Nanobiotix KOL Call to Discuss the Role of NBTXR3 and Immune Oncology in Advancing Head & Neck Cancer

June 18, 2024

IMPORTANT NOTICE AND DISCLAIMER

IMPORTANT: You must read the following before continuing. In accessing this document, you agree to be bound by the following terms and conditions.

References herein to this presentation (the “Presentation”) shall mean and include this document, the oral presentation accompanying this document provided by Nanobiotix SA (the "Company" and, together with its subsidiaries, the “Group”) and any other person as physicians acting as investigator of clinical trial involving product-candidate NBTXR3, any question and answer session following that oral presentation and any further information that may be made available in connection with the subject matter contained herein.

This Presentation has been prepared by the Company and is provisional and for information purposes only. The information presented is provided as of the date of this Presentation only and may be subject to significant changes at any time without notice. Neither the Company, nor its advisors, nor any other person is under any obligation to update such information. Potential risks and uncertainties include the risk that possible adverse events associated with the use of NBTXR3, delays and cost due to additional work or other requirements flowing from regulatory agencies, the possiblity that ongoing clinical study of NBTXR3 will not replicate results from ealier clinical trials and that NDA submissions of NBTXR3 will not resul in product approval. Further information regarding risk related to NBTXR3 and the Group activities is included in reports published in accordance with the rules and regulations applicable to companies listed on the Nasdaq Global Select Market and on the regulated market of the Euronext in Paris under the framework of requirements of the U.S. Securities and Exchange Commission (the "SEC") and the French Financial Markets Authority (Autorité des Marchés Financiers -- the "AMF"), including the risk factors described in the Company's most recent universal registration document filed with the AMF and the most recent Annual Report on Form 20-F filed with the SEC, as updated from time to time by the Company's other public reports, which are available free of charge on the Company's website (www.nanobiotix.com) and the respective websites of the AMF (www.amf-france.org) and the SEC (www.sec.gov).

The Presentation and any of its statements, other than statements of historical fact, are forward-looking statements, including within the meaning of the U.S. Private Securities Litigation Reform Act of 1995. These statements are not guarantees of the Company’s future performance. Such statements reflect the current view of the Company's management and are subject to a variety of risks and uncertainties as they relate to future events and are dependent on circumstances that may or may not materialize in the future. Forward-looking statements cannot, under any circumstance, be construed as a guarantee of the Company’s future performance as to strategic, clinical, regulatory, financial or other matters, and the Company’s actual performance, including its financial position, results and cash flow, as well as the trends in the sector in which the Company operates, may differ materially from those proposed or reflected in the forward-looking statements contained in this Presentation. Even if the Company’s performance, including its clinical results and developments were to conform to the forward-looking statements contained in this Presentation, such results or developments cannot be construed as a reliable indication of the Company’s future results or developments. The Company expressly declines any obligation to update or to confirm any prospective information in order to reflect an event or circumstance that may occur after the date of this Presentation.

Each reader is cautioned that assumptions used in the preparation of any forward-looking information may prove to be incorrect and that study results could change over time as the study is continuing to follow up all subjects and new data are continually being received which could materially change study results. Caution should be exercised when interpreting results from separate trials involving product candidates, including NBTXR3. There are differences in the clinical trial design, patient populations, and the product candidates themselves, and the results from the clinical trials of distinct product candidates may have no interpretative value with respect to our existing or future results. Similarly, caution should be exercised when interpreting results relating to a small number of patients or individually presented case studies.

The Information does not constitute an offer to sell or subscribe or a solicitation to purchase or subscribe for securities, nor shall there be any sale of these securities in the United States or any other jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction. No public offering of securities may be conducted in any member state of the European Economic Area (including France) prior to the publication in the relevant member state of a prospectus that complies with the provisions of Regulation 2017/119.

All persons accessing the Information are deemed to agree to all the limitations and restrictions set out above.

Agenda

Welcome – Craig West, SVP Investor Relations

Introductions and Agenda – Jeffery Bockman, PhD

How NBTXR3 works and its local and systemic responses – Sébastien Paris, PhD

How patients present and are treated in this setting; unmet needs – Ari Rosenberg, MD

NBTXR3 in R/M HNSCC, the 1100 study – Colette Shen, MD, PhD

Q&A and Panel Discussion - All

Conclusion

Introductions

Colette Shen, MD, PhD
University of North Carolina Lineberger Comprehensive Cancer Care Center

Ari Rosenberg, MD
University of Chicago School of Medicine

Sébastien Paris, PhD
Nanobiotix

Jeffrey Bockman, PhD
Lumanity

How NBTXR3 Works and its Local and Systemic Responses – Sebastien Paris, PhD

NBTXR3: A First-In-Class Radioenhancer

Aqueous suspension of inorganic crystalline hafnium oxide (HfO_2) nanoparticles

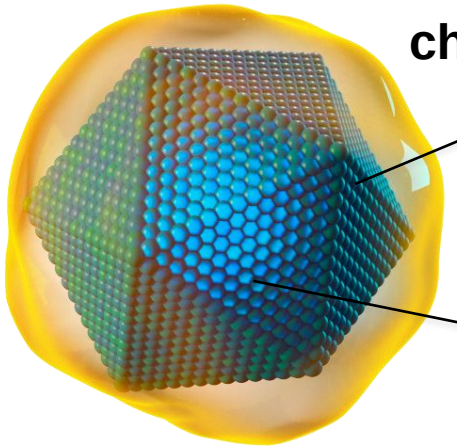
High atomic number (Z=72) and electron density

Inert in the absence of ionizing radiation: “Off “status
Activated by ionizing radiation: “On” status

One-time intratumoral administration, remains in tumor

Efficacy and safety demonstrated in a randomized Phase 2/3 trial in locally advanced soft tissue sarcoma[1]

Universal mode of action targeting all solid tumors



Negative surface charge for stability at neutral pH in aqueous medium
+ Nanometer scale to fit inside cell

» Facilitates entry into tumor cells

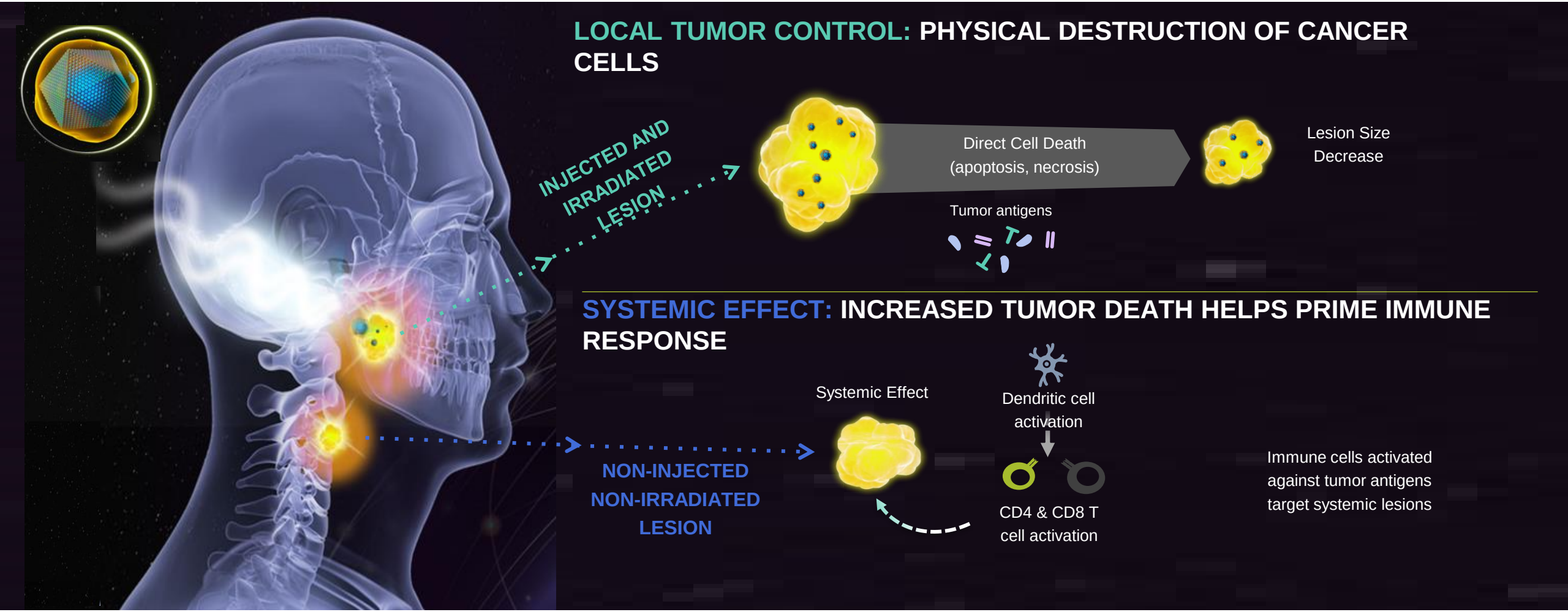
High atomic number (72) and high e^- density

» Increased local absorption of ionizing radiation

1 Bonvalot, Sylvie et al. The Lancet. Oncology (2019); RT: Radiotherapy

Local Cell Destruction Induced by NBTXR3 Activates Immune Priming

Local and systemic benefits through cell death and immune activation against tumor antigens



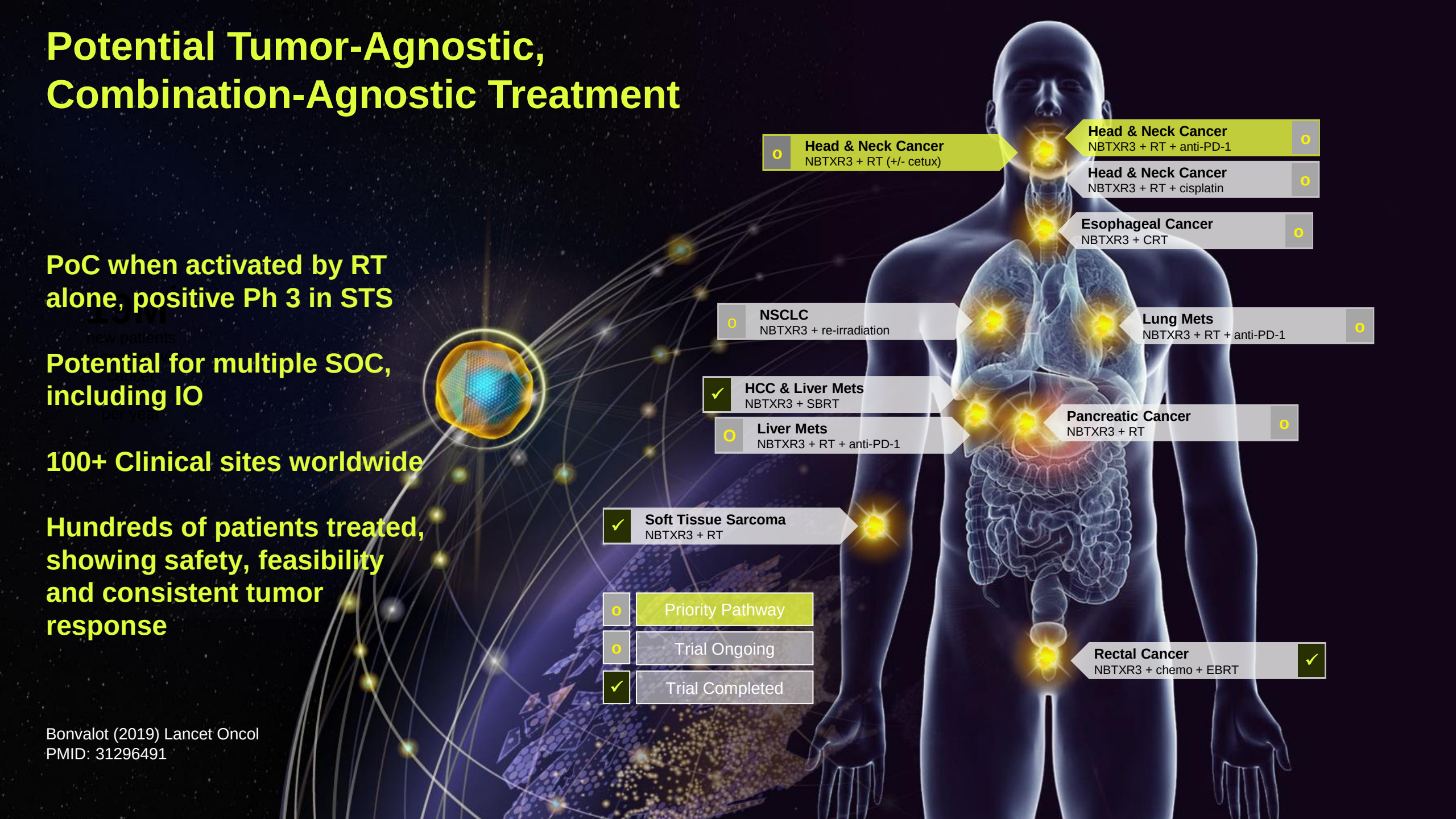
Potential Tumor-Agnostic, Combination-Agnostic Treatment

PoC when activated by RT alone, positive Ph 3 in STS

Potential for multiple SOC, including IO

100+ Clinical sites worldwide

Hundreds of patients treated, showing safety, feasibility and consistent tumor response



Bonvalot (2019) Lancet Oncol
PMID: 31296491

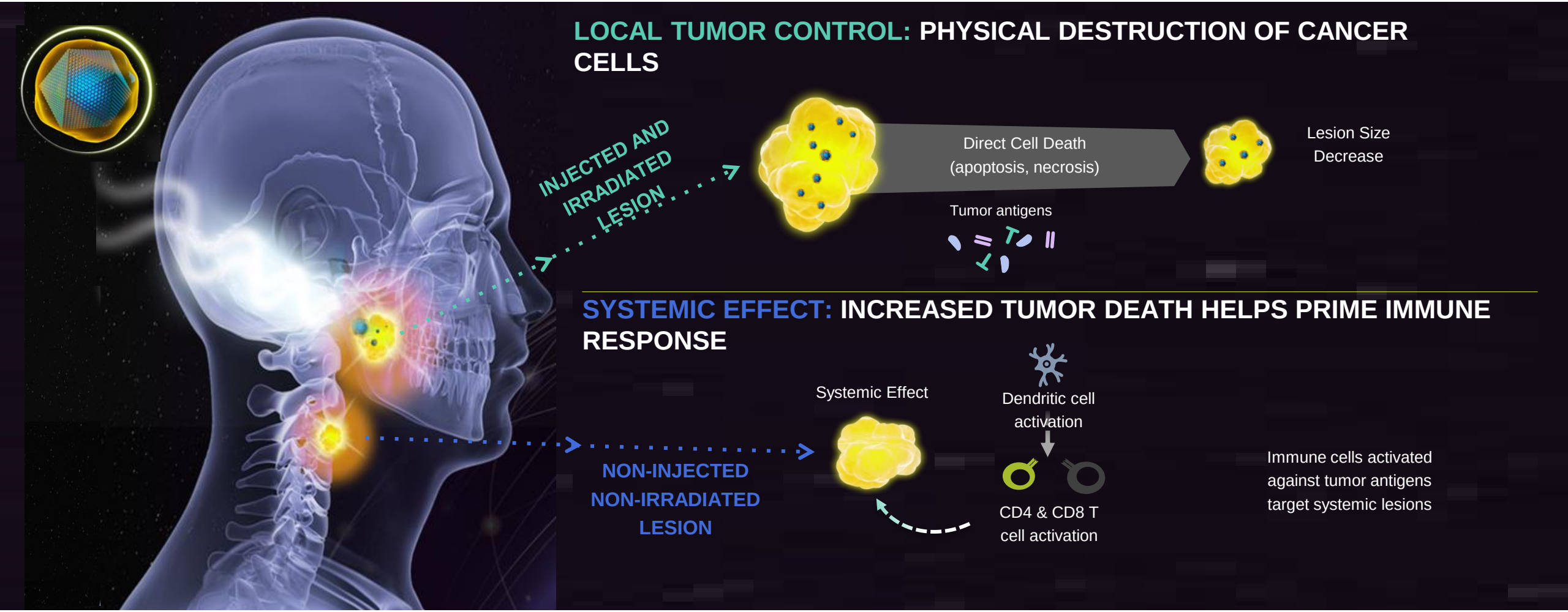
Pipeline-in-a-Product Strategy

Patients (Current Study)	N	Phase 1	Phase 2	Phase 3	Operational Sponsor
Head & Neck					
Elderly Cisplatin-ineligible (NANORAY-312, RT-R3 +/- cetuximab vs RT +/- cetuximab)	500				Nanobiotix Janssen
R/M IO Naïve (Study 1100, RT-R3 fb anti-PD-1)	35+				Nanobiotix
R/M IO Resistant (Study 1100, RT-R3 fb anti-PD-1)	35+				Nanobiotix
R/M (MDA-0541, RT-R3 fb anti-PD-1)	60				MD Anderson Cancer Center
Lung					
Inoperable, Stage 3	NA				Janssen
Inoperable, Recurrent (MDA-0123, Reirradiation RT-R3)	24				MD Anderson Cancer Center
Expansion Opportunities					
Soft Tissue Sarcoma (Act.In.Sarc, RT-R3 fb resection)	180				Nanobiotix
Rectal (Study 1001, RT-R3 concurrent CT)	32				Nanobiotix
Advanced Solid (MDA-0618, RT-R3 with anti-PD-1)	40				MD Anderson Cancer Center
Cisplatin-eligible H&N (Study 1002, RT-R3 concurrent CT)	12				Nanobiotix
HCC & Liver Mets (Study 103, RT-R3)	23				Nanobiotix
Pancreas (MDA-1001, RT-R3)	24				MD Anderson Cancer Center
Esophageal (MDA-0122, RT-R3 concurrent CT)	24				MD Anderson Cancer Center
IO Resistant Multiple Primary Tumors (Study 1100, RT-R3 fb anti-PD-1)	35+				Nanobiotix

Nanobiotix granted Janssen a worldwide license for the development and commercialization of NBTXR3 as announced July 10, 2023; IO Resistant Mets: Metastases from different primary tumors in IO resistant patients; RT-R3: RT activated NBTXR3; fb: followed by; CT: chemotherapy.

