Head and Neck Cancer Highlights ASCO 2021

John Kaczmar MD
Hollings Cancer Center, MUSC

Disclosure of Conflict(s) of Interest

John Kaczmar, MD reported the following relevant financial relationships or relationships they have with ineligible companies of any amount during the past 24 months:

Consultant: Regeneron, Bicara

Overview

- Establishment of a new standard of care in R/M nasopharynx cancer
- A new TKI for DTC
- Targeting and surveilling HPV+ OPSCC
- Highlighting an important targeted therapy trial in progress

2021 ASCO ANNUAL MEETING

CAPTAIN-1ST: CAMRELIZUMAB VERSUS PLACEBO IN COMBINATION WITH GEMCITABINE AND CISPLATIN AS FIRST-LINE TREATMENT FOR RECURRENT OR METASTATIC NASOPHARYNGEAL CARCINOMA: A MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PHASE 3 TRIAL

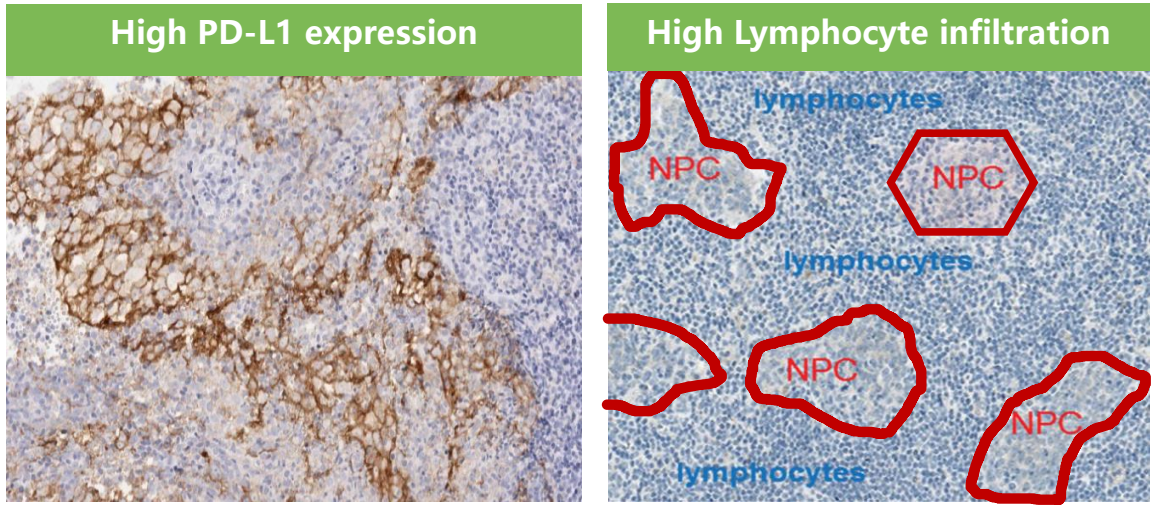
Li Zhang, MD

Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Guangzhou, China.

June 7, 2021

Background

- Standard first-line treatment for recurrent or metastatic NPC (R/M-NPC) is platinum-based chemotherapy.
  - Gemcitabine + cisplatin (GP): ORR, 64%; median PFS, 7.0 months; median OS, 29.1 months.[3]
- Endemic NPC tumors are characterized by high PD-L1 expression and intensive infiltration of non-malignant lymphocytes.[4]
- First-line camrelizumab plus GP showed encouraging anticancer activity (ORR, 91%; 12-month PFS rate, 61.4%).[5]
- **Objective:** This multicenter, randomized, double-blind, phase 3 study was conducted to investigate camrelizumab plus GP *vs* placebo plus GP for R/M-NPC in the first-line setting.



3. Zhang L, et al. Lancet 2016; 388:1883-92; 4. Larbcharoensub N, et al. Am J Clin Oncol 2018; 41:1204-10; 5. Fang W, et al. Lancet Oncol 2018; 19:1338-50.
Abbreviations: ORR, objective response rate; PFS, progression-free survival; OS, overall survival.

Study Design (NCT03707509)

Key eligibility criteria:

- Aged 18-75 years;
- Pathologically confirmed R/M-NPC;
- Had not received previous systemic therapy for R/M-NPC (disease progression at least 6 months after induction, adjuvant, or concurrent chemoradiotherapy were eligible);
- ECOG performance status of 0 or 1;
- At least one measurable lesion according to RECIST version 1.1;

R 1 : 1

Camrelizumab (200 mg on day 1)
+ gemcitabine (1000 mg/m^2 on days 1 and 8)
+ cisplatin (80 mg/m^2 on day 1)

Q3W for 4-6 cycles

Camrelizumab (200 mg on day 1)

Q3W until disease progression, unacceptable toxicity, withdrawal of consent

Stratification factors:

- Liver metastases (yes *vs* no).
- Previous radical concurrent chemoradiotherapy (yes *vs* no).
- ECOG performance status (0 *vs* 1)

Placebo
+ gemcitabine (1000 mg/m^2 on days 1 and 8)
+ cisplatin (80 mg/m^2 on day 1)

Q3W for 4-6 cycles

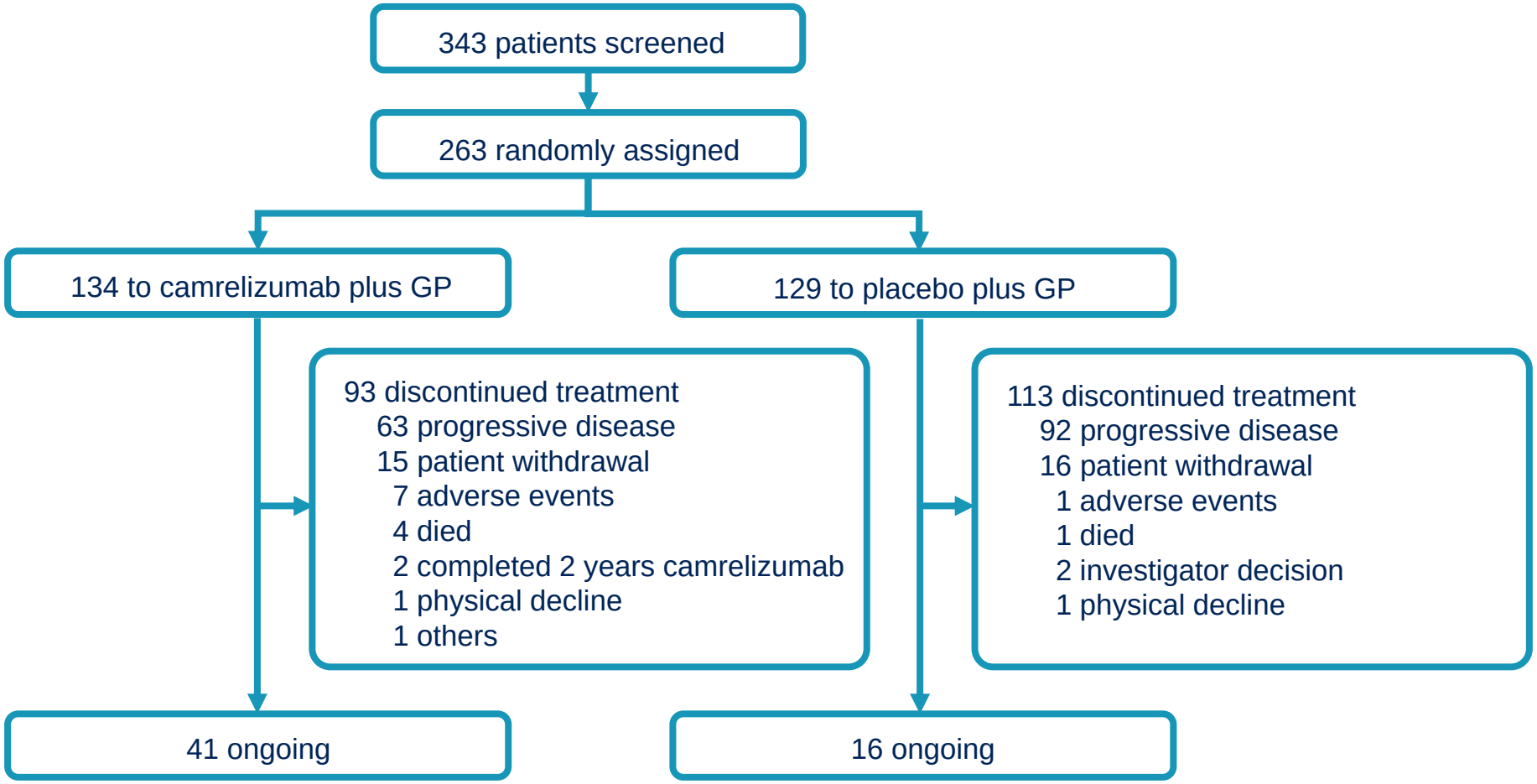
Placebo

Q3W until disease progression, unacceptable toxicity, withdrawal of consent

- Primary endpoint: independent review committee (IRC)-assessed PFS
- Secondary endpoints: investigator-assessed PFS, ORR, DCR, DoR, OS and safety

ECOG, Eastern Cooperative Oncology Group; RECIST, Response Evaluation Criteria in Solid Tumors; DCR, disease control rate; DoR, duration of response

Trial Profile (data cutoff on Dec 31, 2020)



