2024 Updates in Head and Neck Cancer

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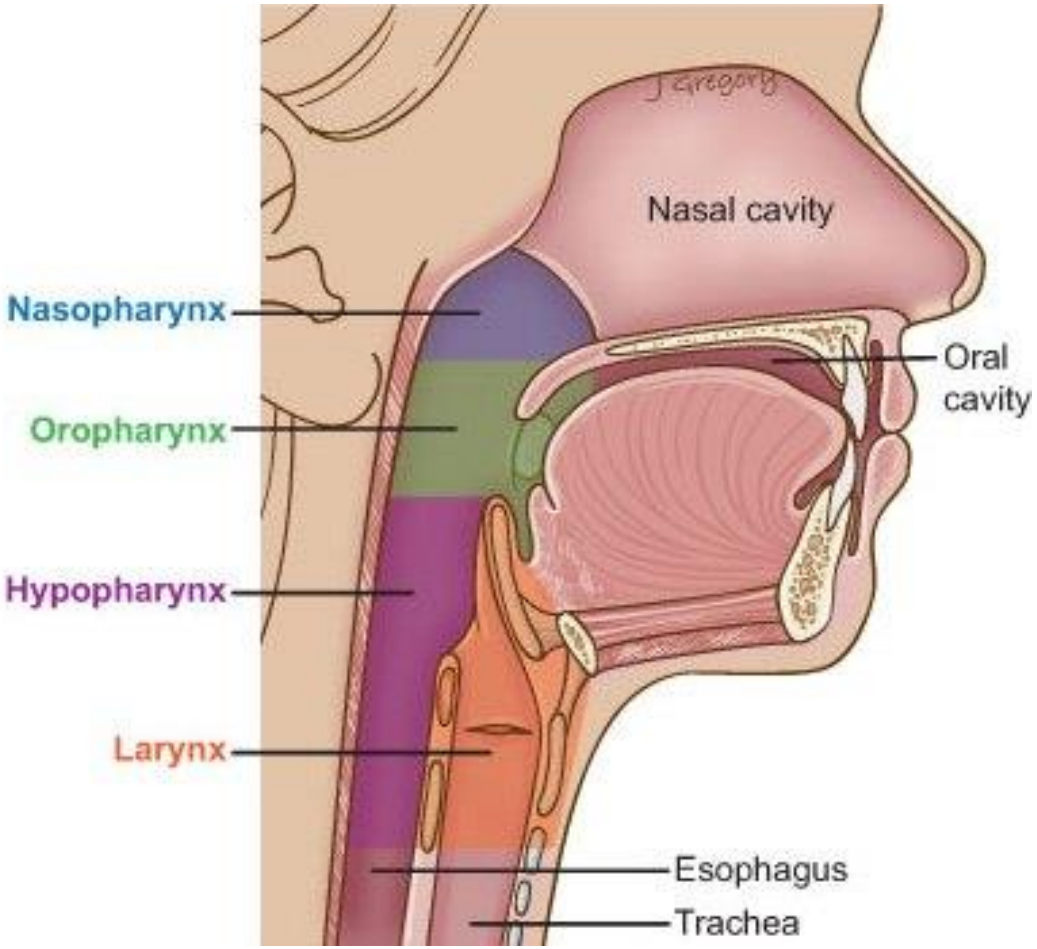
OUTLINE

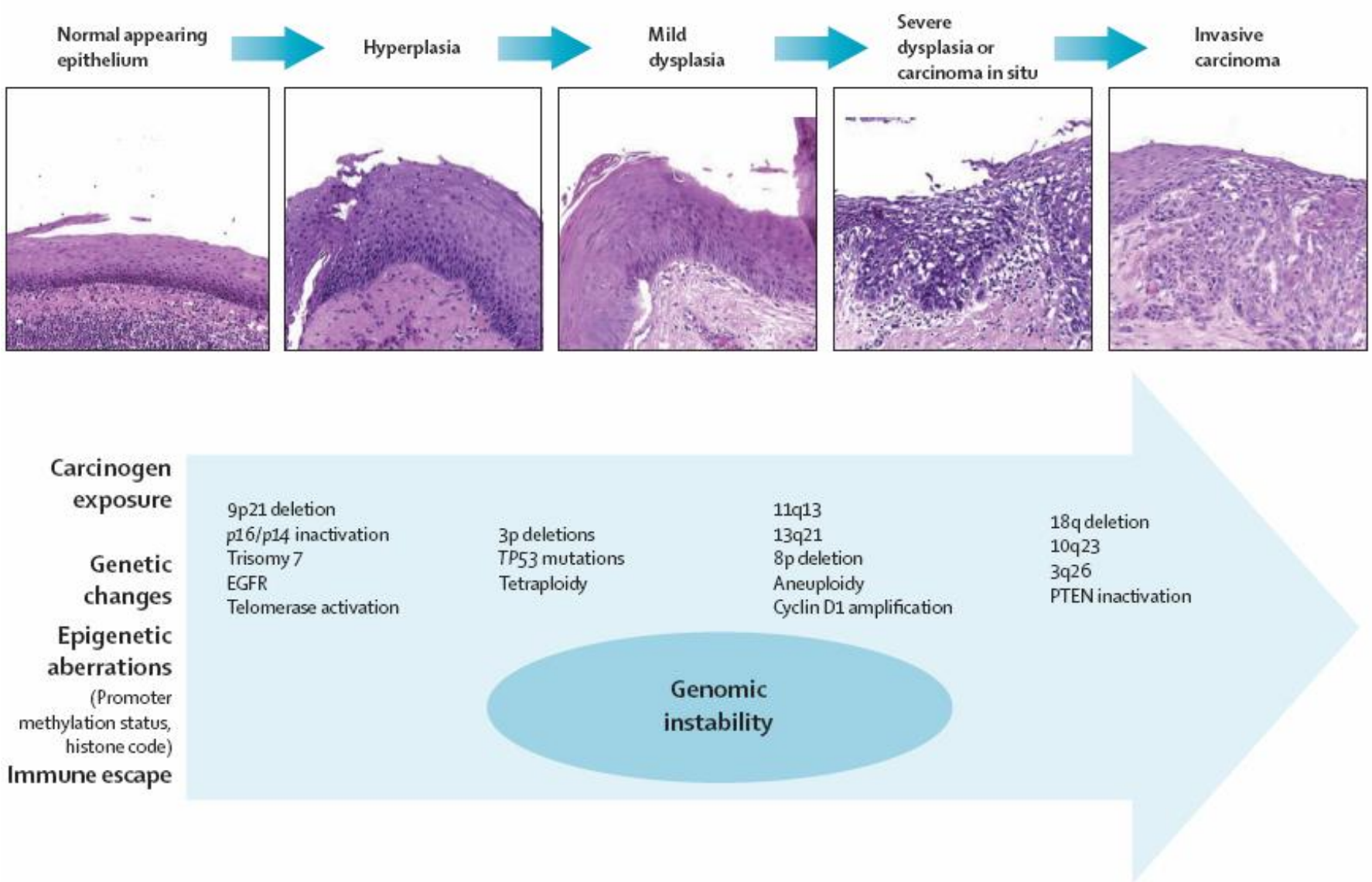
- Background
- Recurrent/metastatic head and neck cancer (RMHNSCC)
- Locally advanced head and neck cancer (LAHNSCC)

Background

Epithelial malignancies of the head and neck

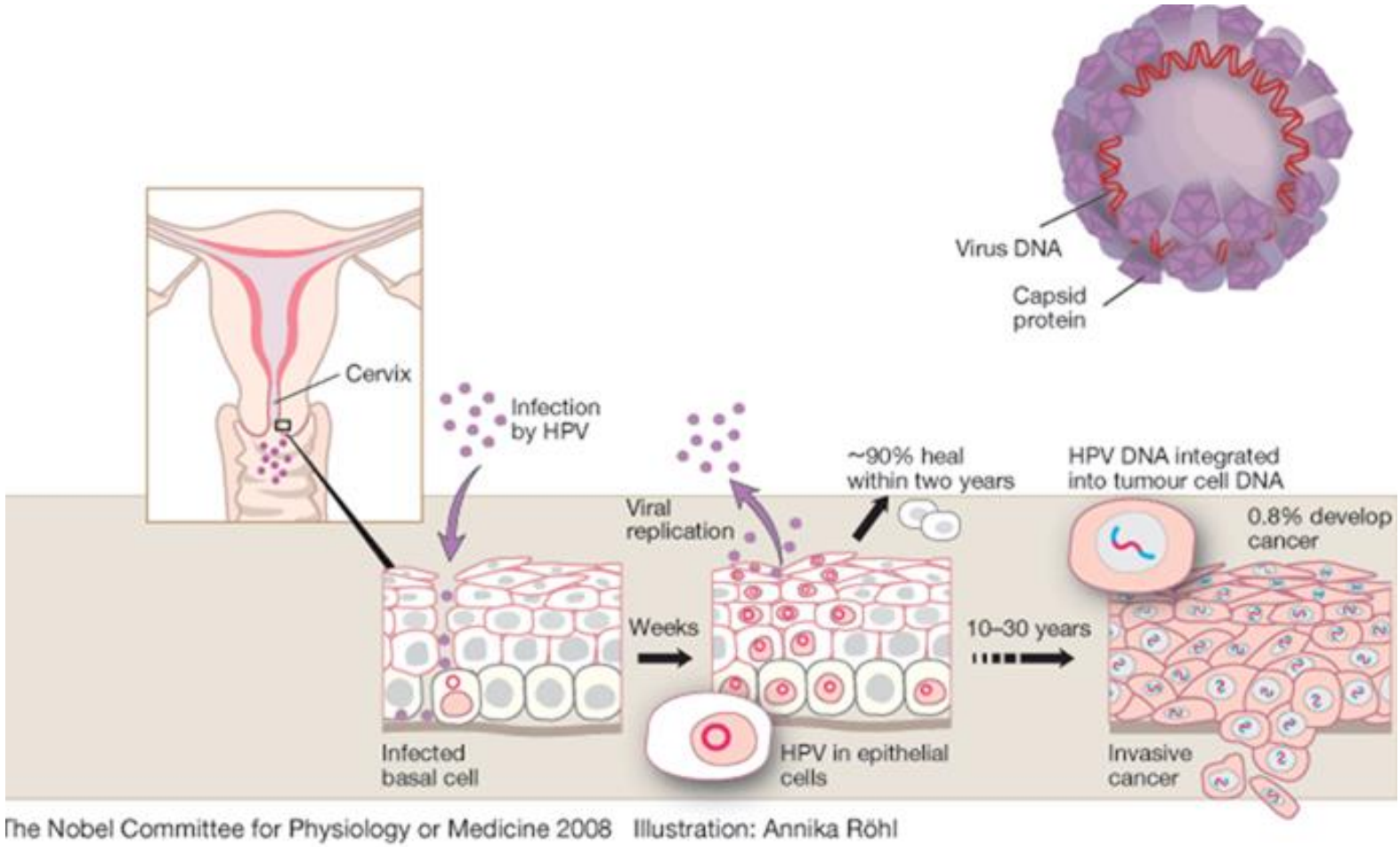


- 90% squamous cell carcinomas
- Most common mucosal sites oropharynx, oral cavity, larynx, hypopharynx
- Tobacco, alcohol in OC, L, HP
- Virus in OPC