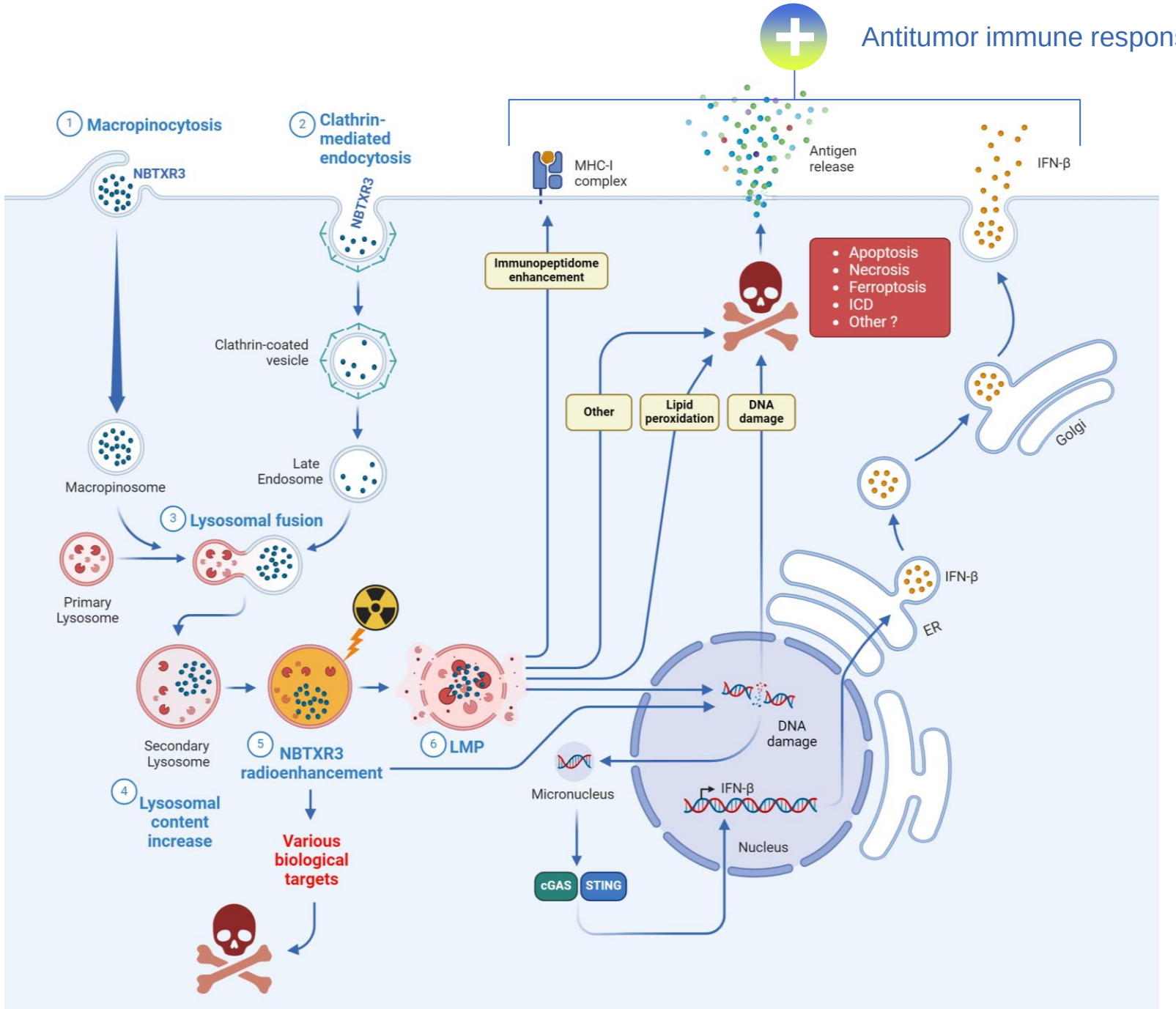
Local Cell Destruction Induced by NBTXR3 Activates Immune Priming

Local and systemic benefits through cell death and immune activation against tumor antigens



NBTXR3

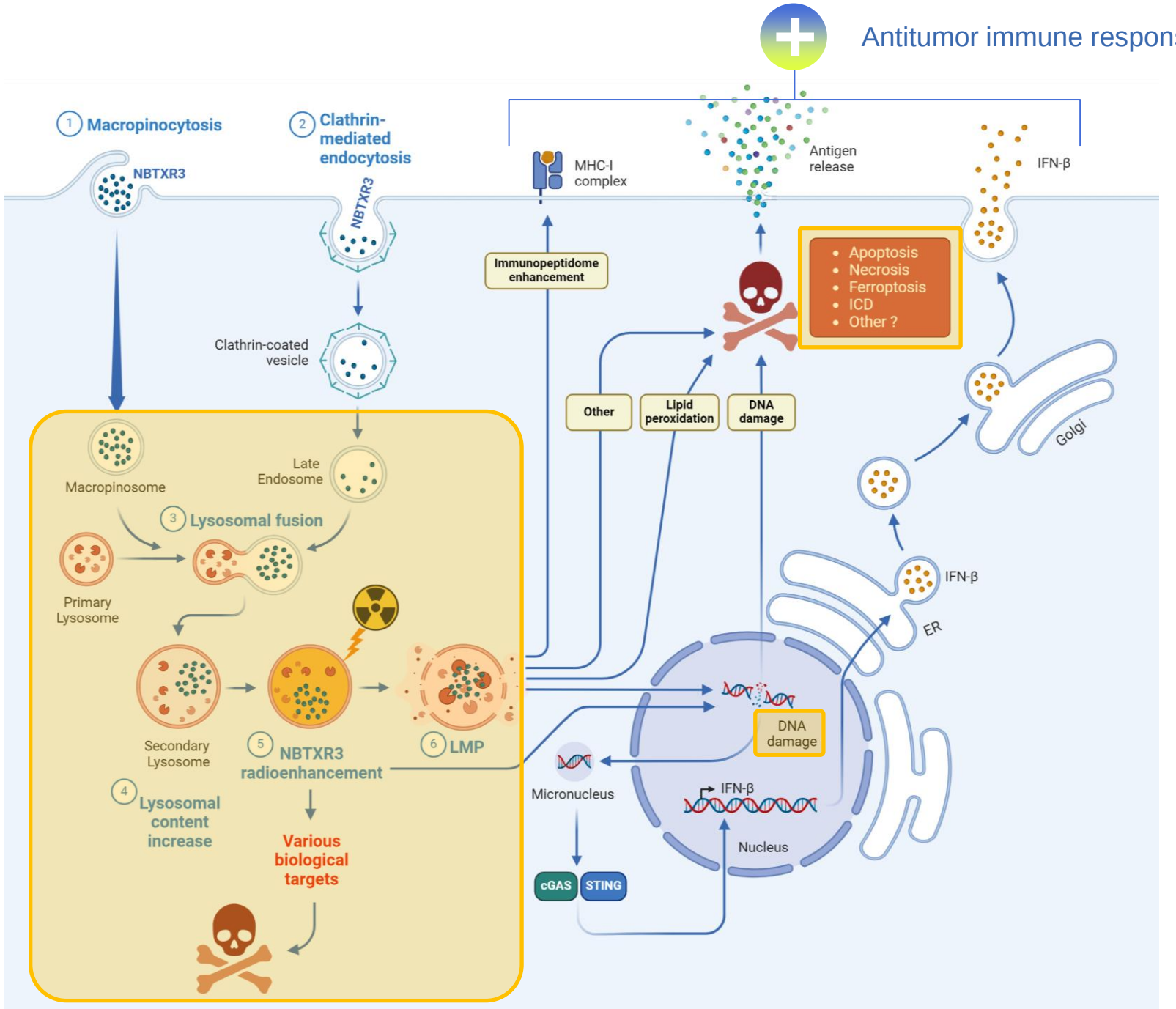
Physical and pleiotropic universal mode of action



Da silva (2024) JECCR
PMID: 38173001

NBTXR3

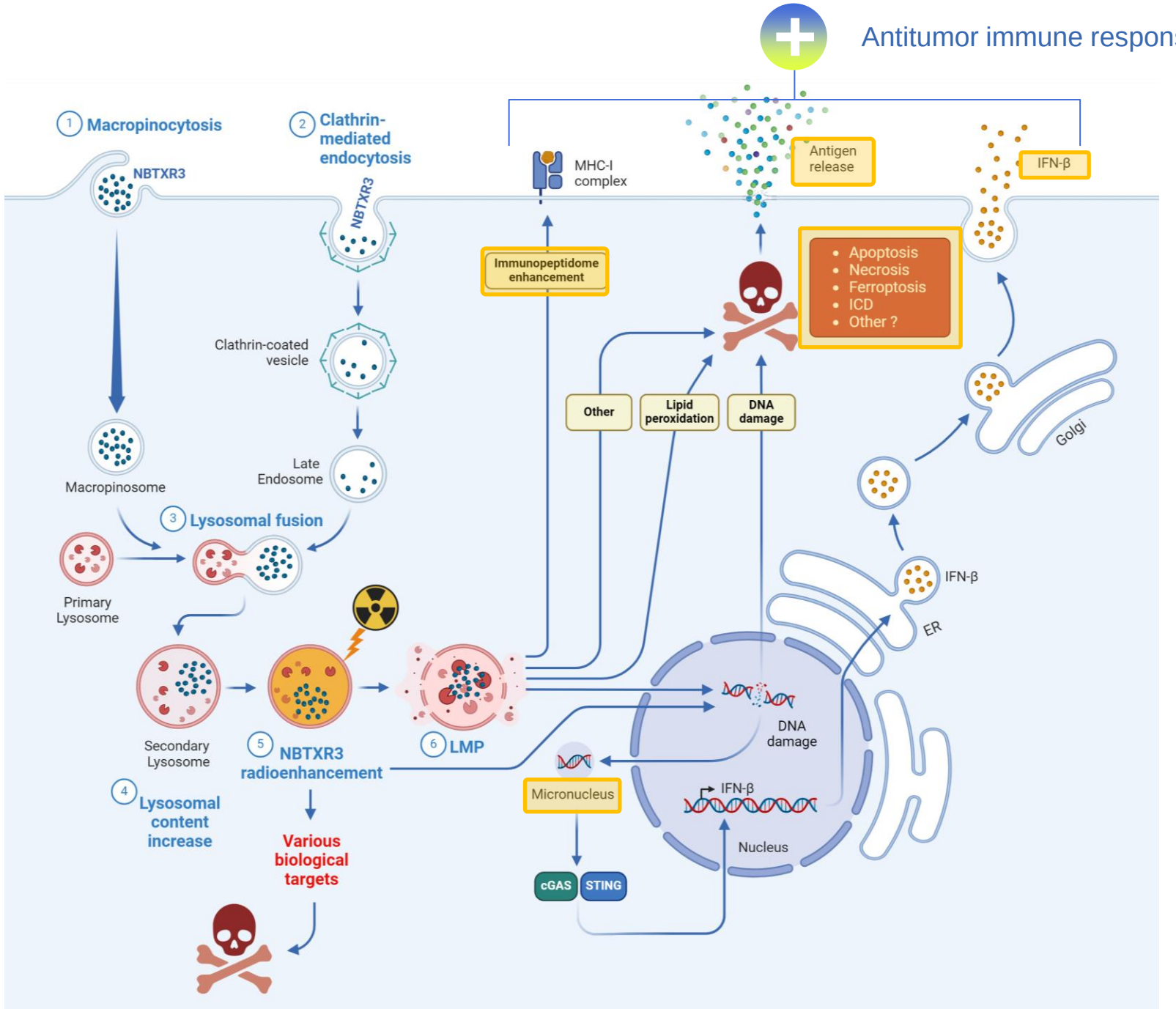
Physical and pleiotropic universal mode of action



Da silva (2024) JECCR
PMID: 38173001

NBTXR3

Subsequent priming of antitumor immune response via multiple pathways

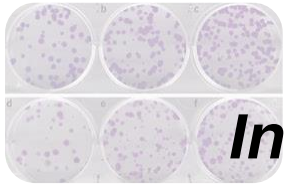


Da silva (2024) JECCR
PMID: 38173001

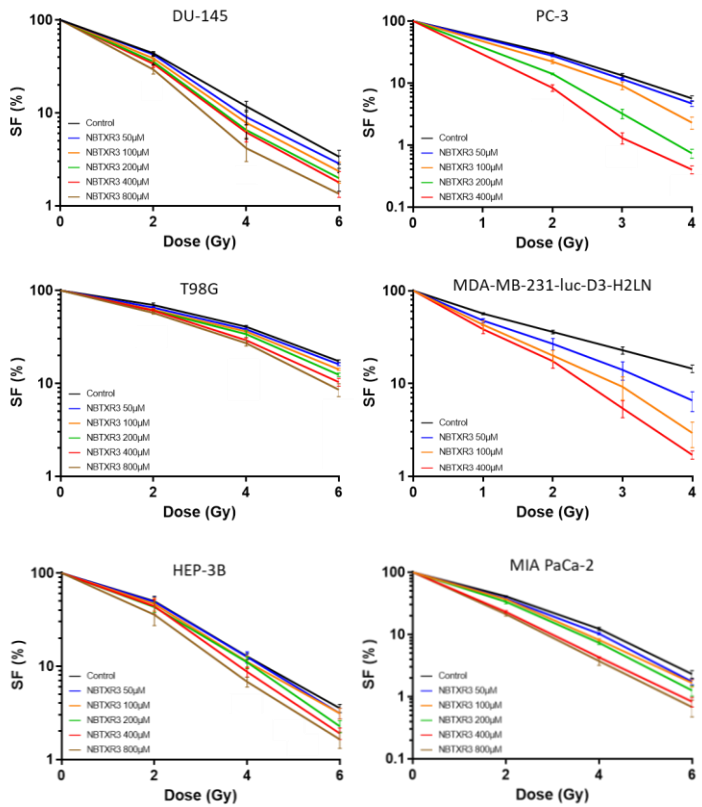
NBTXR3

Direct cell death enhancement leading to improved local control

Zhang (2021) Int J Nanomedicine PMID: 33880022; Zhang (2020) Int J Nanomedicine PMID: 32581534; Marill (2019) Radiotherapy & Oncology PMID: 31439450; Marill (2014) Radiation Oncology PMID: 24981953; Maggiorella (2012) Future Oncol. PMID: 23030491

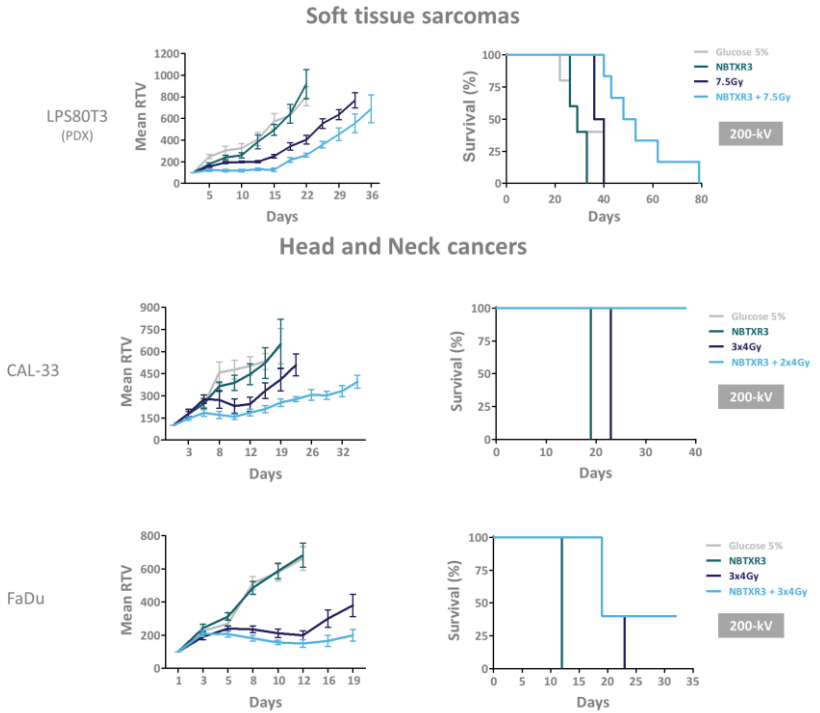


In vitro



⇨ **15 cancer cell lines tested**

In vivo



⇨ **11 cancer cell lines tested**

NBTXR3

Multiple pathways priming the immune response

Darmon (2022) Cancer Cell Int.
PMID: 35659676

AACR 2019
SITC 2022

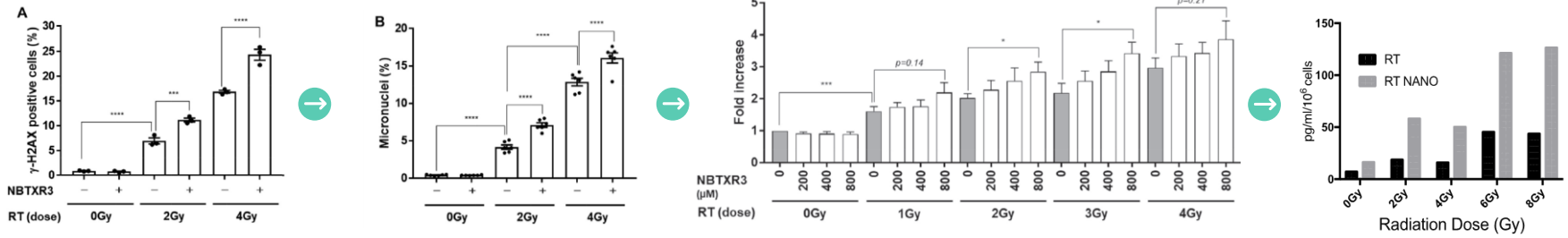
Marill (2019) Radiotherapy & Oncology
PMID: 31439450

DNA damages, cGAS/STING activation and IFN-β secretion

HCT116 cells

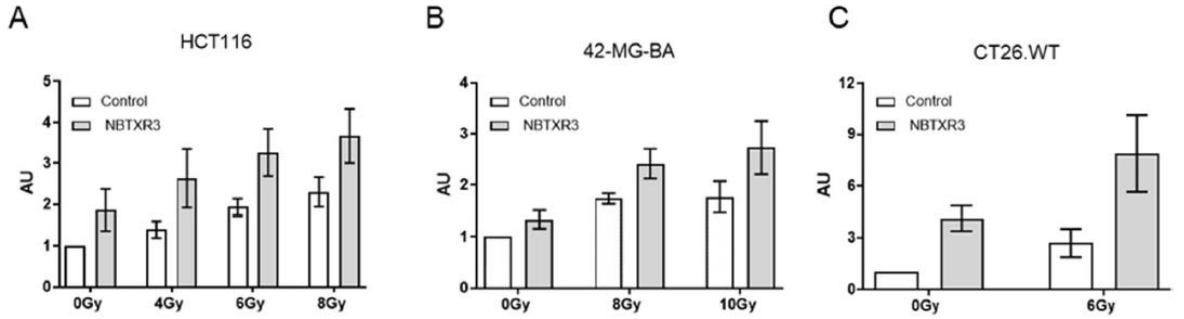
Weill Cornell Medicine

γ-H2AX (DSBs) → Micronuclei → cGAS/STING → IFN-β



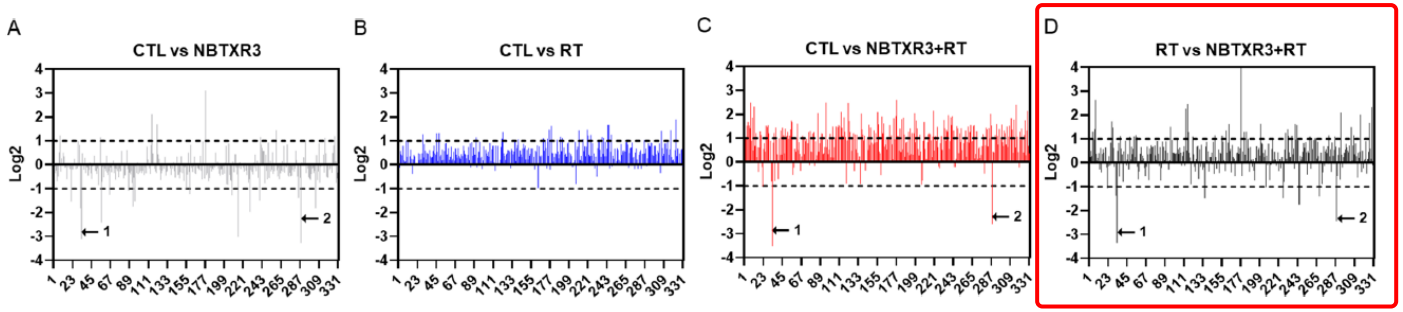
Immunogenic Cell Death (ICD)

ecto-CALR



Immunopeptidome modulation

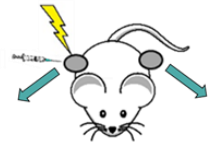
CT26 cells



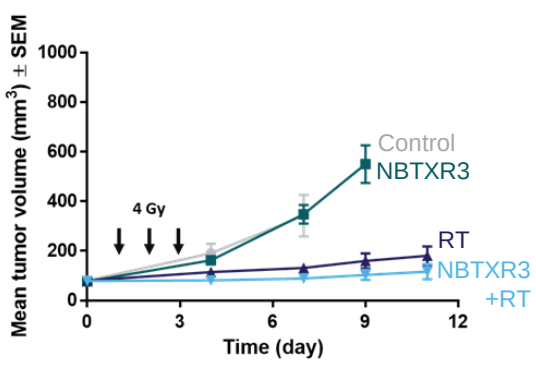
NBTXR3+RT Achieves Immune Effects that RT Alone Cannot Accomplish