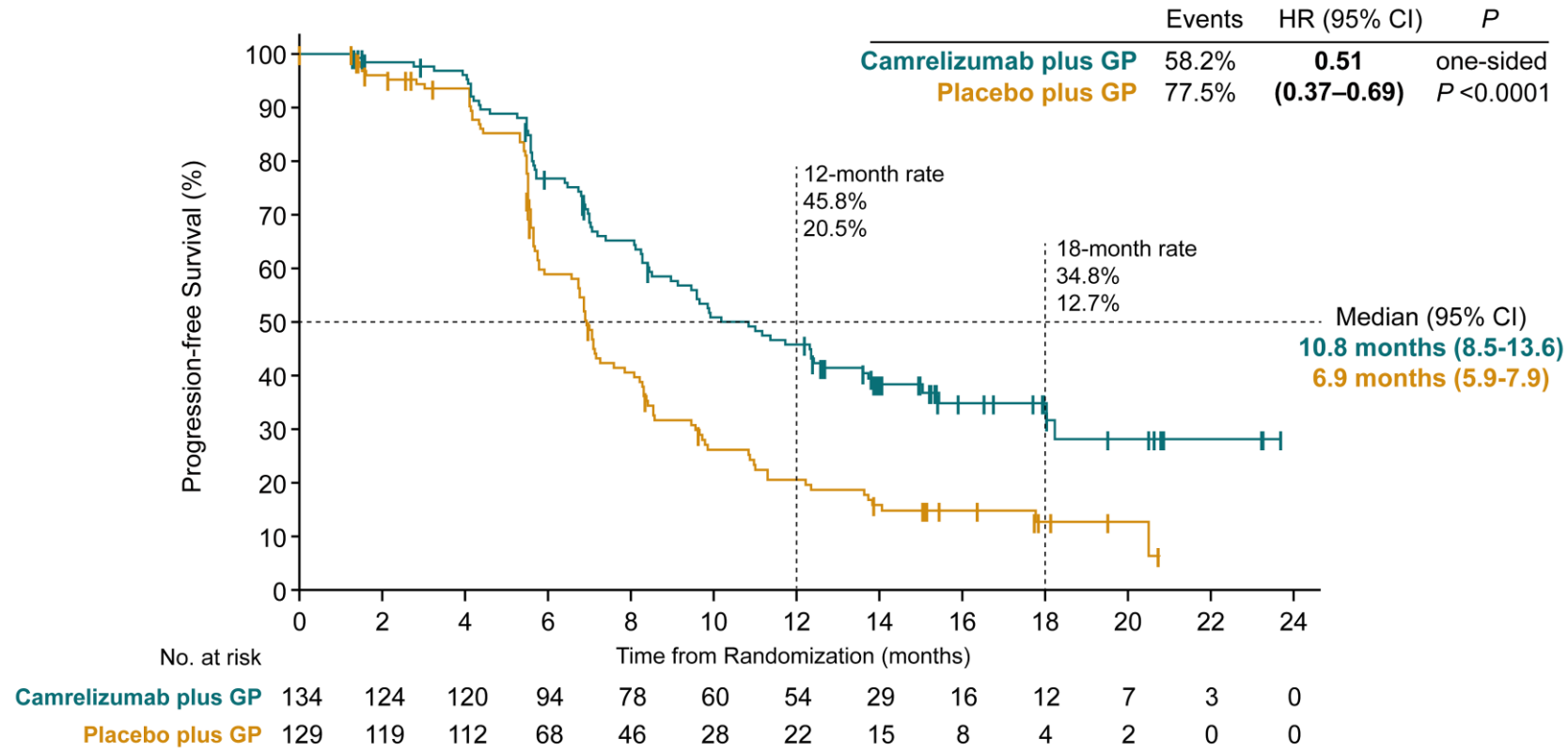
Baseline Characteristics

Characteristic	Camrelizumab plus GP (N = 134)	Placebo plus GP (N = 129)
Age (years)		
Median (range)	52 (25-73)	49 (24-74)
<50	59 (44%)	73 (57%)
≥50	75 (56%)	56 (43%)
Male	113 (84%)	105 (81%)
ECOG performance status		
0	47 (35%)	44 (34%)
1	87 (65%)	85 (66%)
Baseline plasma EBV DNA level		
Positive	95 (71%)	86 (67%)
Negative	39 (29%)	43 (33%)
WHO classification		
Keratinizing	1 (<1%)	1 (<1%)
Non-keratinizing differentiated	21 (16%)	21 (16%)
Non-keratinizing undifferentiated	110 (82%)	106 (82%)
Others	2 (1%)	1 (<1%)

Characteristic	Camrelizumab plus GP (N = 134)	Placebo plus GP (N = 129)
Lung metastases		
Yes	66 (49%)	61 (47%)
No	68 (51%)	68 (53%)
Liver metastases		
Yes	70 (52%)	66 (51%)
No	64 (48%)	63 (49%)
Concurrent chemoradiotherapy history		
Yes	86 (64%)	83 (64%)
No	48 (36%)	46 (36%)
No. of metastatic organs		
1	44 (33%)	48 (37%)
2	56 (42%)	42 (33%)
≥3	34 (25%)	39 (30%)
Stage		
Primary metastases	47 (35%)	42 (33%)
Recurrence with distant metastases	87 (65%)	87 (67%)

Data are n (%) unless otherwise indicated. EBV, Epstein-Barr virus.

PFS per IRC



- **Camrelizumab plus GP improved PFS compared with placebo plus GP, with a 49% lower risk of disease progression or death.**

Data cutoff on Dec 31, 2020

Overall Survival

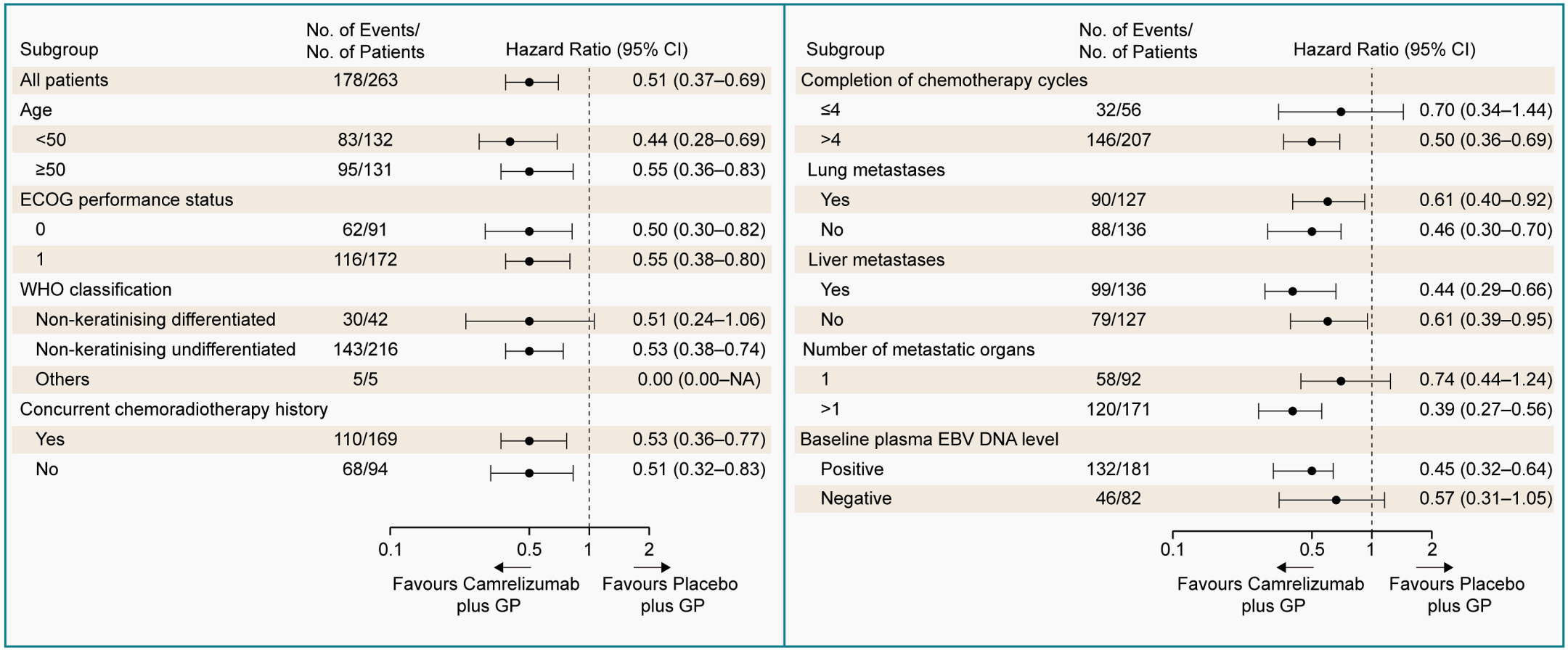
	Camrelizumab plus GP (N = 134)	Placebo plus GP (N = 129)
Events, n (%)	28 (20.9)	38 (29.5)
Median (95% CI), months	NR (NR-NR)	22.6 (19.2-NR)
Hazard ratio (95% CI)	**0.67 (0.41-1.11); *P* = 0.0576**	
12-month rate, % (95% CI)	85.0 (77.7-90.1)	83.4 (75.6-88.8)
24-month rate, % (95% CI)	70.0 (53.9-81.4)	NR (NR-NR)

- **Although the OS was immature in both groups, a trend of survival benefit was observed in the camrelizumab plus GP group.**

NR, not reached.

Data cutoff on Dec 31, 2020.

Subgroup Analyses: PFS



- **PFS benefit with the addition of camrelizumab was observed across all subgroups.**

Data cutoff on Dec 31, 2020. Assessed by IRC.

