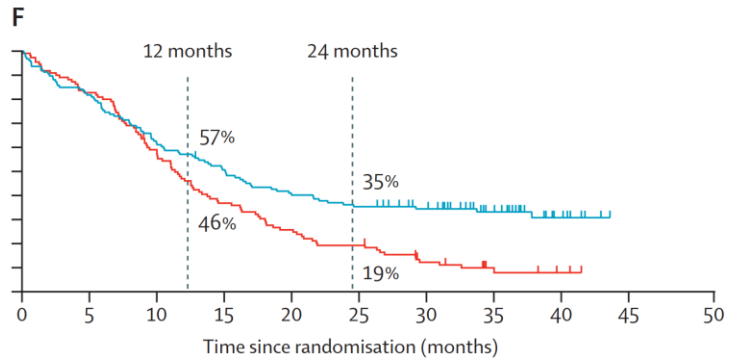
*Barbara Burtness, Kevin J Harrington, Richard Greil, Denis Soulières, Makoto Tahara, Gilberto de Castro Jr, Amanda Psyrri, Neus Basté, Prakash Neupane, Åse Bratland, Thorsten Fuereder, Brett G M Hughes, Ricard Mesía, Nuttapong Ngamphaiboon, Tamara Rordorf, Wan Zamaniah Wan Ishak, Ruey-Long Hong, René González Mendoza, Ananya Roy, Yayan Zhang, Burak Gumuscu, Jonathan D Cheng, Fan Jin, Danny Rischin, on behalf of the KEYNOTE-048 Investigators**

www.thelancet.com **Published online October 31, 2019**

CPS ≥20 PFS



CPS ≥20 OS



First Subsequent Therapy Following PD

Key Eligibility Criteria

- SCC of the oropharynx, oral cavity, hypopharynx, or larynx
- R/M disease incurable by local therapies
- ECOG PS 0 or 1
- Tissue sample for PD-L1 assessment[a]
- Known p16 status in the oropharynx[b]

Stratification Factors

- PD-L1 expression[a] (TPS ≥50% vs <50%)
- p16 status in oropharynx (positive vs negative)
- ECOG performance status (0 vs 1)

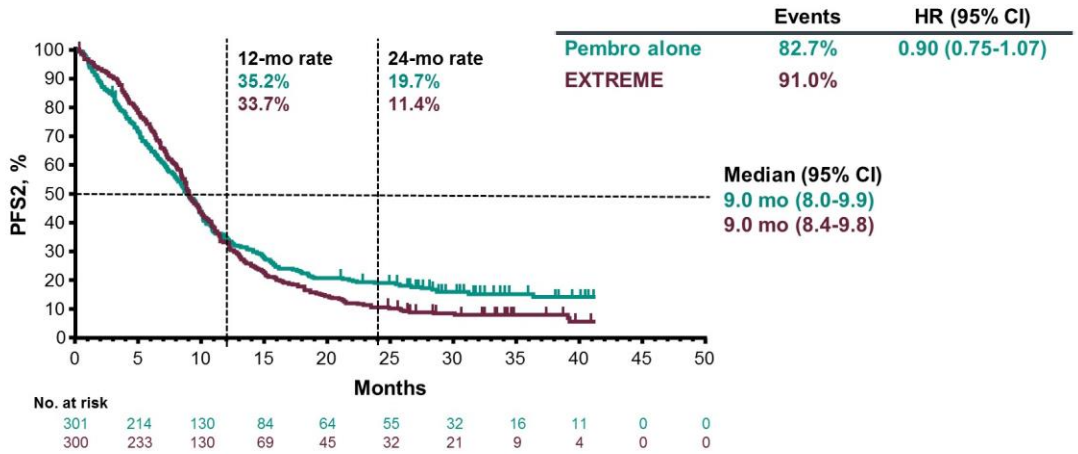
R 1:1:1

- Pembro → Pembro 200 mg Q3W for up to 35 cycles
- Pembro + Chemo → Pembro 200 mg Q3W for up to 35 cycles total + Chemo[d]
- EXTREME → Cetuximab 250 mg/m² Q1W[c] + Chemo[d]

PD → Subsequent Therapy (Investigator's choice)