Direct antitumor response and immune priming lead to systemic response

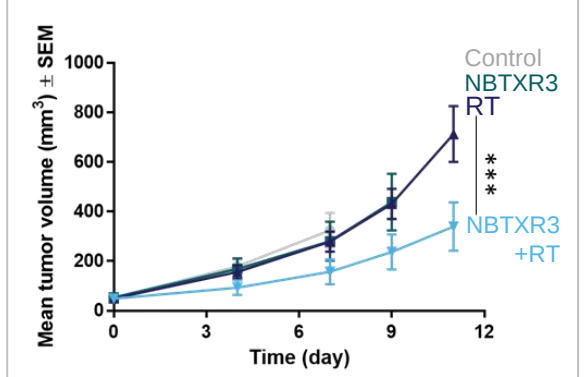
No CPI

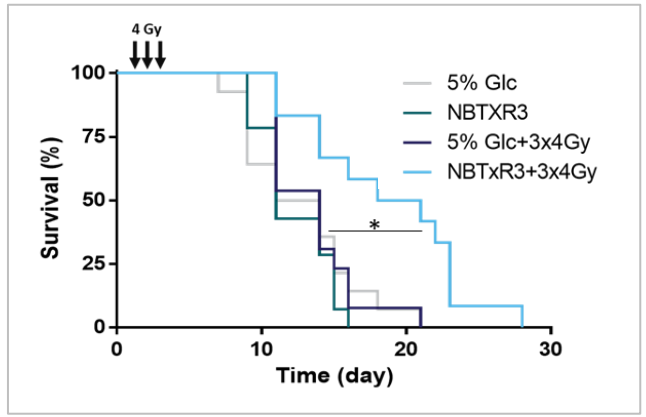


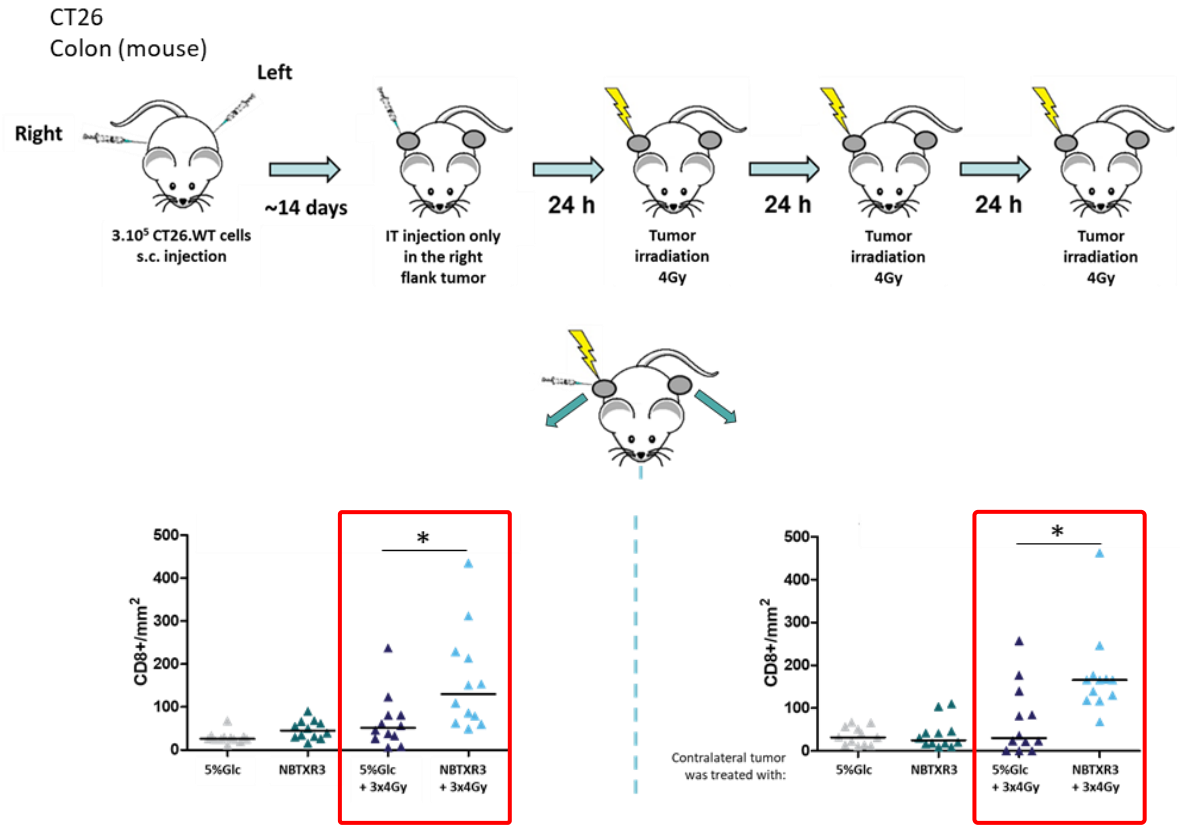
Treated



Untreated





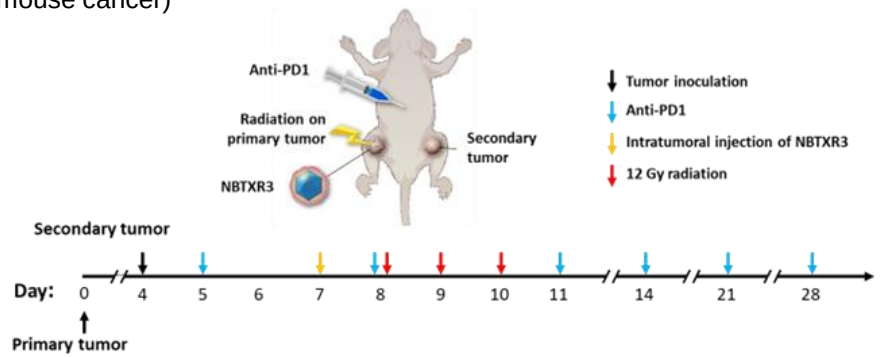


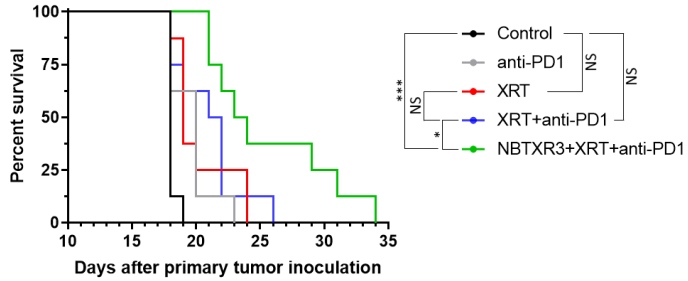
Zhang (2021) Int J Nanomedicine PMID: 33880022

NBTXR3 Overcomes Anti-PD-1 Resistance

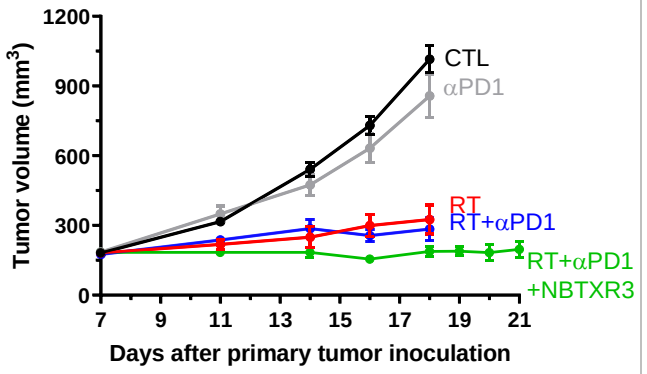
Combination with checkpoint inhibitors in anti-PD-1 resistant model

344SQR cells (lung mouse cancer)

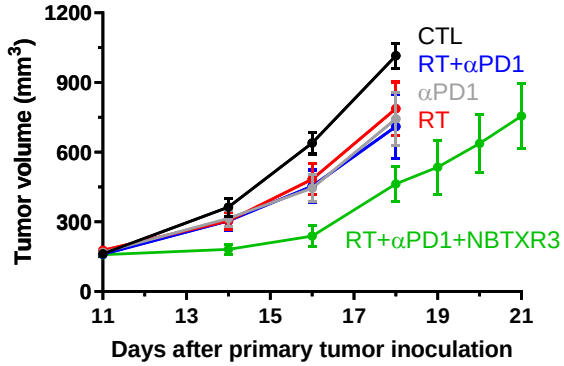


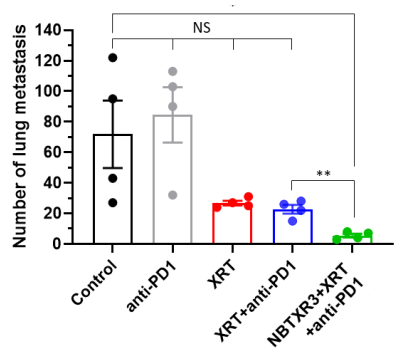


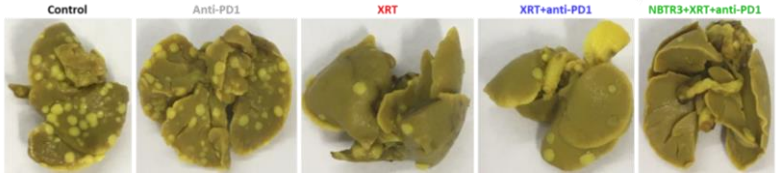
Treated



Untreated



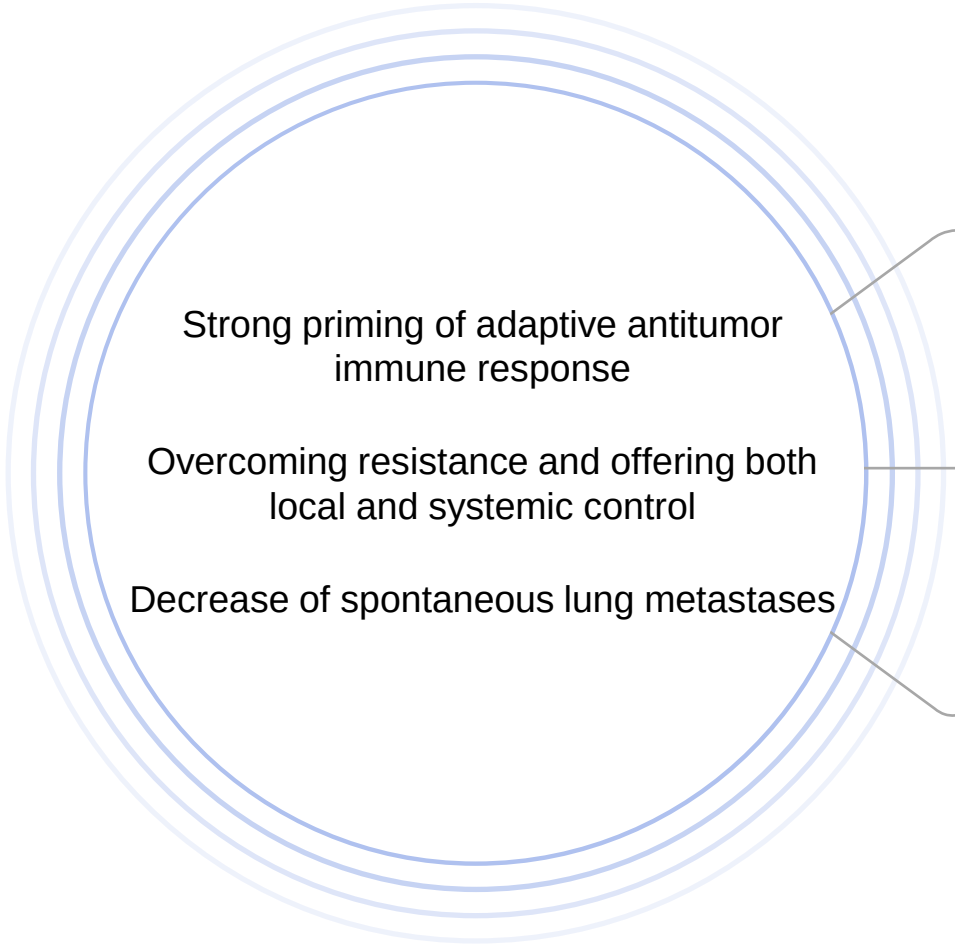




Hu et al. (2021) Int J Radiat Oncol Biol Phys. PMID: 34242713

NBTXR3 Overcomes Anti-PD1 Resistance

Combination with checkpoint inhibitors in anti-PD-1 resistant model



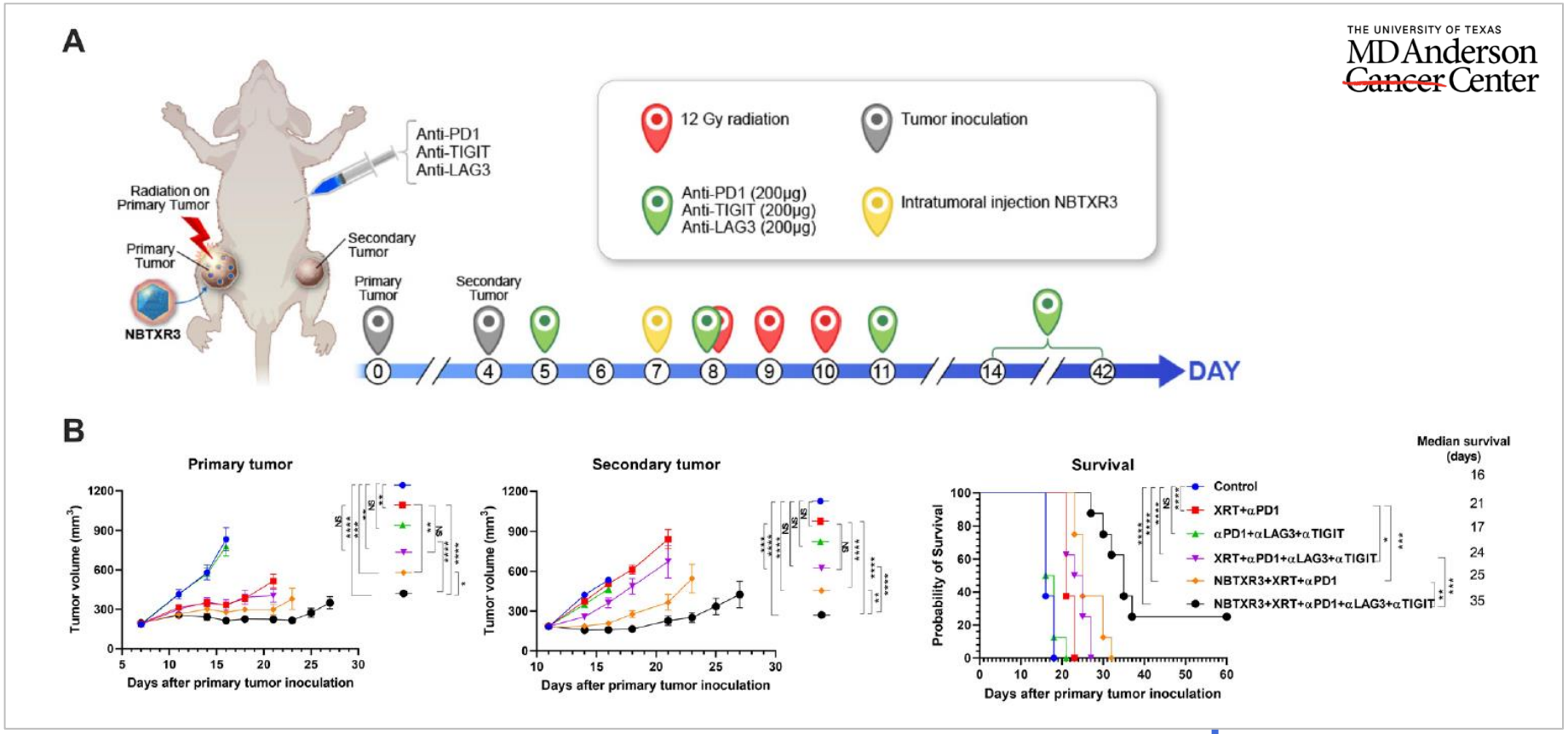
01 **Anti-PD-1 + anti-LAG3 + anti-TIGIT**
Hu (2022) J. Nanobiotech. PMID 36123677

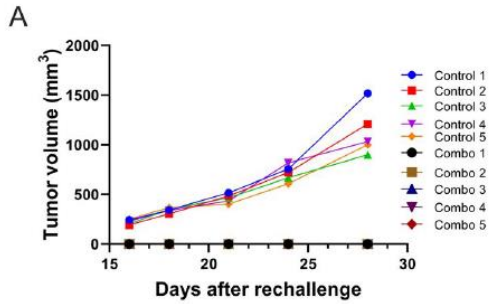
02 **Anti-PD-1 + anti-CTLA4**
Hu (2021) J Nanobiotechnology. PMID: 34895262

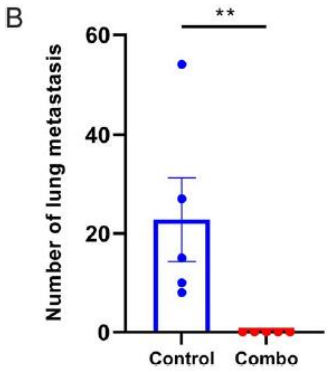
03 **Anti-PD-1 + NF-anti-CTLA4**
Hu (2022) Front. Immunol. PMID: 36405757

Efficient Antitumor Immune Response by NBTXR3 and CPIs Triggers Long Lasting Memory Response

Combination Anti-PD-1 + Anti-TIGIT + Anti-LAG3 in anti-PD-1 resistant model





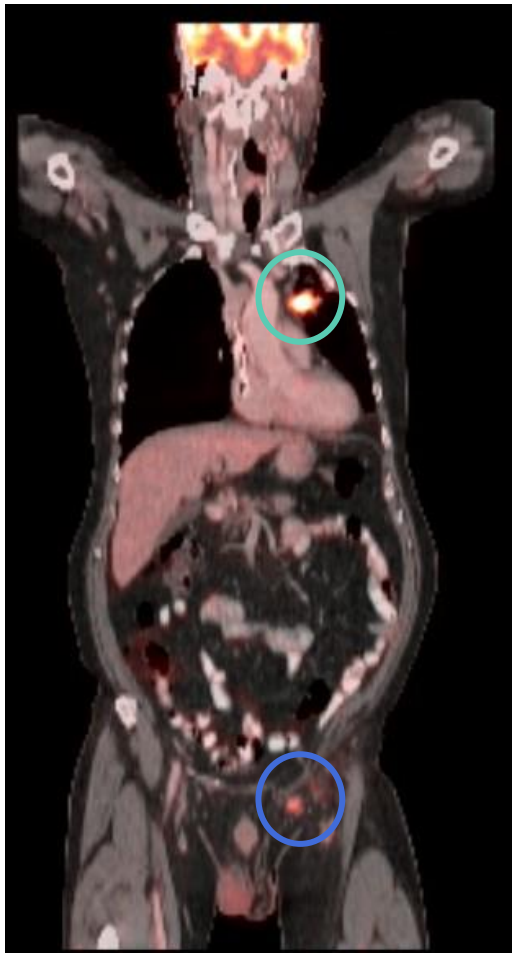


Hu (2022) J Nanobiotechnology PMID: 36123677

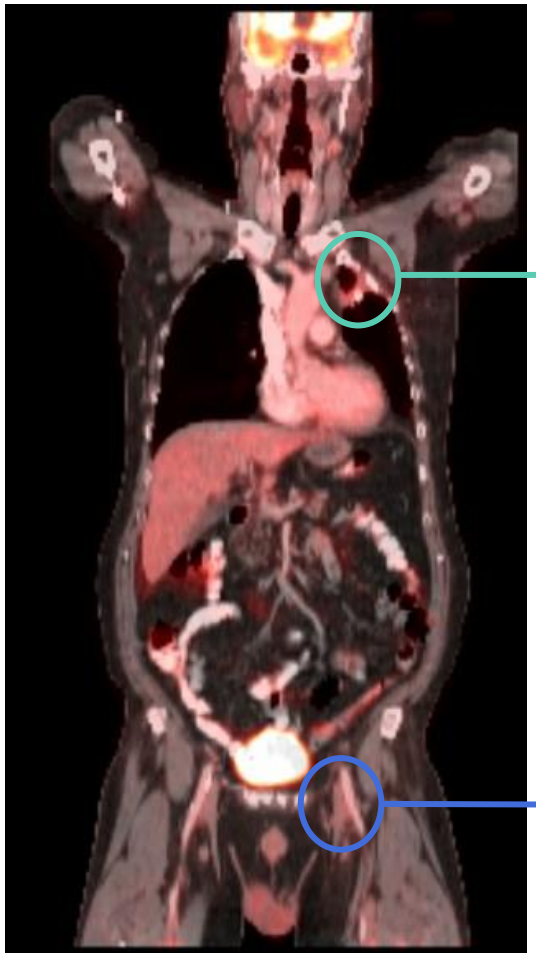
NBTXR3 Achieves Both Local & Systemic Control in PD-1 Refractory Patient