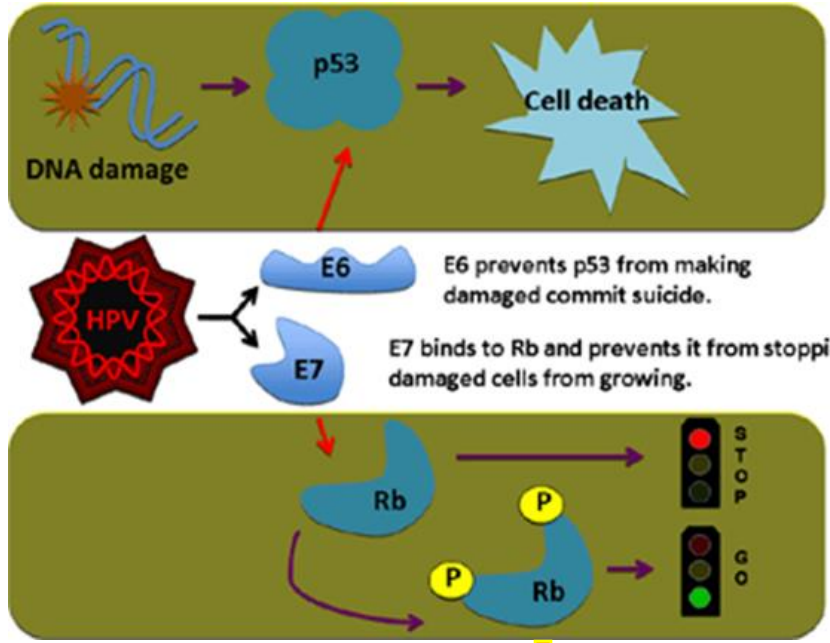


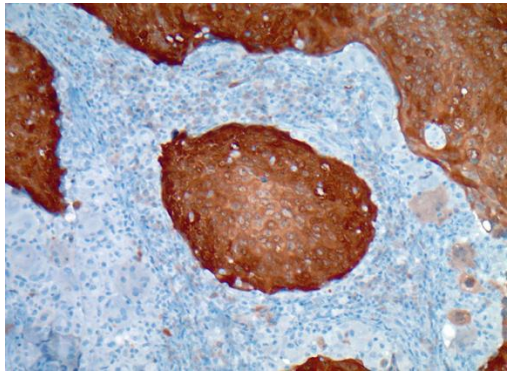
Argiris et al. Lancet. 2008 May 17;371(9625):1695-709.

HPV+ oropharynx cancer: a distinct entity with a viral association



The Nobel Committee for Physiology or Medicine 2008 Illustration: Annika Röhl

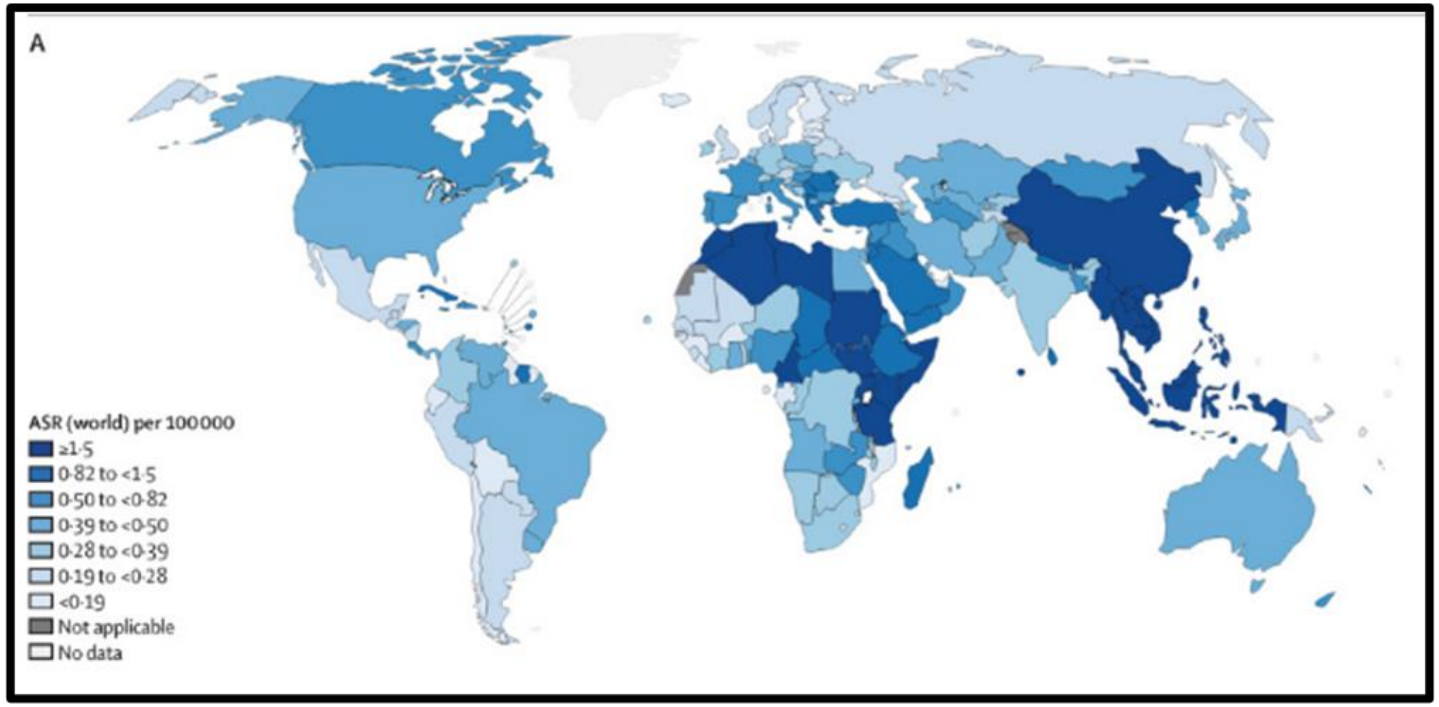




p16 upregulation

Nasopharyngeal Carcinoma

- Distinct epidemiology
- WHO classification
- Endemic disease is EBER+
- Brisk lymphocytic infiltrate



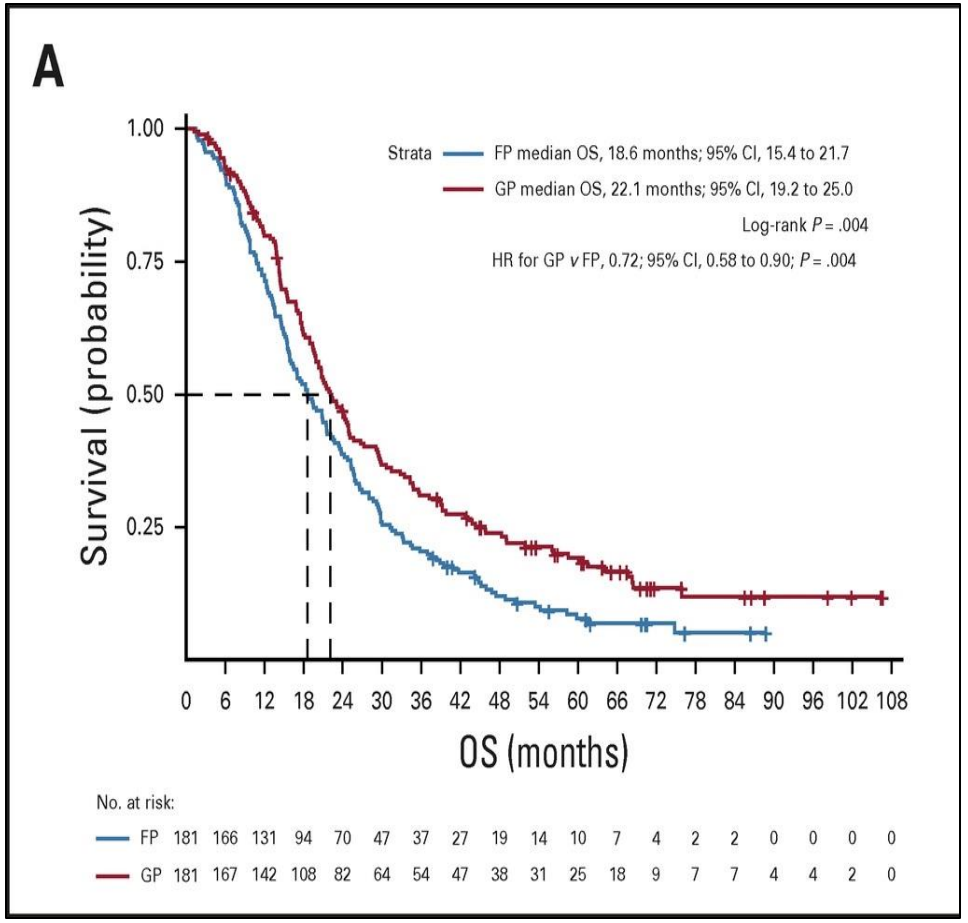
Chen et al, Lancet 2019

Recurrent/metastatic head and neck cancer (RMHNSCC)

- Immune checkpoint inhibitors in R/M NPC
- Novel combinations in R/M HNSCC
  - TKI
  - HPV directed approaches
  - Bispecific antibodies

Recurrent/Metastatic NPC

- 30% recur after curative intent therapy
- Multiple active systemic agents
- Gemcitabine+Cisplatin (GC): PFS advantage over 5-FU+Cisplatin in endemic population
  - ORR: 64%
  - Median PFS: 7 months
  - Median OS: 22 months



Zhang et al, Lancet, 2016.
Hong et al, JCO, 2021

Recurrent/Metastatic NPC and PD1 inhibition

- Near universal PD1 expression in endemic disease
- Characterized by robust tumor immune cell infiltration

Author	Agent	N	PD-L1 status	ORR
Wang (2021)	Toripalimab	190	any	20.5%
Wang (2019)	Tislelizumab	20	any	20%
Fang (2018)	Camrelizumab	93	any	34%
Fang (2018)	Camrelizumab+ GC	22		91%
Ma (2018)	Nivolumab	44	any	20.5%
Hsu (2017)	Pembrolizumab	27	PD-L1 ≥1%	25.9%

Phase III clinical trials in 1st line R/M NPC

Trial	Treatment Arms	Results in PD-L1 arm	High Grade AEs	ORR/mDOR
JUPITER -02[1]	GC + placebo vs GC + toripalimab	PFS and OS advantage	89% vs 89.5%	66.4% (5.7 mo) 77.4% (10 mo)
CAPTAIN-1ST[2]	GC + placebo vs GC + camrelizumab	PFS advantage	91% vs 94%	80.6 (5.6 mo) 87.3% (8.5 mo)
RATIONALE-309[3]	GC + placebo vs GC + tislelizumab	PFS advantage	80.9% VS 81.8%	55.3 (6.1 mo) 69.5 (8.5 mo)

[1]Mai et al. Nat Med 2021
[2]Yang et al. Lancet Oncology 2021
[3]Yang et al. Cancer Cell 2023