Summary of Adverse Events

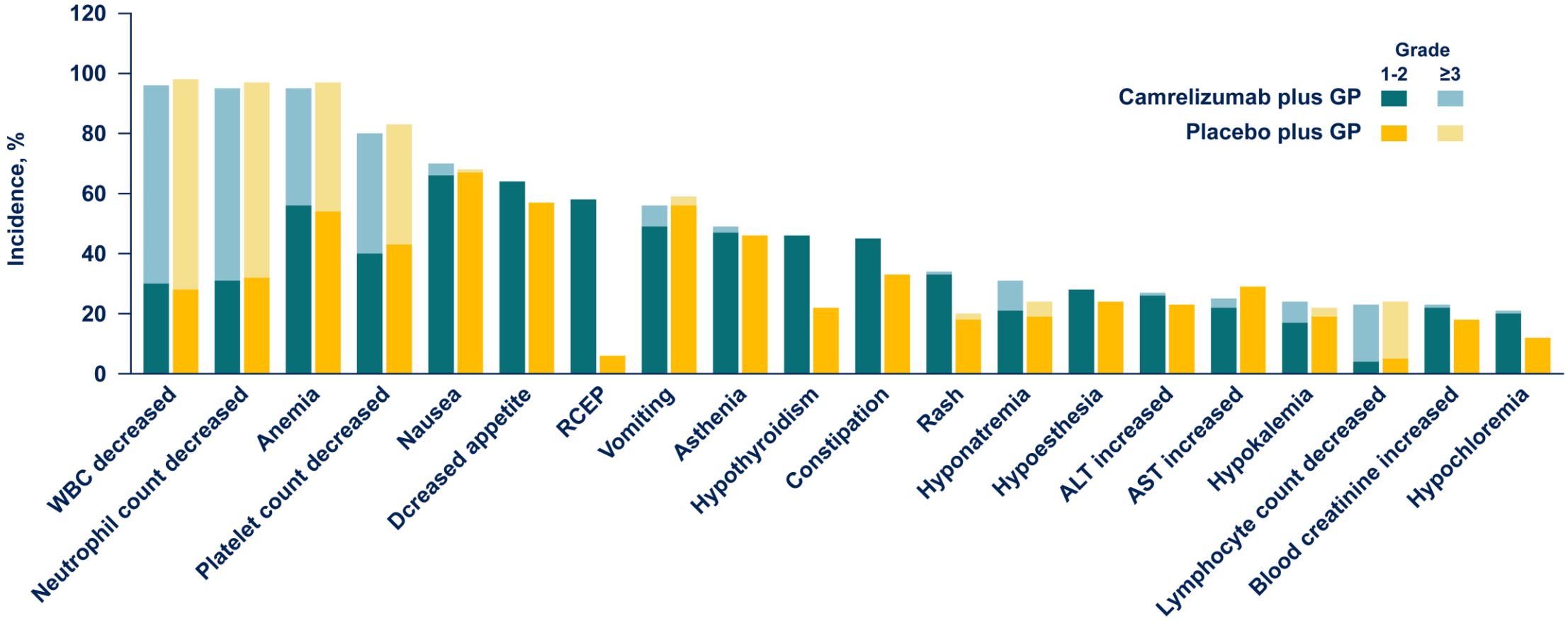
	Camrelizumab plus GP (N = 134)	Placebo plus GP (N = 129)
Any adverse event	134 (100%)	129 (100%)
Grade ≥3	126 (94%)	118 (91%)
Any treatment-related event	134 (100%)	129 (100%)
Grade ≥3	124 (93%)	116 (90%)
AEs Leading to discontinuation	13 (10%)	7 (5%)
TRAEs leading to discontinuation	12 (9%)	6 (5%)
AEs leading to death	10 (7%)	7 (5%)
TRAEs leading to death	5 (4%)	1 (<1%)

*Two patients died of unknown cause of death, one patient died of multiple organ dysfunction syndrome, one died of pharyngeal haemorrhage, and one died of arrhythmia.
#One patient died of unknown cause of death. AE, adverse event; TRAE, treatment-related adverse event

Data cutoff on Dec 31, 2020.

Treatment-related Adverse Events

Treatment-related adverse events with all grade incidence ≥20%



➢ **The frequency and grade of TRAEs were comparable between treatment groups, except for RCEP.**

WBC, white blood cell; RCEP, reactive capillary endothelial proliferation; ALT, alanine aminotransferase increased; AST, aspartate aminotransferase; TRAEs, treatment-related adverse events

Data cutoff on Dec 31, 2020.

Conclusions

- Addition of camrelizumab to gemcitabine and cisplatin significantly prolonged PFS than placebo in patients with R/M-NPC.
  - Median, **10.8** *vs* **6.9** months; HR, **0.51 (95% CI 0.37-0.69)**; one-sided *P* < 0.0001
- Median DoR was longer in the camrelizumab plus chemotherapy group than in the placebo plus chemotherapy group.
  - Median, **9.9** *vs* **5.7** months; HR, **0.48 (95% CI 0.34-0.68)**
- Although OS was immature in both groups, preliminary data revealed an improving trend of survival in patients with camrelizumab plus chemotherapy.
  - Median, not reached *vs* 22.6 months; HR, **0.67 (95% CI 0.41-1.11)**
- The safety profiles of camrelizumab plus gemcitabine and cisplatin were manageable.

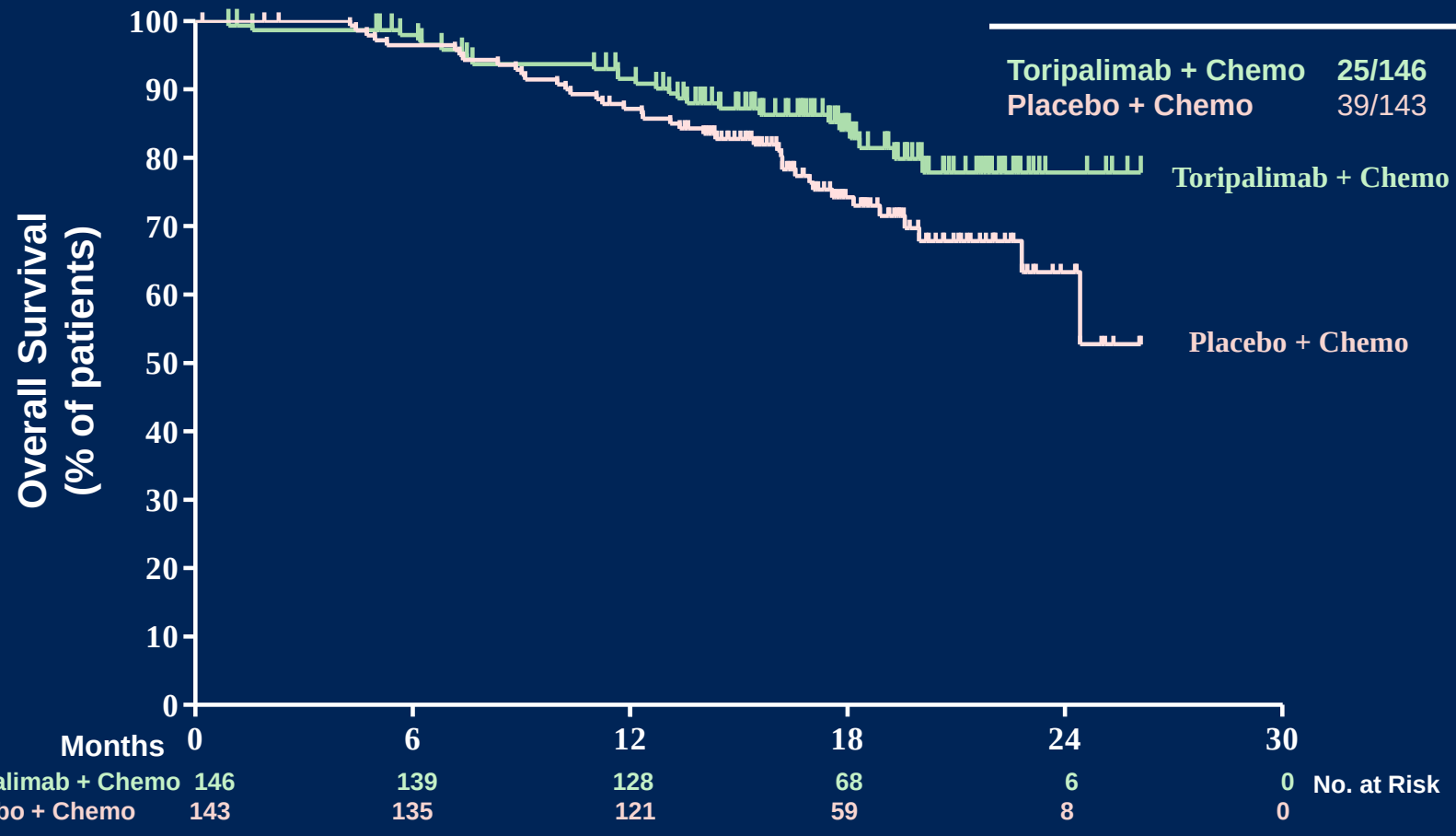
My Take

- Jupiter-2, also presented basically the same design with toripalimab
  - PFS 11.7 vs. 8.0 months
  - DOR 10 vs. 5.7 months
- NRG-HN007 utilizing nivolumab
- Chemo-immunotherapy, as it is in HNSCC, is a front-line option for NPC
  - *Backbone differs*

Overall Survival Update Jupiter-02

Nine-month OS update after PFS Interim Analysis on Feb 18, 2021

	No. of Deaths/ Total No. of Patients	Median Overall Survival (95% CI) *mo*	1-Yr Overall Survival Rate % (95% CI)	2-Yr Overall Survival Rate % (95% CI)
Toripalimab + Chemo	25/146	NE (NE, NE)	91.6 (85.6, 95.1)	77.8 (68.0, 85.0)
Placebo + Chemo	39/143	NE (22.8, NE)	87.1 (80.4, 91.7)	63.3 (49.8, 74.1)

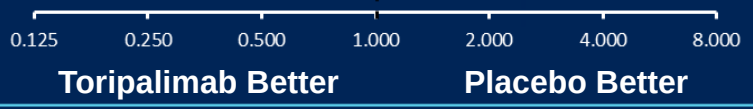


Stratified HR for death,

0.603 (95% CI 0.364-0.997); P=0.0462

Progression Free Survival by BIRC in Key Subgroups

Subgroup	No. of Patients	Unstratified Hazard Ratio (95% CI)
Overall	289	0.51 (0.356-0.728)
Age		
<=50 yr	166	0.42 (0.261-0.648)
>50 yr	123	0.65 (0.373-1.126)
Sex		
Female	49	0.41 (0.187-0.889)
Male	240	0.54 (0.360-0.806)
Baseline ECOG		
0	164	0.51 (0.317-0.811)
1	125	0.49 (0.281-0.861)
Baseline disease stage		
Recurrent	172	0.46 (0.284-0.750)
Metastatic	117	0.57 (0.333-0.981)
Baseline EBV copy number		
<2000	108	0.59 (0.313-1.114)
>=2000	181	0.46 (0.300-0.717)
Baseline PD-L1 expression level		
TC>=1% or IC>=1%	218	0.59 (0.388-0.893)
TC<1% and IC<1%	45	0.35 (0.153-0.808)