SITC 2022: Anti-PD-1 resistant patient case study

Patient progressing at enrollment after ~ 1-year anti-PD-1 treatment



PET Baseline



PET Follow-Up Visit 1

Target Lesion

PR in injected and irradiated tumor

Non-Target Lesion

CR in non-injected and non-irradiated distal lesion suggesting systemic response

AT THE FOREFRONT
UChicago Medicine

Challenges and Opportunities in Recurrent/Metastatic Head and Neck Cancer

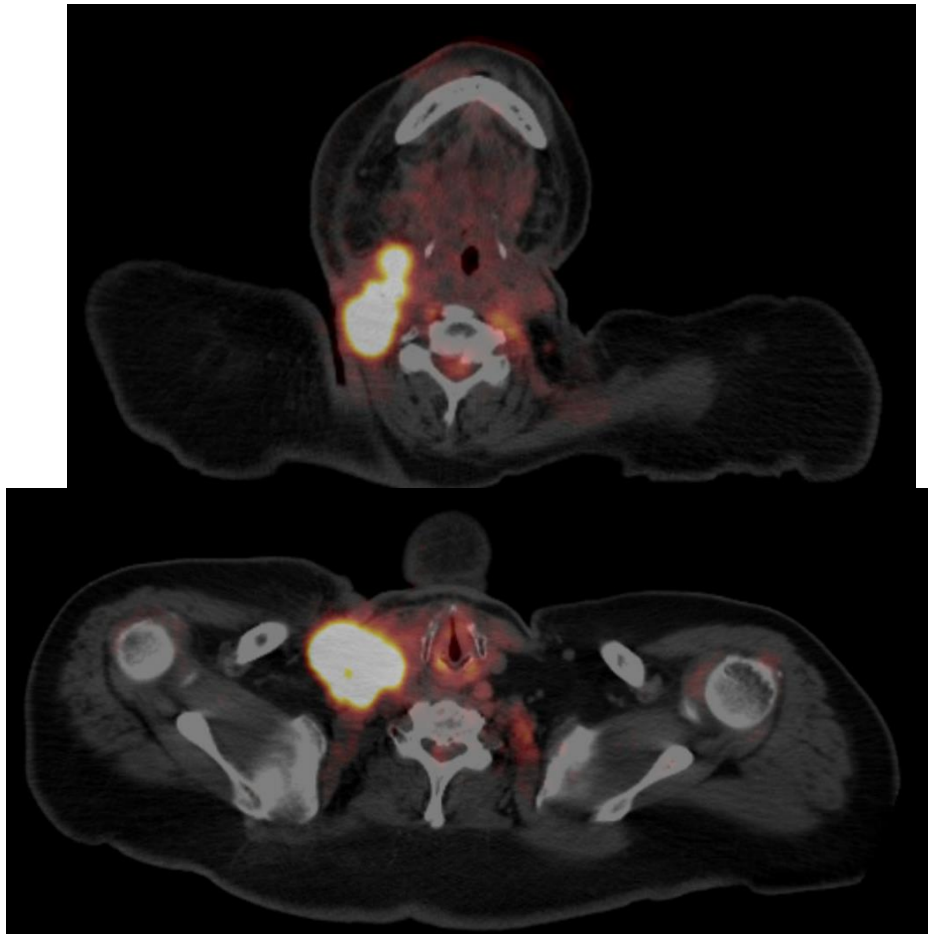
Ari Rosenberg, MD
Assistant Professor of Medicine
The University of Chicago

Disclosures

- Consulting/advisory: Galectin, Privo, Nanobiotix,
  EMD Serono, Vaccitech, Novartis, Eisai, Astellas, Regeneron, Coherus.
- Research funding: Hookipa, EMD Serono, Purple Biotech, BeiGene,
  BMS/Celgene, AbbVie, Nanobiotix, Seagen.

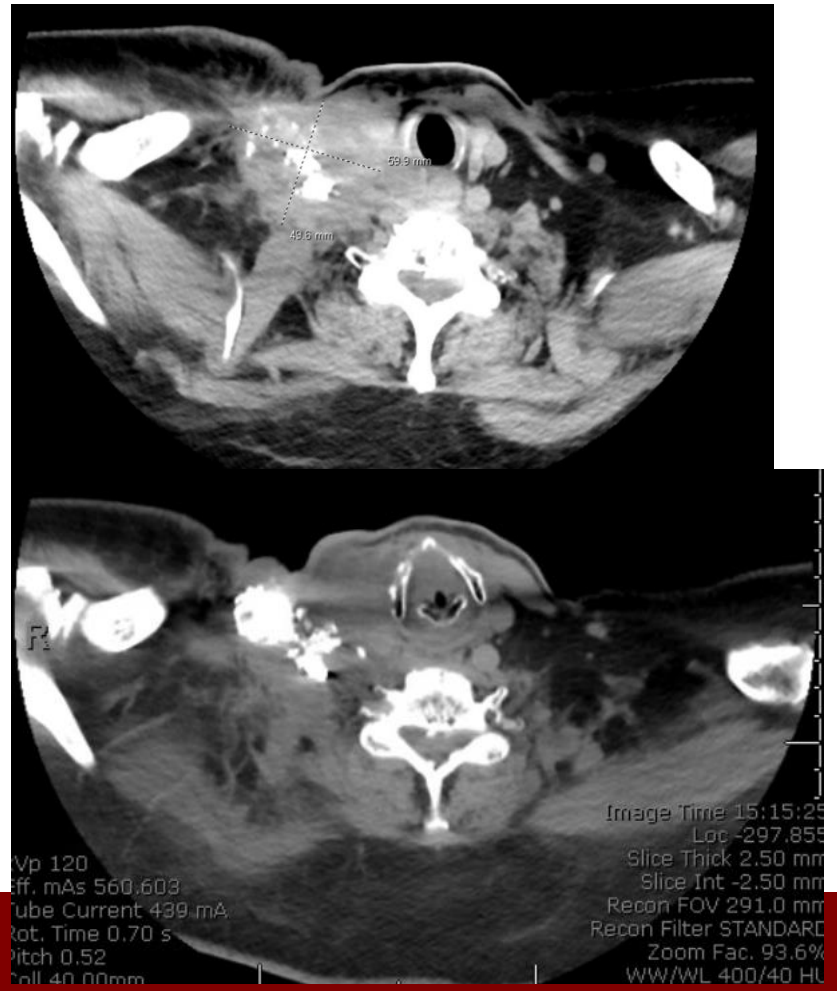
DJ: 68 yo W with recurrent HNSCC

- 2016: Diagnosed with T3N3 SCC of supraglottis treated with induction chemotherapy followed by chemoradiation (TFHX) and salvage neck dissection with pCR.
- 2020: Enlarging neck mass biopsy demonstrating SCC, PD-L1 CPS 0



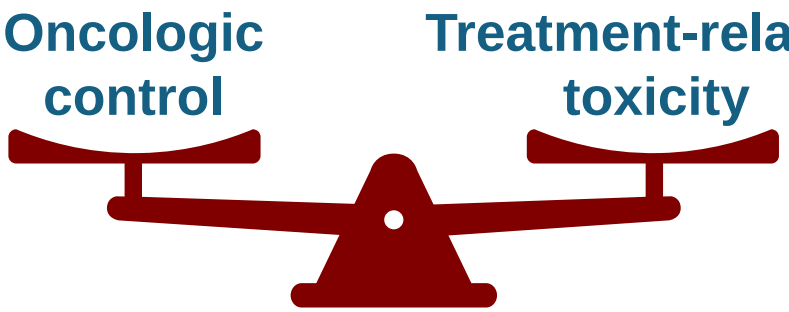
Disease regression with NBTXR3/SBRT/IO

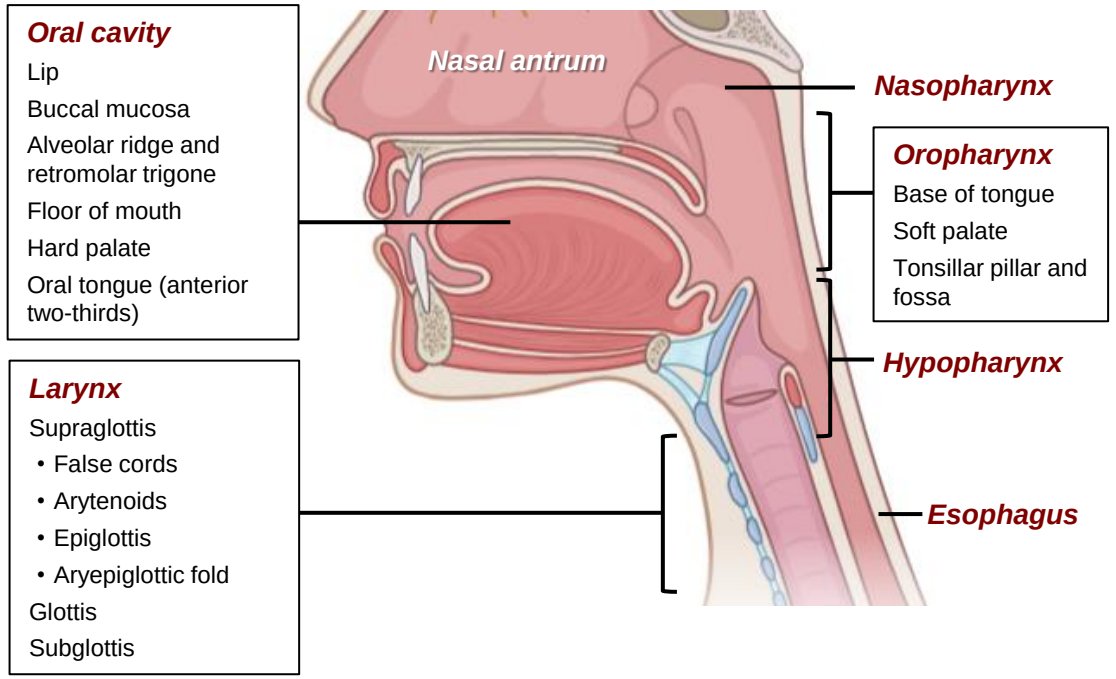
- Enrolled on 1100 study
- Injected with NBTXR3 -> SBRT -> Nivolumab
- Completed 2 years of IO treatment without disease progression



Patients with SCCHN are treated with curative intent minimizing toxicities and preserving organ function[1,2]

- Goals:
  - Cure
  - Function/QoL
- Treatment approaches:
  - Systemic therapy
  - Radiotherapy

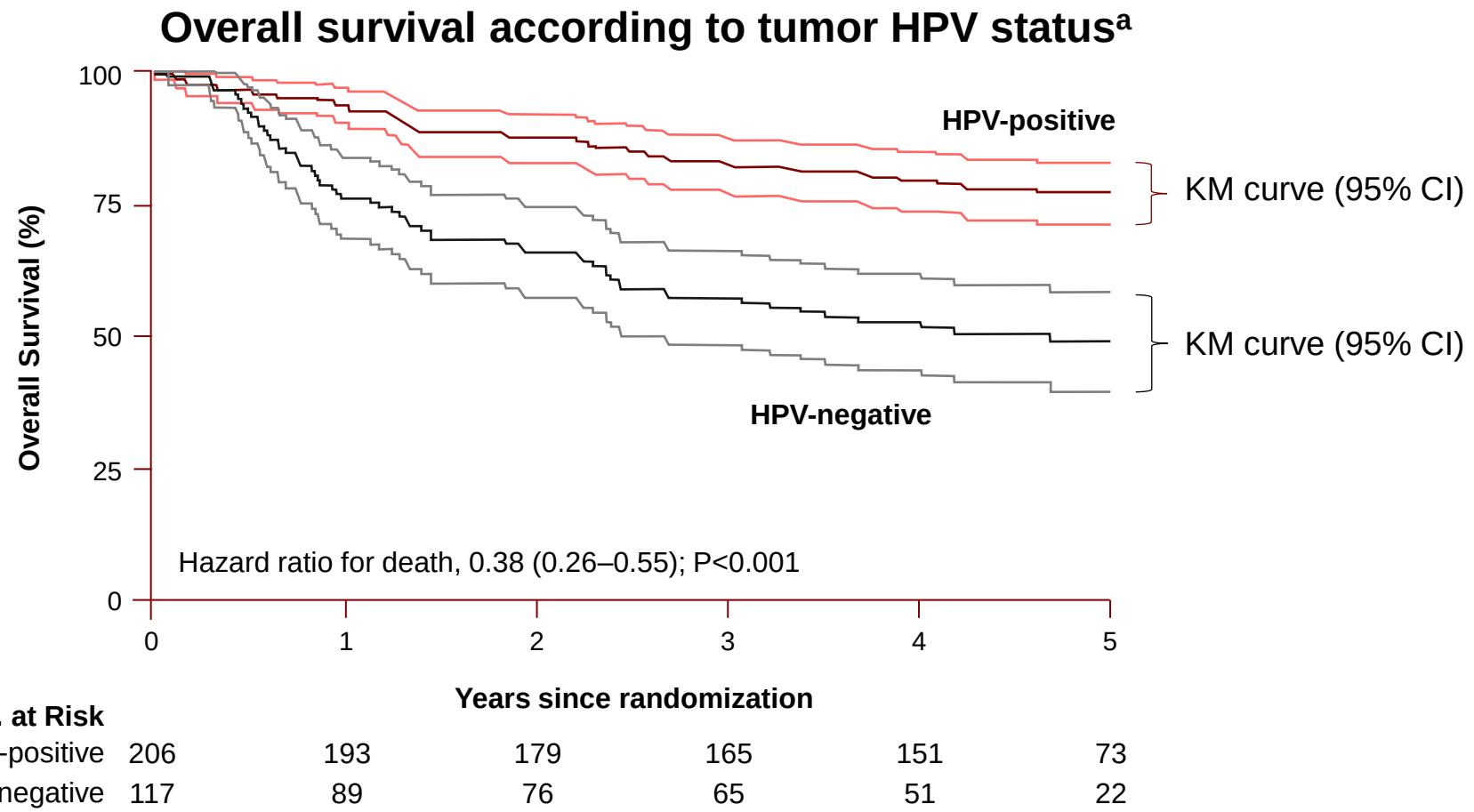




LA SCCHN, locally advanced squamous cell carcinoma of the head and neck; QoL, quality of life.

1. Machiels J-P. *Ann Oncol*. 2020;31(11):1462–1475; 2. Johnson DE et al. *Nat Rev Dis Primers*. 2020;6(1):92.

Despite curative-intent treatment, survival in patients with HPV-negative LA SCCHN is poor[1]



[a]p16-expression status.

CI, confidence interval; HPV, human papillomavirus; KM, Kaplan-Meier; LA SCCHN, locally advanced squamous cell carcinoma of the head and neck.

1. Ang KK, et al. *N Engl J Med.* 2010;363(1):24–35.

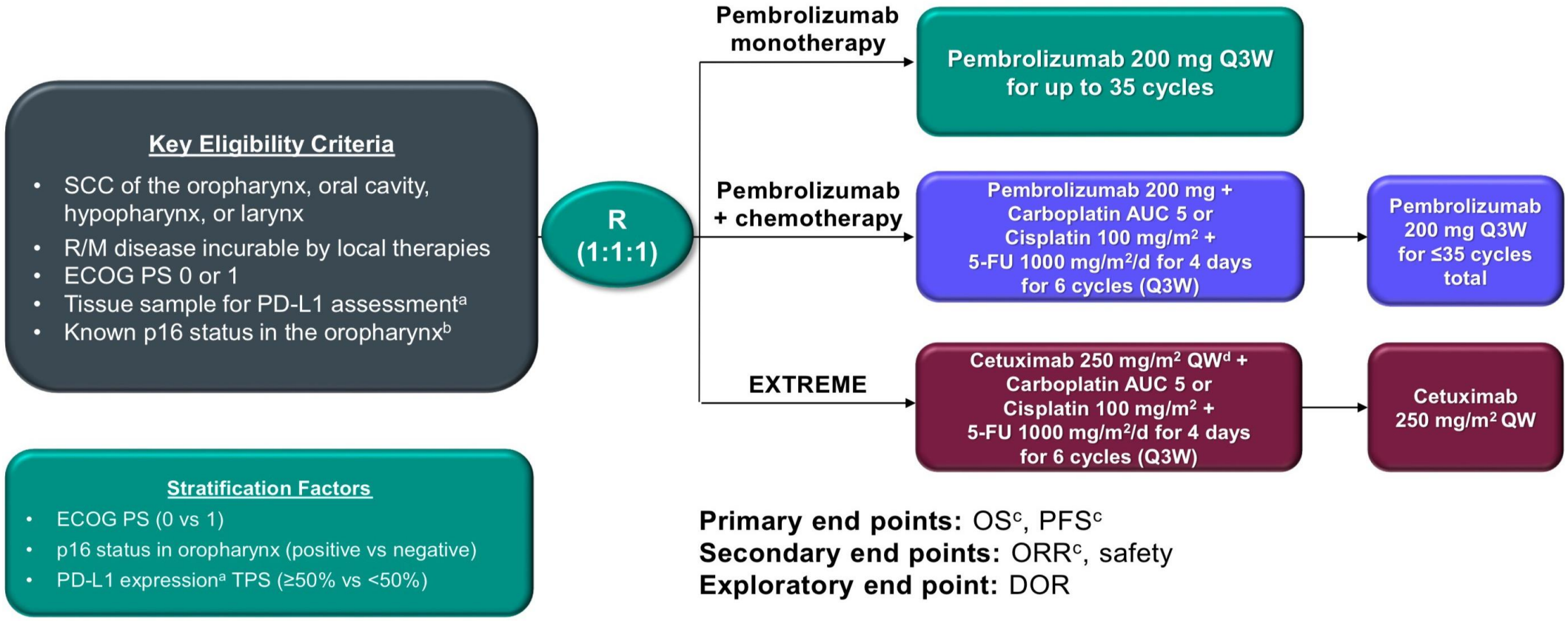
Standard of Care for Locoregionally Advanced HNSCC

- **Oral Cavity:** Surgery, +/- Radiation, +/- Chemo
- **Oropharynx:** Radiation + Chemotherapy vs TORS +/- Radiation and Chemotherapy
- **Larynx:** Radiation + Chemotherapy vs. Laryngectomy
- **Nasopharynx:** Chemotherapy + Radiation +/- induction (and/or adjuvant) chemotherapy (immunotherapy evolving role)
- **Definitive Radiation Dose** ~66-75 Gy
- **Adjuvant Radiation Dose** ~60-66 Gy Standard Chemotherapy - Cisplatin

Recurrent and/or Metastatic HNSCC is associated with poor survival

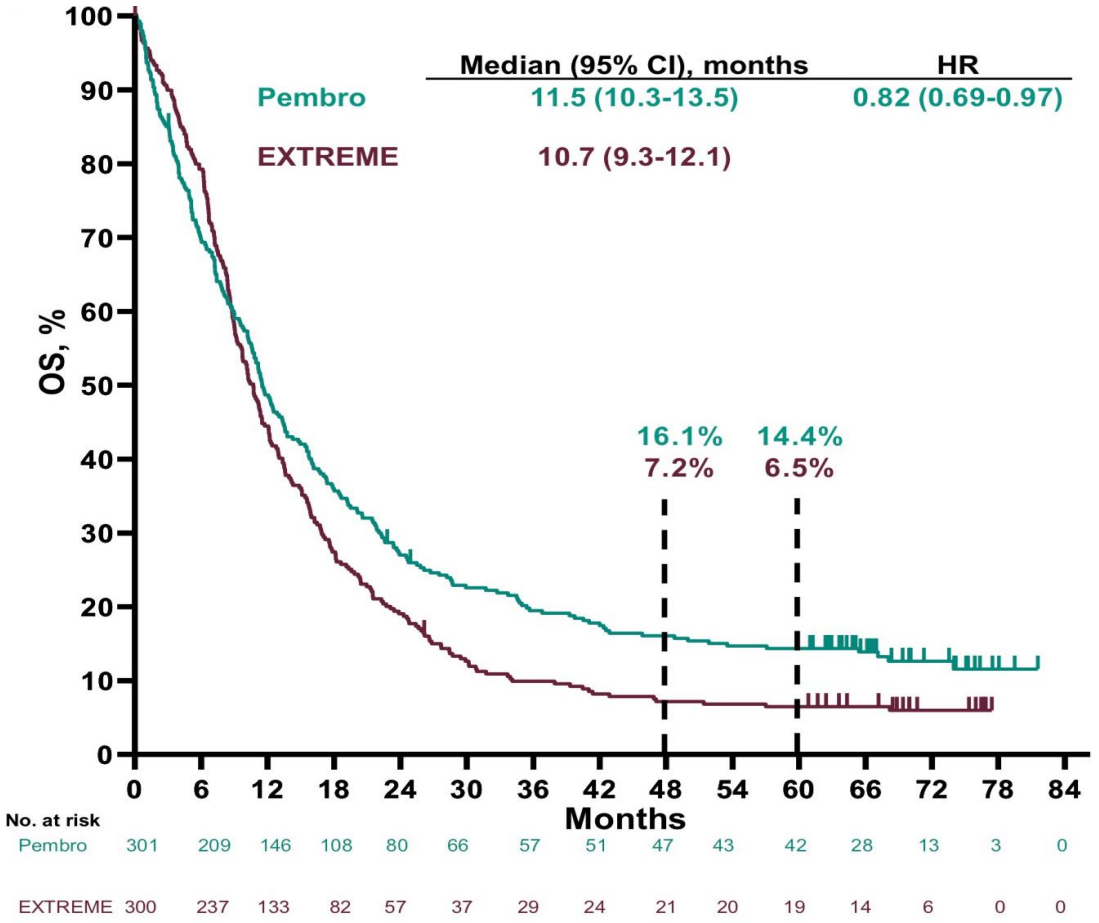
- Patients can develop locoregionally recurrent and/or distant metastatic disease
  - » Approximately 1/3 Locoregionally recurrent only
  - » ~1/3 Distant metastatic disease only
  - » ~1/3 both locoregionally recurrent and distant metastatic
- Median survival: ~11-13 months