Ongoing investigation in R/M NPC

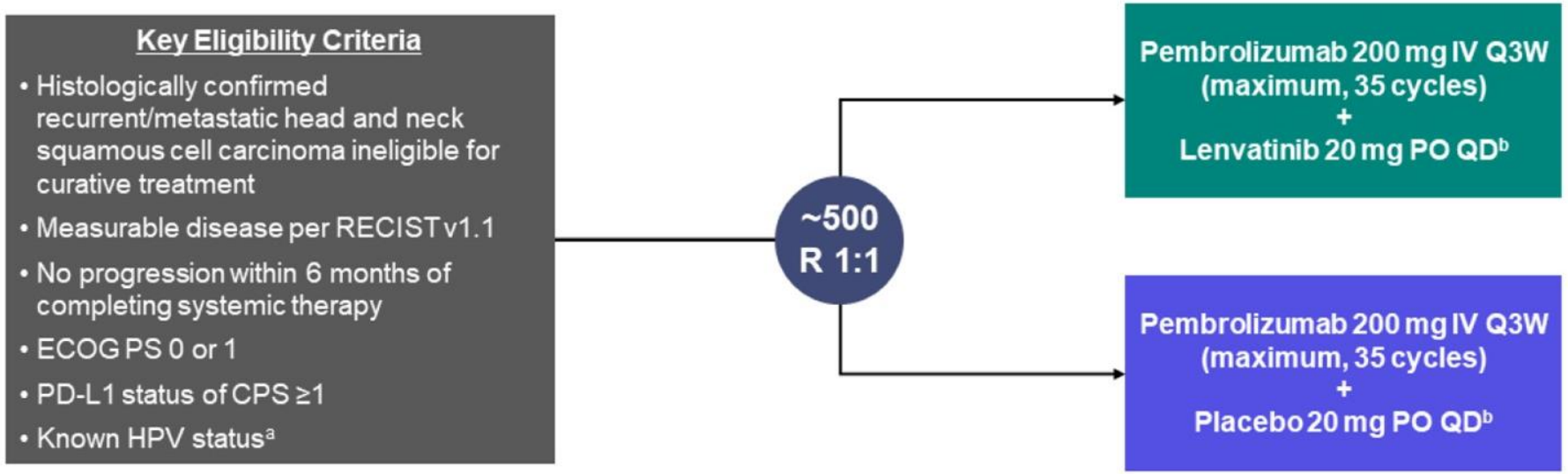
- Maintenance therapy combinations
  - NRG HN011 relatlimab+ nivolumab vs nivolumab alone
- Chemoimmunotherapy in non-endemic populations
  - TRANSPARENT study gemcitabine+cisplatin+ toripalimab
- Post chemoimmunotherapy regimens
  - A092105 (Alliance) nivolumab/ipilimumab/cabozantinib vs nivolumab/ipilimumab in 2nd line setting

Options for Non NPC RMHNCC

- Standards of care
  - Pembrolizumab monotherapy in CPS ≥1
  - Chemo+ pembrolizumab in any CPS
  - Pembrolizumab OR nivolumab monotherapy post cisplatin
- Suboptimal ORR rates, toxicity with chemotherapy
- Need for well tolerated, effective first line options

Novel combinations in R/M HNSCC

LEAP-010 Study Design



Stratification Factors
- PD-L1 expression (TPS <50% vs ≥50%)
- HPV status[a] (positive vs negative)
- ECOG PS (0 vs 1)

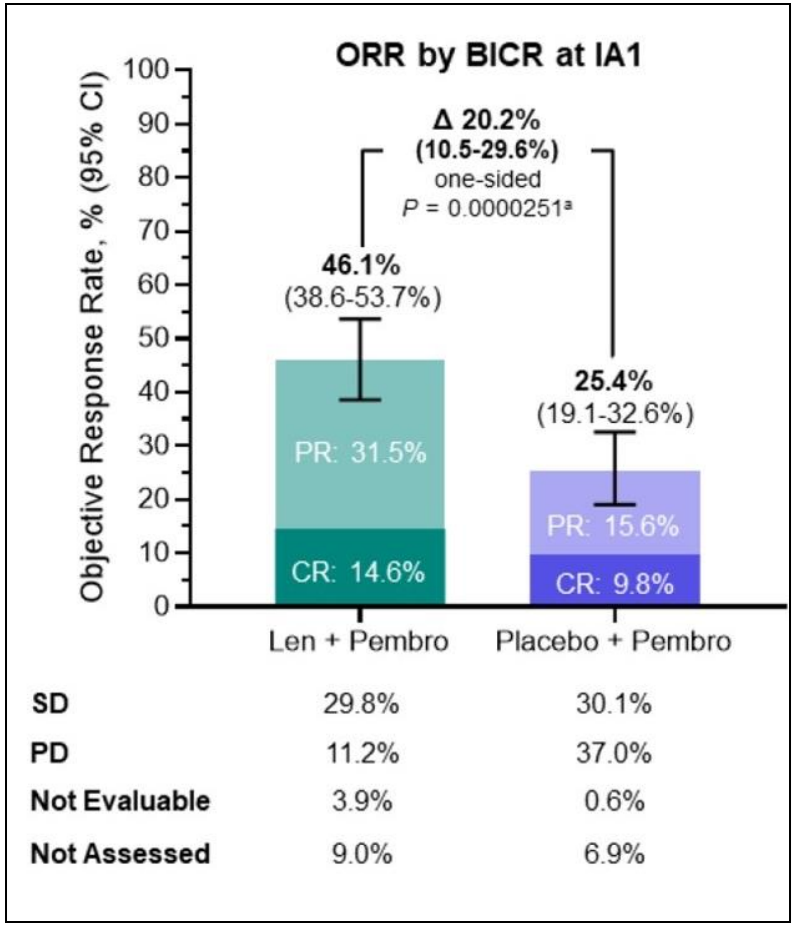
- **Primary Endpoints:** ORR and PFS, assessed per RECIST v1.1 by blinded, independent central review (BICR), and OS
- **Secondary Endpoints:** DOR, assessed per RECIST v1.1 by BICR, and safety

[a]HPV status for oropharynx cancer determined by p16 immunohistochemistry; for patients without oropharynx cancer, HPV status was considered negative. [b]Lenvatinib or placebo could continue to be given after 35 cycles of pembrolizumab.
ClinicalTrials.gov identifier: NCT04199104.

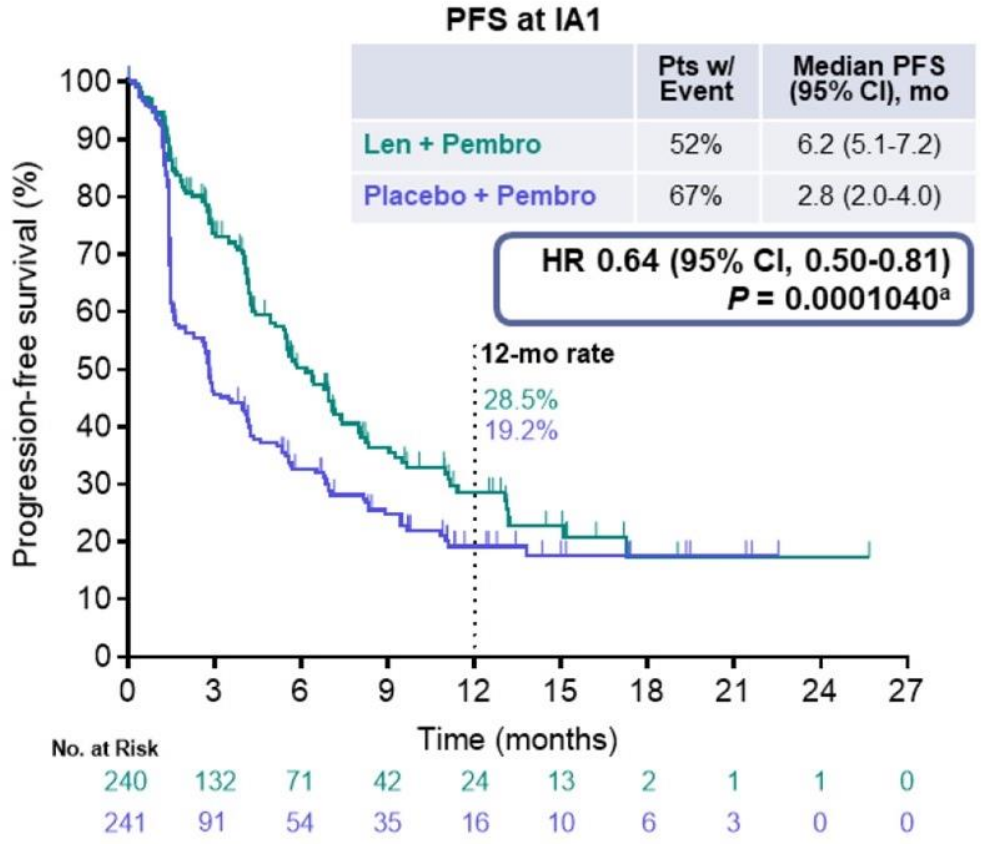
Licitra et al. MHNCS 2024.

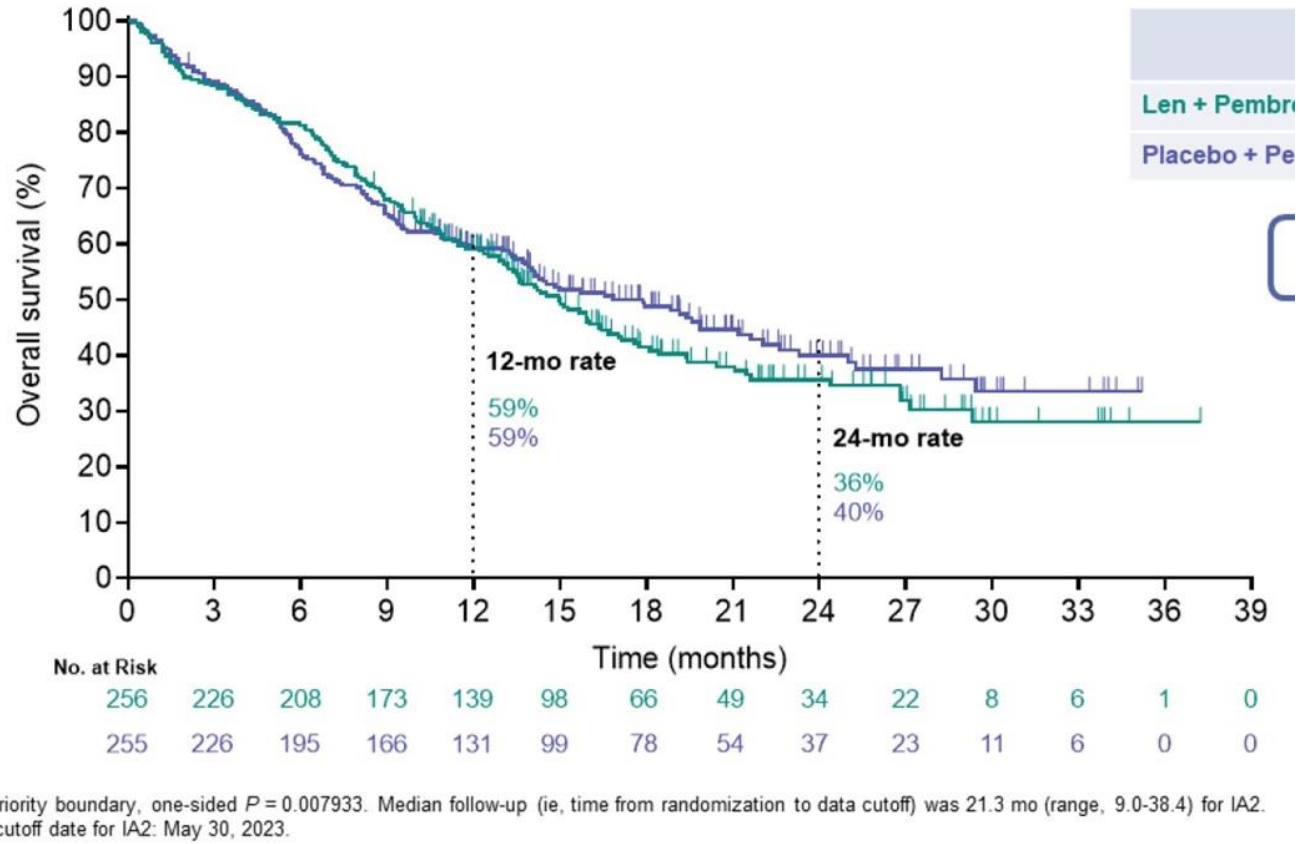
LEAP 010

- Most patients enrolled in europe and asia
- 22% HPV + OPC
- 45% ECOG 0
- 27-32% CPS 1
- 76-88% smoking history



LEAP 010





aSuperiority boundary, one-sided $P = 0.007933$. Median follow-up (ie, time from randomization to data cutoff) was 21.3 mo (range, 9.0-38.4) for IA2. Data cutoff date for IA2: May 30, 2023.