Data cut-off date: 30/May/2020

2021 ASCO ANNUAL MEETING

Cabozantinib Versus Placebo in Patients With Radioiodine-Refractory Differentiated Thyroid Cancer Who Have Progressed After Prior VEGFR-targeted Therapy: Results From the Phase 3 COSMIC-311 Trial

Marcia S. Brose,[1] Bruce Robinson,[2] Steven I. Sherman,[3] Barbara Jarzab,[4] Chia-Chi Lin,[5] Fernanda Vaisman,[6] Ana O. Hoff,[7] Erika Hitre,[8] Daniel W. Bowles,[9] Leonardo Faoro,[10] Kamalika Banerjee,[10] Jennifer W. Oliver,[10] Bhumsuk Keam,[11] Jaume Capdevila[12]

[1]Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, USA; [2]Sydney Medical School, The University of Sydney, Sydney, New South Wales, Australia; [3]Department of Endocrine Neoplasia and Hormonal Disorders, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [4]Department of Nuclear Medicine and Endocrine Oncology, Maria Sklodowska Curie National Research Institute of Oncology Gliwice Branch, Gliwice, Poland; [5]Department of Oncology, National Taiwan University Hospital, Taipei, Taiwan; [6]Instituto Nacional de Câncer, Rio de Janeiro, Brazil; [7]Department of Endocrinology, Instituto do Câncer do Estado de São Paulo, Universidade de São Paulo, São Paulo, Brazil; [8]Department of Medical Oncology and Clinical Pharmacology "B," Országos Onkológiai Intézet, Budapest, Hungary; [9]Division of Medical Oncology, Department of Medicine, University of Colorado Anschutz Medical Campus, Aurora, CO, USA ; [10]Exelixis, Inc., Alameda, CA, USA; [11]Department of Internal Medicine, Seoul National University Hospital, Seoul, Republic of Korea; [12]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Universitat Autònoma de Barcelona, Barcelona, Spain

Abstract 6001
June 7, 2021

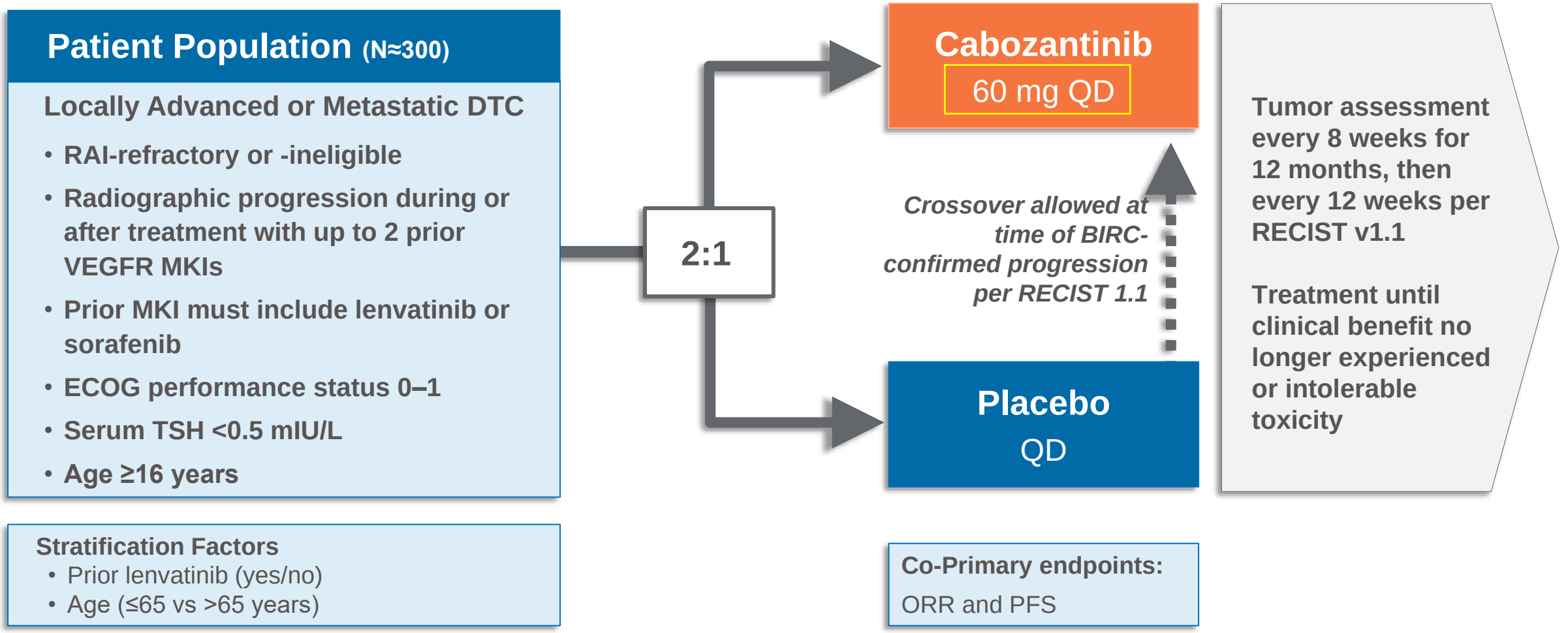
Background

- Patients with RAI-refractory DTC who progress on prior VEGFR-targeted therapies have poor prognosis and no standard of care[1,2]
- Cabozantinib is an inhibitor of VEGFR2, MET, AXL, and RET, which are implicated in the pathogenesis of DTC[3-9]
- Cabozantinib showed clinical activity in patients with RAI-refractory DTC in early-phase studies[10-12]
- COSMIC-311 is a randomized, double-blind, phase 3 study, which evaluated the efficacy and safety of cabozantinib vs placebo in patients with RAI-refractory DTC who had progressed during or after prior VEGFR-targeted therapy

COSMIC-311 is registered at ClinicalTrials.gov (NCT03690388); DTC, differentiated thyroid cancer; RAI, radioiodine; VEGFR, vascular endothelial growth factor receptor

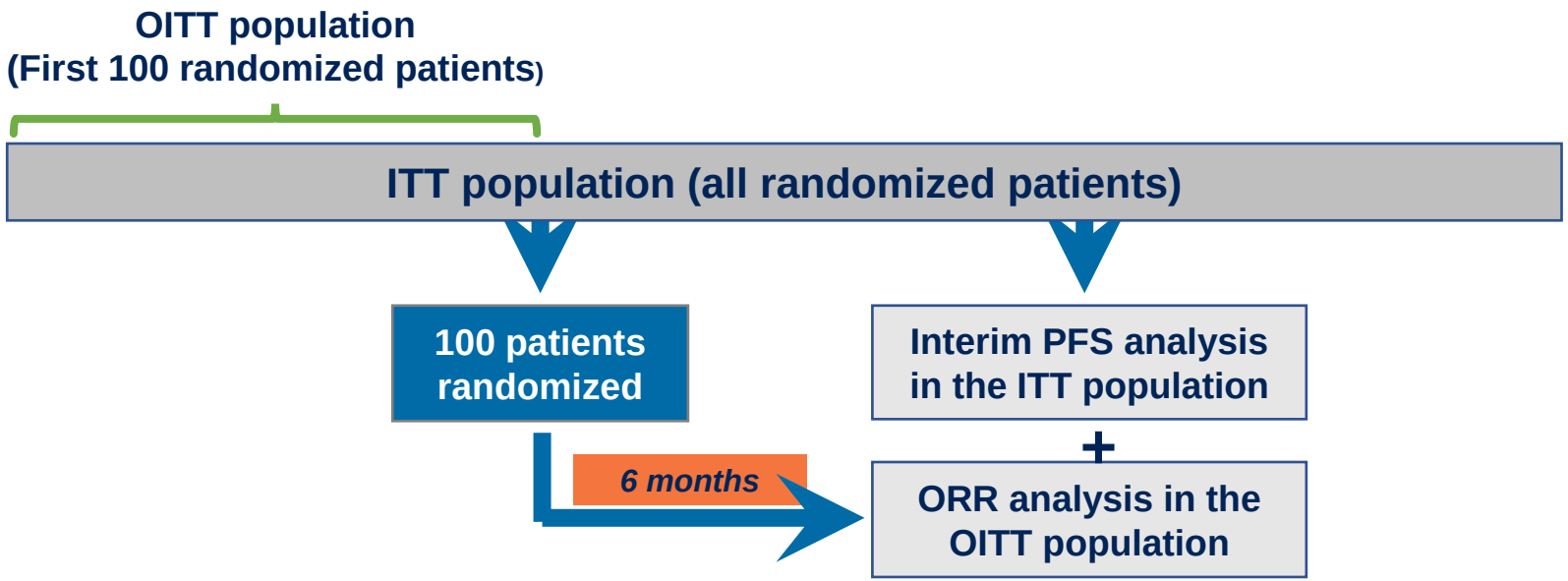
1. Lirov R, et al. *Drugs.* 2017;77:733-45. **2.** Durante C, et al. *J Clin Endocrinol Metab.* 2006;91:2892-9. **3.** Yakes FM, et al. *Mol Cancer Ther.* 2011;10:2298-308. **4.** Ferrari SM, et al. *Front Endocrinol.* 2015;6:176. **5.** Schoumacher M, et al. *Curr Oncol Rep.* 2017;19:19. **6.** Collina F, et al. *Cancers.* 2019;11:785. **7.** Shojaei F, et al. *Cancer Res.* 2010;70:10090-100. **8.** Ruco L, et al. *Biomedicines.* 2014;2:263-74. **9.** Salvatore D, et al. *Nat Rev Endocrinol.* 2021. Epub. **10.** Cabanillas ME, et al. *Thyroid.* 2014;24:1508-14. **11.** Cabanillas ME, et al. *J Clin Oncol.* 2017;35:3315-21. **12.** Brose MS, et al. *J Clin Oncol.* 2018;36(suppl 15):Abstract 6088.

