



Viracta Therapeutics, Inc.

**Key Opinion Leader Webinar on Nana-val for the
Treatment of Advanced EBV+ Solid Tumors**

April 27, 2022

**Precision
Oncology for
Virus-Associated
Cancers**



Introduction:
Dr. Ivor Royston
President and Chief Executive Officer



Forward Looking Statements

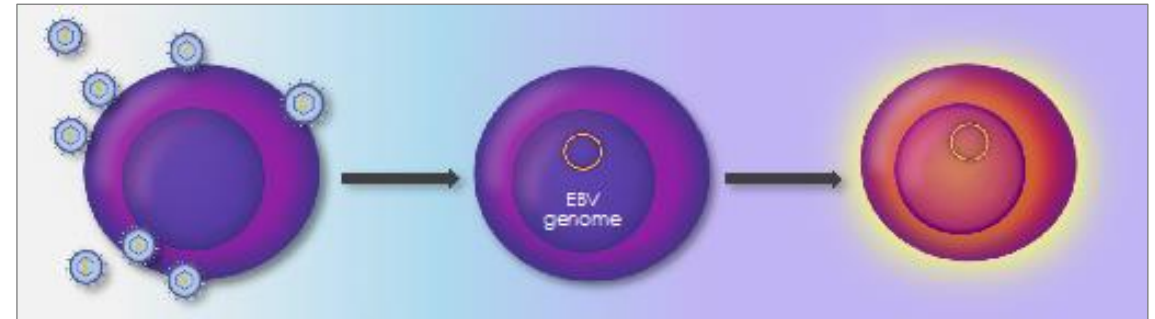
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These risks and uncertainties may be amplified by the COVID-19 pandemic, which has caused significant economic uncertainty. If any of these risks materialize or underlying assumptions prove incorrect, actual results could differ materially from the results implied by these forward-looking statements. Additional risks and uncertainties that could cause actual outcomes and results to differ materially from those contemplated by the forward-looking statements are included under the caption "Risk Factors" and elsewhere in Viracta's most recent filings with the SEC and any subsequent reports on Form 10-K, Form 10-Q or Form 8-K filed with the SEC from time to time and available at www.sec.gov. The forward-looking statements included in this communication are made only as of the date hereof. Viracta assumes no obligation and does not intend to update these forward-looking statements, except as required by law or applicable regulation.

Epstein-Barr Virus (EBV): A High Global Cancer Priority

EBV+ malignancies account for ~2% of all new cancers globally, currently no approved therapies

- ~ 90% of the adult population is infected w/ EBV
- Persists as a life-long latent infection, remaining dormant within cell nuclei
- Latency confers resistance to anti-viral therapies and facilitates evasion of immune detection
- Linked to a variety of cancers
 - ~310,000 new cases/year of lymphoma, NPC and GC
- Poor prognosis, no approved therapies
- Responsible for ~180,000 cancer deaths/year*



EBV infects cells

Latent infection established in subset of cells

Latently infected cells can continue to proliferate, evade immune detection, and become malignant

Today's Topics and Speakers

Introduction

Ivor Royston, MD
President and Chief Executive
Officer, Viracta



Nasopharyngeal Carcinoma Treatment Landscape

Ezra Cohen, MD, FRCPSC, FASCO
Chief of Hematology/Oncology and
Co-director of the Gleiberman Head
and Neck Cancer Center, UCSD



Nana-val MOA and its Potential in Advanced EBV+ Solid Tumors

Ayman Elguindy, PhD
Chief Scientific Officer, Viracta



Nana-val Phase 1b/2 Trial in Advanced EBV+ Solid Tumors

Lisa Rojkjaer, MD
Chief Medical Officer, Viracta



A Question and Answer Session with all Speakers will Follow the Formal Presentations

UC San Diego

NPC Treatment Landscape:

Dr. Ezra Cohen

Chief of Hematology/Oncology

Co-director of the Gleiberman Head and Neck Cancer Center





Nasopharyngeal Carcinoma: Current State and Medical Needs



A Comprehensive Cancer
Center Designated by the
National Cancer Institute

Ezra E.W. Cohen, MD

UC San Diego
MOORES CANCER CENTER

NPC EPIDEMIOLOGY

- Relatively rare in non southern Chinese populations: overall worldwide incidence rate is < 1 case per 100,000 person years
- Highest rates are in Hong Kong and among central region of Guangdong province in Southern China: incidence rate 20 – 50 per 100,000 person years

Fig. 1 Age-specific rates of NPC for combined periods among three different Chinese populations, (a) Males; (b) Females

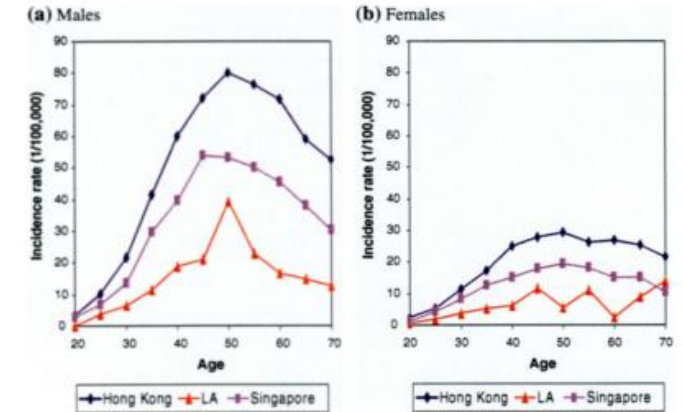
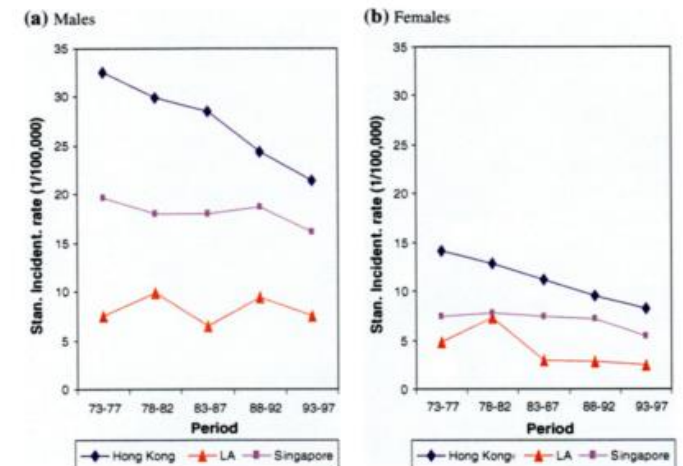


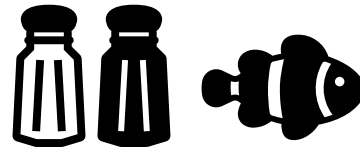
Fig. 2 Age-adjusted incidence rates of NPC in different Chinese populations, (a) Males; (b) Females



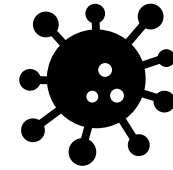
NPC ETIOLOGY



- Risk of NPC in a first-degree family member is as high as 8 times that of the general population
- The majority of first-degree relatives affected are siblings rather than parents and children
- *HLA-A0207 haplotype?*
- *P16 inactivation?*



- Salted fish, eggs, and vegetables
- Nitrosamines
- Wood dust

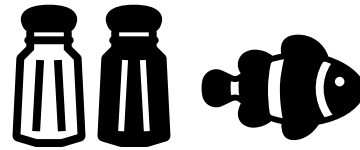


- Epstein-barr virus
- Herpesvirus- DNA virus with a capsid
- Non-NPC pts: **IgG** VCA and EA are raised
- NPC pts: **IgA** VCA and EA are raised
- NPC cells express latent EBV proteins: **EBNA-I** and **LMP-I** and normal NP cells do not

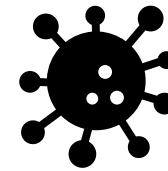
NPC ETIOLOGY



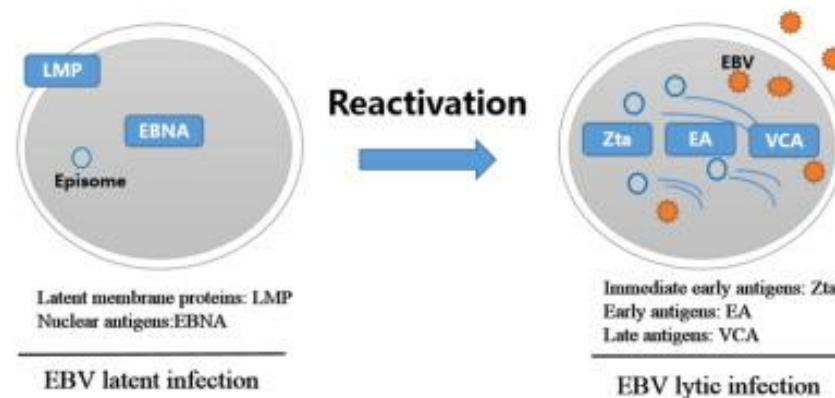
- Risk of NPC in a first-degree family member is as high as 8 times that of the general population
- The majority of first-degree relatives affected are siblings rather than parents and children
- *HLA-A0207 haplotype?*
- *PI6 inactivation?*



- Salted fish, eggs, and vegetables
- Nitrosamines
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- Epstein-barr virus
- Herpesvirus- DNA virus with a capsid
- Non-NPC pts: **IgG** VCA and EA are raised
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- NPC cells express latent EBV proteins: **EBNA-I** and **LMP-I** and normal NP cells do not