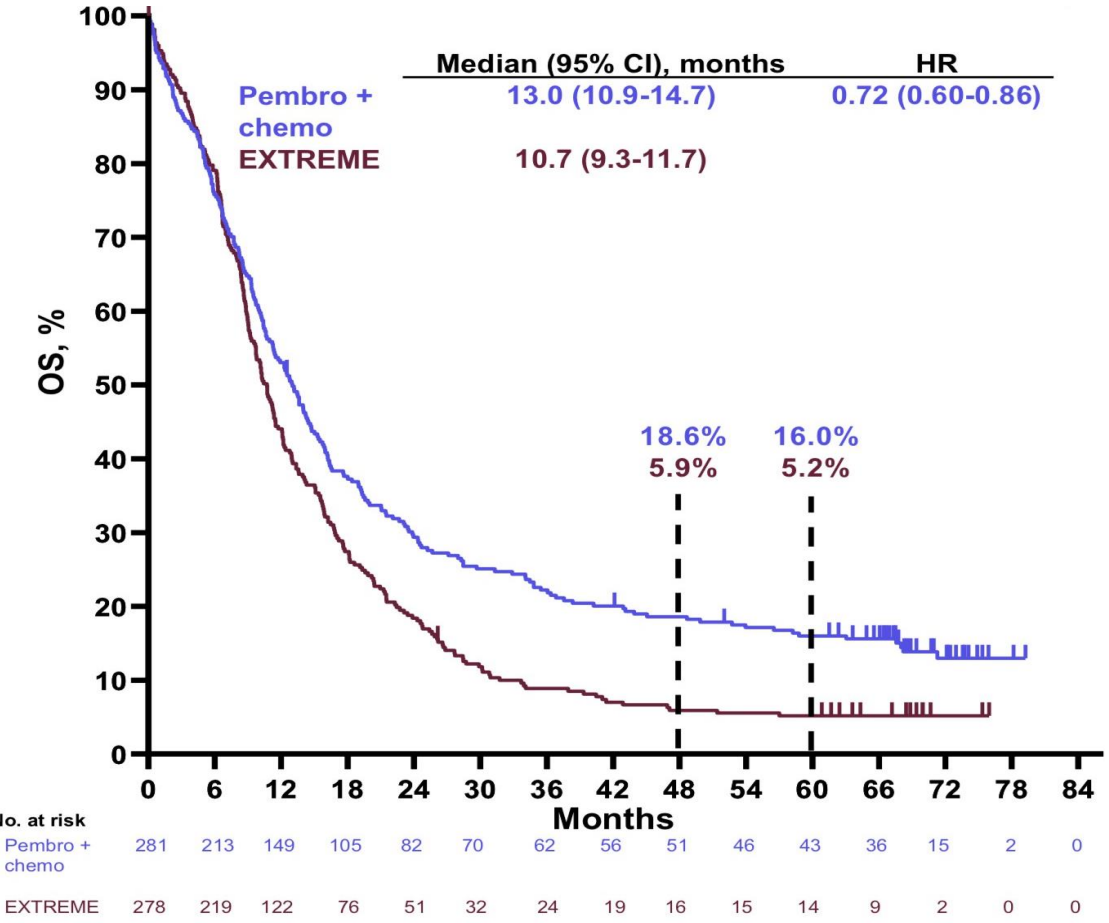
KEYNOTE048 – Study Design



Median follow-up was 69.2 mo (range, 61.2-81.6) for pembrolizumab versus EXTREME and 68.6 mo (range, 61.2-82.1) for pembrolizumab + chemotherapy versus EXTREME.
[a]Assessed using PD-L1 IHC 22C3 pharmDx (Agilent Technologies). TPS = percentage of tumor cells with membranous PD-L1 expression. [b]Assessed using the CINtec p16 histology assay (Ventana); cut point for positivity = 70%. [c]Analyzed in PD-L1 CPS ≥1, PD-L1 CPS ≥20, and total populations. [d]After a loading dose of 400 mg/m². Data cutoff date February 21, 2022.
Burtness B et al. *Lancet*. 2019;394:1915-1928.

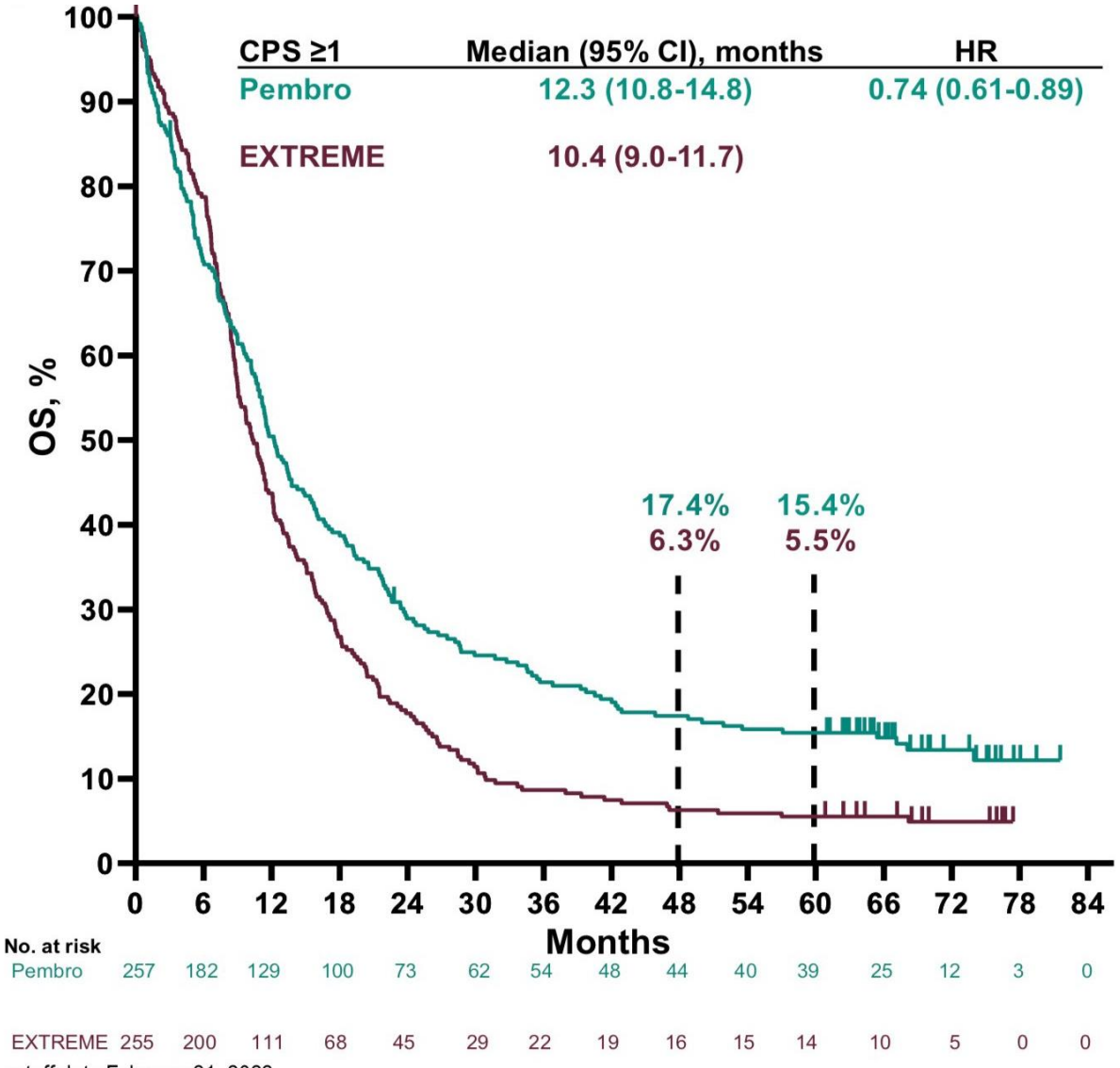
Overall Survival IIT Population

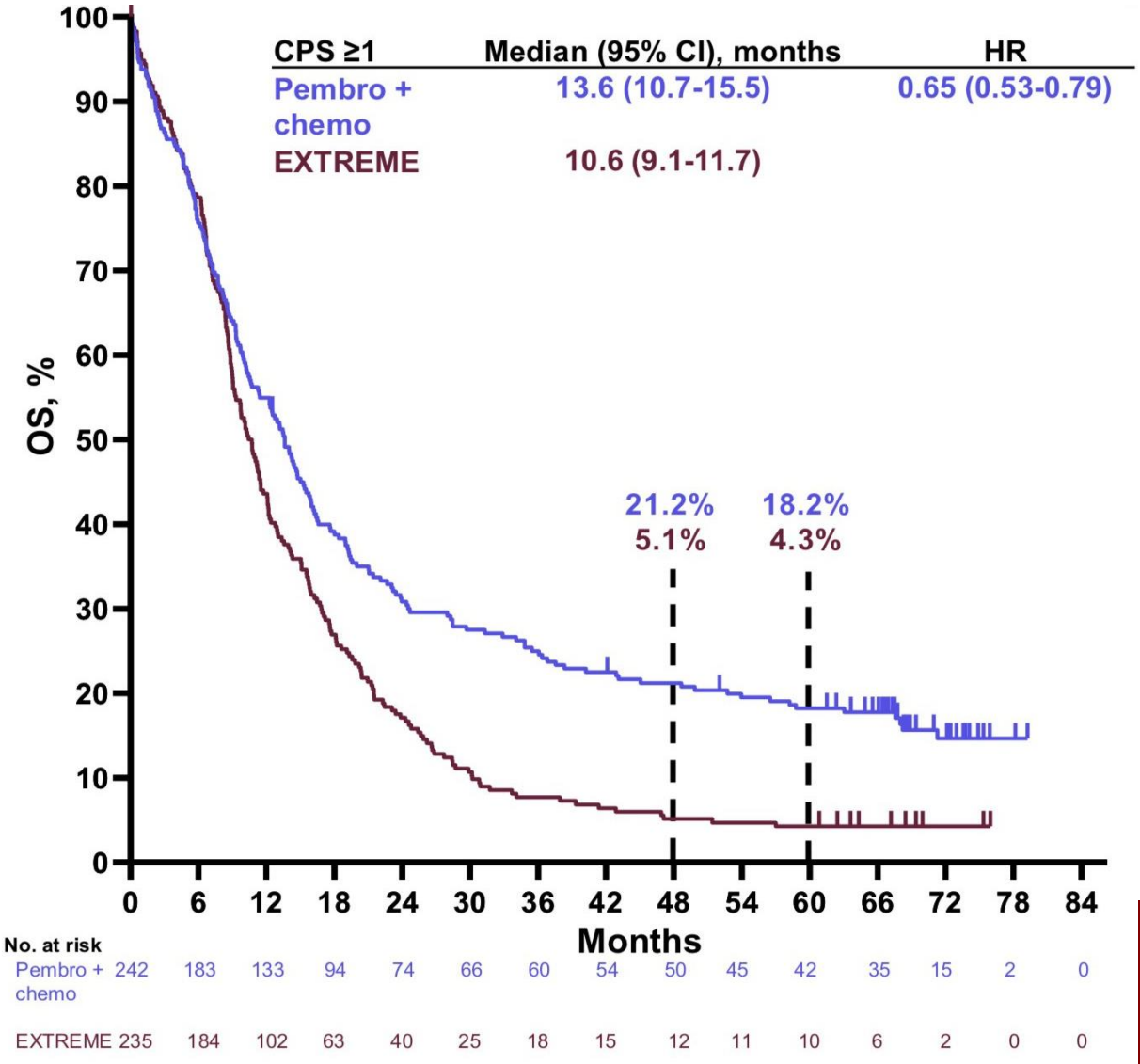




Data cutoff date February 21, 2022.

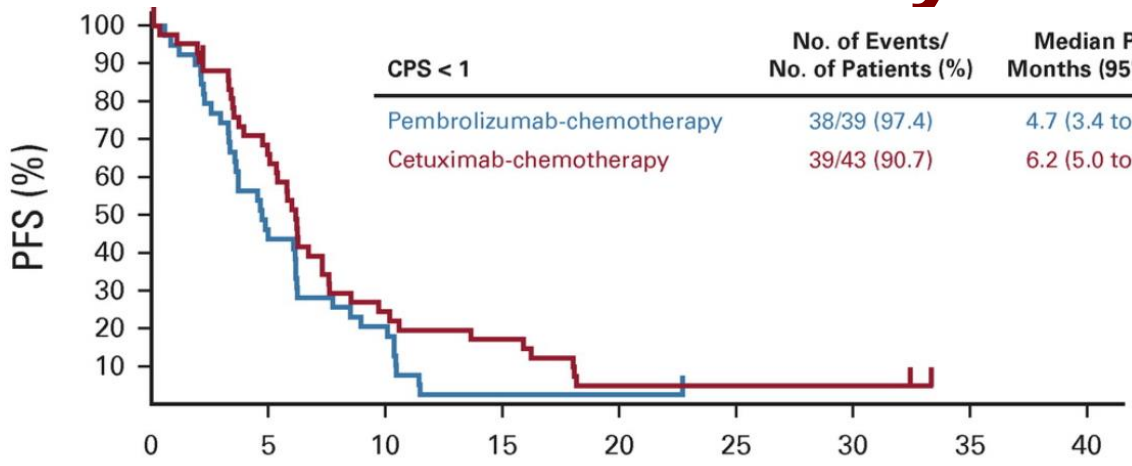
Overall Survival in PD-L1 CPS ≥ 1 Population





Data cutoff date February 21, 2022.

Benefit to pembrolizumab in PD-L1 negative less clear: Keynote-048 subset analysis



CPS < 1	No. of Events/ No. of Patients (%)	Median PFS, Months (95% CI)[a]	HR (95% CI)[b]	Nominal *P*[c]
Pembrolizumab-chemotherapy	38/39 (97.4)	4.7 (3.4 to 6.2)	1.46 (0.93 to 2.30)	.94898
Cetuximab-chemotherapy	39/43 (90.7)	6.2 (5.0 to 7.3)		

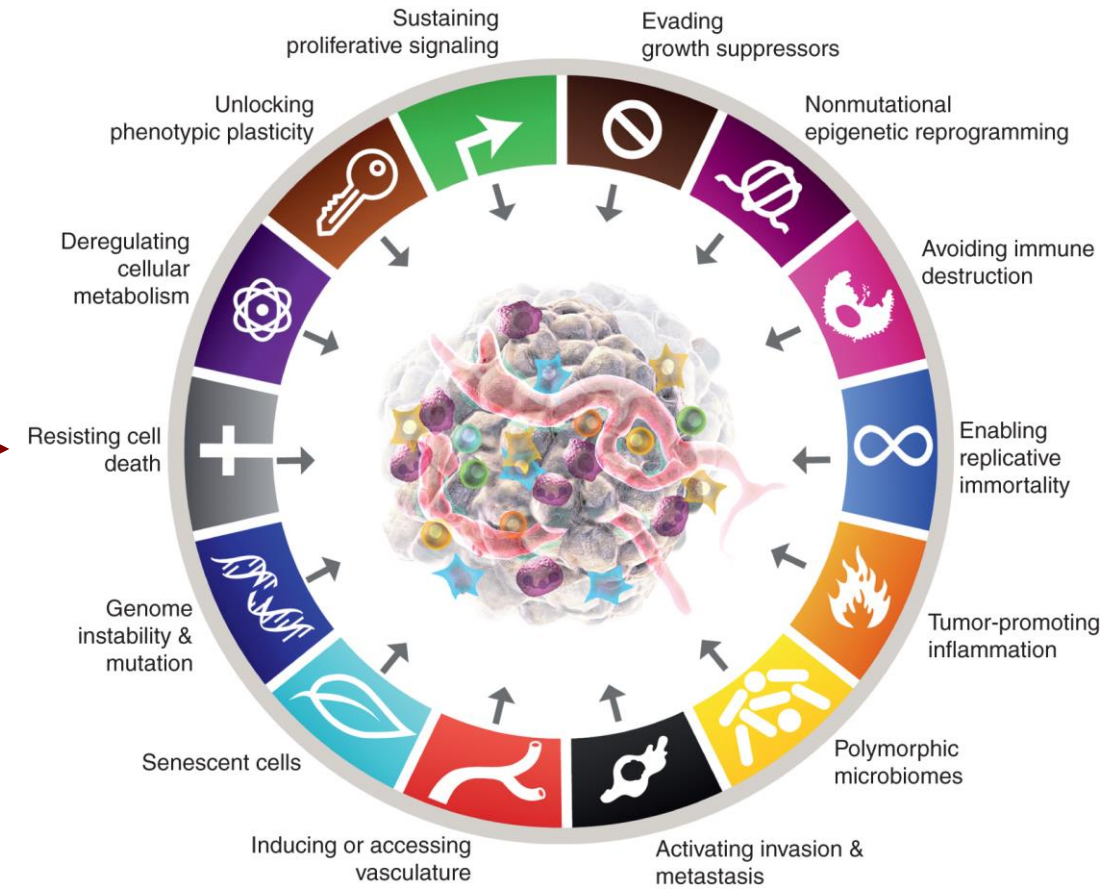
	PD-L1 CPS < 1				PD-L1 CPS 1-19			
	Pembrolizumab Versus Cetuximab-Chemotherapy		Pembrolizumab-Chemotherapy Versus Cetuximab-Chemotherapy[a]		Pembrolizumab Versus Cetuximab-Chemotherapy		Pembrolizumab-Chemotherapy Versus Cetuximab-Chemotherapy[a]	
Confirmed Best Objective Response	Pembrolizumab (n = 44)	Cetuximab-Chemotherapy (n = 45)	Pembrolizumab-Chemotherapy (n = 39)	Cetuximab-Chemotherapy (n = 43)	Pembrolizumab (n = 124)	Cetuximab-Chemotherapy (n = 133)	Pembrolizumab-Chemotherapy (n = 116)	Cetuximab-Chemotherapy (n = 125)
Objective response[b]								
No. (%)	2 (4.5)	19 (42.2)	12 (30.8)	17 (39.5)	18 (14.5)	45 (33.8)	34 (29.3)	42 (33.6)
95% CI	0.6 to 15.5	27.7 to 57.8	17.0 to 47.6	25.0 to 55.6	8.8 to 22.0	25.9 to 42.5	21.2 to 38.5	25.4 to 42.6
CR, No. (%)	(0)	1 (2.2)	1 (2.6)	1 (2.3)	4 (3.2)	3 (2.3)	4 (3.4)	3 (2.4)
PR, No. (%)	2 (4.5)	18 (40.0)	11 (28.2)	16 (37.2)	14 (11.3)	42 (31.6)	30 (25.9)	39 (31.2)
SD, No. (%)	10 (22.7)	18 (40.0)	14 (35.9)	18 (41.9)	32 (25.8)	41 (30.8)	35 (30.2)	39 (31.2)
Progressive disease, No. (%)	22 (50.0)	4 (8.9)	6 (15.4)	4 (9.3)	58 (46.8)	21 (15.8)	23 (19.8)	20 (16.0)
Non-CR/non-PD, No. (%)	3 (6.8)	0 (0)	2 (5.1)	0 (0)	3 (2.4)	5 (3.8)	7 (6.0)	4 (3.2)
Not evaluable or assessed, No. (%)	7 (15.9)	4 (8.9)	5 (12.8)	4 (9.3)	13 (10.5)	21 (15.8)	17 (14.7)	20 (16.0)

Burtness et al. JCO 2022.