COSMIC-311 Study Design



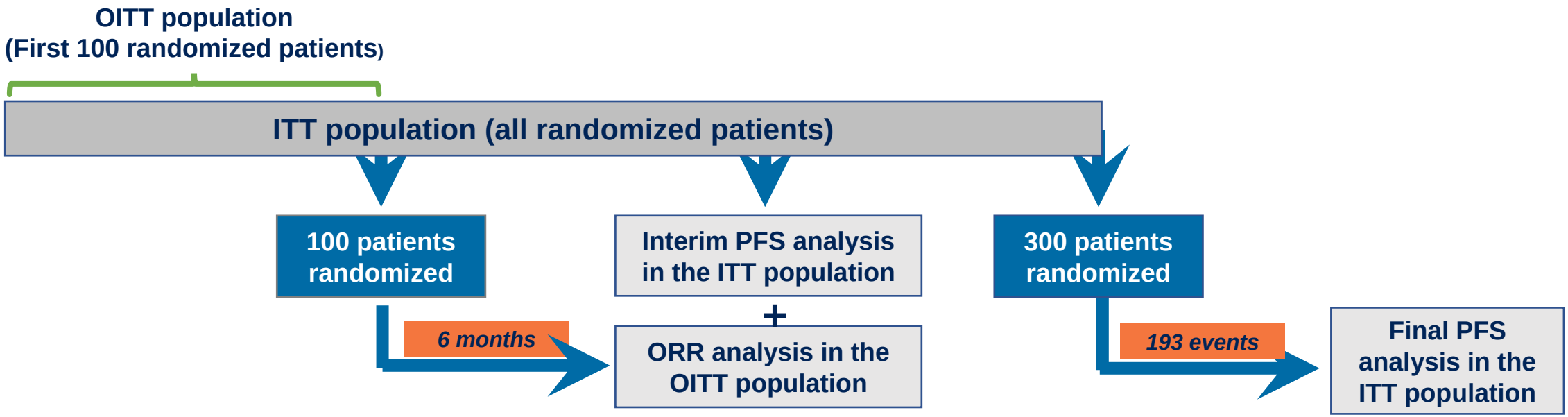
BIRC, blinded independent radiology committee; ECOG, Eastern Cooperative Oncology Group; QD, once daily; RECIST, Response Evaluation Criteria in Solid Tumors; TKI, tyrosine kinase inhibitor; TSH, thyroid-stimulating hormone

Study Endpoints and Statistical Design



ITT, intention-to-treat; OITT, objective response rate ITT; ORR, objective response rate; PFS, progression-free survival

Study Endpoints and Statistical Design



- Primary endpoints: ORR (OITT population) and PFS (ITT population) per RECIST v1.1 by BIRC
  - ORR alpha = 0.01; power of >90%
  - PFS alpha = 0.04 or 0.05 or if null hypothesis for ORR not rejected/rejected; power of 90%
- Meeting either of the primary endpoints would indicate superiority of cabozantinib over placebo
- Other endpoints: OS and safety
- **The IDMC reviewed the data from the first analysis and recommended that enrollment be stopped**

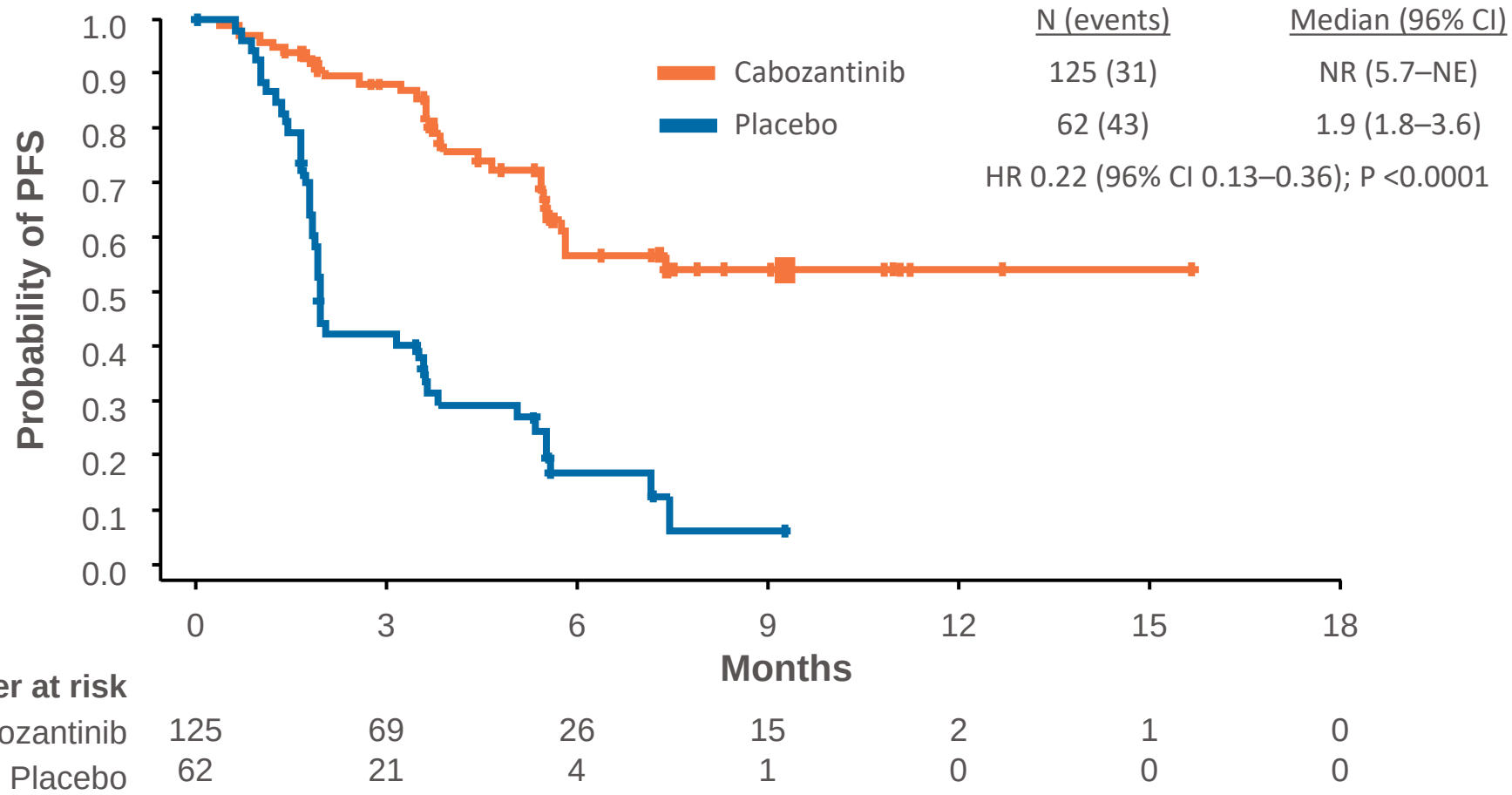
BIRC, blinded independent radiology committee; ITT, intention-to-treat; OITT, objective response rate ITT; ORR, objective response rate; OS, overall survival; PFS, progression-free survival

Baseline Demographics and Clinical Characteristics (ITT Population)

Data cutoff of August 19, 2020 – 187 patients randomized (interim PFS analysis)

		Cabozantinib (N=125)	Placebo (N=62)
Age, years	Median (range)	**65 (32–85)**	**66 (37–81)**
Sex, %	Female	**54**	**55**
Race, %	White	**72**	**66**
	Non-white	**21**	**27**
	Unknown	**7**	**6**
Geographic region, %	Europe	**52**	**52**
	Asia	**13**	**21**
	USA/Canada	**10**	**15**
	Rest of the World	**25**	**13**
ECOG performance status, %	0	**47**	**48**
	1	**53**	**52**
Histologic subtype,* %	Papillary	**54**	**56**
	Follicular	**50**	**45**
Prior lenvatinib, %		**63**	**63**
Prior sorafenib or lenvatinib, %	Sorafenib but not lenvatinib	**37**	**37**
	Lenvatinib but not sorafenib	**38**	**42**
	Lenvatinib and sorafenib	**25**	**21**
Number of prior VEGFR MKIs, %	1	**73**	**77**
	2	**27**	**23**
Metastatic lesions,† %	Bone	**50**	**39**
	Liver	**22**	**10**
	Lung	**70**	**79**
	Other	**83**	**90**

Progression-Free Survival by BIRC (ITT Population)