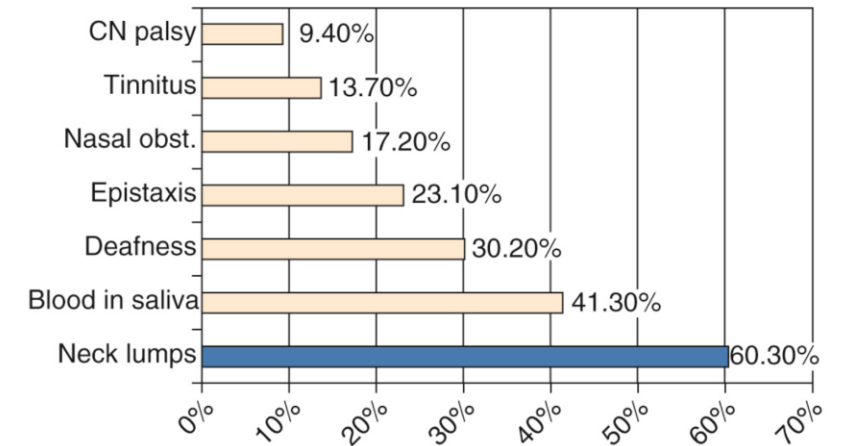


CLINICAL PRESENTATION

Table 1. Presenting symptoms and their frequencies (n=4768)

Symptom	Number of patients		
	Only symptom	First symptom *	Total No. presenting with symptom
	No. (%)	No. (%)	No. (%)
Neck mass	37 (0.8)	1777 (37.3)	3612 (75.8)
Nasal (discharge, bleeding, obstruction)	65 (1.4)	1687 (35.4)	3501 (73.4)
Aural (tinnitus, impairment of hearing)	54 (1.1)	912 (19.1)	2975 (62.4)
Headache	13 (0.3)	175 (3.7)	1657 (34.8)
Ophthalmic (diplopia, squint)	4 (0.1)	48 (1.0)	512 (10.7)
Facial numbness	3 (0.1)	22 (0.5)	361 (7.6)
Weight loss	0	1	329 (6.9)
Trismus	2	2	141 (3.0)
Slurring of speech	0	3 (0.1)	114 (2.4)
Others due to metastatic deposits	0	12 (0.3)	57 (1.2)
Skin lesions due to dermatomyositis	4 (0.1)	6 (0.1)	42 (0.9)

* In patients presenting with multiple symptoms



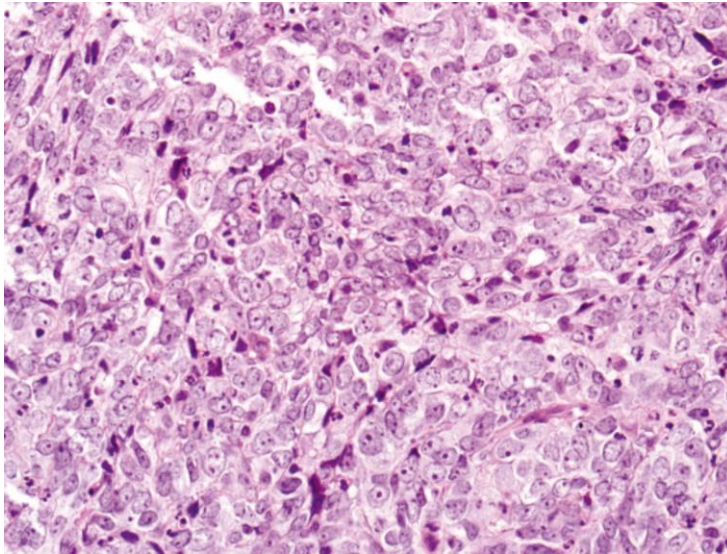
Nasopharyngeal carcinoma: presenting symptoms and duration before diagnosis.

Lee AW, Foo W, Law SC, Poon YF, Sze WM, O SK, Tung SY, Lau WH.

Hong Kong Med J. 1997 Dec;3(4):355-361.

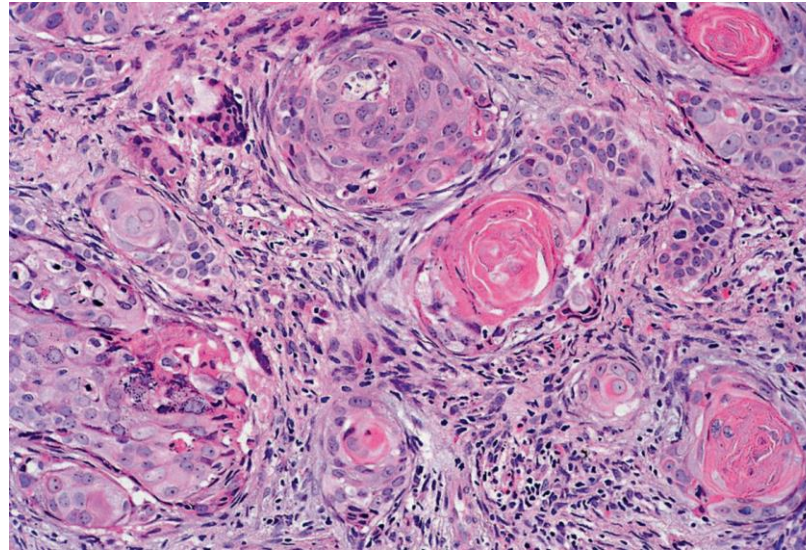
NPC HISTOPATHOLOGY

Nonkeratinizing



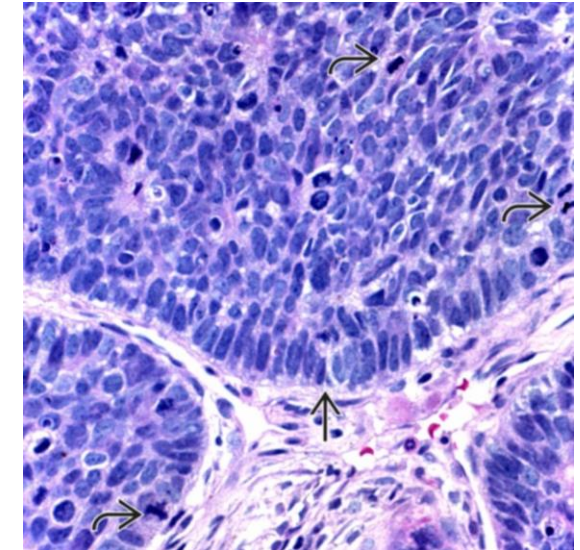
- >95% of cases in endemic areas
- Loosely cohesive tumor cells
- Ill-defined cell borders
- Large nuclei
- Lymphocytes

Keratinizing



- <20% of cases worldwide
- Cells grow in nests
- Well-defined cell borders
- Intercellular bridges
- Keratin pearls

Basaloid



- Extremely rare
- Palisaded basaloid cells

Chemotherapy in Combination With Radiotherapy for Definitive-Intent Treatment of Stage II-IVA Nasopharyngeal Carcinoma: CSCO and ASCO Guideline

**Yu-Pei Chen, MD¹; Nofisat Ismaila, MD²; Melvin L. K. Chua, MD PhD³; A. Dimitrios Colevas, MD⁴; Robert Haddad, MD⁵;
Shao Hui Huang, MD, MRT(T)⁶; Joseph T. S. Wee, MD³; Alexander C. Whitley, MD⁷; Jun-Lin Yi, MD⁸; Sue S. Yom, MD⁹;
Anthony T. C. Chan, MD¹⁰; Chao-Su Hu, MD¹¹; Jin-Yi Lang, MD¹²; Quynh-Thu Le, MD⁴; Anne W. M. Lee, MD¹³; Nancy Lee, MD¹⁴;
Jin-Ching Lin, MD¹⁵; Brigitte Ma, MD¹⁰; Thomas J. Morgan, MR¹⁶; Jatin Shah, MD¹⁴; Ying Sun, MD¹; and Jun Ma, MD¹**

PRIMARY SITE

Recommendation 1.1. For all patients with NPC, intensity-modulated radiotherapy (IMRT) with daily image guidance should be offered. If IMRT is unavailable, patients should be transferred to institutions that could implement IMRT whenever possible (Type: evidence based; benefits outweigh harms; Evidence quality: high; Strength of recommendation: strong).

Recommendation 1.3. For all patients with NPC, a prescribed dose of 70 Gy in 33-35 fractions (2.0-2.12 Gy per fraction) delivered over 7 weeks (once daily, 5 fractions per week) should be offered. Radiation dose may be adjusted according to tumor volume and its response to (chemo-)radiotherapy (Type: evidence based; benefits outweigh harms; Evidence quality: high; Strength of recommendation: strong).

Intensity-modulated RT (IMRT) enables delivery of tumoricidal doses of RT to irregular shapes

CHEMOTHERAPY

Chemotherapy Sequence

Recommendation 2.1. For patients with T2N0 (AJCC 8th) NPC, chemotherapy is not routinely recommended, but may be offered if there are adverse features, such as bulky tumor volumes or high EBV DNA copy number (Type: evidence based; harms outweigh benefits; Evidence quality: intermediate; Strength of recommendation: moderate).