J Clin Oncol 38: 2020 (suppl; abstr 6505)

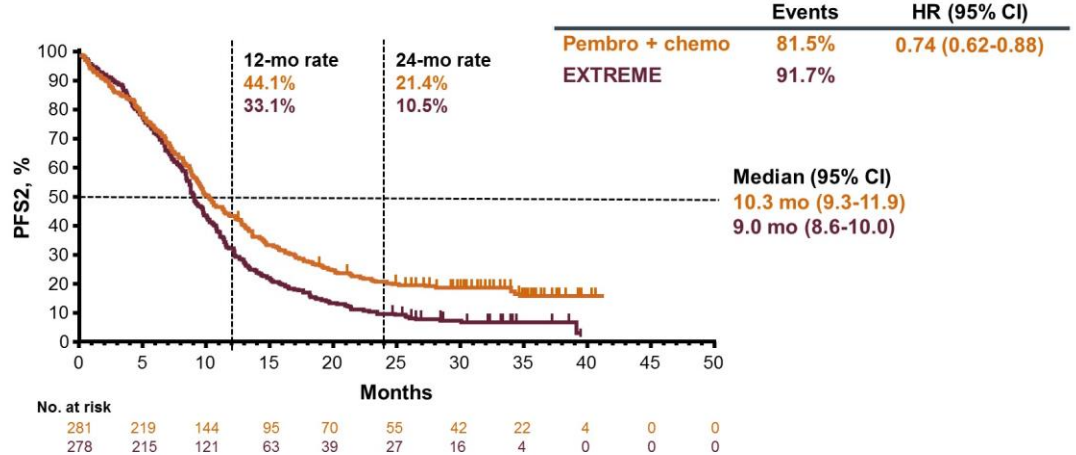
PFS2: Initially Randomized, Pembro vs EXTREME, Total Population



- PFS2 analysis involved patients in the ITT population (Pembro vs EXTREME)

Data cutoff: February 25, 2019 (final analysis).

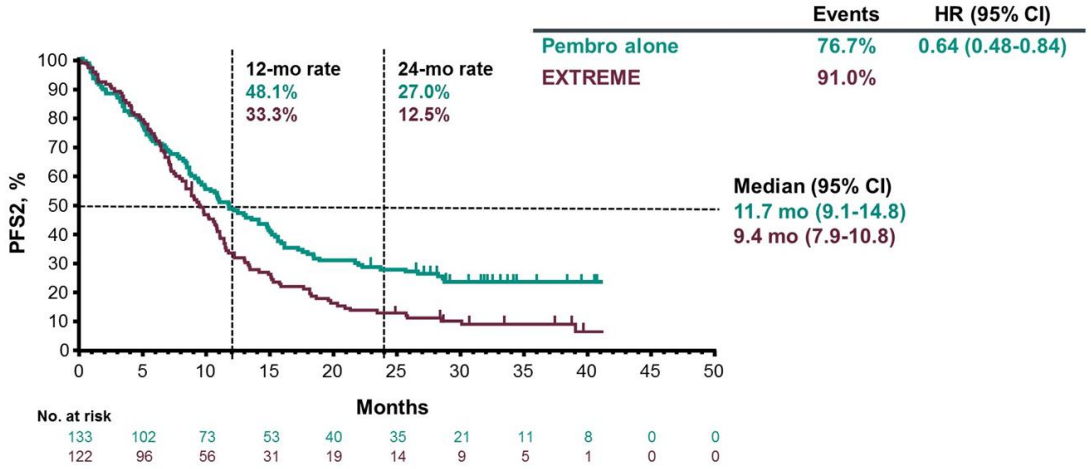
PFS2: Initially Randomized, Pembro + Chemotherapy vs EXTREME, Total Population



- PFS2 analysis involved patients in the ITT population (Pembro + Chemotherapy vs EXTREME)

Data cutoff: February 25, 2019 (final analysis).