Standard of Care Treatment approach in R/M HNSCC

- Front-line treatment
  - » **PD-L1 CPS≥1**: Pembrolizumab +/- chemotherapy
  - » **PD-L1 CPS <1**: Pembro+chemo or Cetuximab+chemo
  - » Chemotherapy: Platinum+5-FU or Platinum+Taxane
- Subsequent-line treatment (regardless of PD-L1)
  - » Cetuximab +/- chemotherapy
  - » Pembrolizumab +/- chemotherapy
- Radiation: Palliative role

Resisting cell death and avoidance of immune destruction are key hallmarks of cancer[1]



Immune-activating mAb

Radiation Enhancement

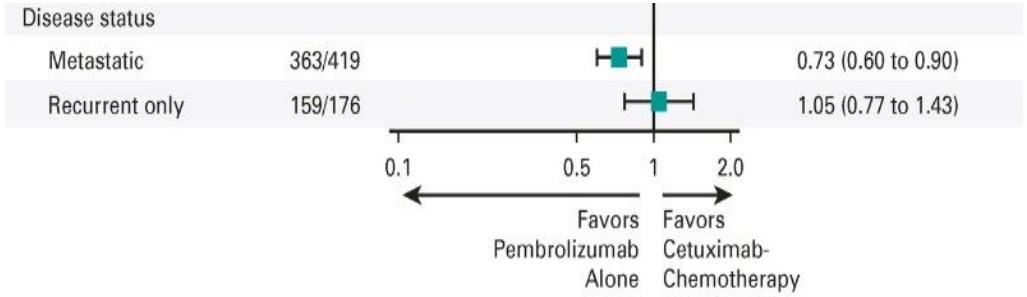
AT THE FOREFRONT
UChicagoMedicine

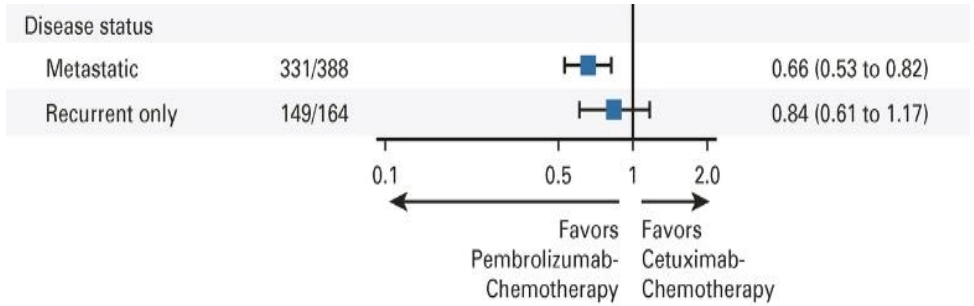
mAb, monoclonal antibody.

1. Hanahan D. *Cancer Discov.* 2022;12(1):31–46.

Unmet need and opportunities

- Locoregionally recurrent disease is associated with substantial morbidity and very difficult to treat
- Novel combinations with pembrolizumab in PD-L1 enriched
- Novel treatment approach post-IO and platinum treatment failure
- Multimodality treatment approaches in R/M HNSCC setting





Conclusions

- Approximately ½ of pts with locoregionally advanced disease treated with curative intent will ultimately recur
- Survival is poor for recurrent/metastatic disease
- Locoregionally recurrent disease is a unique challenge with substantial morbid impact on function and QoL
- Opportunities for novel multimodality treatment approach to improve pt outcomes

NBTXR3 in R/M HNSCC, the 1100 Study –

Colette Shen, MD, PhD

2024 **ASCO** Annual Meeting

Abstract #6035

Early signs of efficacy in patients with anti-PD-1 naïve and anti-PD-1 resistant HNSCC treated with NBTXR3/SBRT in combination with nivolumab or pembrolizumab in the phase I trial Study 1100

Colette Shen[1], Jessica Frakes[2], Trevor Hackman[1], Jiaxin Niu[3], Jared Weiss[1], Jimmy Caudell[2], George Yang[2], Tanguy Seiwert[4], Paul Chang[5], Septimiu Murgu[5], Siddharth Sheth[1], Shetal Patel[1], Kedar Kirtane[2], David Rolando[6], Pavel Tyan[6], Omar I. Vivar[6], Zhen Gooi[5], Aditya Joolori[5], Ari Rosenberg[5]

[1]University of North Carolina School of Medicine, Chapel Hill, North Carolina, USA; [2]Moffitt Cancer Center, Tampa, Florida, USA; [3]Banner MD Anderson Cancer Center, Gilbert, Arizona, USA; [4]Johns Hopkins Medicine, Baltimore, Maryland, USA; [5]The University of Chicago, Chicago, Illinois, USA; [6]Nanobiotix, SA, Paris, France

Disclosures

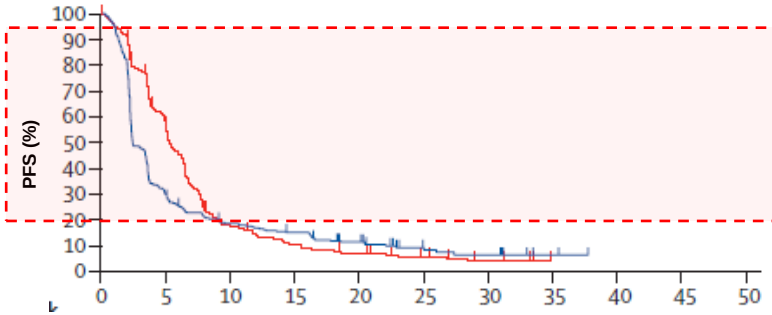
- Consulting: Nanobiotix, Johnson & Johnson, GT Medical Technologies
- Research funding: AstraZeneca

Outcomes Remain Limited for Patients Treated With Anti-PD-1 in 1st, 2nd or Further Lines of treatment: PFS is Short and Many Patients do not Respond

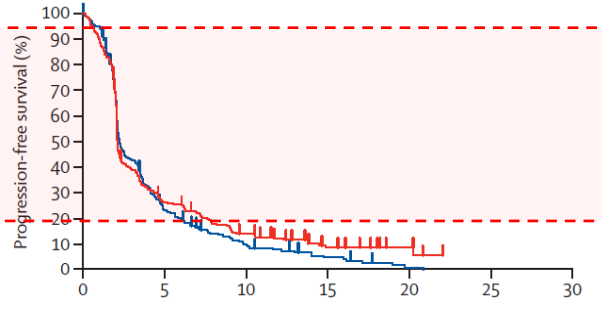
Anti-PD-1 treatment as 1st line of treatment

Anti-PD-1 treatment as 2nd or further line of treatment

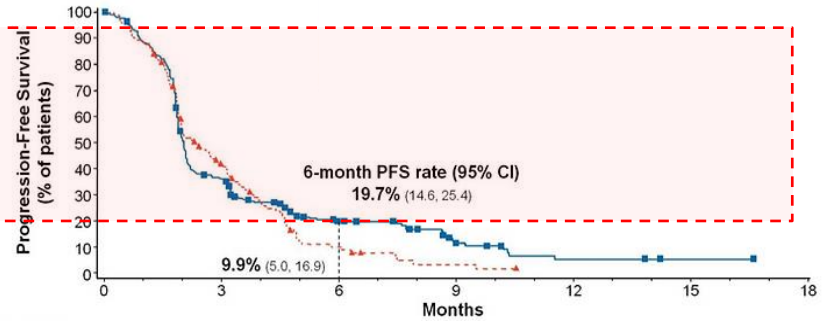
KEYNOTE 048[3] – PFS (all population)



KEYNOTE 040[1] – PFS (all population)



CHECKMATE-141[2] – PFS (all treated)



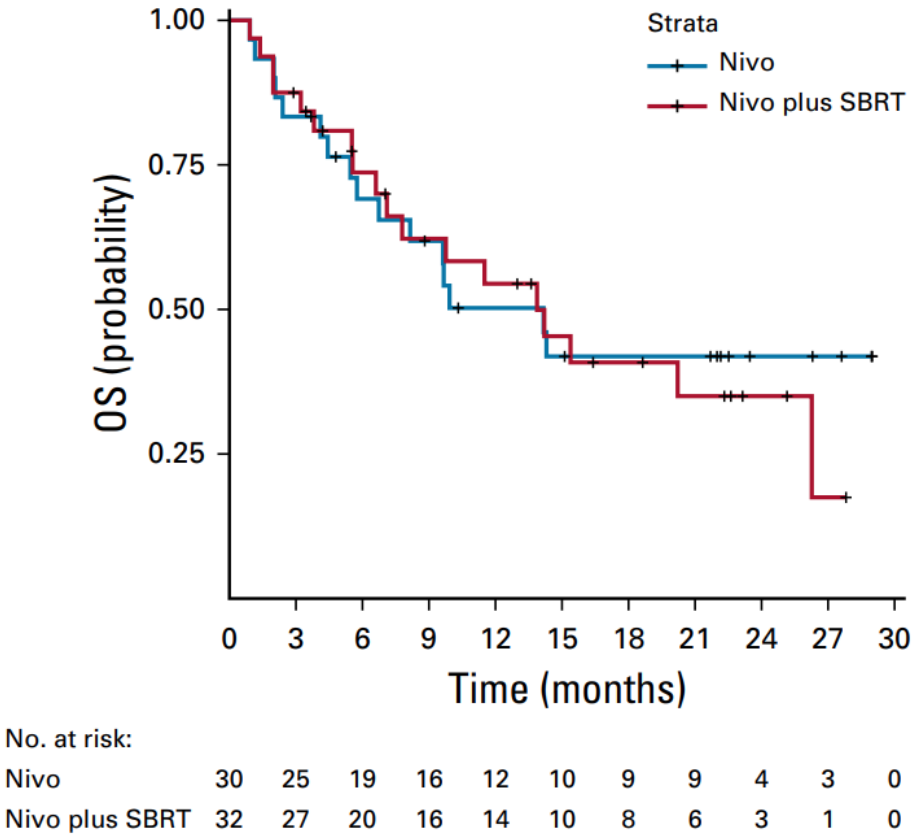
Primary and secondary non-responders to anti-PD-1 treatment

[1] Cohen E. et al, Lancet, 2018; [2] Ferris R. et al, NEJM 2016; [3] Burtness B. et al, Lancet, 2019

MSKCC Phase 2 Trial Exploring Nivolumab vs Nivolumab + SBRT

Addition of RT to nivolumab does not improve OS in anti-PD-1 naïve patients

Overall Survival



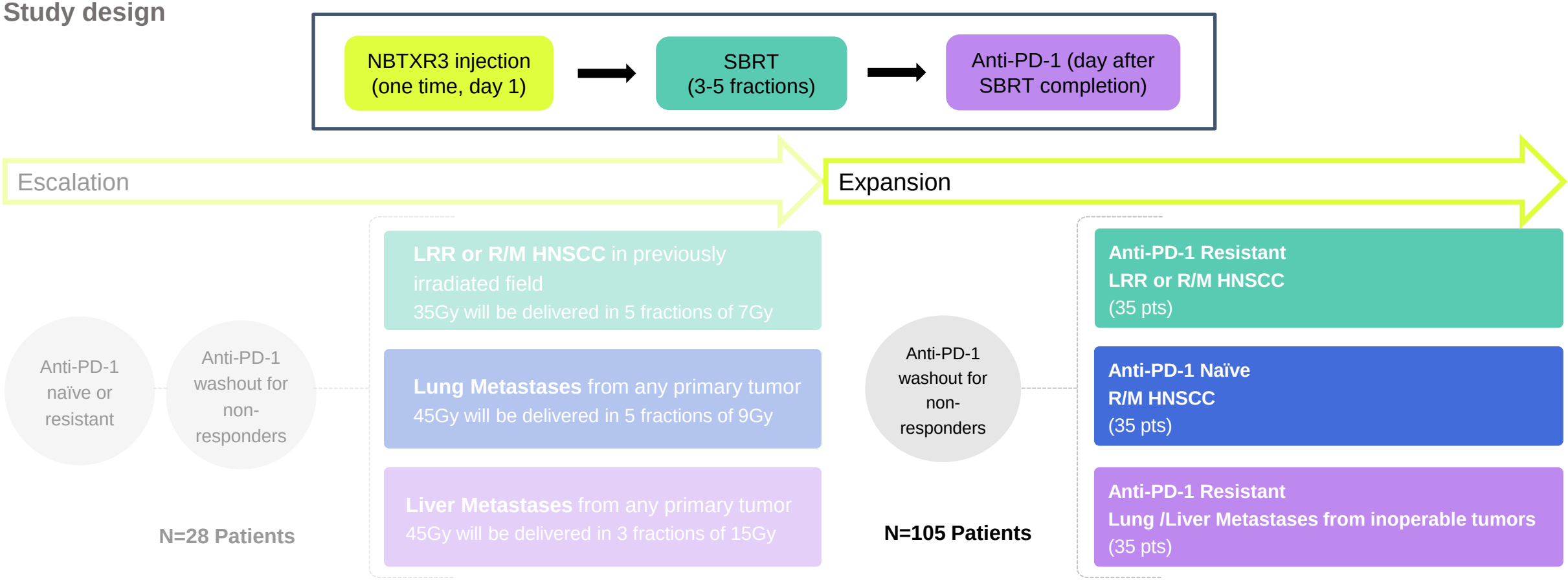
By providing local control and priming an immune response with NBTXR3 + RT, a goal of the 1100 study is to explore whether NBTXR3 + SBRT + anti-PD-1 can:

1. Improve responses and deepness of immune responses for patients naive to anti-PD-1
2. Reverse resistance to anti-PD-1 for refractory patients

McBride S. et. al. JCO 2020

Study 1100 Potential Immunotherapy Combination

Study design



Endpoints

Primary:
Recommended Phase 2 Dose
Secondary:
ORR, Safety and Feasibility, and Body-Kinetics
Exploratory:
Survival Outcomes, Duration of Response, and Biomarkers of Response

Primary:
Further assess the safety profile of RP2D(s)
Secondary:
Evaluate the safety, feasibility, and anti-tumor response of RT-activated NBTXR3 in combination with anti-PD-1
Exploratory:
Survival Outcomes, Duration of Response, Biomarkers of Response, and response in non-injected (target and non-target) lesion(s)

Baseline Characteristics of R/M HNSCC Patients in Study 1100

	ICI Naïve N=33	ICI Resistant N=35	All N=68
Age (years)			
Missing	0	0	0
n	33	35	68
Mean (SD)	64.1 (8.6)	63.5 (9.5)	63.8 (9.0)
Median	63.0	64.0	63.5
Min ; Max	46 ; 80	45 ; 85	45 ; 85
ECOG Performance status			
Missing	1	0	1
n	32	35	67
0	13 (40.6)	16 (45.7)	29 (43.3)
1	17 (53.1)	19 (54.3)	36 (53.7)
2	2 (6.3)		2 (3.0)
Prior anti-PD-1			
Missing	5	3	8
n	28	32	60
Yes	2 (7.1) [(1)]	32 (100)	34 (56.7)
No	26 (92.9)		26 (43.3)
Number of prior treatment lines			
Missing	5	4	9
n	28	31	59
1-2	25 (89.3)	11 (35.5)	36 (61.0)
3-4	2 (7.1)	12 (38.7)	14 (23.7)
5+		8 (25.8)	8 (13.6)

	ICI Naïve N=33	ICI Resistant N=35	All N=68
Number of lesions			
Missing	4	1	5
n	29	34	63
1	10 (34.5)	7 (20.6)	17 (27.0)
2-3	12 (41.4)	7 (20.6)	19 (30.2)
4+	7 (24.1)	20 (58.8)	27 (42.9)
HPV status			
Missing	1	0	1
n	32	35	67
Negative	17 (53.1)	13 (37.1)	30 (44.8)
Positive	11 (34.4)*	18 (51.4)**	29 (43.3)
Unknown	4 (12.5)	4 (11.4)	8 (11.9)
Smoking status			
Missing	0	0	0
n	33	35	68
Former smoker	16 (48.5)	22 (62.9)	38 (55.9)
Nonsmoker	8 (24.2)	10 (28.6)	18 (26.5)
Current smoker	9 (27.3)	3 (8.6)	12 (17.6)
Combined Positive Score (CPS) testing (%)			
Missing	17	9	26
n	16	26	42
< 1%		4 (15.4)	4 (9.5)
[1%-20%]	12 (75.0)	11 (42.3)	23 (54.8)

* 10 ICI naïve patients have Oropharynx cancer and HPV+
** 12 ICI resistant patients have Oropharynx cancer and HPV+

[(1)] Two patients were included approximately two years after having finished ICI therapy as part of definitive/adjuvant therapy: one patient received 4 month Durvalumab treatment, one patient received 10 month nivolumab treatment.

Safety – Few Treatment Emergent Adverse Events (TEAE) Related to NBTXR3

Confirmed safety profile of NBTXR3 activated by RT in both ICI naive and ICI resistant patients

	ICI Naïve N=33 Patients (%) [AEs]	**ICI Resistant** N=35 Patients (%) [AEs]	**All treated** N=68 Patients (%) [AEs]
All TEAEs	24 (72.7) [122]	31 (88.6) [221]	55 (80.9) [343]
Grade ≥ 3 TEAEs:			
related to NBTXR3	1 (3.0) [2] [1]	1 (2.9) [1] [1]	2 (2.9) [3]
related to injection procedure	2 (6.1) [2]	2 (5.7) [2] [1]	4 (5.9) [4]
related to radiotherapy	1 (3.0) [1]	6 (17.1) [6] [1]	7 (**10.3**) [7]
TEAEs related to anti-PD-1	2 (6.1) [5] [1]	2 (5.7) [2]	4 (5.9) [7]
Grade ≥ 3 Serious TEAEs related to radiotherapy or injection procedure or anti-PD-1 or NBTXR3, or a combination	3 (9.1) [5] [1,2]	3 (8.6) [3]	6 (**8.8**) [8]

[1] *Same TEAEs reported several times in each category by investigators due to multiple causalities*

[2] *1 patient experienced Grade 5 pneumonitis related to anti-PD-1 and possibly to NBTXR3; this patient did not receive injection in the lungs*

- A single NBTXR3 intra-tumoral injection followed by SBRT activation was safe and feasible
- Less than 10% of Grade ≥ 3 serious TEAEs related to NBTXR3, injection procedure, radiotherapy or anti-PD-1
- Approximately 10% of Grade ≥ 3 TEAEs were related to radiotherapy, which is in line with reported data
- No unexpected side effect emerged related to radiotherapy/NBTXR3 or anti-PD-1 or injection procedure

AE occurrences are grouped in episodes when there is a chronologic continuity and no change in relationship to NBTXR3, injection, radiotherapy, anti-PD-1, disease or other
Patients = number of patients with at least one TEAE and AEs = number of events.
Events are considered treatment related when reported as 'Possibly related' or 'Related' to NBTXR3, injection procedure, radiotherapy and/or anti-PD-1

Efficacy
Patients Naïve to Anti-PD-1

1100 Data Update (Ongoing study)

Baseline Characteristics of R/M HNSCC Patients Naïve to Anti-PD-1

Similar population as in the Keynote 040 (pembrolizumab) and CheckMate-141 (nivolumab)^

33 patients treated evaluable for safety

25 evaluable for efficacy at the cutoff date

Heavy tumor burden

CPS score

- 75% of patients* **below 20%**

HPV status:

- 10 patients* with oropharynx with HPV+ status among the 33 patients

Number of lesions	ICI Naive (N=33)
Missing	4
n	29
1	10 (**34.5**)
2-3	12 (**41.4**)
4+	7 (**24.1**)