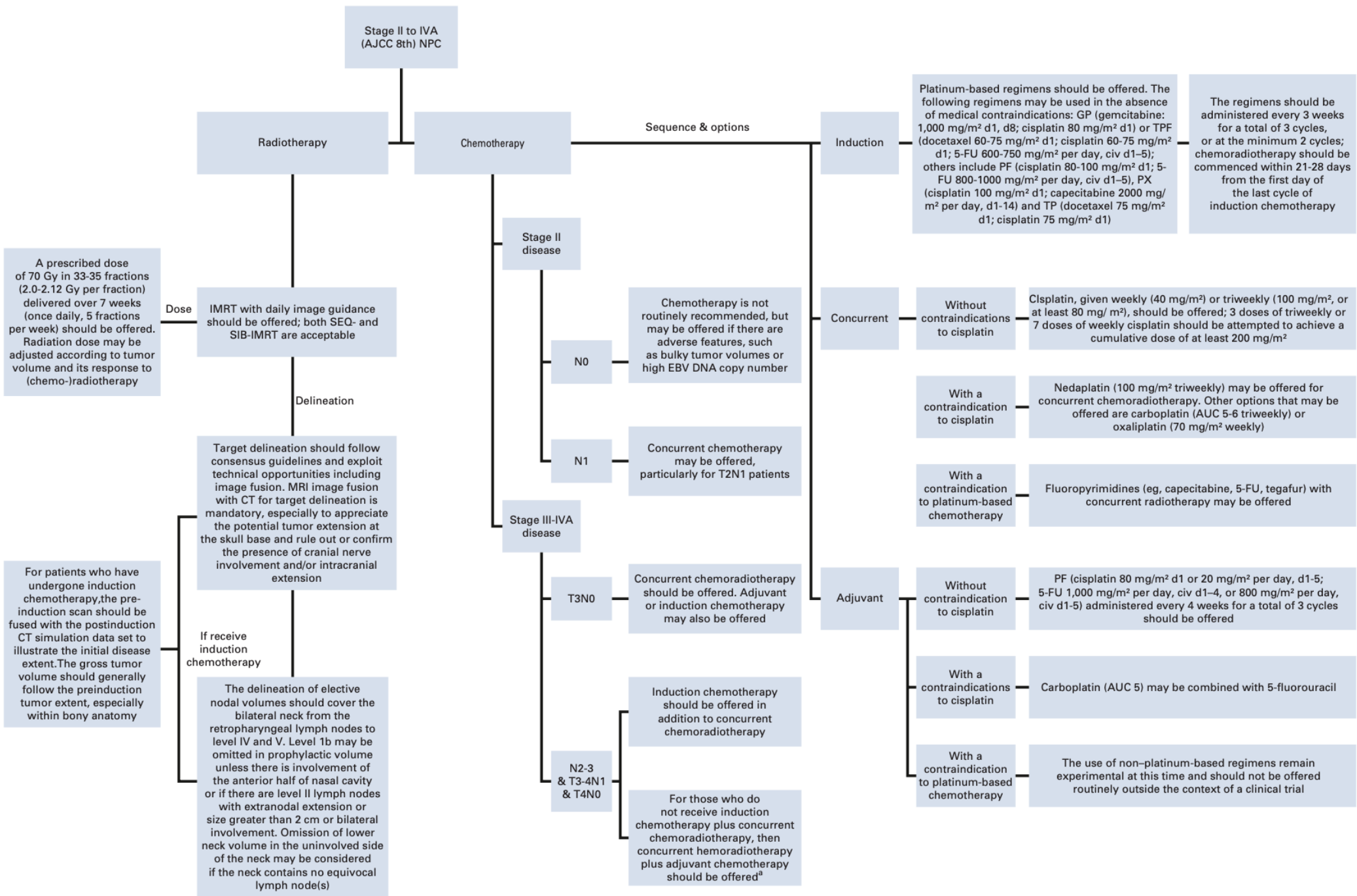
Recommendation 2.2. For patients with T1-2N1 (AJCC 8th) NPC, concurrent chemotherapy may be offered, particularly for T2 N1 patients (Type: evidence based; benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: moderate).

Recommendation 2.3. For patients with Stage III-IVA (except T3N0) (AJCC 8th) NPC, induction chemotherapy should be offered in addition to concurrent chemoradiotherapy (Type: evidence based; benefits outweigh harms; Evidence quality: high; Strength of recommendation: strong).

Recommendation 2.4. For patients with Stage III-IVA (except T3N0) (AJCC 8th) NPC who do not receive induction chemotherapy plus concurrent chemoradiotherapy, then concurrent chemoradiotherapy plus adjuvant chemotherapy should be offered (Type: evidence based; benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: moderate).

NOTE. There is a lack of head-to-head trials comparing induction chemotherapy plus concurrent chemoradiotherapy versus concurrent chemoradiotherapy plus adjuvant chemotherapy, thus which sequence performs better in the contemporary era remains uncertain.

Recommendation 2.5. For patients with T3N0 (AJCC 8th) NPC, concurrent chemoradiotherapy should be offered. Adjuvant or induction chemotherapy may also be offered (Type: evidence based; benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: moderate).



Recurrent/Metastatic Disease



Gemcitabine plus cisplatin versus fluorouracil plus cisplatin in recurrent or metastatic nasopharyngeal carcinoma: a multicentre, randomised, open-label, phase 3 trial

Prof Li Zhang, MD, Yan Huang, MD, Shaodong Hong, MD, Yunpeng Yang, MD, Gengsheng Yu, MD, Jun Jia, MD, Peijian Peng, MD, Xuan Wu, MD, Prof Qing Lin, MD, Prof Xuping Xi, MD, Jiewen Peng, MD, Mingjun Xu, MD, Prof Dongping Chen, MD, Xiaojun Lu, MD, Rensheng Wang, MD, Xiaolong Cao, MD, Xiaozhong Chen, MD, Prof Zhixiong Lin, MD, Jianping Xiong, MD, Qin Lin, MD, Conghua Xie, MD, Zhihua Li, MD, Prof Jianji Pan, MD, Jingao Li, MD, Prof Shixiu Wu, MD, Yingni Lian, MD, Quanlie Yang, MD, Prof Chong Zhao, MD

The Lancet

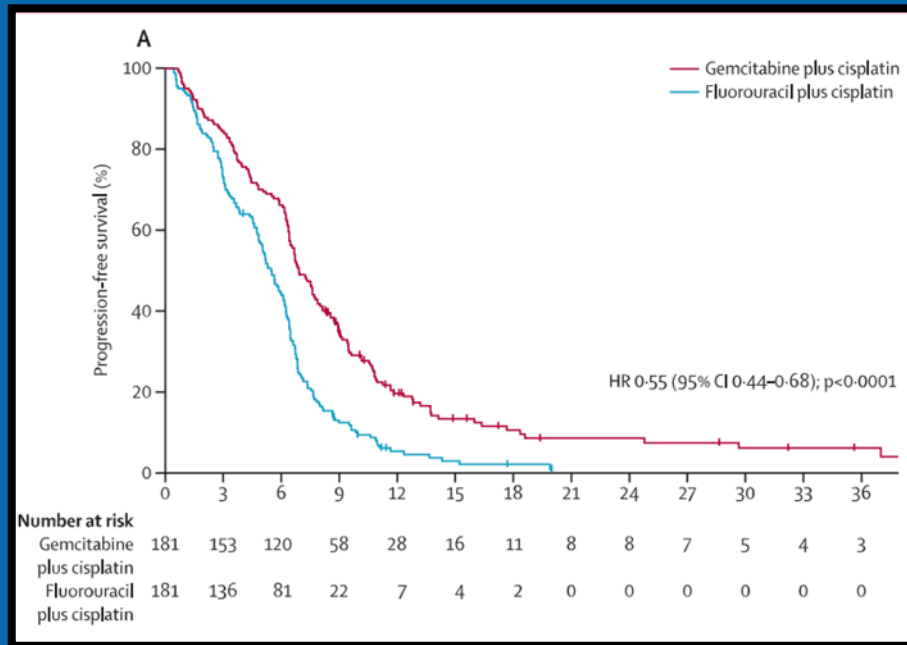
Volume 388 Issue 10054 Pages 1883-1892 (October 2016)

DOI: 10.1016/S0140-6736(16)31388-5

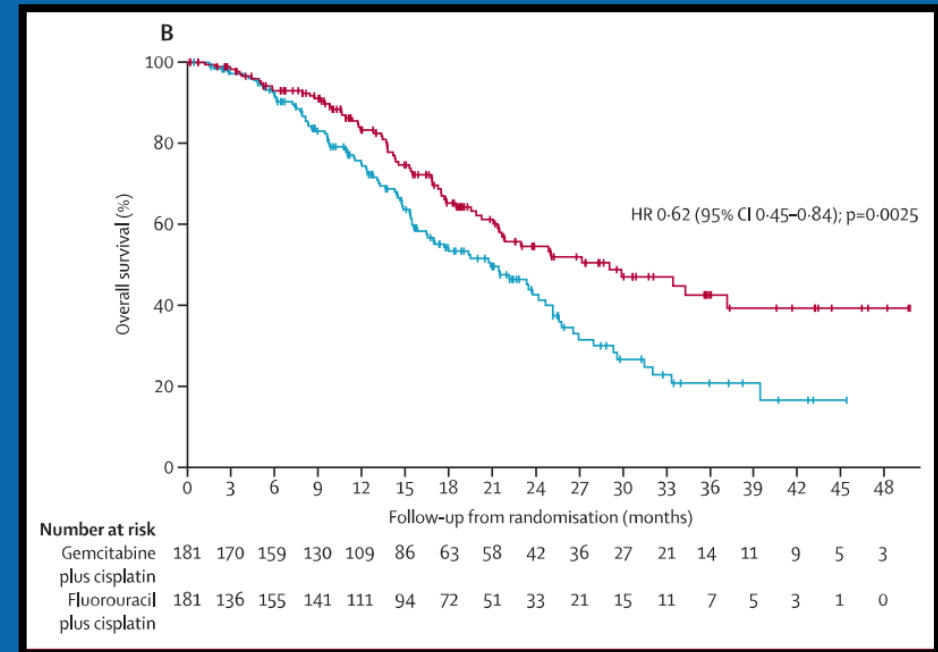


Figure 2: Progression-free survival and overall survival in the intention-to-treat population

A. Progression-free survival



B. Overall survival



JUPITER-02:

The randomized, double-blind, phase 3 study of toripalimab or placebo plus cisplatin and gemcitabine as first-line treatment for recurrent or metastatic nasopharyngeal carcinoma (NPC)

Rui-Hua Xu^{1, *}, Hai-Qiang Mai², Qiu-Yan Chen², Dongping Chen³, Chaosu Hu⁴, Kunyu Yang⁵, Jiyu Wen⁶, Jingao Li⁷, Ying-Rui Shi⁸, Feng Jin⁹, Ruilian Xu¹⁰, Jianji Pan¹¹, Shenhong Qu¹², Ping Li¹³, Chunhong Hu¹⁴, Yi-Chun Liu¹⁵, Yi Jiang¹⁶, Xia He¹⁷, Hung-Ming Wang¹⁸ and Wan-Teck Lim¹⁹, Coherus Biosciences and Shanghai Junshi Biosciences.