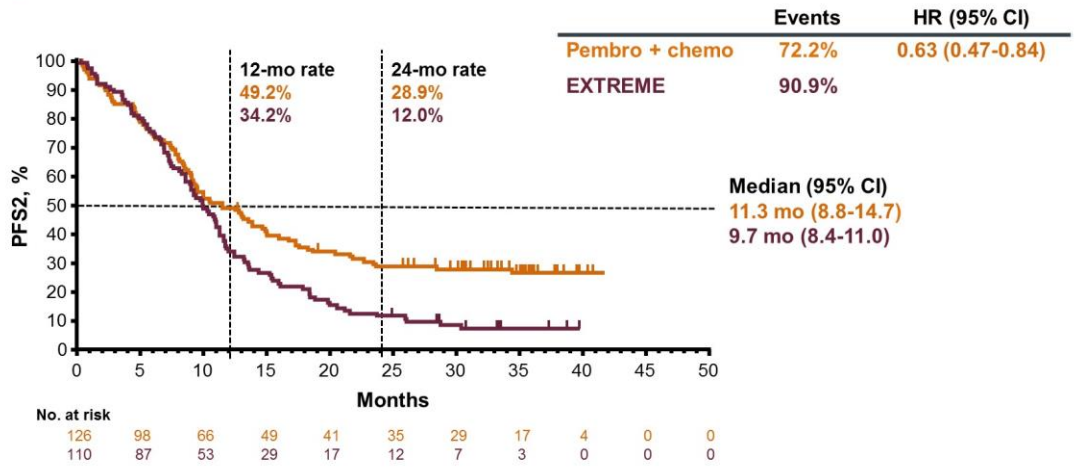
PFS2: Initially Randomized, Pembro vs EXTREME, CPS ≥20 Population



- PFS2 analysis involved patients in the ITT population with PD-L1 CPS≥20 (Pembro vs EXTREME)

Data cutoff: February 25, 2019 (final analysis).

PFS2: Initially Randomized, Pembro + Chemotherapy vs EXTREME, CPS ≥20 Population



- PFS2 analysis involved patients in the ITT population with PD-L1 CPS≥20 (Pembro + Chemotherapy vs EXTREME)

Data cutoff: February 25, 2019 (final analysis).

Randomized phase II study of axitinib versus observation in patients with recurred or metastatic adenoid cystic carcinoma

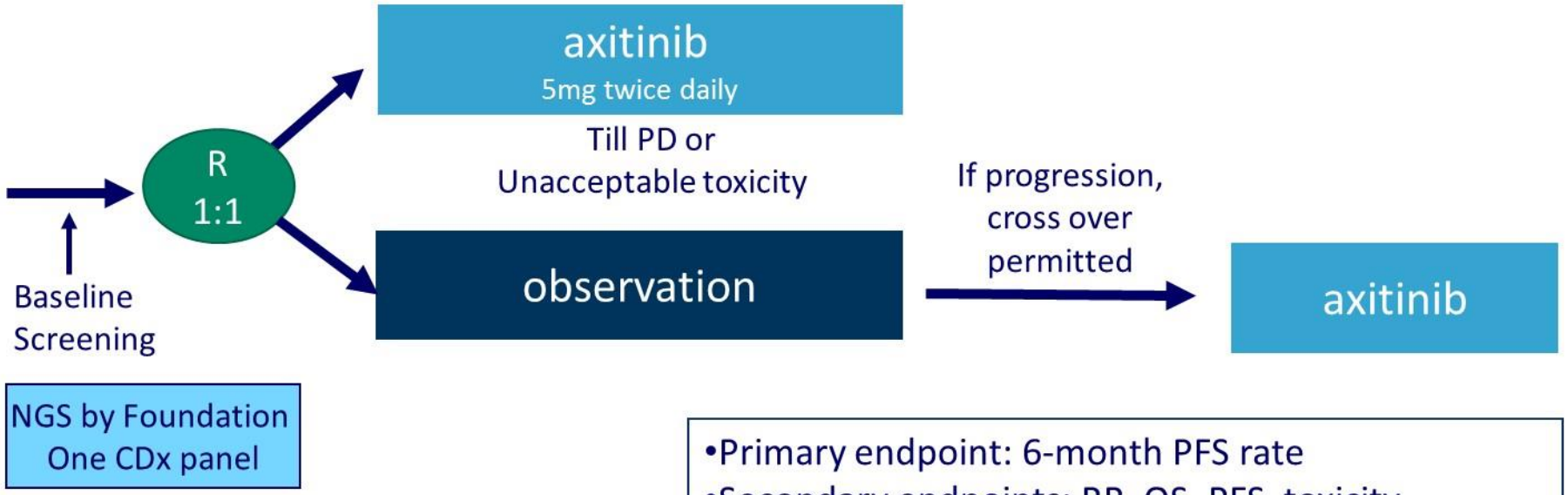
Bhumsuk Keam[1], Eun Joo Kang[2], Myung-Ju Ahn[3], Chan-Young Ock[1], Keun-Wook Lee[4], Jung Hye Kwon[5], Yaewon Yang[6], Yoon Hee Choi[7], Min Kyoung Kim[8], Jun Ho Ji[9], Tak Yun[10], Byung-Ho Nam[11], Sung-Bae Kim[12]