LEAP 010

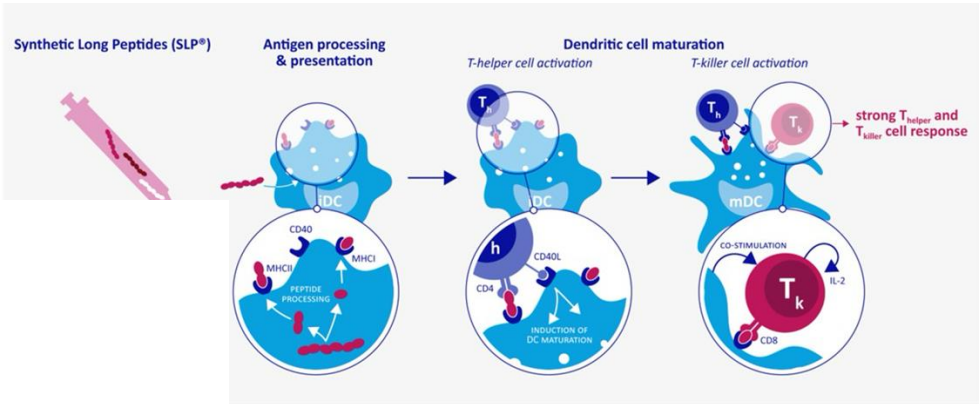
- 61% vs 18% Grade 3 or higher toxicity in len + pembro
- 28% vs 8% treatment discontinuation due to TRAE

Ongoing multitargeted TKI + ICI studies

- STELLAR 305 NCT06082167
  - First line R/M HNSCC
  - Zanzalitinib+ pembro vs pembro

- BiCaZO S2101 NCT05136196
  - Previously immune checkpoint inhibitor exposed
  - Melanoma/HN
  - Currently on hold

Novel first line approaches: HPV directed treatment



n MD MSc

Study design
Double-blind, placebo-controlled, phase II

Eligibility criteria:

- R/M HPV16+ OPC
- ECOG PS 0-1
- No prior treatment with anti-PD1, anti-PD-L1 or therapeutic anti-HPV vaccines
- 1st and 2nd line patients
- For 1st line patients: CPS ≥1

1:1

ISA101b 100 µg/peptide s.c. (3 doses) + **cemiplimab** 350mg i.v. Q3W until PD*, unacceptable toxicity or patient withdrawal

ISA101b matching placebo (3 doses) + **cemiplimab** 350mg i.v. Q3W until PD*, unacceptable toxicity or patient withdrawal

Stratification factors: smoking history, treatment line in the study

*Or up to a maximum of 24 months of treatment (whichever occurs first)

Primary efficacy endpoint:
- ORR by independent review (RECIST 1.1)

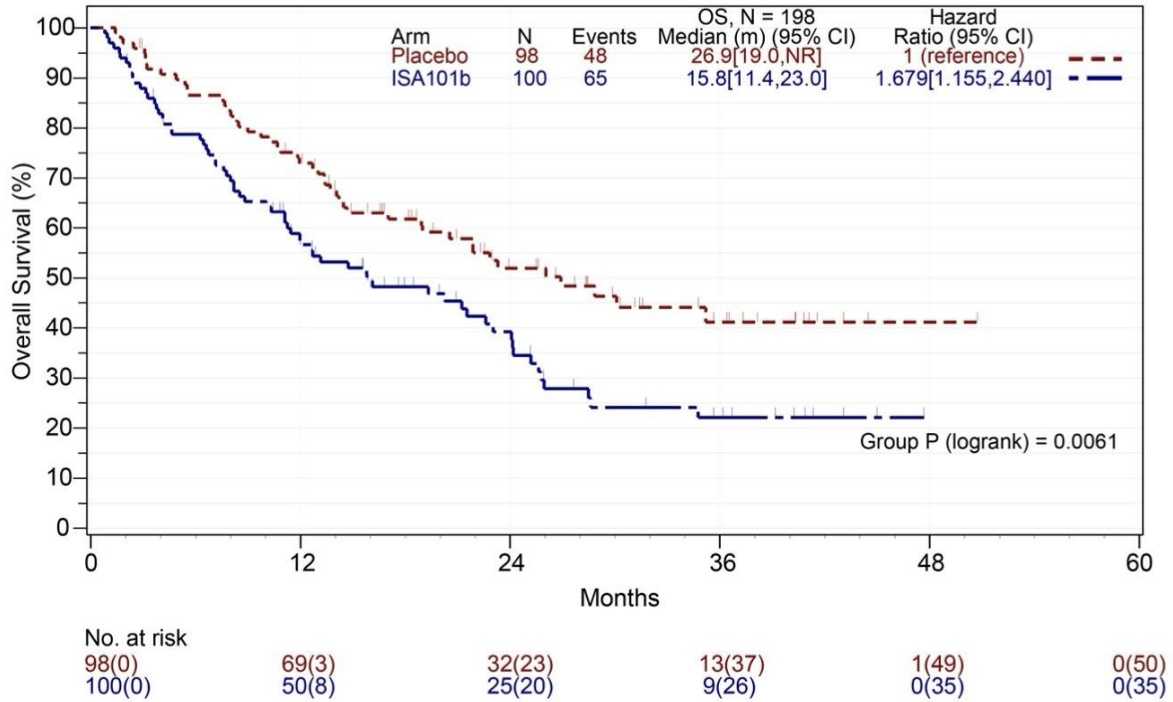
Primary safety endpoint:
- Frequency and severity of toxicities

Secondary endpoints:
- PFS
- OS

Exploratory endpoints:
- Tumor molecular profiling
- Correlative biomarkers

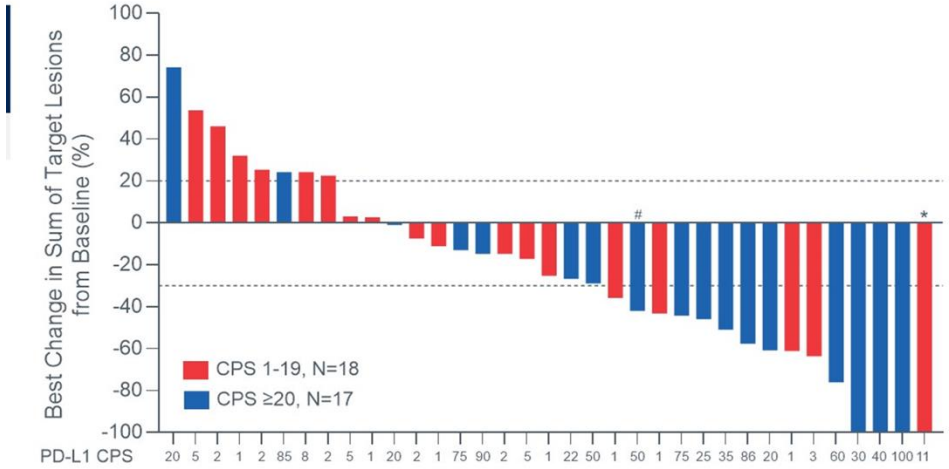
Novel first line approaches: HPV directed treatment

Overall survival in FAS

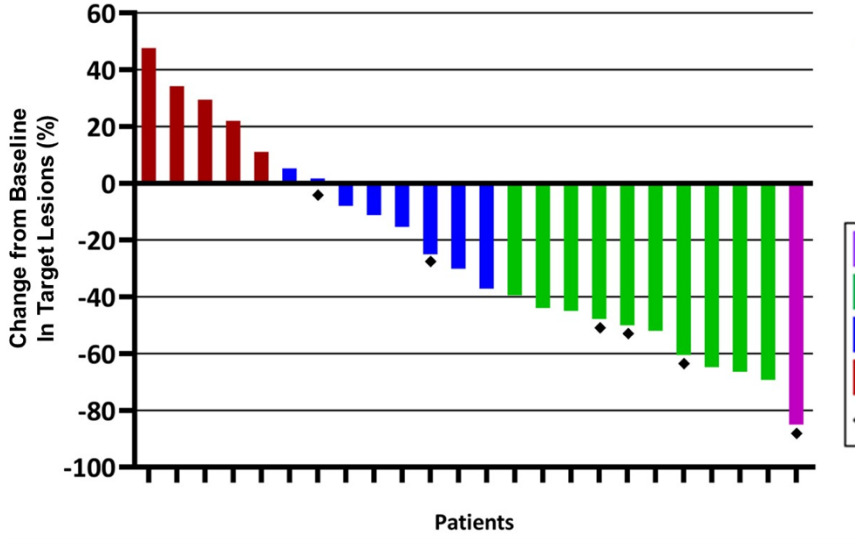


Novel first line approaches: HPV directed treatment

- HB200 + Pembrolizumab
  - Arenavirus vector E6/E7 vaccine + pembro
  - 38 evaluable patients
  - ORR 37%