¹Department of Medical Oncology, Sun Yat-Sen University Cancer Center; State Key Laboratory of Oncology in South China; Collaborative Innovation Center of Cancer Medicine, Guangzhou, China; ² Department of Nasopharyngeal Carcinoma, Sun Yat-Sen University Cancer Center; ³Affiliated Cancer Hospital & Institute of Guangzhou Medical University, Guangzhou, China; ⁴Fudan University Cancer Center, Shanghai, China; ⁵Union Hospital Tongji Medical College Huazhong University of Science and Technology, Wuhan, China; ⁶Affiliated Hospital of Guangdong Medical University, Zhanjiang, China; ⁷Jiangxi Cancer Hospital, Nanchang, China; ⁸Hunan Cancer Hospital and the Affiliated Cancer Hospital of Xiangya School of Medicine, Changsha, China; ⁹Guizhou Cancer Hospital of Guizhou Medical University, Guiyang, China; ¹⁰Shenzhen People's Hospital, Shenzhen, China; ¹¹Fujian Provincial Cancer Hospital, Fuzhou, China; ¹²The People's Hospital of Guangxi Zhuang Autonomous Region, Nanning, China; ¹³West China Hospital of Sichuan University, Chengdu, China; ¹⁴The Second Xiangya Hospital of Central South University, Changsha, China; ¹⁵Taichung Veterans General Hospital, Taichung, Taiwan; ¹⁶Cancer Hospital of Shantou University Medical College, Shantou, China; ¹⁷Jiangsu Cancer Hospital, Nanjing, China; ¹⁸Chang Gung Memorial Hospital, Taoyuan, Taiwan; ¹⁹National Cancer Centre, Singapore City, Singapore

Presented by Rui-Hua Xu, MD, PhD at 2021 ASCO Annual Meeting

JUPITER-02: Study Design

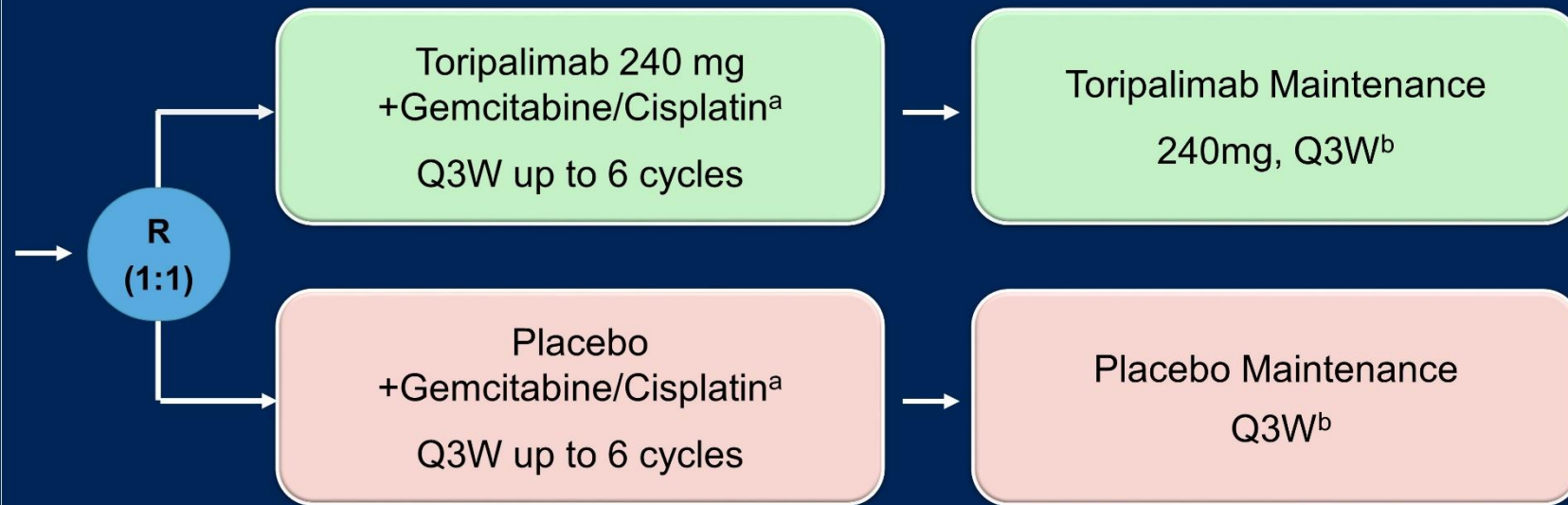
(ClinicalTrials.gov identifier: NCT03581786)

Key Eligibility Criteria

- Primary metastatic NPC or recurrent NPC after curative-intent therapy
- Treatment naïve for recurrent or metastatic (R/M) disease
- ECOG 0-1
- 18-75 yrs
- Measurable disease per RECIST v1.1

Stratification Factors

- Recurrent vs Primary metastatic
- ECOG PS 0 vs 1



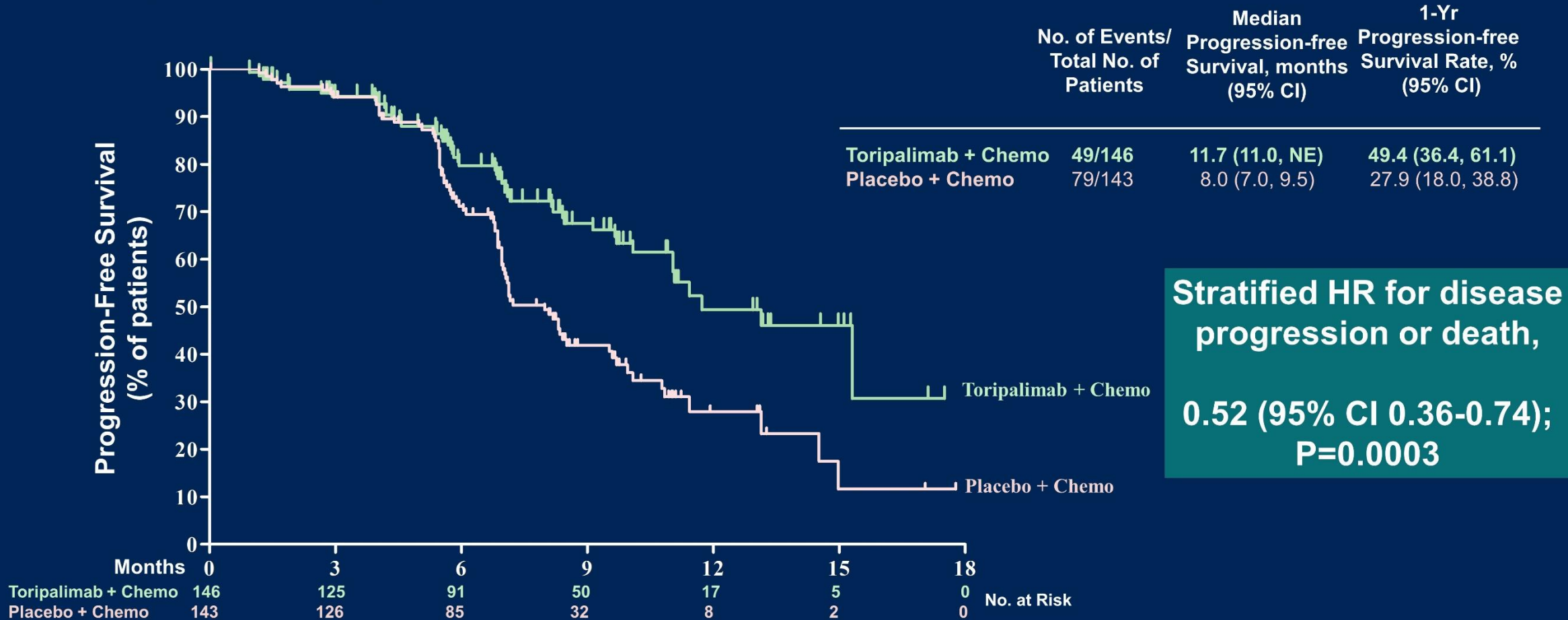
- Primary endpoint: PFS by a blinded independent review committee (BIRC) per RECIST v1.1
- Secondary endpoints: PFS by the Investigator, ORR, DoR, DCR, OS, and PFS & OS 1-year and 2-year rates

^a Gemcitabine 1000mg/m² D1,8 + Cisplatin 80mg/m² D1

^b Until progressive disease, excessive toxicity, withdrawal of consent or investigator's judgement or a maximum treatment of 2 years.