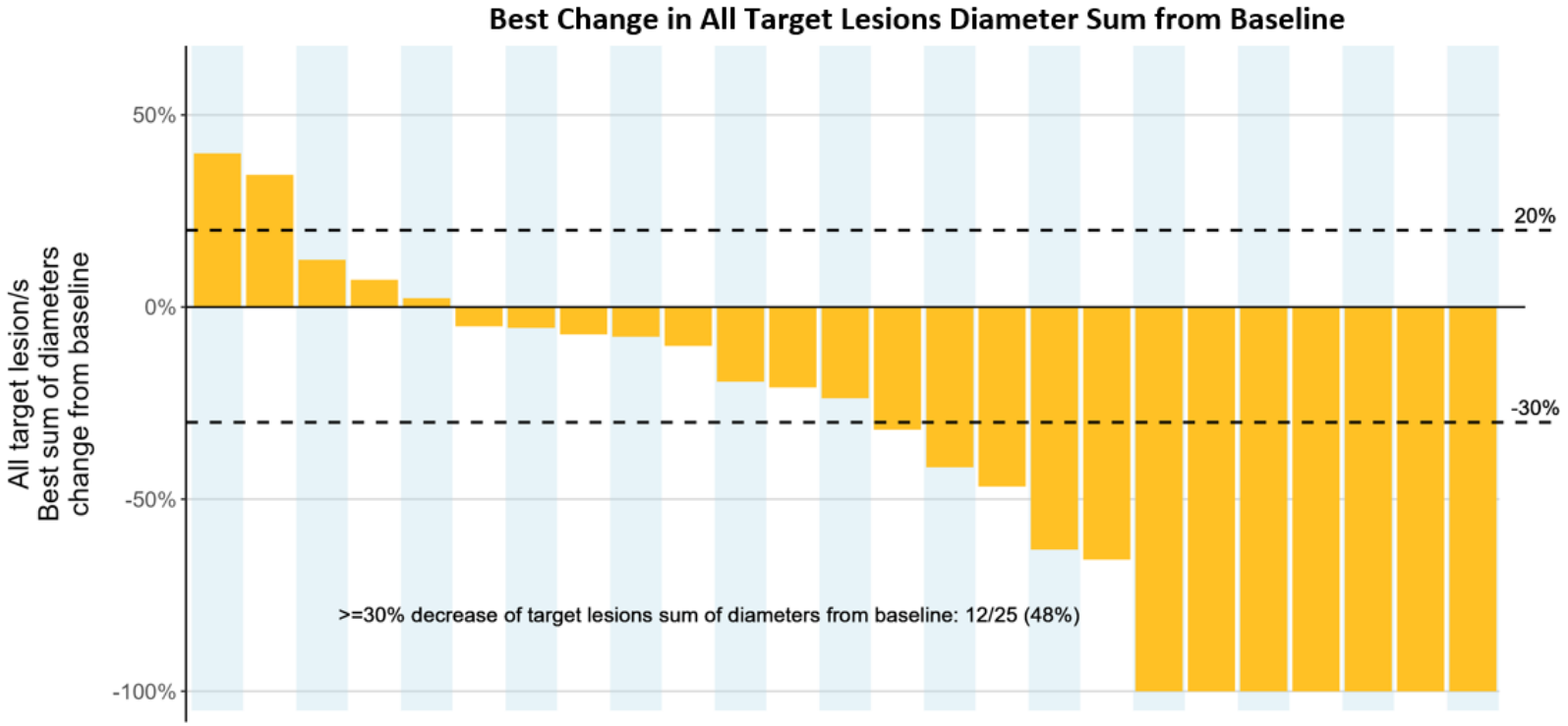
Number of prior treatment lines	ICI Naive (N=33)
Missing	5
n	28
1-2	25 (**89.3**)
3-4	2 (**7.1**)

**among available data at cutoff*

^Note: Study 1100 is a ph. I trial assessing safety as primary endpoint and exploring signals of efficacy as secondary endpoints. The sample size is small, and the trial is ongoing – some of the efficacy data will mature as new data come in.

Best Change in Diameter Sum From Baseline and RECIST Response

ICI Naïve, Evaluable Patients (N=25)



Overall Response (RECIST 1.1)	ICI Naive N=25
Complete Response	3 (12.0)
ORR (CR + PR)	**12 (48.0)**
95% CI	[27.8 - 68.7]
Median duration (days)(1))	54.0
DCR (CR + PR + SD)	**19 (76.0)**
95% CI	[54.9 - 90.6]
Median duration (days)(2)	65.0

(1) Number of days from first to last RECIST assessment with CR or PR
(2) Number of days from first to last RECIST assessment with CR, PR or SD
Best overall response have been derived as single best overall response observed for 11 subjects, either ongoing or with missing data (1 CR, 7 PR, 3 SD and 0 PD)

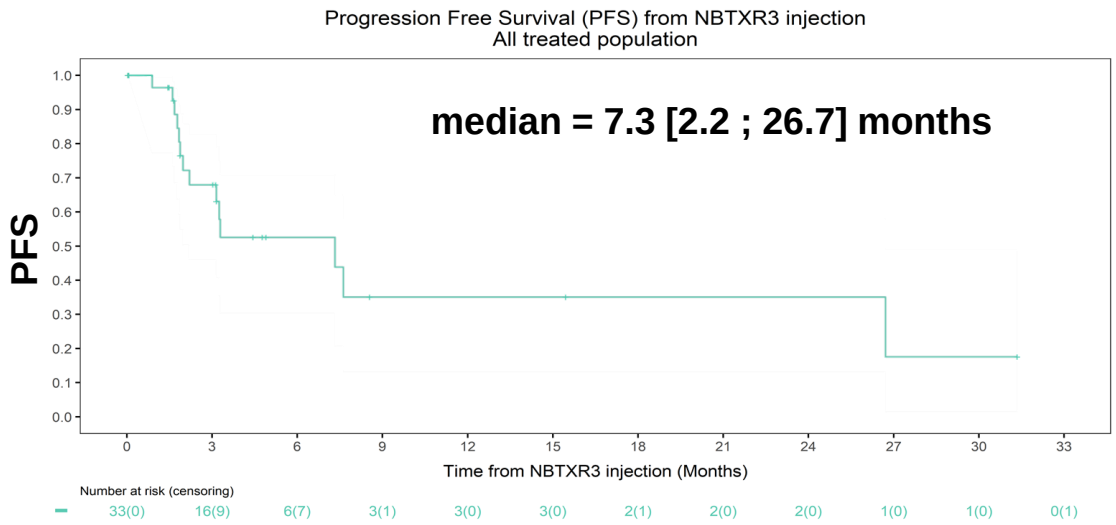
Systemic Control in anti-PD-1 naïve patients with high disease burden
(24% of patients have 4+ lesions; 66% have 2+ lesions)

Progression Free Survival (PFS) and Overall Survival (OS)

All treated R/M HNSCC ICI Naïve patients

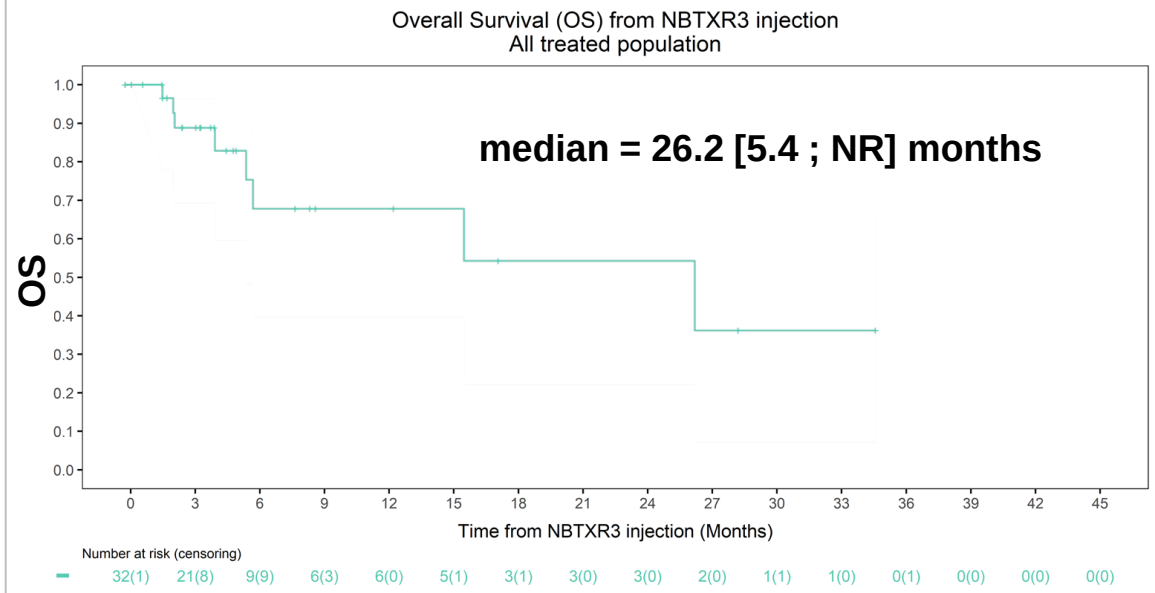
PFS from NBTXR3 injection

All treated population (N=33)



OS from NBTXR3 injection

All treated population (N=32)*



** Ongoing query related to survival data for 1 patient: censored at T = 0 month.*

Illustration / Response and Survival Results for Study 1100 and Reference Studies Keynote 040 and Checkmate-141

ICI-Naïve patient population

	1100 Study – Naïve to Anti-PD-1		Keynote 040	CheckMate-141
	All Treated: N=33 evaluable for efficacy: N=25		**Pembrolizumab** N=247	**Nivolumab** N=240
Response	***All target*** *(N=25)* 48%	***ORR*** *(N=25)* 48%	***ORR*** 14.6%	***ORR*** 13.3%
PFS	7.3 [2.2 ; 26.7] months *(N=33)**		2.1	2.0
OS	26.2 [5.4 ; NR] months *(N=33)**		8.4	7.5

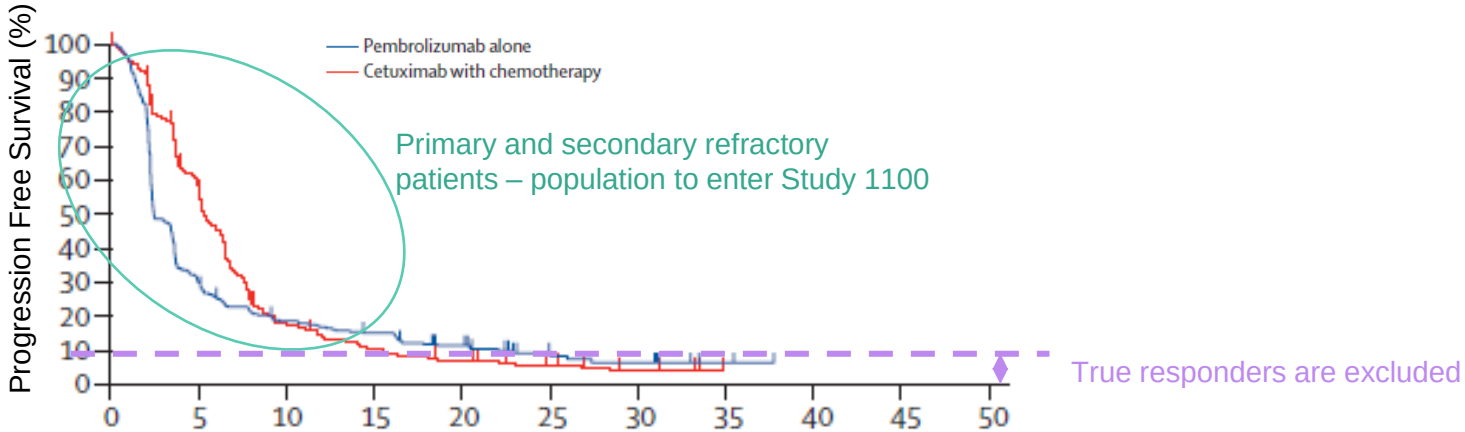
** Ongoing trial – PFS and OS expected to mature with new data coming in*

Efficacy
Patients Resistant to Anti-PD-1

1100 Data Update (Ongoing study)

1100 Study – Treatment of Anti-PD-1 Resistant Patient Population

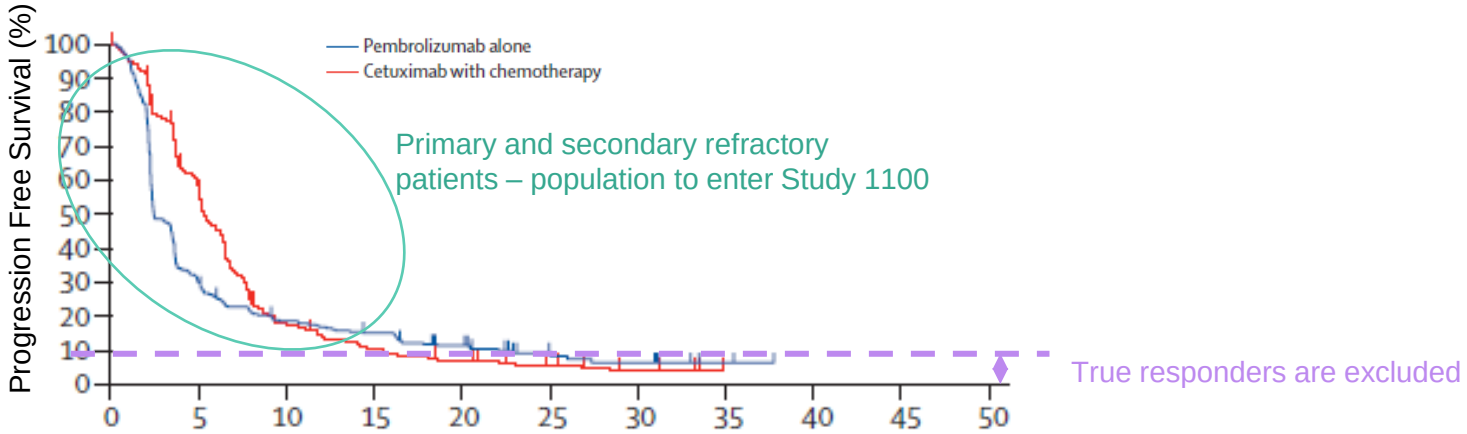
83% of H&N resistant patients entered the 1100 study after having been recorded in progression in their last treatment line
17% have unknown status before entering the study, but supposed to be considered as in progression

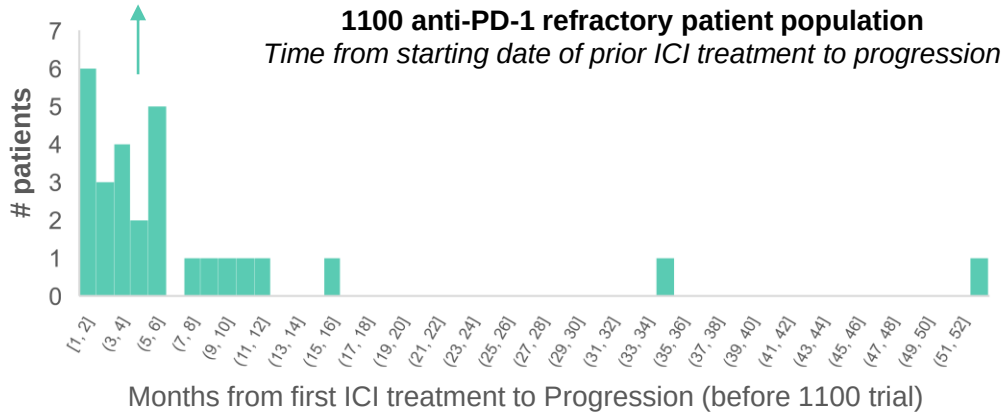


ASCO 2024 data *Ongoing trial: data are subject to change*

1100 Study – Treatment of Anti-PD-1 Resistant Patient Population

83% of H&N resistant patients entered the 1100 study after having been recorded in progression in their last treatment line
17% have unknown status before entering the study, but supposed to be considered as in progression





ASCO 2024 data *Ongoing trial: data are subject to change*

Baseline Characteristics of R/M HNSCC Patients Resistant to Anti-PD-1

35 patients treated evaluable for safety

25 evaluable for efficacy at the cutoff date

83% of patients entered the 1100 study « in progression » in their last treatment line (17% have unknown status but supposed to be in progression (not recorded yet))

Heavy tumor burden

Highly pre-treated patients

CPS score

- 15% of patients* have a CPS score < 1%
- 58% of patients* below 20%

HPV status:

- 12 patients* with oropharynx with HPV+ status among the 35 patients

Number of lesions	ICI Resistant (N=35)
Missing	1
n	34
1	7 (**20.6**)
2-3	7 (**20.6**)
4+	20 (**58.8**)

Number of prior treatment lines	ICI Resistant (N=35)
Missing	4
n	31
1-2	11 (**35.5**)
3-4	12 (**38.7**)

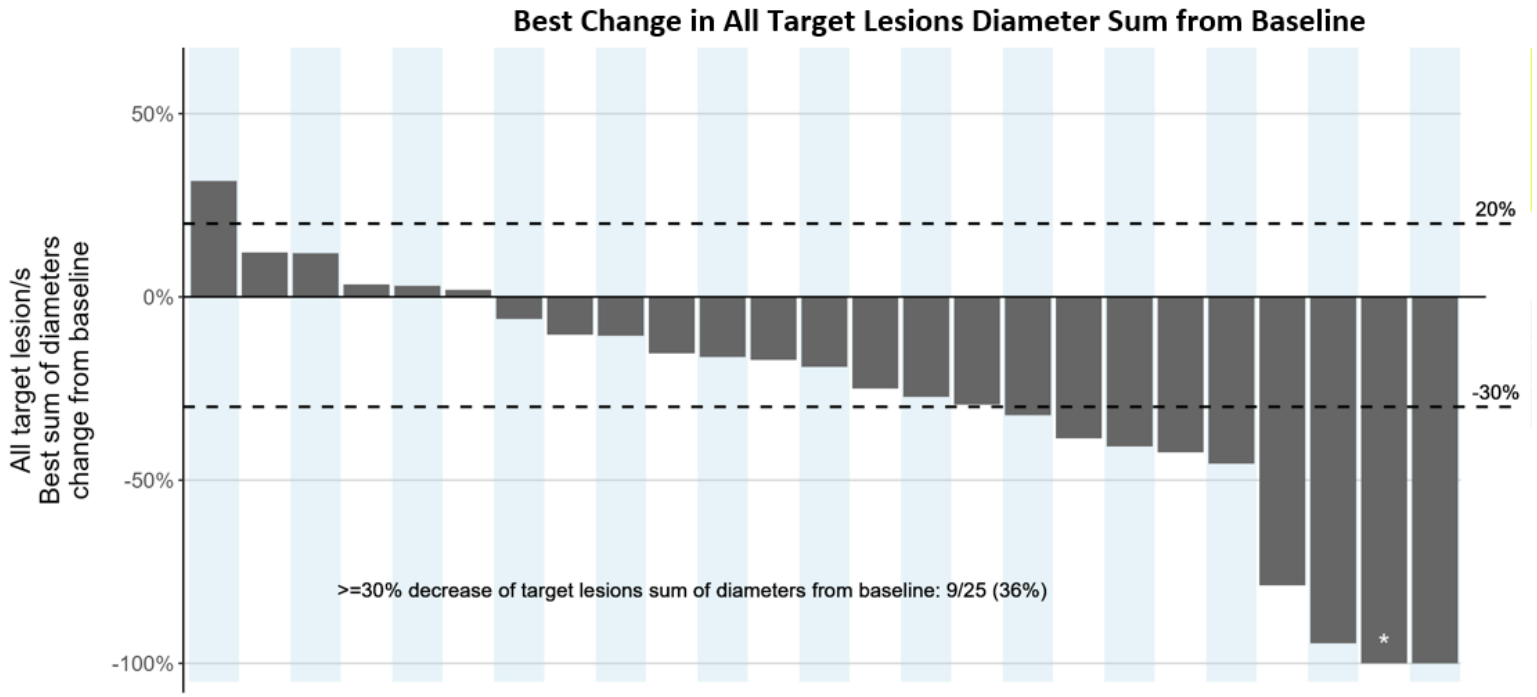
Similar population as **Keynote-040 treatment beyond progression** (pembrolizumab), and **CheckMate-141 treatment post-failure** (nivolumab)^

**among available data at cutoff*

^Note: Study 1100 is a ph. I trial assessing safety as primary endpoint and exploring signals of efficacy as secondary endpoints. The sample size is small, and the trial is ongoing – some of the efficacy data will mature along with new data comes in.