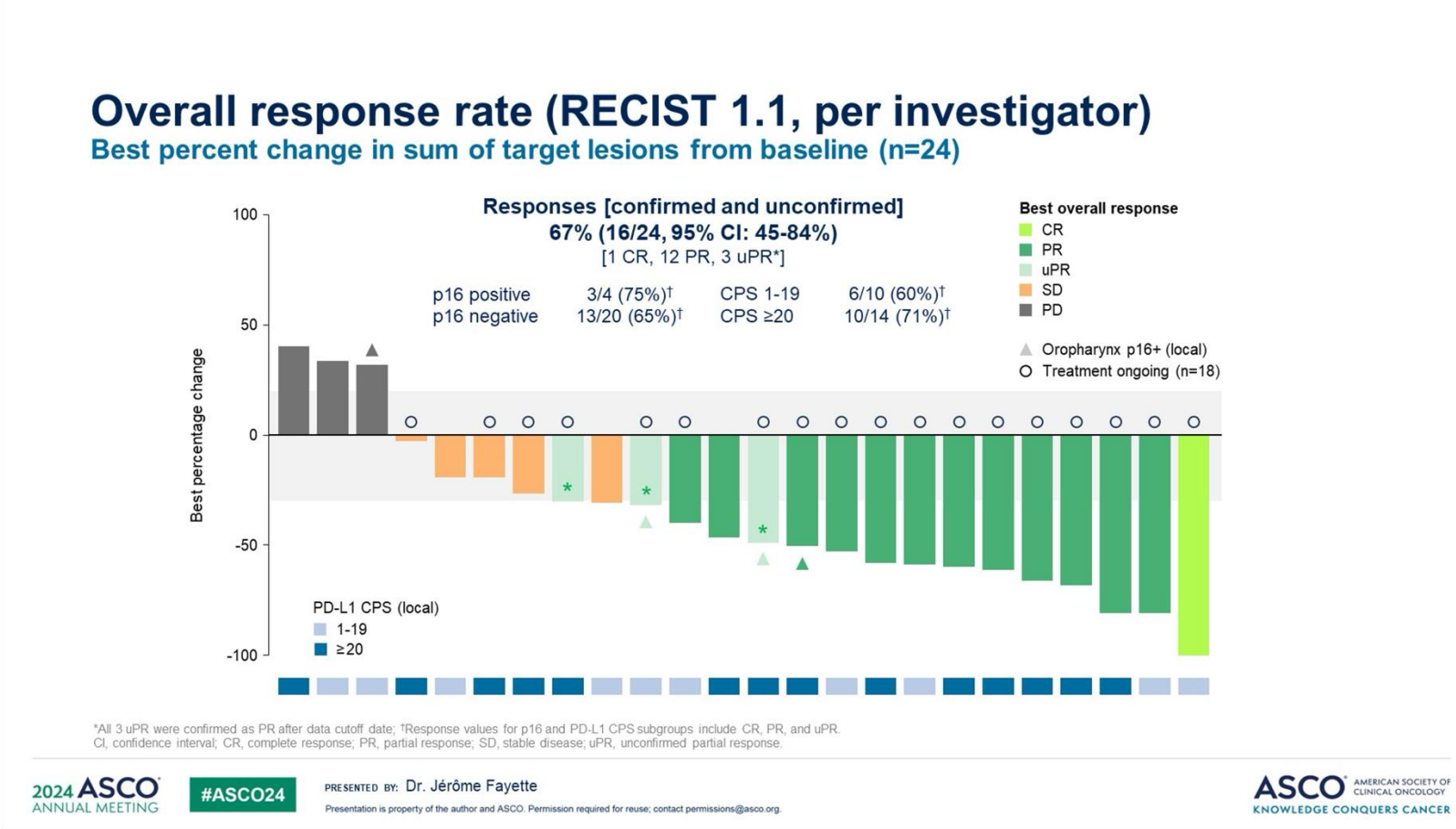


- CUE101 + Pembrolizumab
  - Novel fusion with E7 epitope
  - Engages tumor spec Tcells
  - 24 evaluable patient
  - ORR 46%



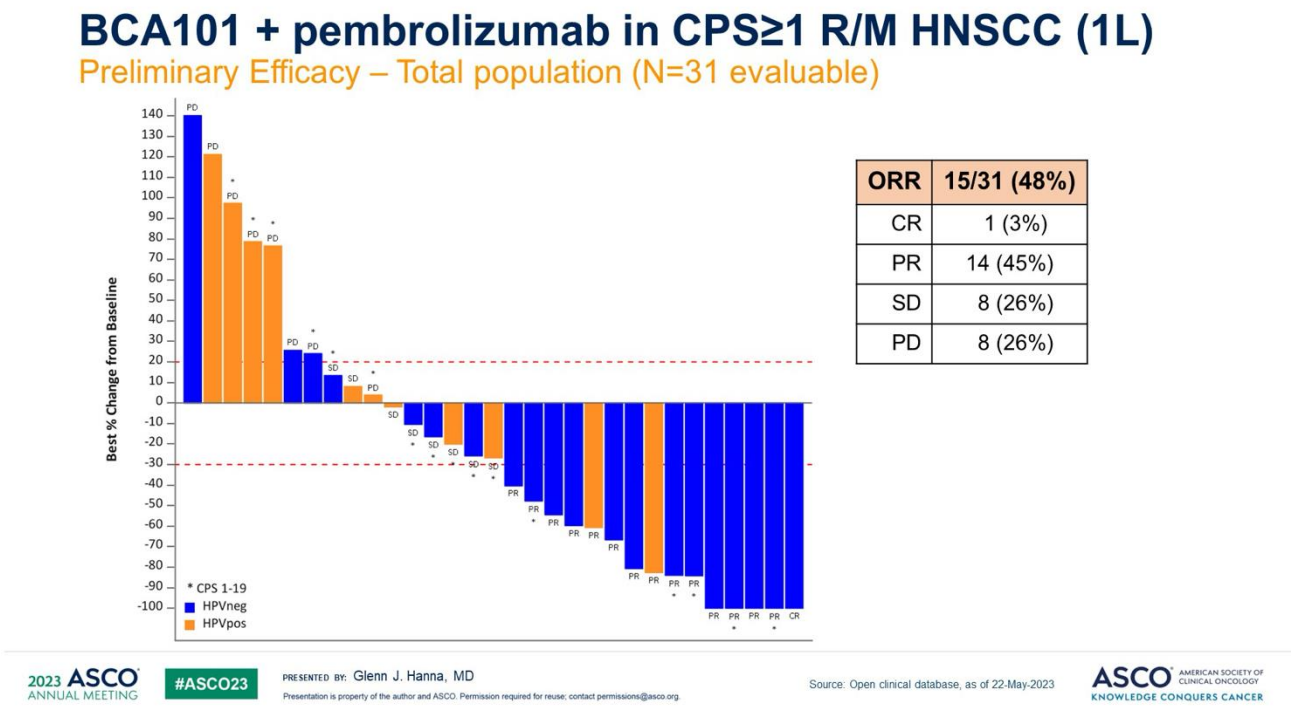
Novel first line approaches: bispecific Ab

- Petosemtamab: bispecific mAb to EGFr and LGR5
- Phase 2 study in first line setting
- N=45, 24 evaluable
- Grade ≥3 AEs in 40%



Novel first line approaches: bispecific Ab

- BCA 101: anti EGFr and TGFb
- Phase 1/1b study in first line setting
- N=41, 39 evaluable
- ORR 46%
- Grade ≥3 AEs in 40%

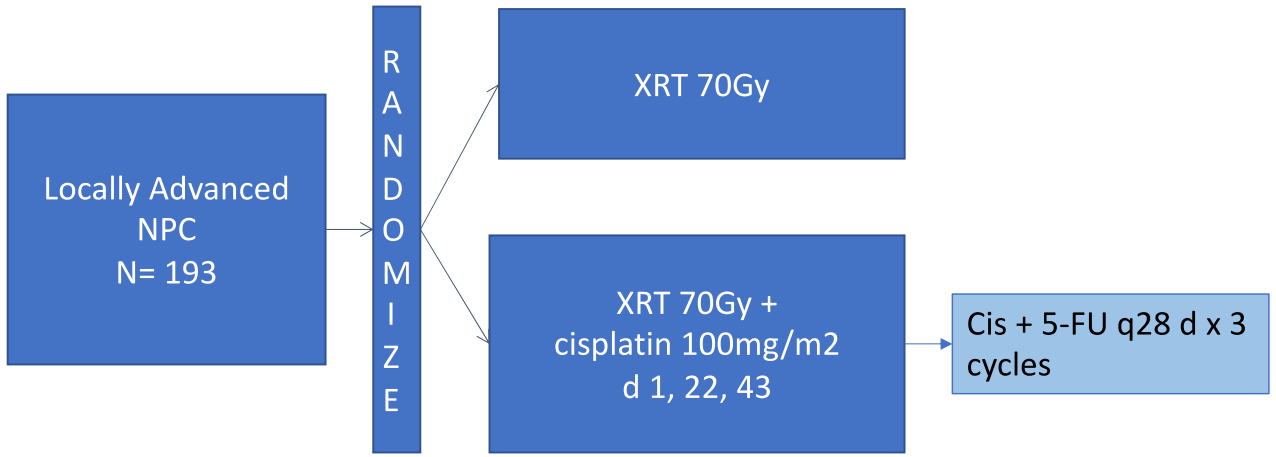


Locally advanced head and neck cancer (LAHNSCC)

- Incorporating ICI into curative intent NPC
- Proton radiation therapy
- Postoperative de-escalation in HPV+ OPC

Chemoradiation in LA NPC

- Intergroup 0099 established curative intent standard in North American population