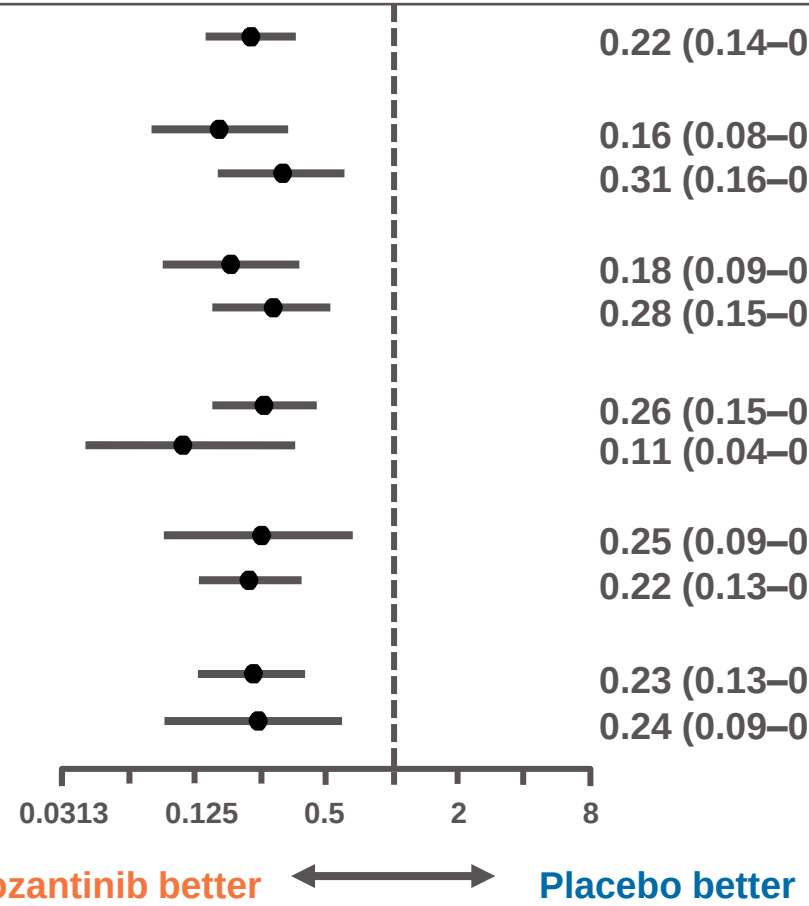


Primary endpoint of PFS was met at planned interim analysis (critical p-value of 0.00036)

Median follow-up 6.2 months; HR, hazard ratio; NE, not estimable; NR, not reached; PFS per RECIST v1.1

Progression-Free Survival in Key Subgroups by BIRC

	Cabozantinib Events / N	Placebo Events / N	HR (95% CI)
Overall (stratified)	31 / 125	43 / 62	0.22 (0.14–0.35)
Age			
≤ 65	14 / 67	24 / 30	0.16 (0.08–0.33)
> 65	17 / 62	19 / 32	0.31 (0.16–0.60)
Prior sorafenib			
Yes	13 / 48	22 / 26	0.18 (0.09–0.37)
No	18 / 79	21 / 36	0.28 (0.15–0.53)
Prior lenvatinib			
Yes	27 / 79	30 / 39	0.26 (0.15–0.44)
No	4 / 46	13 / 23	0.11 (0.04–0.35)
Prior sorafenib and lenvatinib			
Yes	9 / 31	9 / 14	0.25 (0.09–0.65)
No	22 / 94	34 / 49	0.22 (0.13–0.38)
No. of prior VEGFR TKI			
1	21 / 91	33 / 48	0.23 (0.13–0.39)
2	10 / 34	10 / 14	0.24 (0.09–0.59)



Cabozantinib was favored over placebo for all prespecified subgroups

PFS per RECIST v1.1

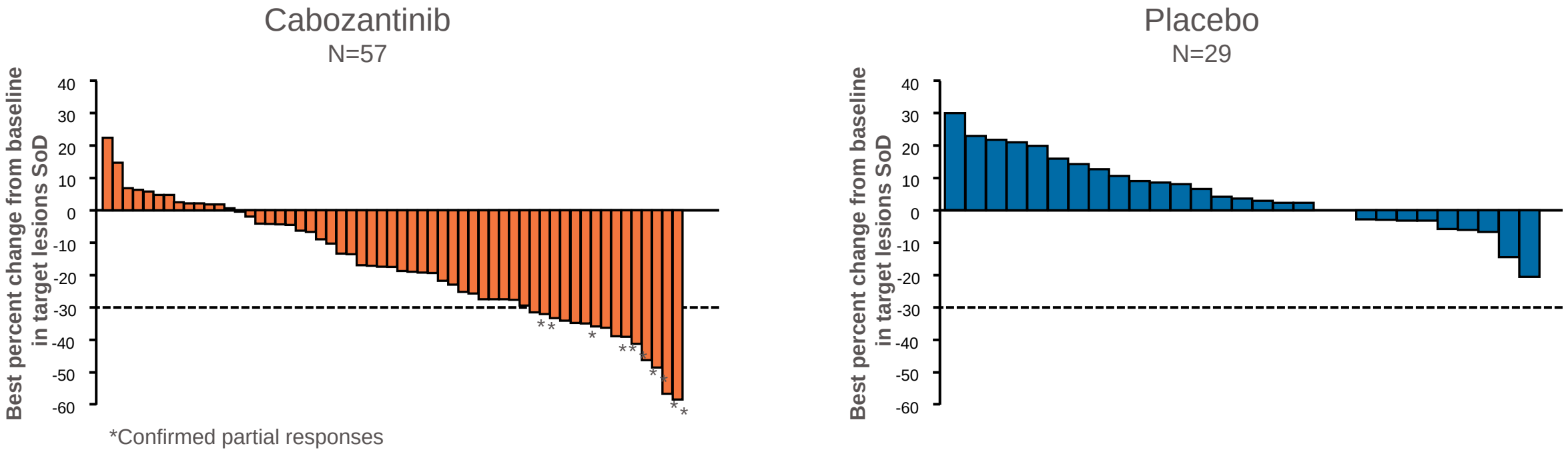
Objective Response Rate by BIRC (OITT Population)

	Cabozantinib (N=67)	Placebo (N=33)
Objective response rate, % (99% CI)	15 (5.8–29.3)	0 (0–14.8)
	P=0.028	
Best overall response, RECIST 1.1, %		
Confirmed complete response	0	0
Confirmed partial response	15	0
Stable disease	69	42
Progressive disease	6	55
Stable disease ≥16 weeks, %	45	27
Disease control rate (ORR + SD for ≥16 weeks), %	60	27
Duration of response, median (95% CI), months	NR (4.1–NE)	NA

The primary endpoint of ORR was not met (critical p-value of 0.01)

CI, confidence interval; NA, not applicable; NE, not estimable; NR, not reached; ORR per RECIST v1.1

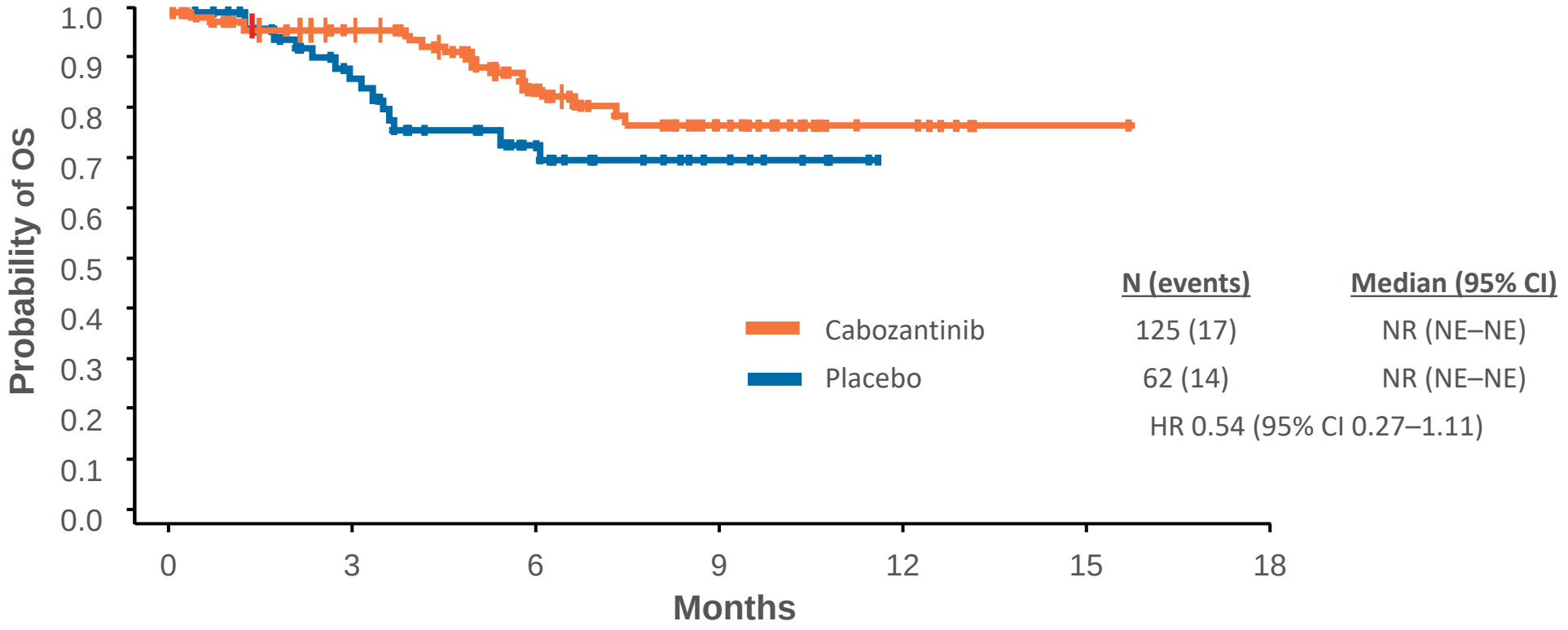
Maximum Percent Tumor Reduction from Baseline in Target Lesions for Individual Patients by BIRC (OITT Population)



At 6 months minimum follow-up, any reduction in target lesions:
76% for cabozantinib vs 29% for placebo

SoD, sum of diameters; ORR per RECIST v1.1

Overall Survival (ITT Population)



Number at risk

Cabozantinib	125	90	54	24	7	1	0
Placebo	62	42	24	9	0	0	0

Median follow-up, 6.2 months

Treatment-Emergent AEs

	Cabozantinib (N=125)			Placebo (N=62)		
	Any Grade	Grade 3	Grade 4	Any Grade	Grade 3	Grade 4
Any AE, %	94	51	6	84	23	3
Diarrhea	51	7	0	3	0	0
Hand foot skin reaction	46	10	0	0	0	0
Hypertension	28	8	1	5	3	0
Fatigue	27	8	0	8	0	0
ALT increased	24	1	0	2	0	0
Nausea	24	3	0	2	0	0
AST increased	23	0	0	2	0	0
Decreased appetite	23	3	0	16	0	0
Hypocalcemia	23	5	2	2	2	0
Weight decreased	18	1	0	5	0	0
Asthenia	15	2	0	15	0	0
Dyspnea	15	3	0	18	2	2
Proteinuria	15	1	0	3	0	0