J Clin Oncol 38: 2020 (suppl; abstr 6503)

- Prospective, open-label, randomized phase II trial (NCT02859012)

Key inclusion criteria

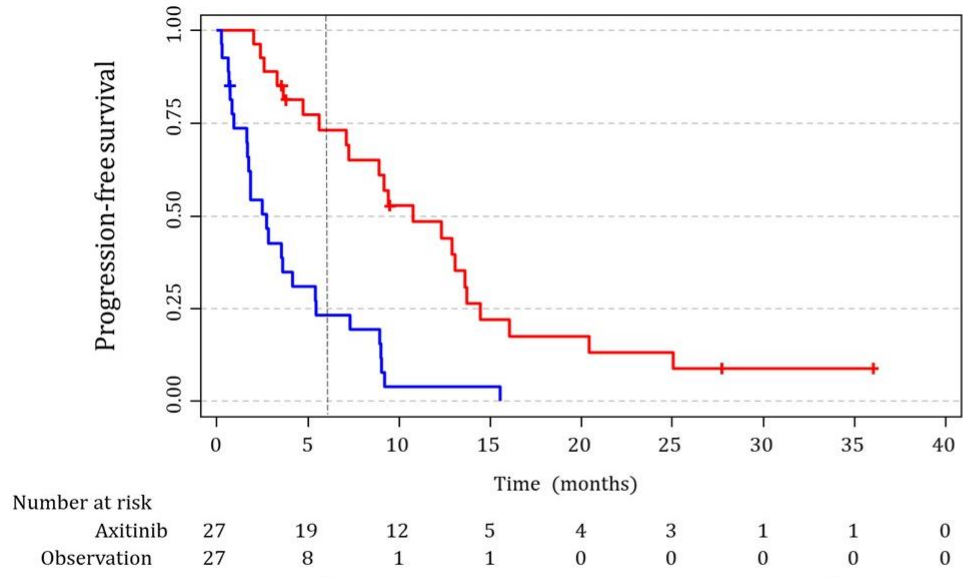
- Recurred/ metastatic / unresectable ACC
- Disease progression within 9 months prior informed consents
- ECOG PS 0-1
- Age ≥ 20
- Measurable lesion
- Prior chemotherapy is allowed (any chemo line)



- Primary endpoint: 6-month PFS rate
- Secondary endpoints: RR ,OS, PFS, toxicity, exploring predictive genomic alteration
- N= 60 (30per each arm)