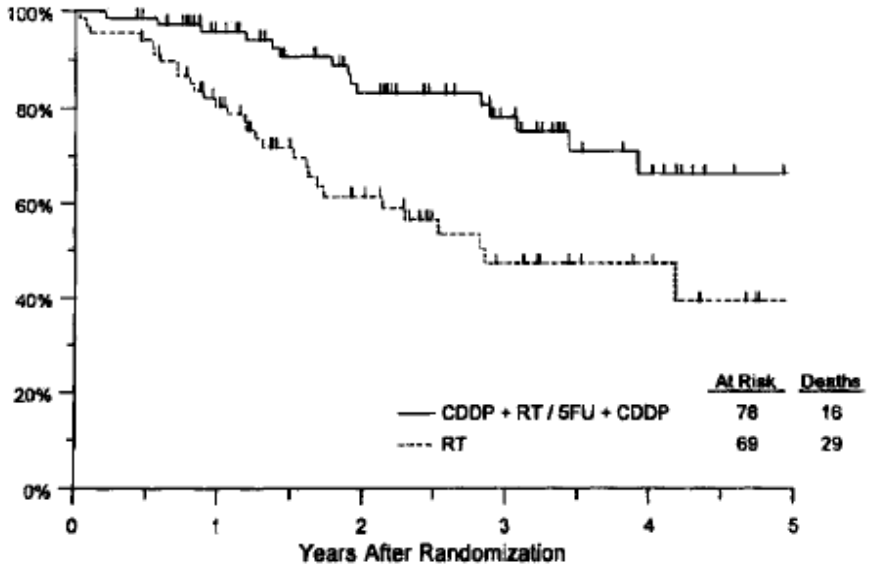
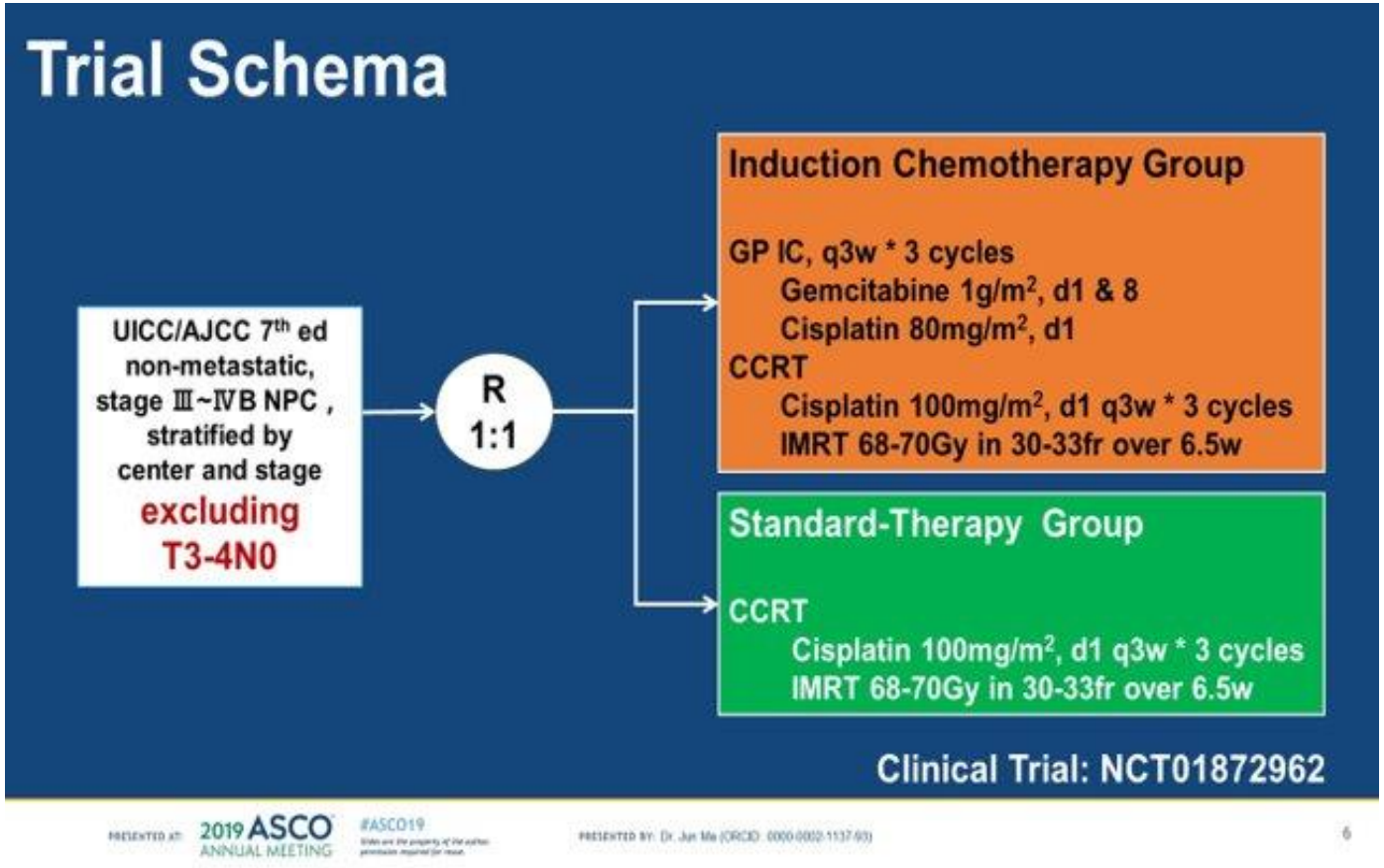
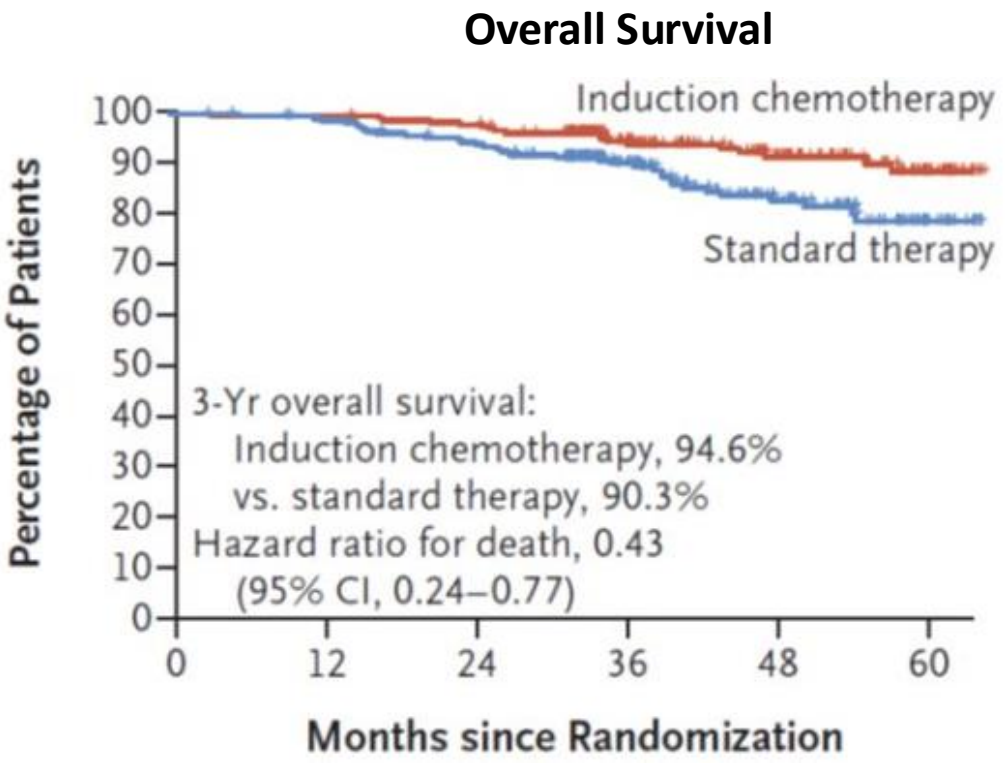


Fig 2. Overall survival for completely eligible patients on RT only and combined CT/RT (----).