AEs of any cause occurring in ≥15% of patients in either treatment arm

Grade 5 AEs: 9 (7%) in the cabozantinib arm, 7 (11%) in the placebo arm. None of the Grade 5 AEs were treatment-related per investigator

ALT, alanine aminotransferase; AST, aspartate aminotransferase

COSMIC-311 Conclusions

- Cabozantinib significantly improved PFS compared to placebo in previously-treated RAI-refractory DTC
- ORR favored cabozantinib over placebo (15% vs 0%), although this difference was not statistically significant
- AEs were consistent with the known safety profile of cabozantinib and were managed with supportive care, dose holds and dose modifications
- These results support cabozantinib as a potential new treatment option for previously-treated RAI-refractory DTC

My Take

- Cabozantinib appears to represent a new second line option after failure of Lenvatinib (or sorafenib)

Quick Hits: Target HPV

- Starting to see encouraging results
  - Phase II evaluation of the triple combination of PDS0101, M9241, and bintrafusp alfa in patients with HPV 16 positive malignancies

2021 ASCO ANNUAL MEETING

PHASE II EVALUATION OF THE TRIPLE COMBINATION OF PDS0101, M9241, AND BINTRAFUSP ALFA IN PATIENTS WITH HPV 16 POSITIVE MALIGNANCIES

Julius Strauss[1], Charalampos S. Floudas[2], Houssein Abdul Sater[2], Michell Manu[3], Elizabeth Lamping[2], Deneise C Francis[2], Lisa M Cordes[2], Jenn Marte[2], Renee N Donahue[1], Caroline Jochems[1], Jason Redman[2], Ravi A Madan[2], Marijo Bilusic[2], Fatima Karzai[2], Scott Norberg[2], Christian S. Hinrichs[2], Lauren V Wood[4], Frank K Bedu-Addo[4], Jeffrey Schlom[1], James L Gulley[2]

[1]Laboratory of Tumor Immunology and Biology, NCI; [2]Genitourinary Malignancies Branch, NCI; [3]Leidos Biomedical Research, Inc.; [4]PDS Biotechnology, Princeton, NJ

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Results

	All patients N=25
Age, median (range), years	50 (37-80)
Female, n (%)	17 (68)
Tumor type, n (%)	
Cervical	10 (40)
Anal	6 (24)
Head & Neck SCC	6 (24)
Vulvar/ Vaginal	3 (12)
Number of prior anticancer therapies, n (%)	
1	5 (20)
2	11 (44)
≥3	9 (36)
Prior chemotherapy, n (%)	25 (100)
Prior radiotherapy, n (%)	24 (96)
Prior PD-(L)1 inhibitor therapy, n (%)	14 (56)
HPV status, n (%)	
HPV 16	18 (72)
HPV type other than 16	6 (24)
Negative	1 (4)

- Key baseline patient and disease characteristics
- As of 01 MAR 2021, 25 patients had received the triple combination of PDS0101, M9241 & bintrafusp alfa
  - The median follow-up is 8 months

Results

	All patients N=25	HPV 16+ N=18	HPV 16+ CPI Naïve N=6	HPV 16+ CPI Refractory N=12
BOR, n (%) Complete response (CR) Partial response (PR)	 2 (8) 8 (32)	 2 (11.1) 8 (44.4)	 1 (16.7) 4 (66.7)	 1 (8.3) 4 (33.3)
ORR (CR+PR), n (%)	10 (40)	10 (55.6)	5 (83.3)	5 (41.7)
Disease Reduction, n (%)	13 (52)	12 (66.7)	5 (83.3)	7 (58.3)
Ongoing response, n/n (%)	8/10 (80)	8/10 (80%)	4/5 (80%)	4/5 (80%)
Overall Survival, n/n (%)*	20/25 (80)	16/18 (88.9)	6/6 (100)	10/12 (83.3)

* Median 8 months of follow up

Patient Outcomes

- ORR 55.6% (tumor reduction 66.7%) in HPV 16+ disease
- ORR 83.3% in CPI *naïve* HPV 16+ disease
- ORR 41.7% (tumor reduction 58.3%) in CPI *refractory* HPV 16+ disease
- After a median 8 months of follow up:
  - 80% of responses are ongoing
  - 6/6 (100%) pts with HPV 16+ CPI naïve disease remain alive (historical median OS is 7-11 mo)[1-6]
  - 10/12 (83.3%) pts with HPV 16+ CPI refractory disease remain alive (historical median OS is 3-4 mo)[7]

1. Bauml J, et al. *J Clin Oncol* 2017;35:1542–49; 2. Ott PA, et al. *Ann Oncol.* 2017;28:1036–41; 3. Mehra R, et al. *Br J Cancer.* 2018;119:153–59; 4. Ferris RL, et al. *N Engl J Med*. 2016;375:1856–67; 5. Morris VK, et al. *Lancet Oncol*. 2017;18:446–53; 6. Chung HC, et al. *J Clin Oncol* 2019;37: 1470-8; 7. Strauss J, et al. J Immunother Cancer. 2020 Dec;8(2):e001395

Quick Hits: HPV detection

- HPV related OPSCC can be detected and monitored in plasma and saliva

2021 ASCO ANNUAL MEETING

Ultra-sensitive detection and quantification of HPV DNA in the plasma of patients with oropharyngeal squamous cell carcinoma (OPSCC) enrolled in the OPTIMA 2 treatment de-escalation trial

Hillary Sloane[1*], Evgeny Izumchenko[2], Austin Mattox[3], Rifat Hasina[2], Aashay Patel[4], Frederick S. Jones[1], Hannah Quinn[1], Kimberly Schmitt[1], Jennifer Preston[1], Kirsten Keyser[5], Johannes Fredebohm[5], Frank Holtrup[5], Alexander T. Pearson[2], Everett E. Vokes[2], Tanguy Y. Seiwert[3], Daniel L. Edelstein[1], Ari Rosenberg[2], Nishant Agrawal[2]

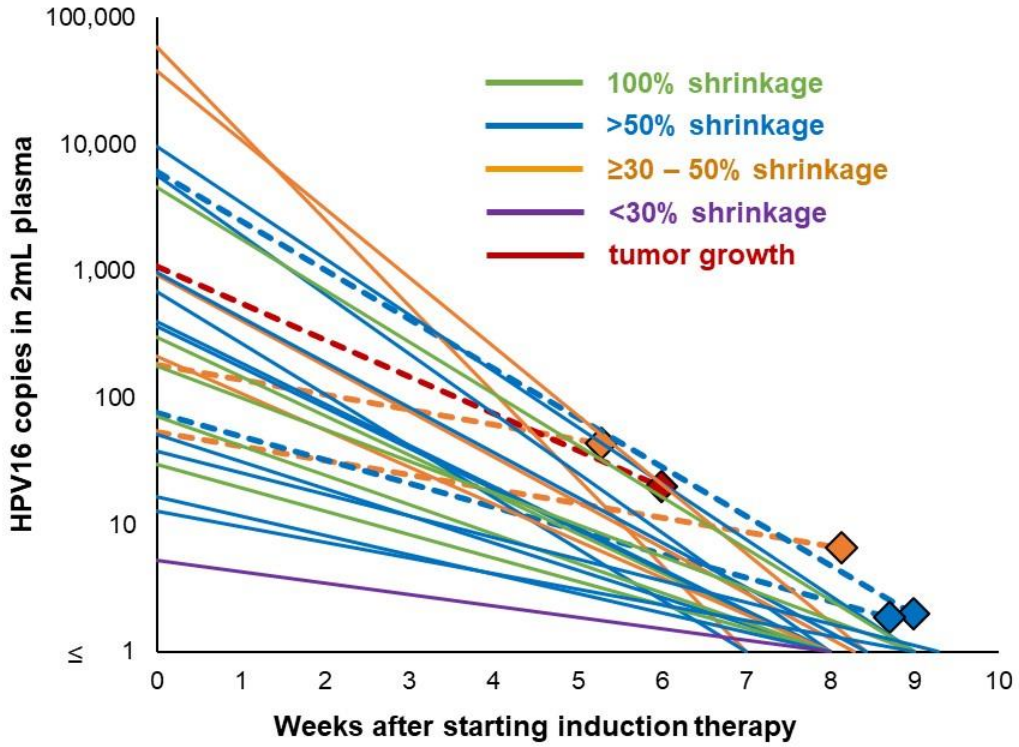
[1]Sysmex Inostics, Inc., Baltimore, MD, USA; [2]University of Chicago, Chicago, IL, USA; [3]Johns Hopkins University, Baltimore, MD USA; [4]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [5]Sysmex Inostics GmbH, Hamburg, Germany

*sloane.hillary@sysmex-inostics.com

Longitudinal cfHPV-DNA analysis

- Plasma samples collected at 2 serial time-points (baseline and 6-9 weeks after beginning induction therapy) were available for analysis in 31 patients.
  - cfHPV-DNA was detected at baseline in 25 patients.

- All 25 patients with baseline cfHPV-DNA showed a decrease in cfHPV-DNA level at follow-up, with complete clearance observed in 20/25 (80%) of patients
  - This is consistent with tumor response (shrinkage) to induction therapy observed in 24/25 (96%) patients.



Trend lines are colored according to radiographic response to induction therapy. Dashed lines indicate patients with persistent cfHPV-DNA at follow-up; residual cfHPV-DNA data points are indicated with a ♦

Longitudinal cfHPV-DNA analysis

- Of 5 patients with persistent cfHPV-DNA detected post-induction therapy (*yellow highlighted rows*): 1 patient progressed on induction therapy, 1 patient demonstrated subsequent recurrence and death, and 1 patient demonstrated concern for distant metastasis followed by death.