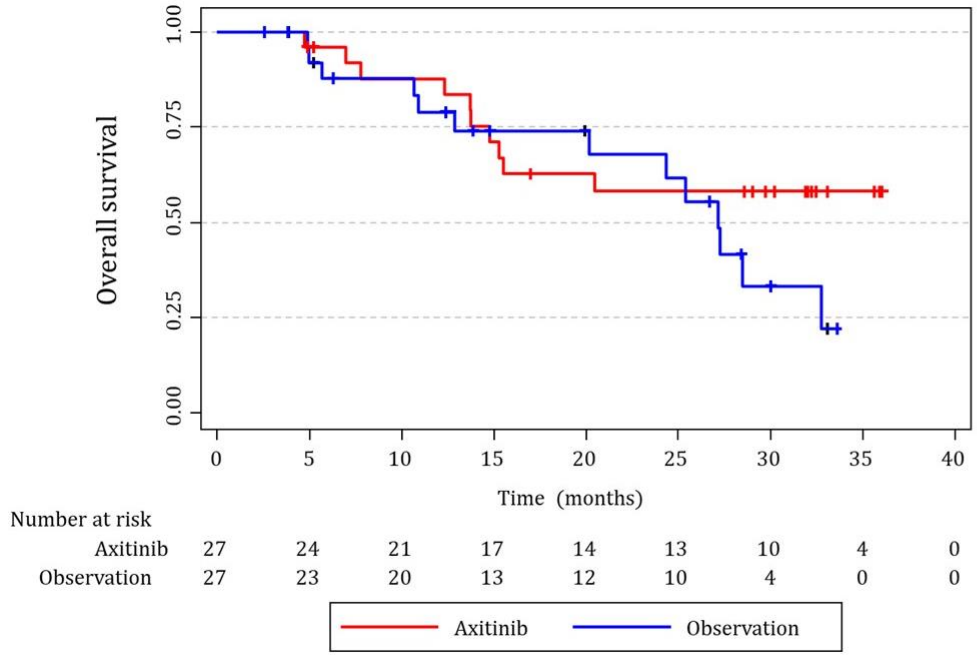
J Clin Oncol 38: 2020 (suppl; abstr 6503)

PFS



	Axitinib (N=27)	Observation (N=27)
6-month PFS rate, % (95% CI)	73% (52-86%)	23% (9-41%)
Median PFS, months (95% CI)	10.8 (7.1-13.6)	2.8 (1.7-4.2)
Hazard Ratio (95% CI)	0.25 (0.14-0.48) p<0.0001	

OS



	Axitinib (N=27)	Observation (N=27)
Median OS, months (95% CI)	NR(14.8-)	27.2(20.2-32.8)
Hazard Ratio (95% CI)	0.60 (0.26-1.38) P=0.2262	
Median follow-up, months	31.9	28.4

J Clin Oncol 38: 2020 (suppl; abstr 6503)

Most frequently observed AEs

Adverse Events	Axitinib(N=30), N(%)			Observation arm (N=30) , N(%)		
	Grade 1-2	Grade3-4	Total	Grade 1-2	Grade3-4	Total
Stomatitis/mucositis	13(43.3)	0(0.0)	13(43.3)	1(3.3)	0(0.0)	1(3.3)
Anorexia	10(33.3)	1(3.3)	11(36.7)	0(0.0)	0(0.0)	0(0.0)
Fatigue	7(23.3)	4(13.3)	11(36.7)	2(6.7)	0(0.0)	2(6.7)
Hypertension	7(23.3)	7(23.3)	14(46.7)	0(0.0)	0(0.0)	0(0.0)
Proteinuria	10(33.3)	0(0.0)	10(33.3)	0(0.0)	0(0.0)	0(0)
Hand-foot syndrome (PPE)	5(16.7)	0(0.0)	5(16.7)	0(0.0)	0(0.0)	0(0.0)
Diarrhea	4(13.3)	3(10.0)	7(23.3)	0(0.0)	0(0.0)	0(0.0)
Dyspepsia	4(13.3)	1(3.3)	5(16.7)	4(13.3)	0(0.0)	4(13.3)
Weight loss	6(20.0)	1(3.3)	7(23.3)	0(0.0)	0(0.0)	0(0.0)
Aspartate aminotransferase (AST) increased	2(6.7)	1(3.3)	3(10.0)	1(3.3)	0(0.0)	1(3.3)
Dyspnea	4(13.3)	1(3.3)	5(16.7)	0(0.0)	0(0.0)	0(0.0)
Headache	4(13.3)	0(0.0)	4(13.3)	2(6.7)	0(0.0)	2(6.7)
QT prolongation	0(0.0)	1(3.3)	1(3.3)	0(0.0)	0(0.0)	0(0.0)
Constipation	4(13.3)	0(0.0)	4(13.3)	2(6.7)	0(0.0)	2(6.7)
Nausea	3(10.0)	0(0.0)	3(10.0)	1(3.3)	0(0.0)	1(3.3)
Skin rash(maculopapular)	2(6.7)	0(0.0)	2(6.7)	0(0.0)	0(0.0)	0(0.0)

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