Al- Sarraf et al, JCO 1998

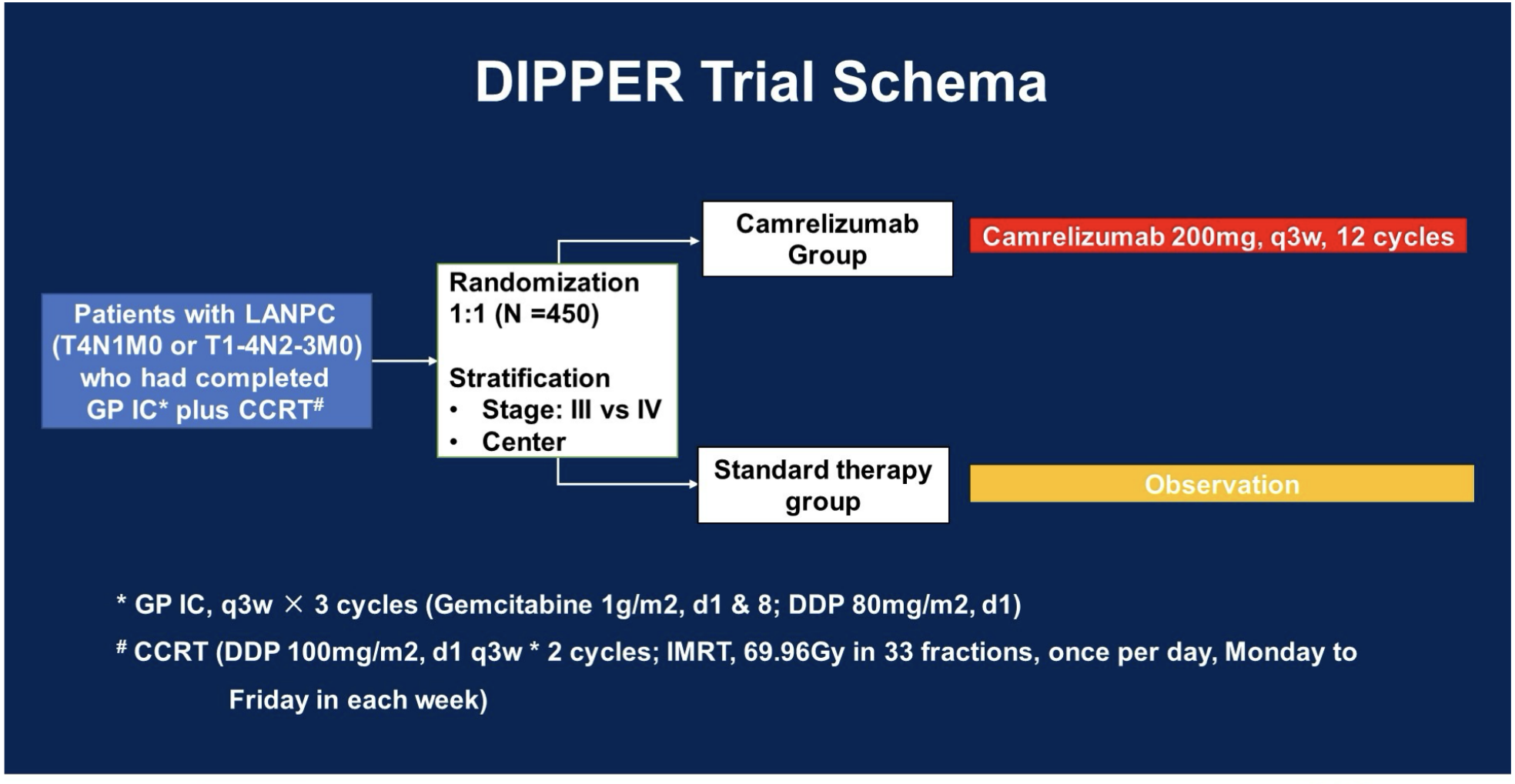
Neoadjuvant Strategy in LA NPC





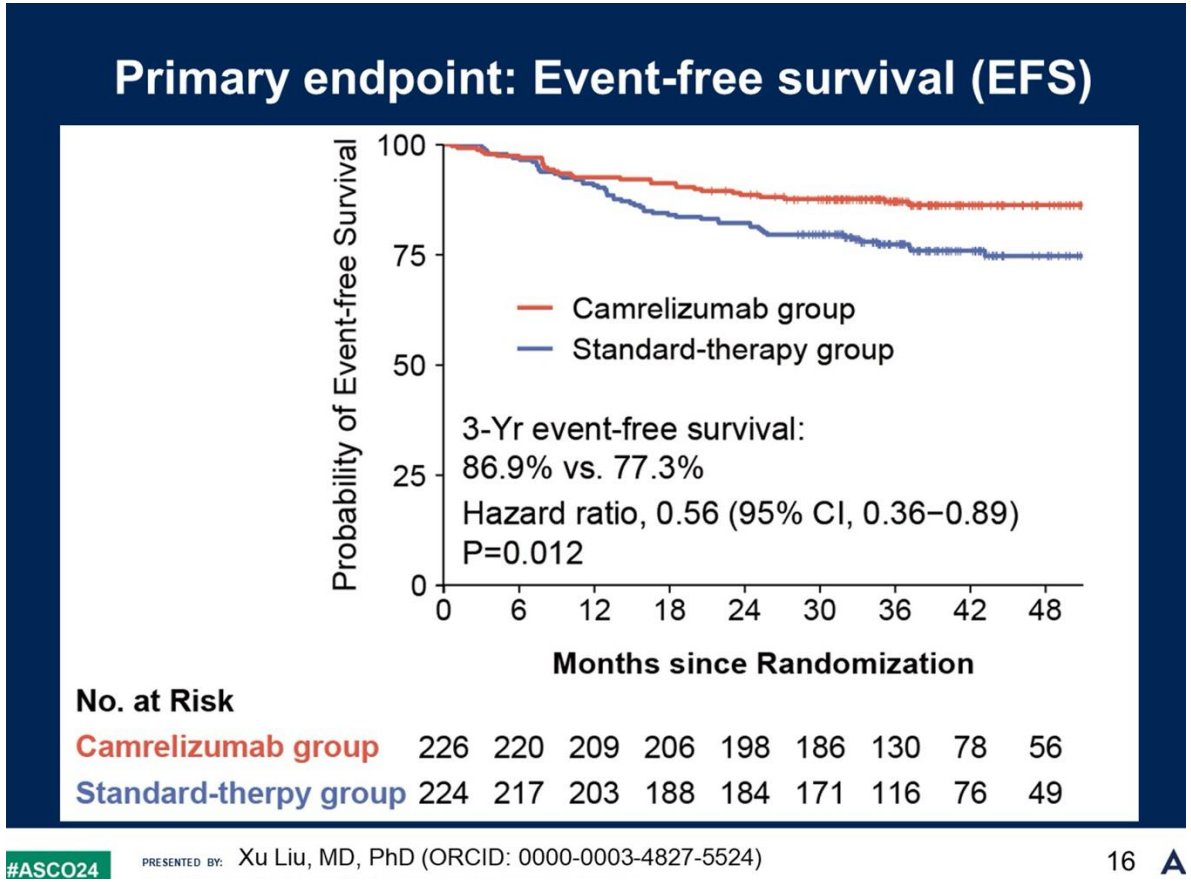
Zhang et al. N Engl J Med. 2019 May 31

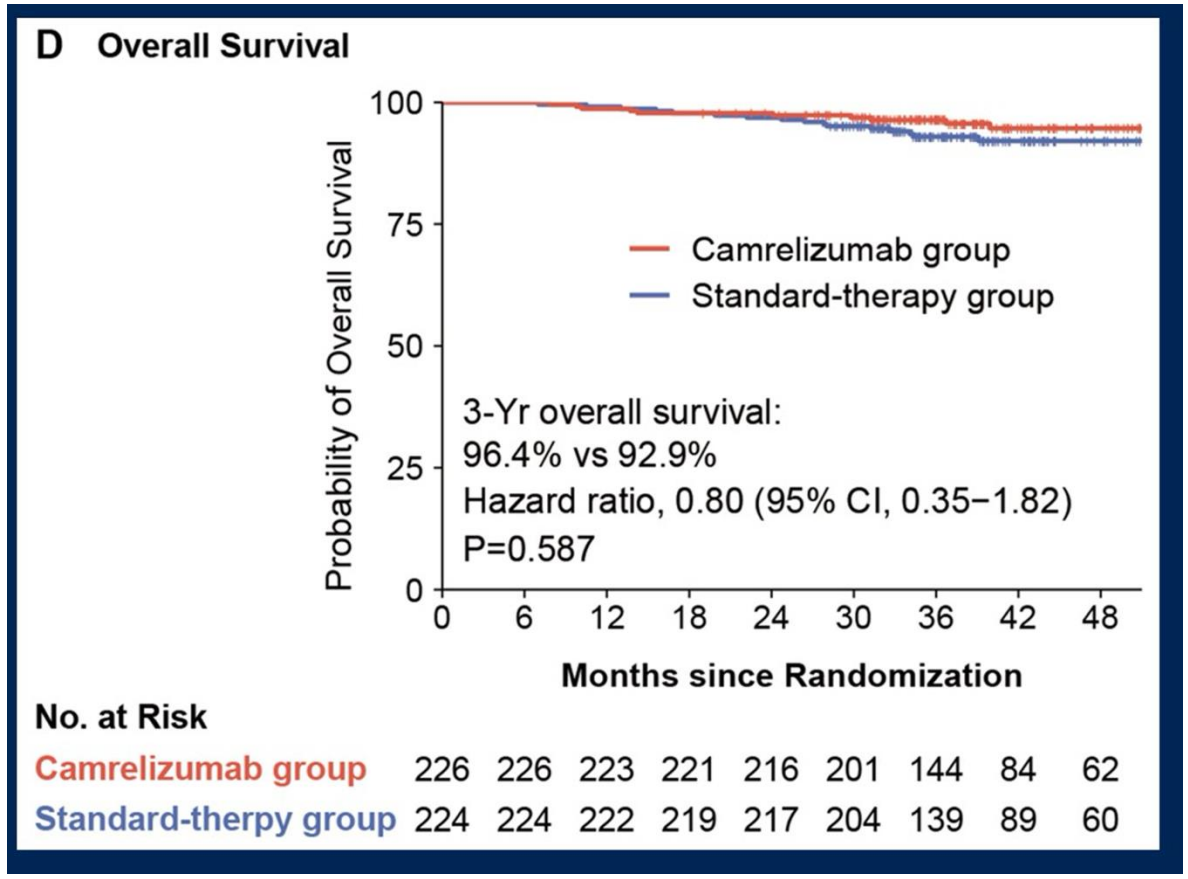
Incorporating ICI in curative intent NPC



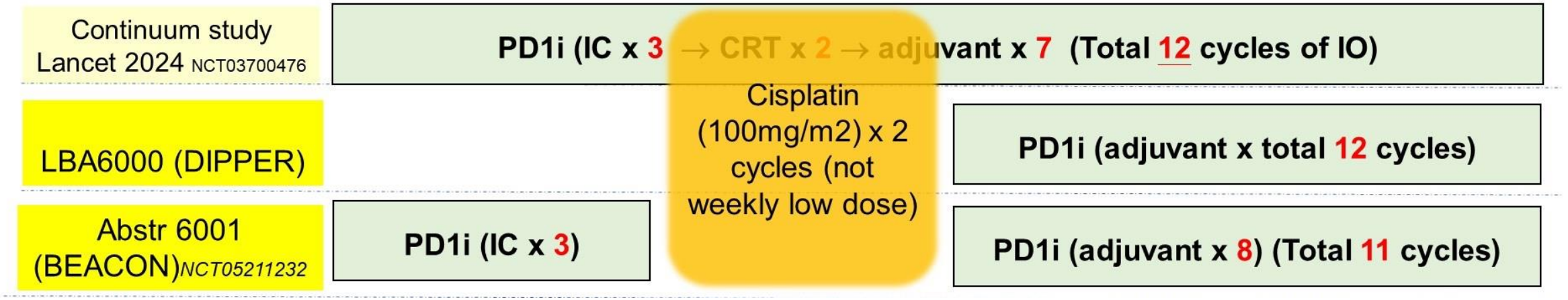
PRESENTED BY: Xu Liu, MD, PhD (ORCID: 0000-0003-4827-5524)

Incorporating ICI in curative intent NPC





Adding immunotherapy to SoC: Strategies phase III evaluation

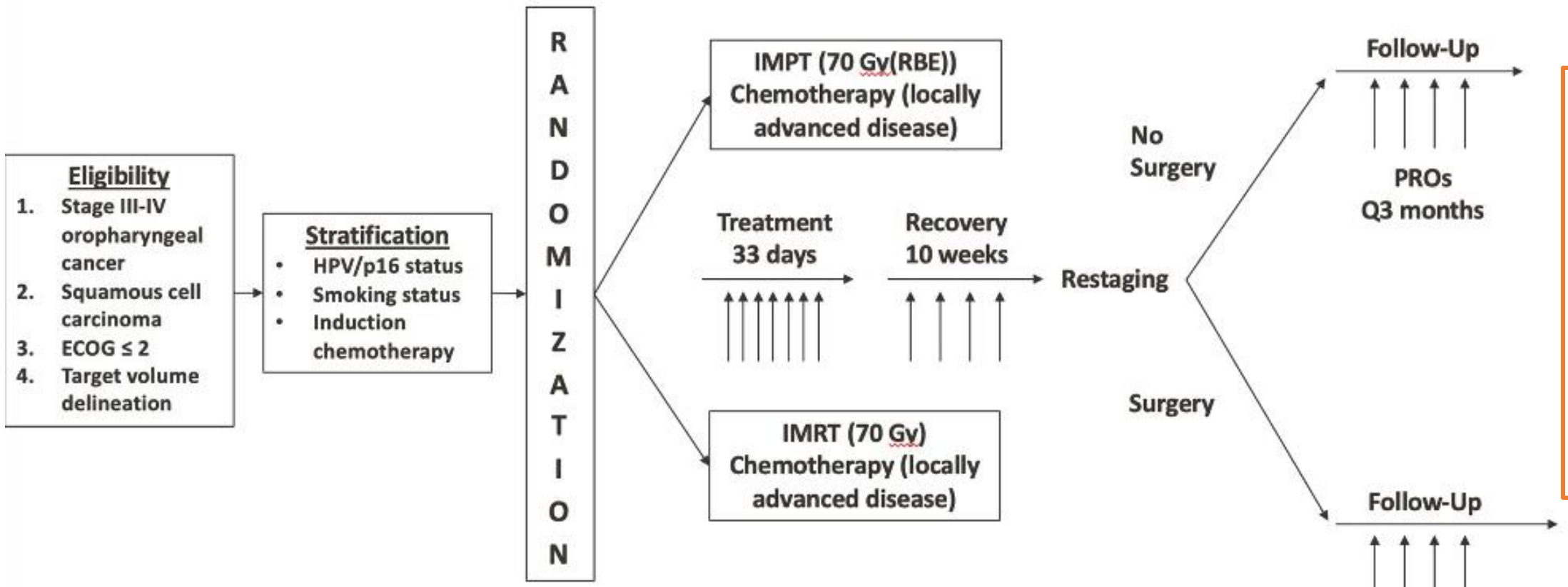


- Encouraging activity and tolerability
- No overall survival advantage (as of yet)
- Timing of ICI unclear

Therapeutic goals in LAHNSCC

- Most are candidates for curative intent therapy
- Dual challenge of optimizing oncologic and functional outcomes