Progression-Free Survival by BIRC per RECIST v1.1

Interim Analysis Data cut-off Date: May 30, 2020



**Stratified HR for disease progression or death,
0.52 (95% CI 0.36-0.74);
P=0.0003**

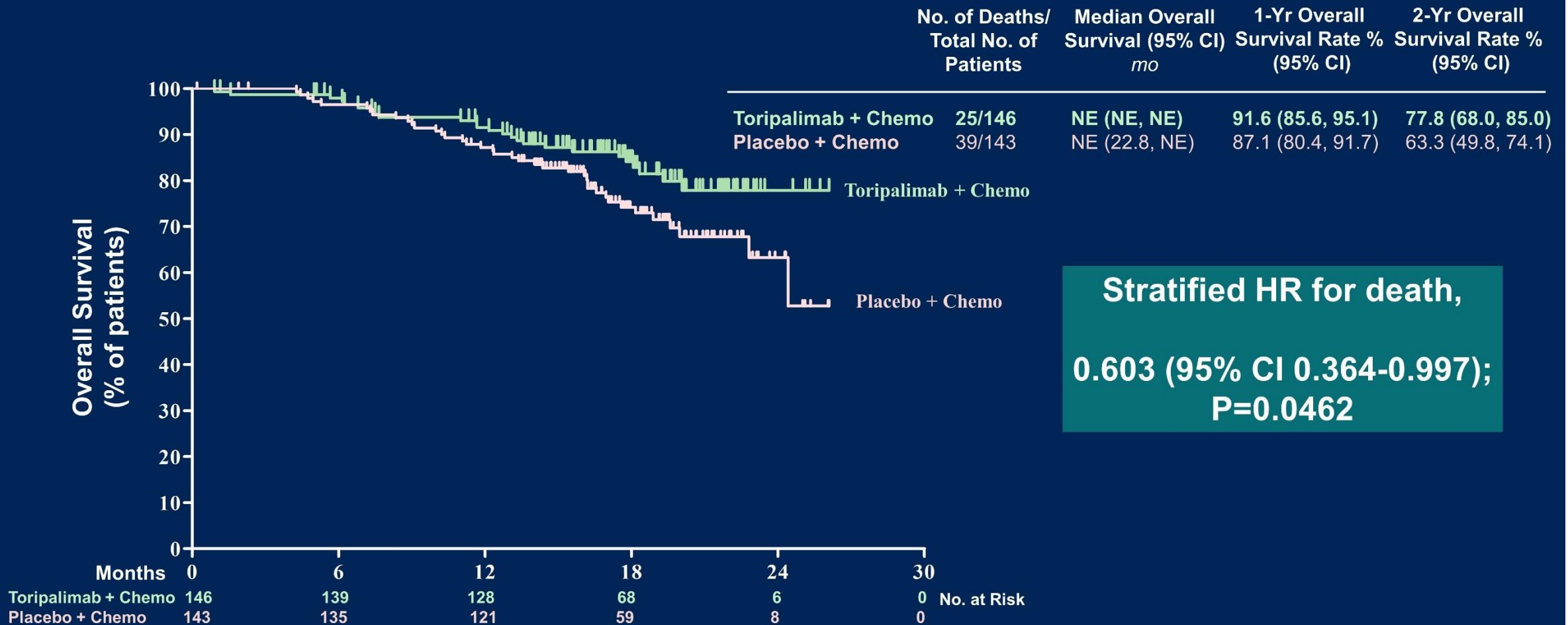
Presented By: Rui-Hua Xu, MD, PhD

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ANNUAL MEETING

Overall Survival Update

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



**Stratified HR for death,
0.603 (95% CI 0.364-0.997);
P=0.0462**

Presented By: **Rui-Hua Xu, MD, PhD**

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Response and Duration of Response by BIRC per RECIST v1.1

Characteristic (%)	Toripalimab + GP (N=146)	Placebo + GP (N=143)
Objective Response Rate ^a	77.4	66.4
95% CI	(69.8, 83.9)	(58.1, 74.1)
<i>P</i> value	0.0335	
Best Overall Response ^a		
Complete Response	19.2	11.2
Partial Response	58.2	55.2
Stable Disease	10.3	13.3
Progressive Disease	3.4	5.6
Not evaluable	6.2	5.6
Non-CR/non-PD ^b	2.7	8.4
No evidence of disease ^c	0	0.7
Median DoR, (95%CI), months	10.0 (8.8, NE)	5.7 (5.4, 6.8)
HR (95%CI)	0.50 (0.33-0.78)	
<i>P</i> value	0.0014	

^a All CR and PR were confirmed.

^b Non-CR/non-PD included subjects who didn't have target disease at baseline by BIRC. ^c

No evidence of disease included subjects who didn't have lesion at baseline by BIRC.

Data cut-off date: 30/May/2020.

Presented By: **Rui-Hua Xu, MD, PhD**

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2021 ASCO[®]
ANNUAL MEETING

Results of KEYNOTE-122: a Phase 3 Study of Pembrolizumab Monotherapy vs Chemotherapy for Platinum-Pretreated, Recurrent or Metastatic Nasopharyngeal Carcinoma

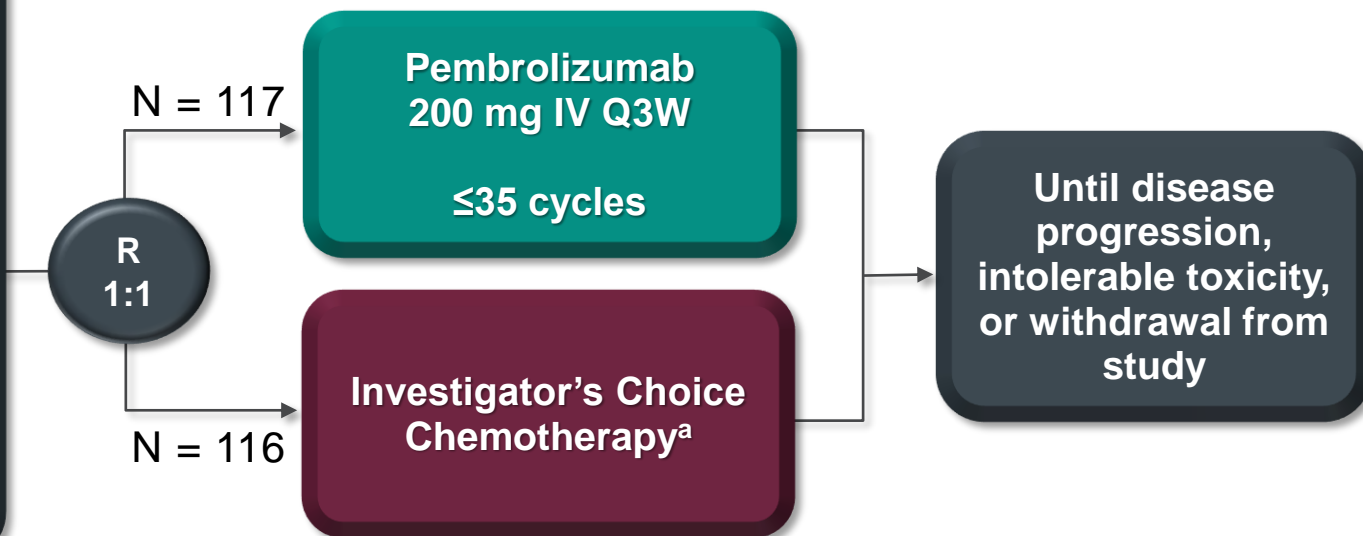
Anthony T.C. Chan¹; Victor Lee²; Ruey-Long Hong³; Myung-Ju Ahn⁴; Wan Qin Chong⁵; Sung-Bae Kim⁶; Gwo Fuang Ho⁷; Priscilla B. Caguioa⁸; Nuttapong Ngamphaiboon⁹; Cheryl Ho¹⁰; Mohamed Amir Shah Abdul Aziz¹¹; Quan Sing Ng¹²; Chia-Jui Yen¹³; Nopadol Soparattanapaisarn¹⁴; Roger Kai-Cheong Ngan¹⁵; Swee Kiong Kho¹⁶; Ramona Swaby^{17,a}; Sanatan Saraf¹⁷; Joy Ge¹⁷; Jianda Yuan¹⁷; Lillian L. Siu¹⁸

¹The Chinese University of Hong Kong, China Hong Kong; ²The University of Hong Kong, China Hong Kong; ³National Taiwan University Hospital, Taipei, China Taiwan; ⁴Samsung Medical Center, Seoul, South Korea; ⁵National University Cancer Institute, Singapore; ⁶Asan Medical Center, Seoul, South Korea; ⁷University of Malaya Medical Centre, Kuala Lumpur, Malaysia; ⁸St. Luke's Medical Center, University of Santo Tomas Faculty of Medicine and Surgery, Manila, The Philippines; ⁹Ramathibodi Hospital, Mahidol University, Bangkok, Thailand; ¹⁰University of British Columbia, Vancouver, BC, Canada; ¹¹Gleneagles Penang Clinical Research Center, Gleneagles Hospital Penang, Penang, Malaysia; ¹²National Cancer Centre Singapore, Singapore; ¹³National Cheng Kung University Hospital, Tainan, China Taiwan; ¹⁴Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand; ¹⁵Queen Elizabeth Hospital, Kowloon, HK SAR, China; ¹⁶Hospital Umum Sarawak, Kuching, Sarawak, Malaysia; ¹⁷Merck & Co., Inc., Kenilworth, NJ, USA; ¹⁸Princess Margaret Cancer Centre, University of Toronto, Toronto, ON, Canada

KEYNOTE-122 Study Design (NCT02611960)

Key Eligibility Criteria

- Histologically confirmed nonkeratinizing differentiated (WHO type II) or undifferentiated (WHO type III) NPC
- Recurrent or metastatic disease
- EBV-positive disease
- Prior treatment with platinum
- Measurable disease per RECIST v1.1
- ECOG PS 0 or 1

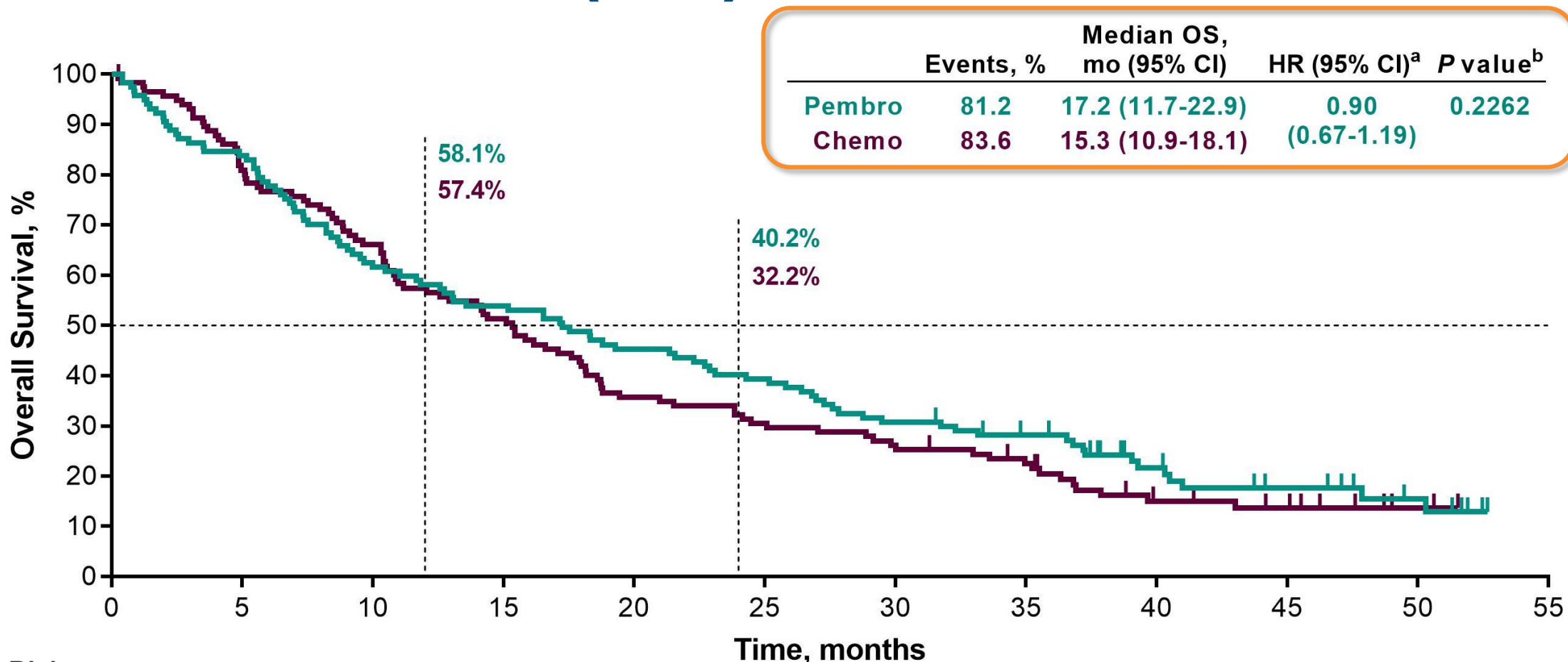


Stratification: presence/absence of liver metastases

ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; Q3W, every 3 weeks; WHO, World Health Organization.