Patient ID	Clinical stage	Clinical risk	Baseline cfHPV16	Follow-up sample		Post-induction response (% shrinkage)	Clinical follow-up / outcome
				cfHPV16	Weeks from baseline		
UC005	T3N0	LR	**4,622.75**	*0.00*	9	100	NER
UC017	T2N2b	LR	**302.63**	*0.42*	8	100	NER
UC023	T4N2c	HR	**180.45**	*0.00*	9	100	NER
UC064	T2N2b	HR	**71.73**	*0.00*	8	100	NER
UC030	T2N2b	LR	**30.09**	*0.00*	8	100	NER
UC019	T3-4N2b	HR	*0.05*	*0.00*	8	100	NER
UC011	T3N1	HR	**76.57**	**1.83**	9	87.7	NER
UC014	T4N2c	HR	**6,173.74**	**1.97**	9	81.6	Concern for lung met (deceased)
UC016	T4N3	HR	**9,740.48**	*0.00*	9	74.6	NER
UC027	T2N2c	HR	**401.31**	*0.68*	8	73.3	NER
UC008	T1N2	HR	**694.18**	*0.00*	7	68.8	NER
UC024	T1N2a	LR	**51.71**	*0.33*	8	65.7	NER
UC013	T2N2b	LR	**5,705.97**	*0.00*	8	64.5	NER
UC067	T1N2b	LR	**365.26**	*0.00*	8	63.9	NER
UC068	T2N1	HR	*0.32*	*0.00*	9	63.0	NER
UC028	T1N2b	HR	**12.86**	*0.00*	9	60.7	NER
UC062	T2N2b	LR	**16.72**	*0.00*	8	55.3	NER
UC018	T2N1	LR	**38.44**	*0.00*	9	55.1	NER
UC066	T1N2b	LR	*0.38*	*0.00*	8	54.6	NER
UC015	T2N2b	LR	*1.09*	*0.00*	8	53.3	NER
UC009	T1N2a	LR	**985.17**	*0.00*	8	51.9	NER
UC022	T2N2b	HR	*0.10*	*0.00*	8	50.7	NER
UC070	T1N2b	HR	**946.06**	*0.00*	8	48.0	NER
UC020	T2N2b	LR	**54.77**	**6.50**	8	46.9	RECURRENCE (deceased)
UC003	T1N2	LR	**37,855.87**	*0.00*	8	45.5	NER
UC063	T1N2b	LR	**215.82**	*0.00*	8	45.5	NER
UC001	T2N2a	LR	*0.16*	*0.00*	8	38.5	NER (deceased)
UC039	T2N2b	HR	**59,050.56**	*0.75*	7	37.5	NER
UC040	T2N2	LR	**184.92**	**44.03**	5	30.0	NER
UC007	T2N2b	HR	**5.32**	*0.00*	8	28.6	NER
UC073	T4N2b	HR	**1,084.91**	**19.94**	6	**2% GROWTH**	NER

Summary of patients included in longitudinal cfHPV-DNA analysis. *HPV values in grey italics are below assay cut-off; LR: Low risk; HR: High risk; NER: No evidence of recurrence.*

Conclusions

- The SafeSEQ cfHPV-DNA Test exhibits robust quantitative detection of HPV across a broad range, enabling high-resolution molecular monitoring for HPV+ OPSCC patients.
- Prospective studies are underway to further evaluate the kinetics of cfHPV-DNA as a predictor of response to therapy in order to more precisely guide the management of patients with HPV+ OPSCC.

Washington University in St. Louis

Evaluating a clinically validated circulating tumor HPV DNA assay in saliva as a proximal biomarker in HPV+ oropharyngeal squamous cell carcinoma

Abstract #6063

Sophie P. Gerndt[1], Ricardo J. Ramirez[1], Benjamin M. Wahle[1], Charlotte Kuperwasser[2], Alicia Gunning[2], Aadel A Chaudhuri[3], Jose P. Zevallos[1]

[1]Department of Otolaryngology – Head and Neck Surgery, Washington University School of Medicine, St. Louis, MO; [2]Naveris Inc., Natick, MA;
[3]Department of Radiation Oncology, Washington University School of Medicine, St. Louis, MO

SITEMAN CANCER CENTER
WASHINGTON UNIVERSITY SCHOOL OF MEDICINE
BARNES-JEWISH HOSPITAL

- 46 patients with HPV+ OPSCC had paired pre-treatment plasma and saliva samples
  - 44 saliva evaluable, 43 plasma

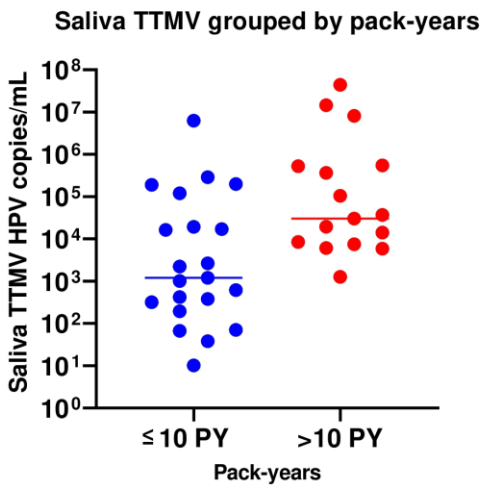
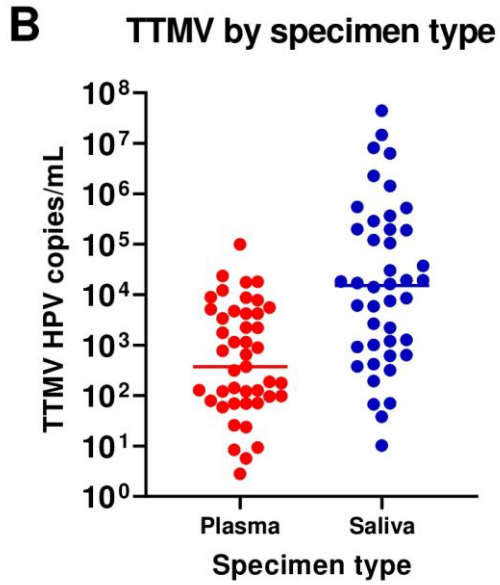


Figure 2. TTMV in saliva was significantly increased in >10 pack-years smokers (p=0.0124, Mann-Whitney U test), whereas this difference was not observed in plasma samples.



Quick Hits: Tipifarnib

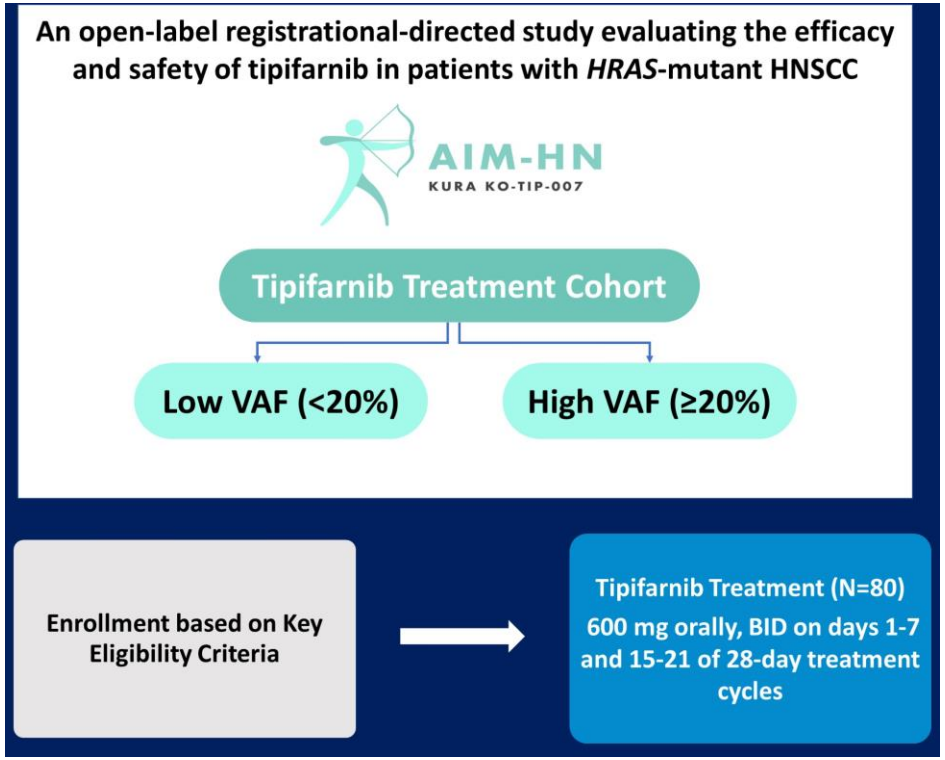
- HRAS mutations present in ~5% of HNSCC
- Inhibits farnesyltransferase required for HRAS activity

TPS6087

The AIM-HN Study: A registrational-directed study evaluating the efficacy of tipifarnib in patients with recurrent or metastatic head and neck squamous cell carcinoma with *HRAS* mutations

Robert Haddad[1], Douglas Adkins[2], Lisa Licitra[3], Justine Yang Bruce[4], Maura Gillison[5], Myung-Ju Ahn[6], Ching-Yun Hsieh[7], Hung-Ming Wang[8], Amanda Psyrri[9], Jean-Pascal Machiels[10], Binaifer Balsara[11], Mollie Leoni[11], Kevin Harrington[12], Nabil F. Saba[13], Alan Ho[14]

- Previous Phase 2 data from ASCO 2020
  - PFS 5.6 months
  - OS 15.4 months
  - Median 2 prior lines
- Current study ongoing
  - NCT03719690
  - Inclusion
    - HRAS missense mutation known
    - Failure of most recent therapy and previous platinum exposure



Conclusion

- Chemo-immunotherapy for NPC should be first line therapy for R/M disease
- Cabozantinib is a second line option for DTC
- More targeted therapies and tailored surveillance are emerging for HPV+ OPSCC
- We may soon have a truly targeted therapy for a subset of HNSCC patients