Best Change in Diameter Sum From Baseline and Study Duration

ICI Resistant, Evaluable Patients (N=25)



Overall Response (RECIST 1.1)	ICI Resistant N=25
Complete Response	2 (8.0)
ORR (CR + PR)	**7 (28.0)**
95% CI	[12.1 - 49.4]
Median duration (days)(1))	128.0
DCR (CR + PR + SD)	**17 (68.0)**
95% CI	[46.5 - 85.1]
Median duration (days)(2)	58.0

(1) Number of days from first to last RECIST assessment with CR or PR

(2) Number of days from first to last RECIST assessment with CR, PR or SD

One subject is in complete pathological response (pCR) and has been included in the CR category of this table

Best overall response have been derived as single best overall response observed for 7 subjects, either ongoing or with missing data (0 CR, 3 PR, 2 SD and 2 PD)

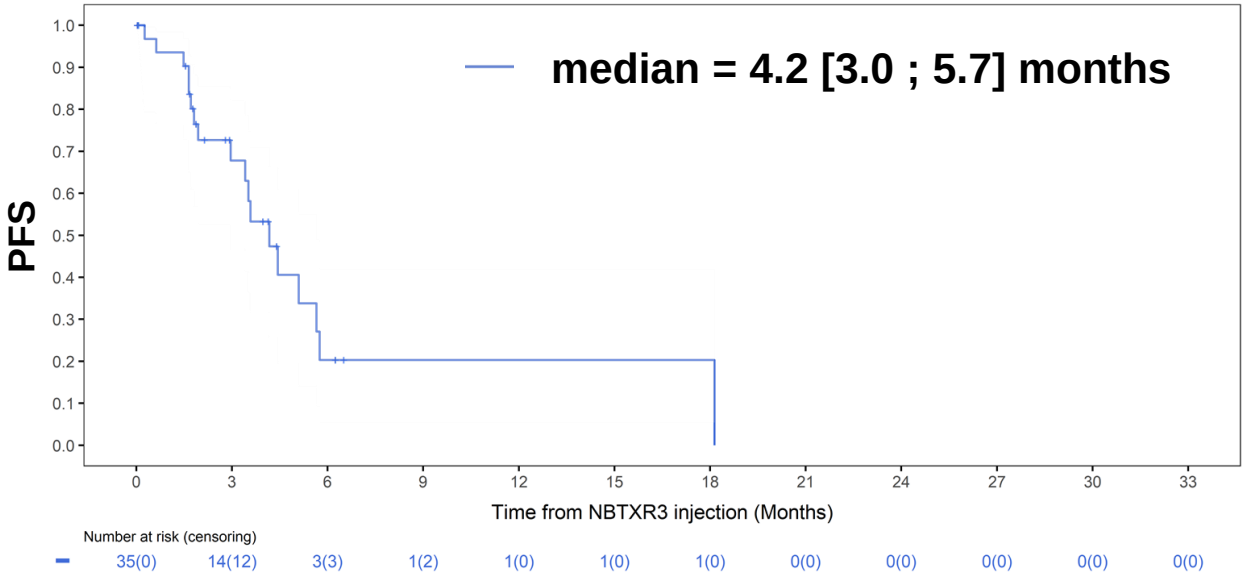
Systemic Control in resistant to anti-PD-1 and in progression metastatic patients with high disease burden
(59% of patients have 4+ lesions; 79% have 2+ lesions)

Progression Free Survival (PFS) and Overall Survival (OS)

ICI resistant, all treated HNSCC patients

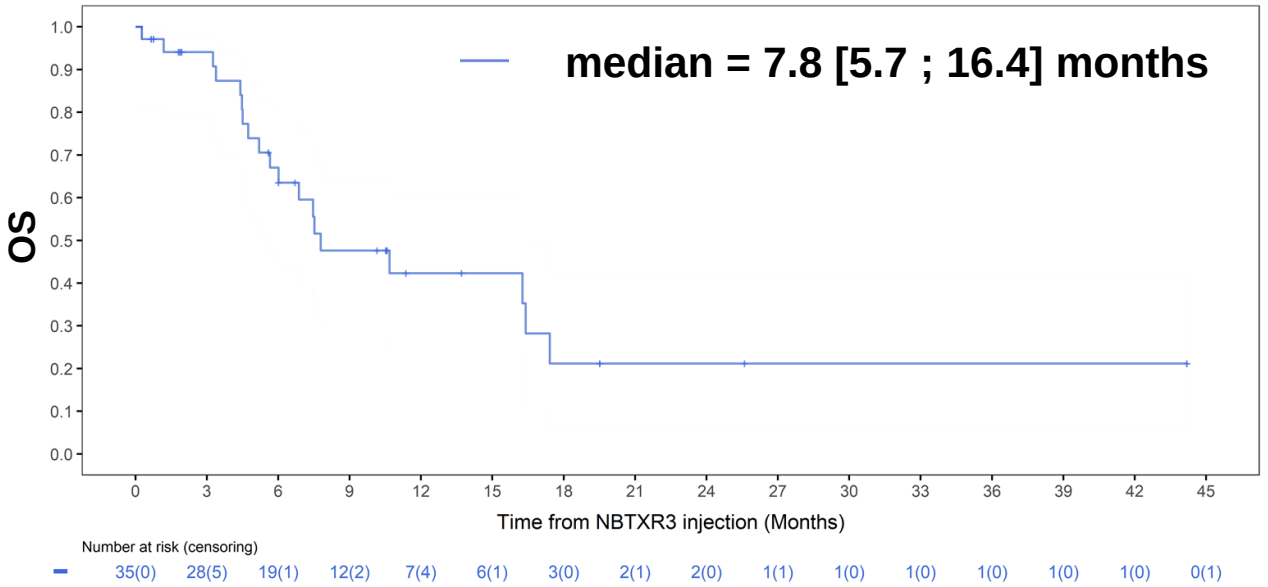
PFS from NBTXR3 injection

All treated population (N=35)



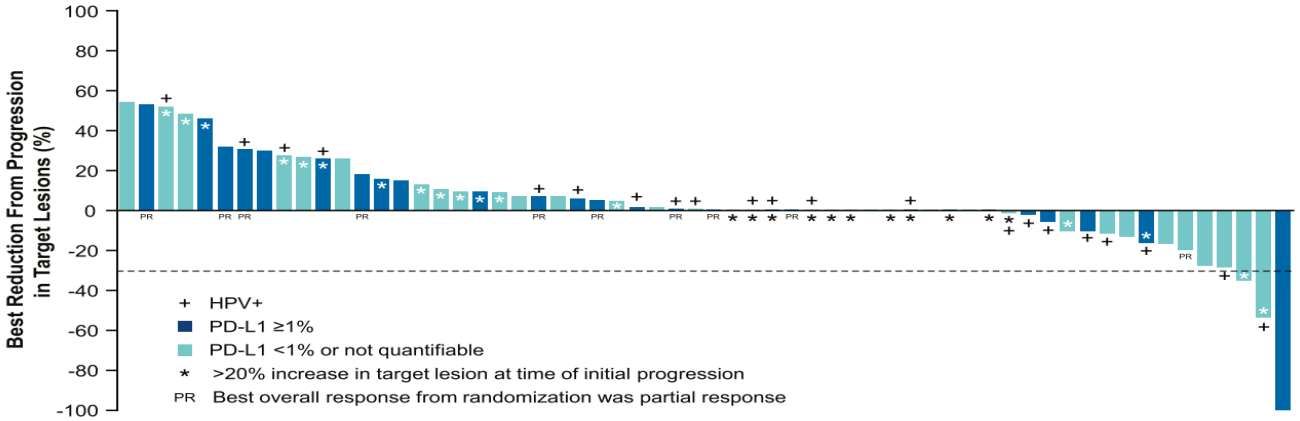
OS from NBTXR3 injection

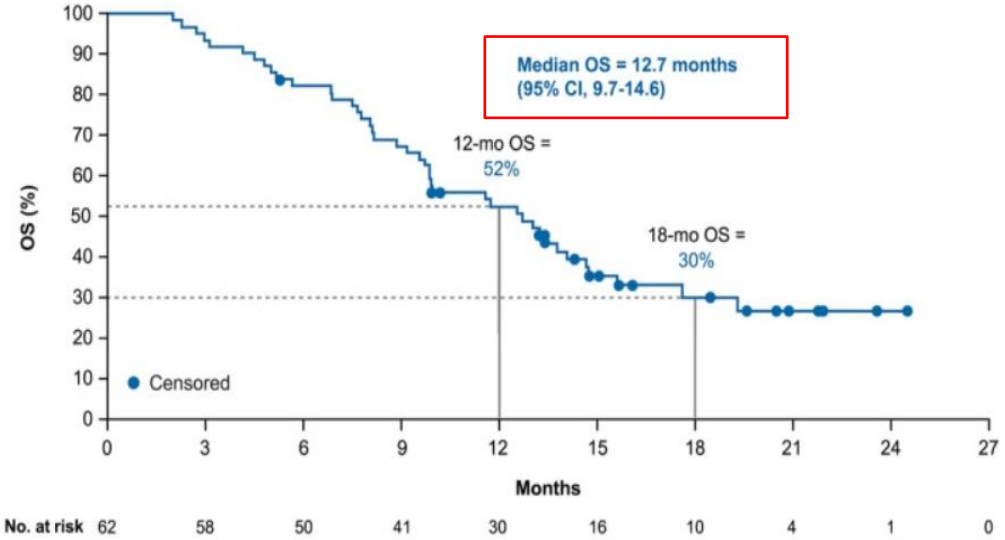
All treated population (N=35)



R/M HNSCC Immune Checkpoint Inhibitor Refractory Populations

CheckMate 141 Nivolumab Trial – patients treated with anti-PD-1 beyond progression





Haddad R. et al., Cancer 2019

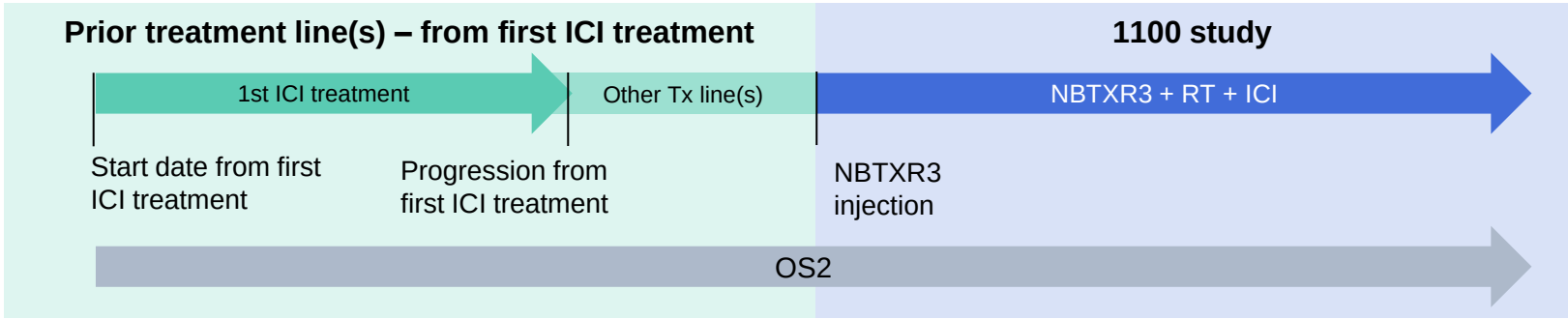
Overall Survival 2 (OS2)

From first ICI treatment

ICI resistant
All treated HNSCC patients

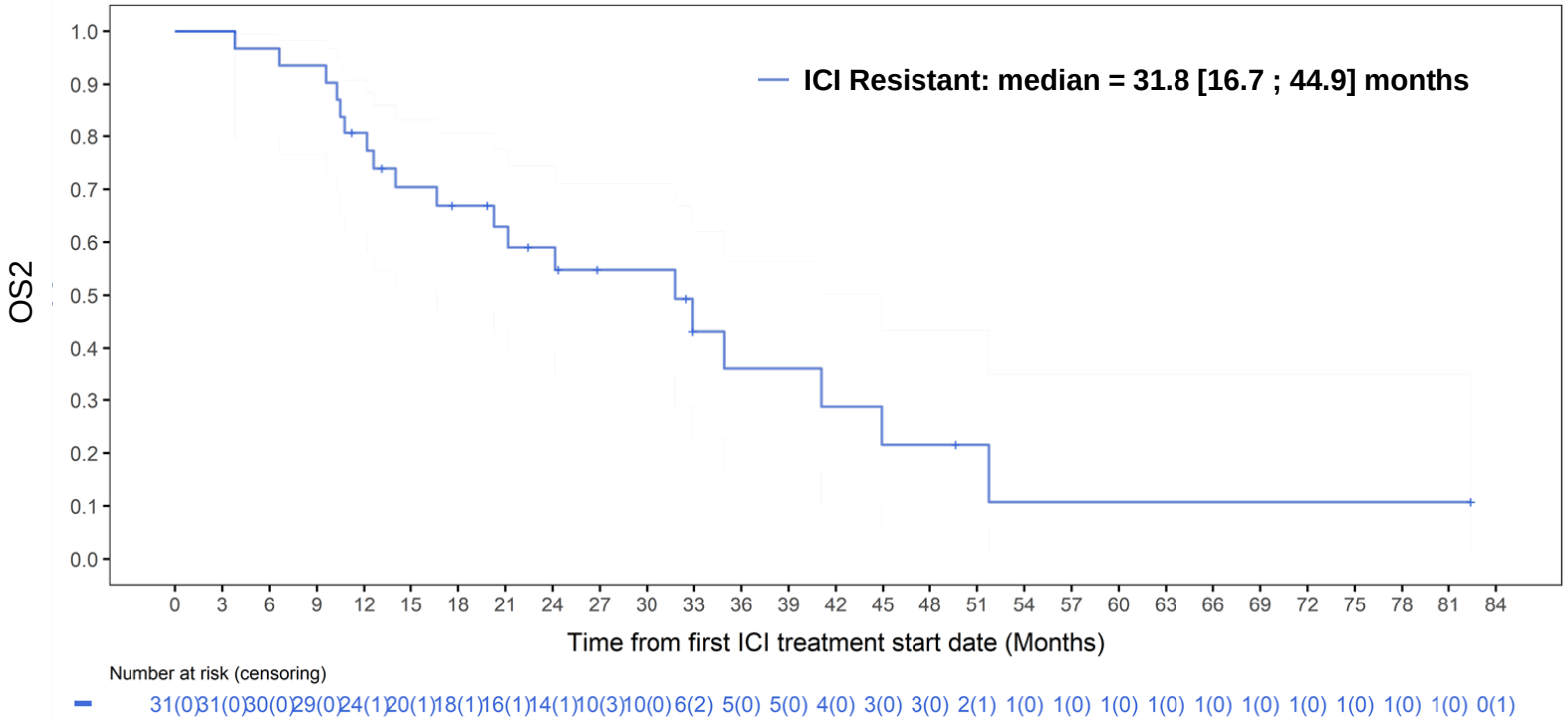
Cut-off: 17 April 2024
N=31*

**4 patients have missing data for prior treatment*



OS2: Overall Survival From First ICI Treatment Start Date

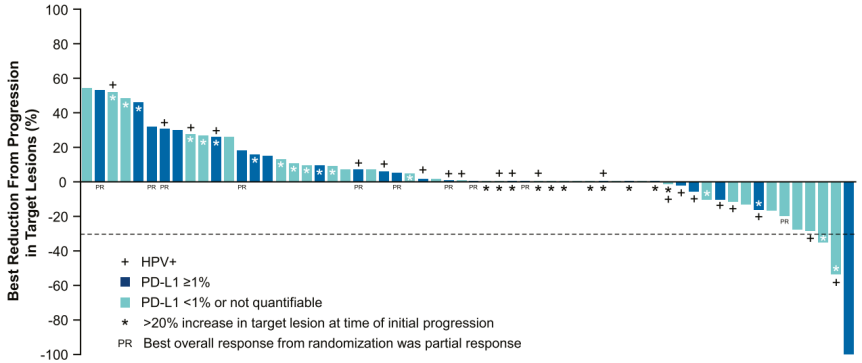
*All treated population (N=31)**

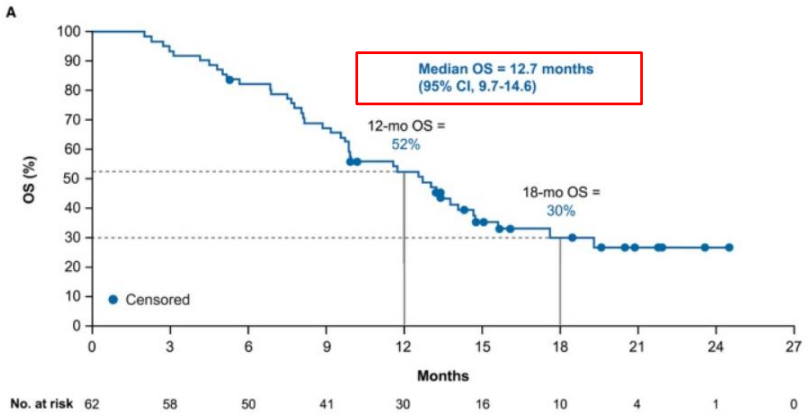


R/M HNSCC Immune Checkpoint Inhibitor Refractory Populations

CheckMate 141 – Nivolumab Trial

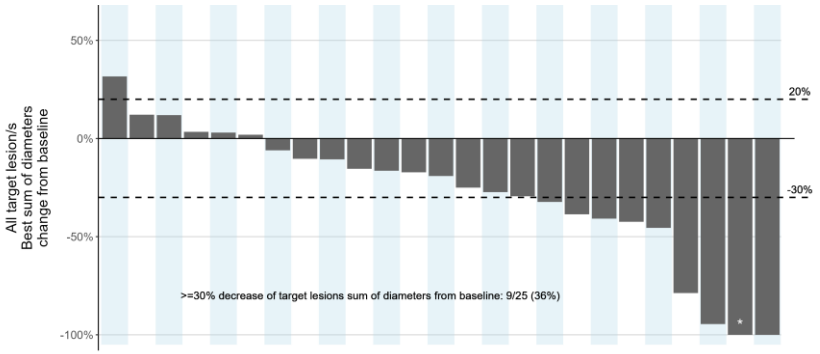
Anti-PD-1 treatment beyond progression

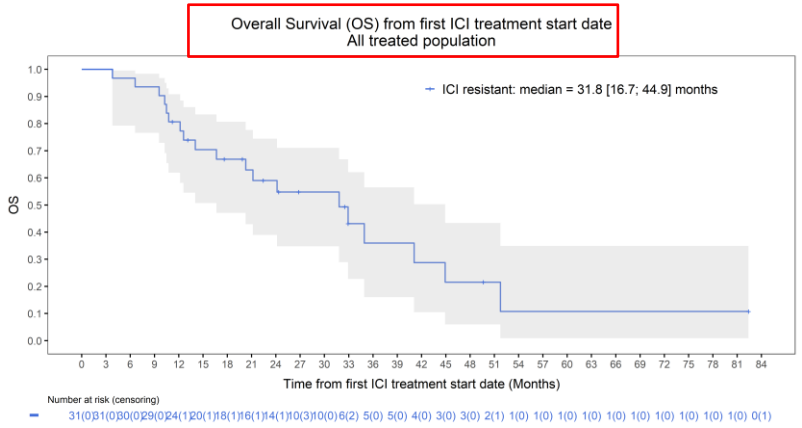




Study 1100 – ICI Resistant Patients

RT+NBTXR3 and anti-PD-1 treatment beyond progression





*Rough comparison only, study 1100 patients may have had other treatment lines after initial anti-PD-1 progression

Study 1100 Results Warrant Further Exploration in Randomized Trials for Both ICI Naïve and Resistant Patients with HNSCC

Feasible and safe with no unexpected findings

- NBTXR3 intra-tumoral injection **was feasible and safe** in heavily pretreated patients with R/M HNSCC
- **Less than 10% of Grade ≥ 3 serious TEAEs** related to radiotherapy, injection procedure, anti-PD-1 or NBTXR3
- No specific or unexpected adverse events emerging

High response rate with metastatic patients (naïve or refractory to anti-PD-1) suggests systemic component of control

	ICI Naïve patients	ICI Resistant patients
ORR	***48% (12/25)***	28% (7/25)
DCR	76% (19/25)	68% (17/25)
mPFS	7.3 months	4.2 months
mOS	26.2 months	7.8 months
mOS from first ICI treatment	--	31.8 months

ASCO 2024 data *Ongoing trial: data are subject to change*

Q&A

THANK YOU