^aCapecitabine 1000 mg/m² (up to 1250 mg/m² from cycle 2 based on tolerability and local practices) PO BID on days 1-14 per 3-week cycle, gemcitabine 1250 mg/m² IV on days 1 and 8 per 3-week cycle, or docetaxel 75 mg/m² IV on day 1 per 3-week cycle. Data cutoff: November 30, 2020.

Overall Survival (ITT)



No. at Risk

Pembro	117	98	72	63	53	46	36	30	17	11	6	0
Chemo	116	93	76	59	41	35	30	23	12	9	2	0

^aBased on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by presence of liver metastasis. ^b1-sided P value based on log-rank test stratified by presence of liver metastasis. Data cutoff: November 30, 2020.

Subsequent Oncologic Therapy

n	Pembro n = 117	Chemo n = 116
≥1 subsequent therapy ^a	78	71
1 subsequent therapy		
Chemotherapy	9	8
Targeted therapy	0	0
Immunotherapy ^b	0	1
Gene therapy	0	1
≥2 subsequent therapies ^c		
Chemotherapy	204	138
Targeted therapy	12	18
Immunotherapy ^b	7	34
Gene therapy	0	0

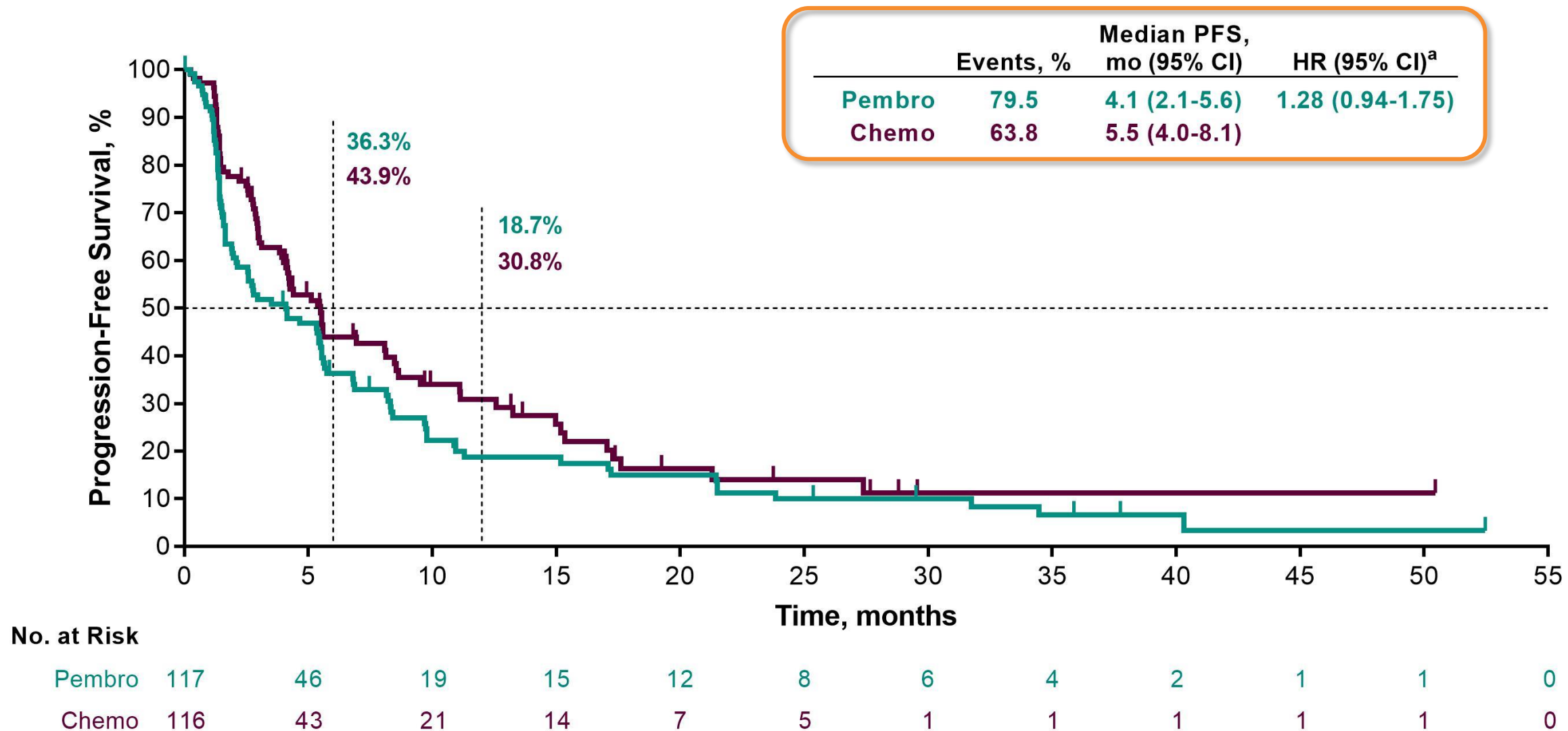
^aPatients could have received ≥1 therapy.

^bIncludes antibodies, cellular-based immunotherapy, and vaccines.

^cTotal number of therapies and not number of patients, in each treatment arm

Data cutoff: November 30, 2020.

PFS per RECIST v1.1 by BICR (ITT)



^aBased on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by presence of liver metastasis. Data cutoff: November 30, 2020.

Opportunities

- 3rd line R/M
 - Agents available but nothing approved → placebo comparator?
 - Many patients fit enough to receive 3rd line
- 2nd line R/M
 - Most patients will be anti-PD1 refractory
 - Single agent cytotoxic represents standard practice
 - Anti-PD1 alone did not improve survival
- 1st line R/M
 - Chemotherapy + anti-PD1 is SOC
 - High bar: 2-yr OS ~75%
 - Potential to combine
 - Potential for maintenance or adjuvant therapy for patients with persistent plasma EBV DNA post-treatment
- Locally advanced
 - Lots of possibilities, long readout
 - Potential for maintenance or adjuvant therapy for patients with persistent plasma EBV DNA post-treatment



**Nana-val MOA and its Potential in
Advanced EBV+ Solid Tumors:**

Dr. Ayman Elguindy
Chief Scientific Officer



Nana-val: All-Oral Combination Drug Product of Nanatinostat and Valganciclovir

Precisely eradicates EBV⁺ tumor cells

nanatinostat:

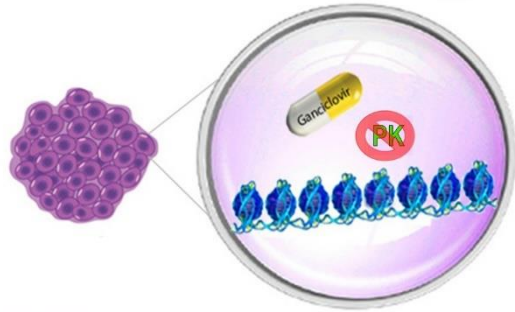
- Epigenetic agent, selective for EBV gene activation and immune enhancement
- Class I HDACi, selective for HDACs 1, 2 & 3
- Potent inducer of expression of the EBV protein kinase (BGLF4) at a low dose

valganciclovir:

- Synthetic nucleoside analog
- Antiviral prodrug, converted into a cytotoxic agent by viral enzymes (kinases)

Viracta's Oral "Kick and Kill" Approach Selectively Targets EBV+ Cancer Cells

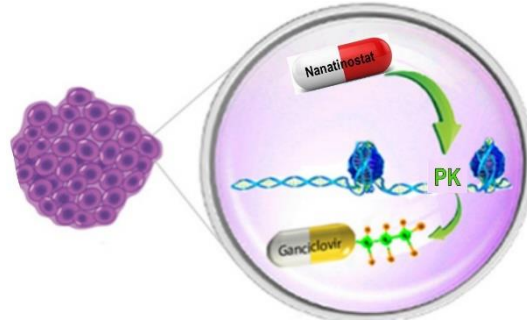
Nanatinostat sensitizes EBV+ tumors to the cytotoxic effects of ganciclovir



LATENCY

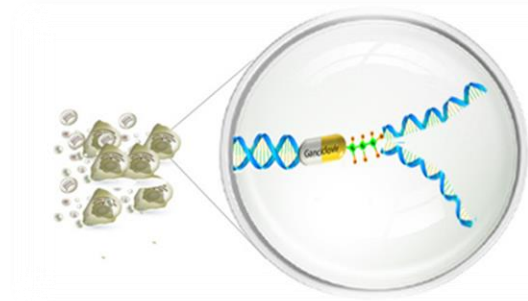
EBV is latent in cancer cells and viral kinase genes are silenced epigenetically.

Valganciclovir, an antiviral prodrug of ganciclovir (GCV), is inactive in the absence of the expression of the viral protein kinase (PK)



THE KICK

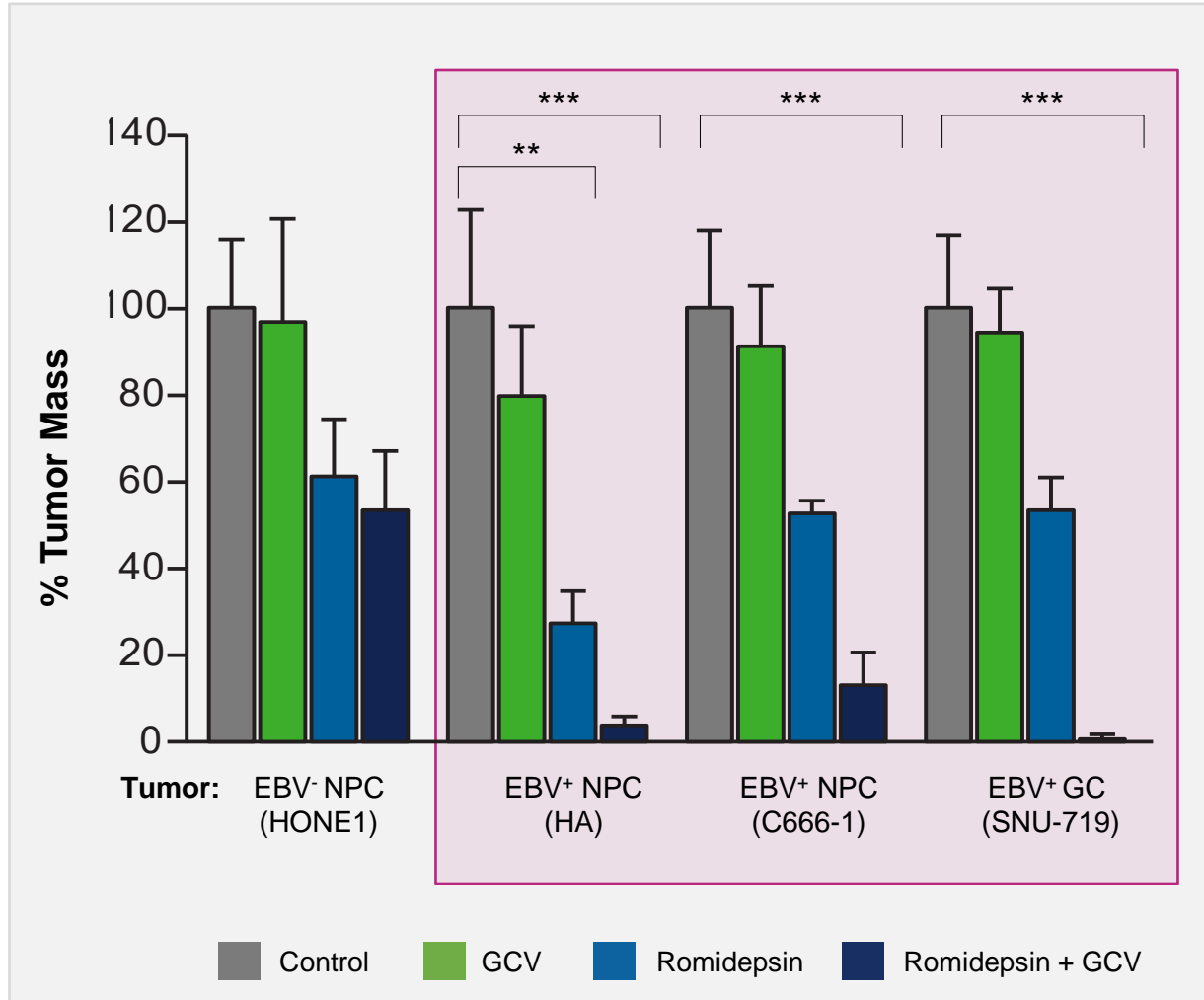
Nanatinostat selectively and potently induces expression of EBV protein kinase (PK), which activates GCV and converts it to its cytotoxic form



THE KILL

Cytotoxic GCV inhibits DNA replication by chain termination leading to apoptosis in EBV+ cancer cells. This combination approach is a form of synthetic lethality

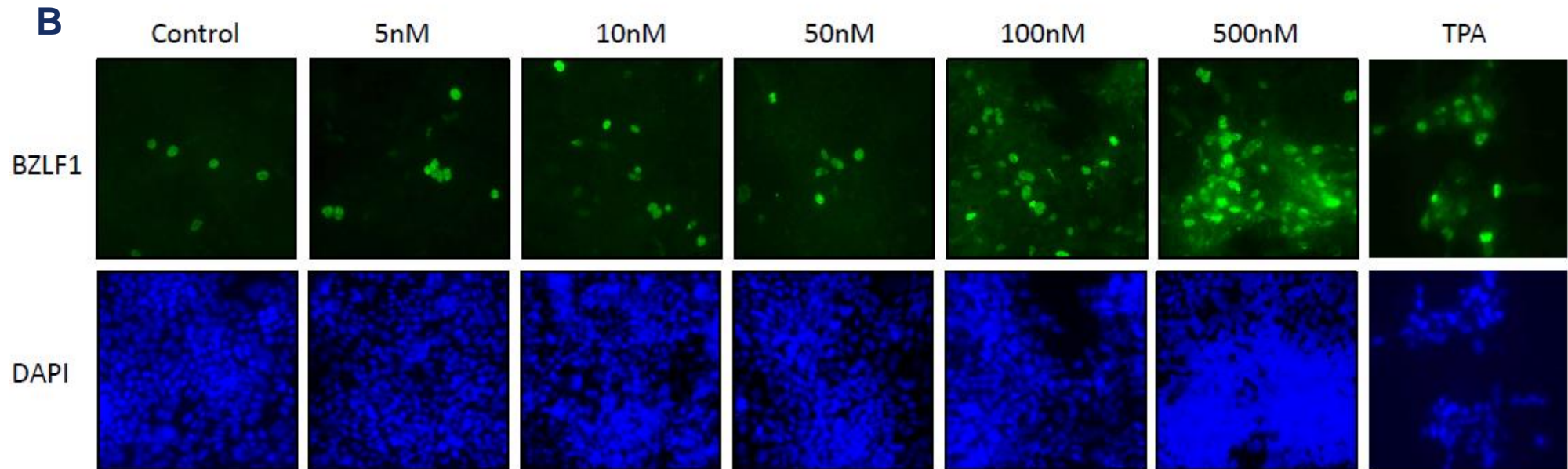
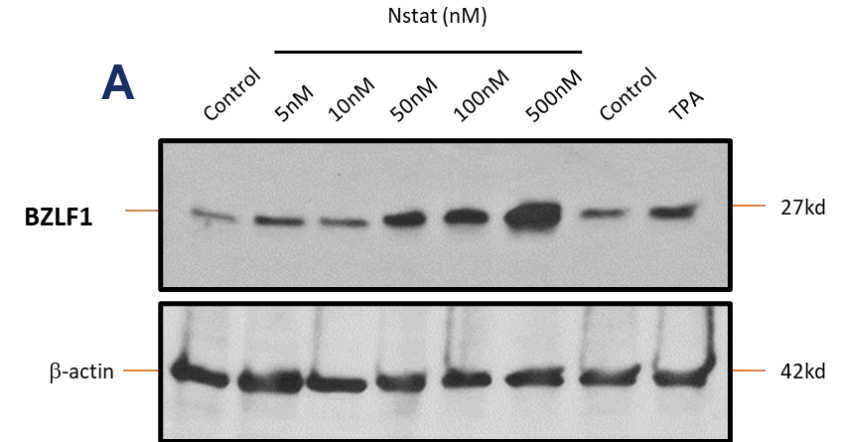
Preclinical Proof of Concept for Nana-val in EBV+ Solid Tumors



- Annual incidence of nasopharyngeal carcinoma (NPC) and gastric carcinoma (GC):
 - North America: ~5,500
 - Global: ~218,000
- High unmet need, especially for R/R disease
- Efficacy of combination approach initially reported in murine models of EBV+ NPC and GC using a first generation intravenous (IV) HDACi + IV ganciclovir

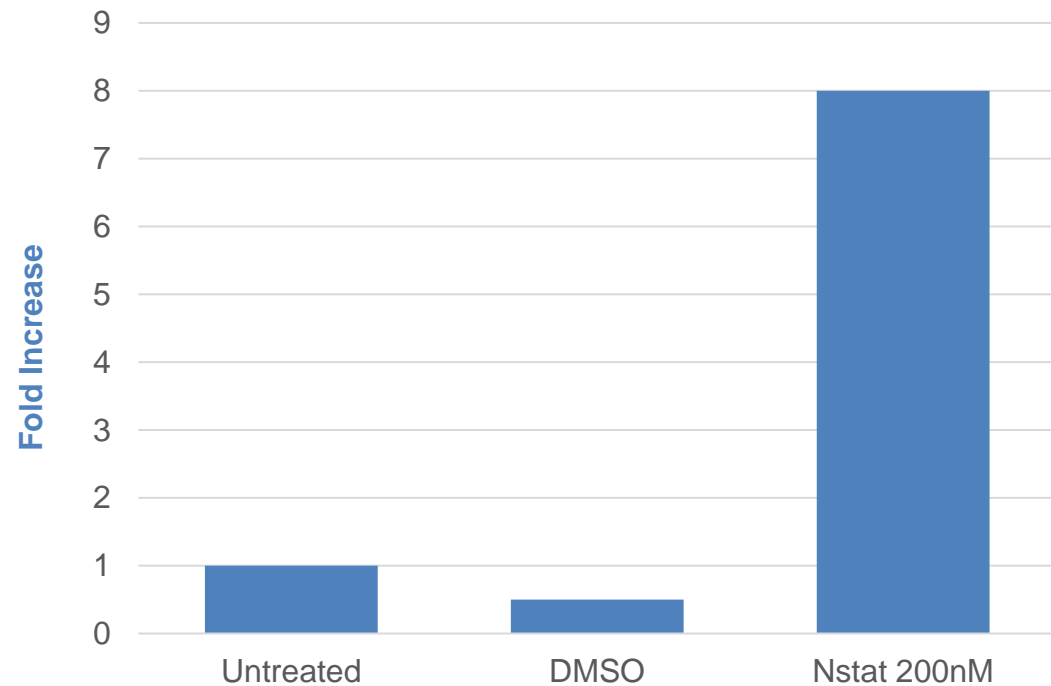
Nanatinostat Induces the EBV Lytic Cycle in NPC Cells

- Different concentrations of nanatinostat activate the expression of BZLF1, the master EBV lytic cycle switch protein;
A) Western blot, B) Immunofluorescence, of BZLF1
- BZLF1 drives expression of lytic viral proteins including BGLF4, the viral protein kinase

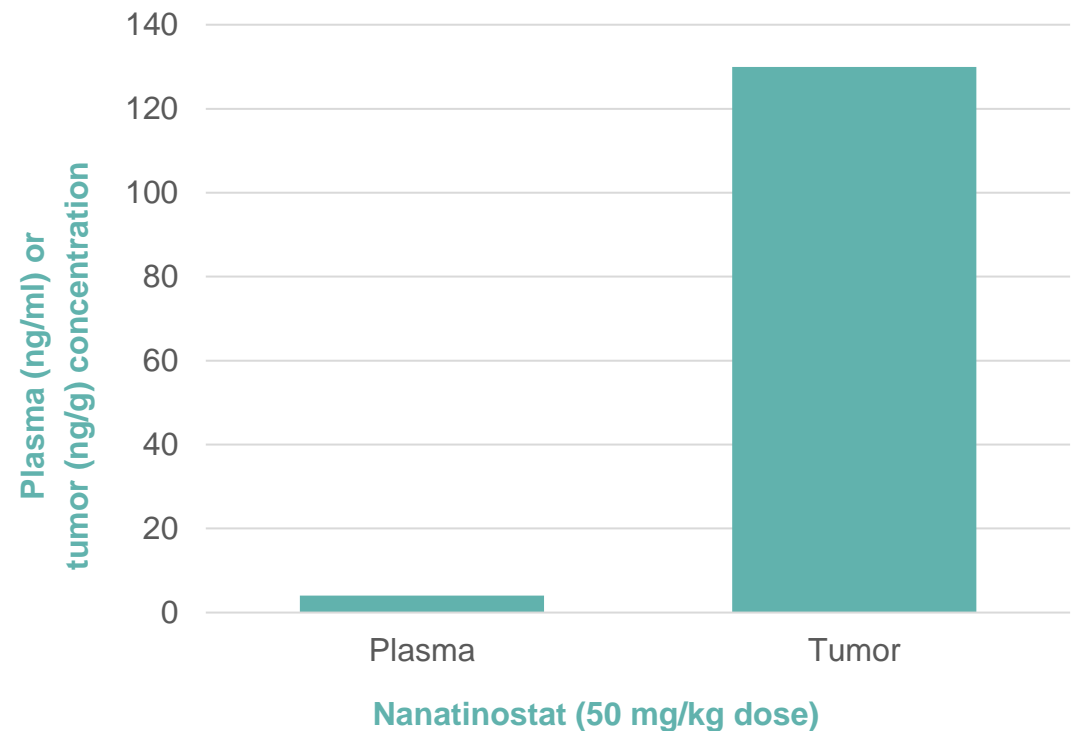


Nanatinostat Induction of EBV Protein Kinase in Tumor Cells and Accumulation in Tumor Tissue

Induction by Nanatinostat of EBV Protein Kinase RNA in SNU-719 EBV+ Gastric Carcinoma Cell Line



High Tumor Uptake of Nanatinostat in a Murine Xenograft Tumor Model





**Nana-val Phase 1b/2 Trial in
Advanced EBV+ Solid Tumors:**
Dr. Lisa Rojkjaer
Chief Medical Officer



Nana-val Clinical Activity Demonstrated in Recurrent EBV+ Lymphoma

Potential tissue agnostic approach to EBV+ cancers

- The all-oral combination of nanatinostat and valganciclovir (Nana-val) has demonstrated promising results in a Phase 1b/2 study in heavily pre-treated, refractory EBV+ lymphoma patients (NCT03397706):
 - Nana-val was generally well-tolerated with a safety profile characterized primarily by reversible cytopenias, low grade gastrointestinal adverse events/creatinine elevations
 - Complete responses in DLBCL, T and NK-cell lymphomas, and immunodeficiency-associated lymphoproliferative disorders
 - Median duration of response of 10.4 months

Considerations for the Solid Tumor Study Design

Potential synergies with checkpoint inhibitors

- EBV⁺ nasopharyngeal cancer has high PD-L1 expression
 - PD-1 inhibitors have ORR of 20-30% in R/M-NPC¹
- Reactivation of EBV leads to the expression of highly immunogenic proteins and could induce an immune response towards the tumor cells containing the virus
- Thus, EBV antigen expression makes this disease amenable to EBV-targeted and immunotherapy approaches

The Phase 1b/2, open label, multicenter study will evaluate the safety, tolerability, pharmacokinetics and preliminary activity of Nana-val in patients with advanced EBV⁺ solid tumors

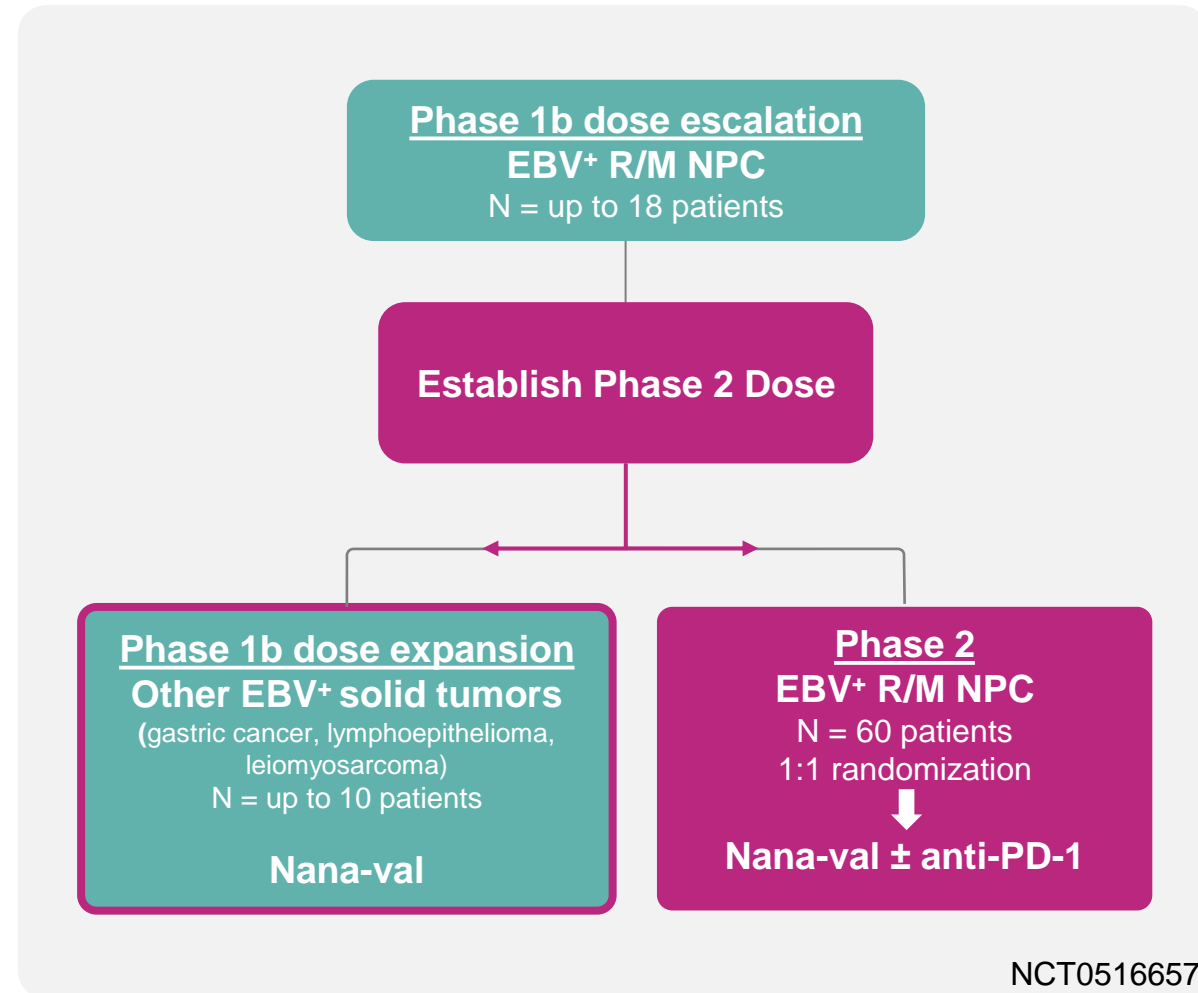
Additionally, the combination of pembrolizumab together with Nana-val will be evaluated in EBV⁺ R/M-NPC patients

Phase 1b/2 “301” Study in EBV+ Solid Tumors

Overview

- **Phase 1b:** N≤18 (*currently enrolling*)
 - Dose escalation to determine the recommended Phase 2 dose (RP2D) of Nana-val in patients with EBV+ R/M NPC
 - Dose expansion at the RP2D in patients with other advanced EBV+ solid tumors
- **Phase 2:** N=60
 - 1:1 randomization to Nana-val +/- pembrolizumab in patients with EBV+ R/M NPC
- **Endpoints:**
 - Primary:
 - Phase 1b: Incidence of dose limiting toxicities
 - Phase 2: ORR by RECIST v1.1
 - Secondary: Safety, efficacy, pharmacokinetics

Preliminary safety/efficacy data anticipated in H2 2022



NCT05166577



Ezra Cohen, MD
UCSD



Ivor Royston, MD
Viracta President & CEO



Lisa Rojkjaer, MD
Viracta CMO



Ayman Elguindy, PhD
Viracta CSO



Daniel Chevallard, CPA
Viracta COO & CFO

Question and Answer Session



Closing Remarks:

Dr. Ivor Royston

President and Chief Executive Officer





Thank you