Phase III Trial of IMPT vs IMRT for Oropharyngeal Tumors



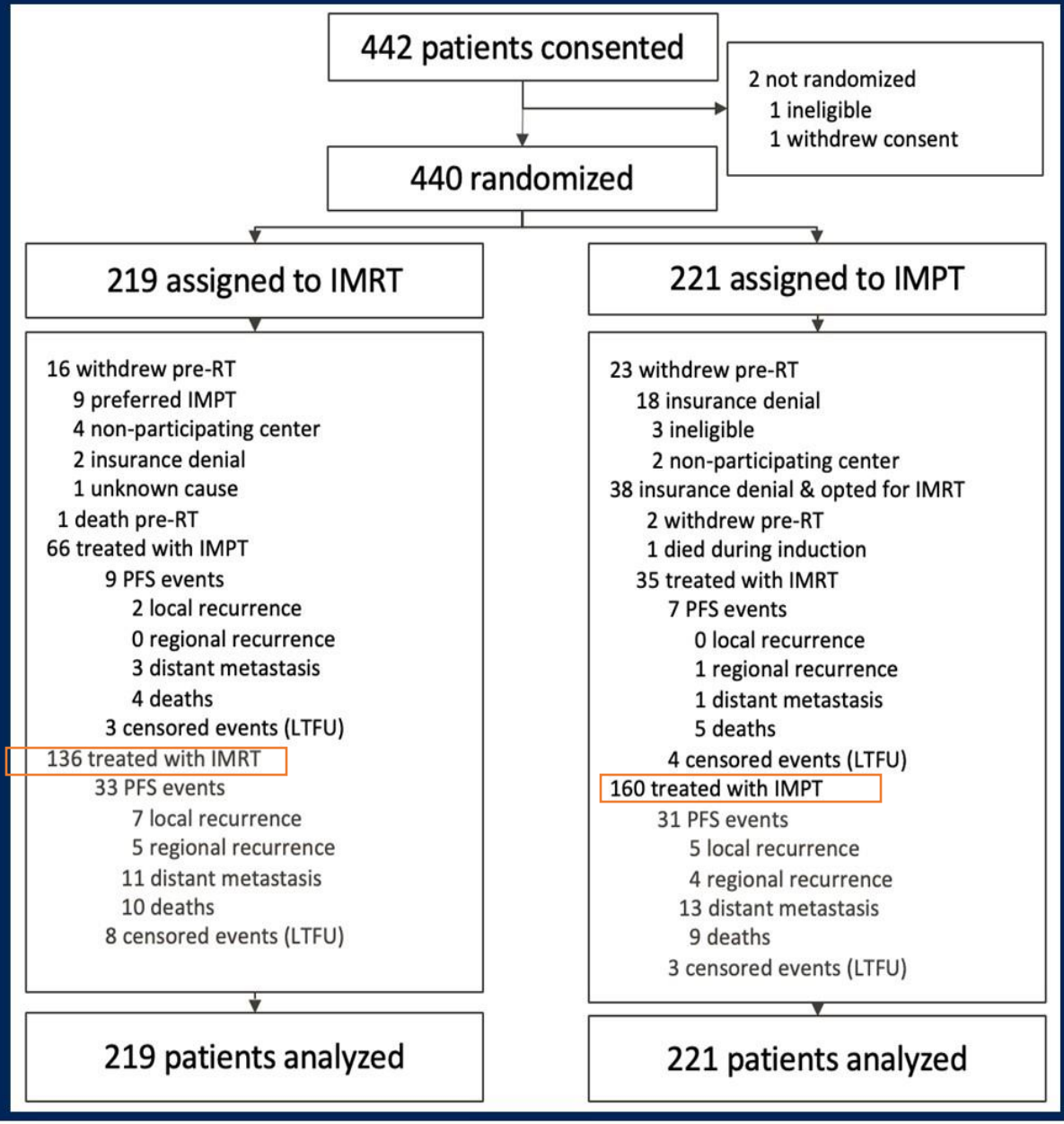
Frank SJ *Seminars in Radiation Oncology 2018*

Primary Endpoint: 3-year PFS

Secondary Endpoints: OS, malnutrition, G-tube dependent

Frank et al, Abstract #6006, ASCO 2024

Consort
[PFS – ITT]

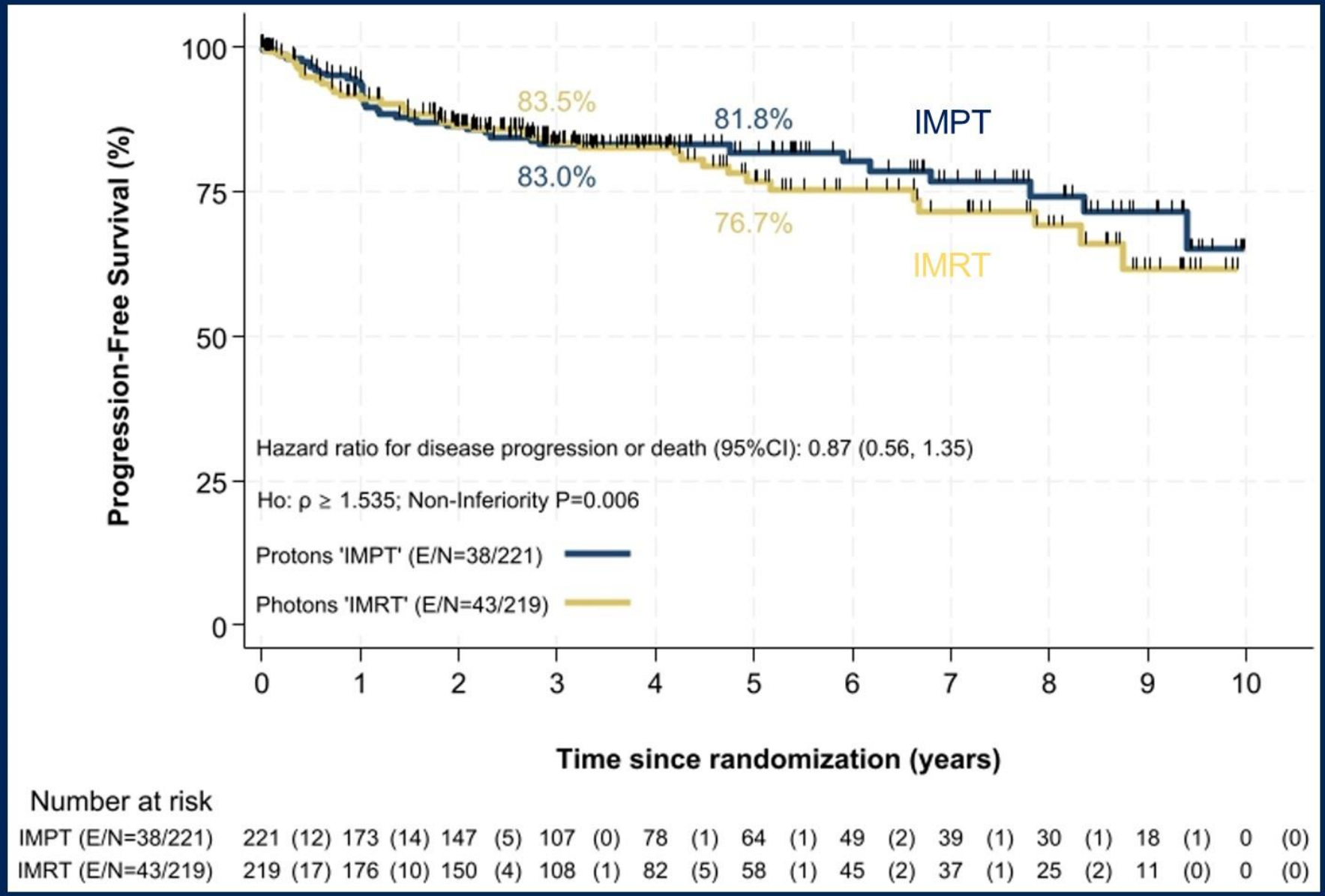


440 patients
- 90% male
- 93% white
- 62% age <65
- 76% ECOG=0
- 95% HPV+

Frank et al, Abstract #6006, ASCO 2024

Progression-Free Survival (ITT)

IMPT is **Non-Inferior** to IMRT



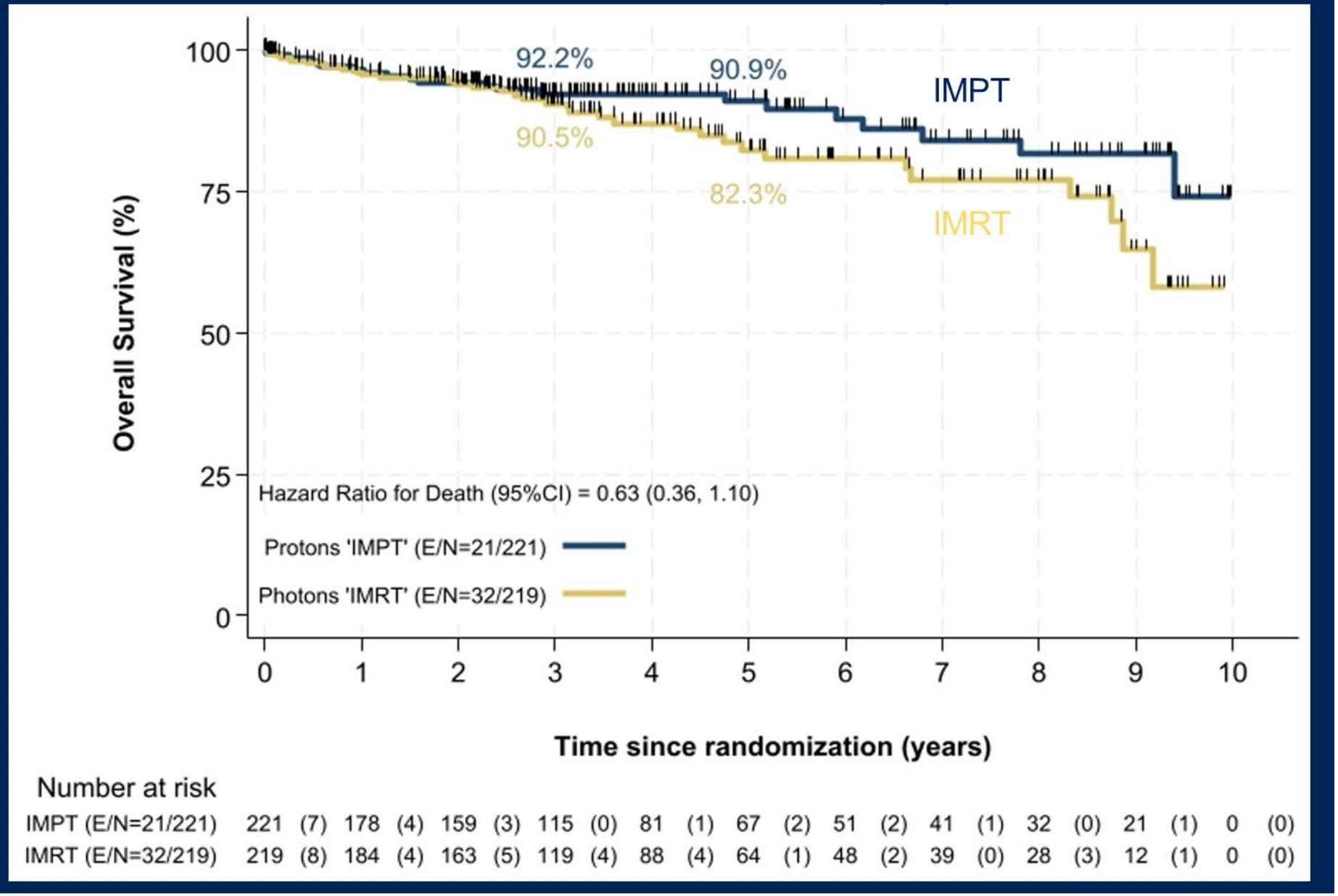
Number at risk

IMPT (E/N=38/221)	221	(12)	173	(14)	147	(5)	107	(0)	78	(1)	64	(1)	49	(2)	39	(1)	30	(1)	18	(1)	0	(0)
IMRT (E/N=43/219)	219	(17)	176	(10)	150	(4)	108	(1)	82	(5)	58	(1)	45	(2)	37	(1)	25	(2)	11	(0)	0	(0)

PRESENTED BY: Steven J Frank, MD

Frank et al, Abstract #6006, ASCO 2024

Overall Survival (ITT)

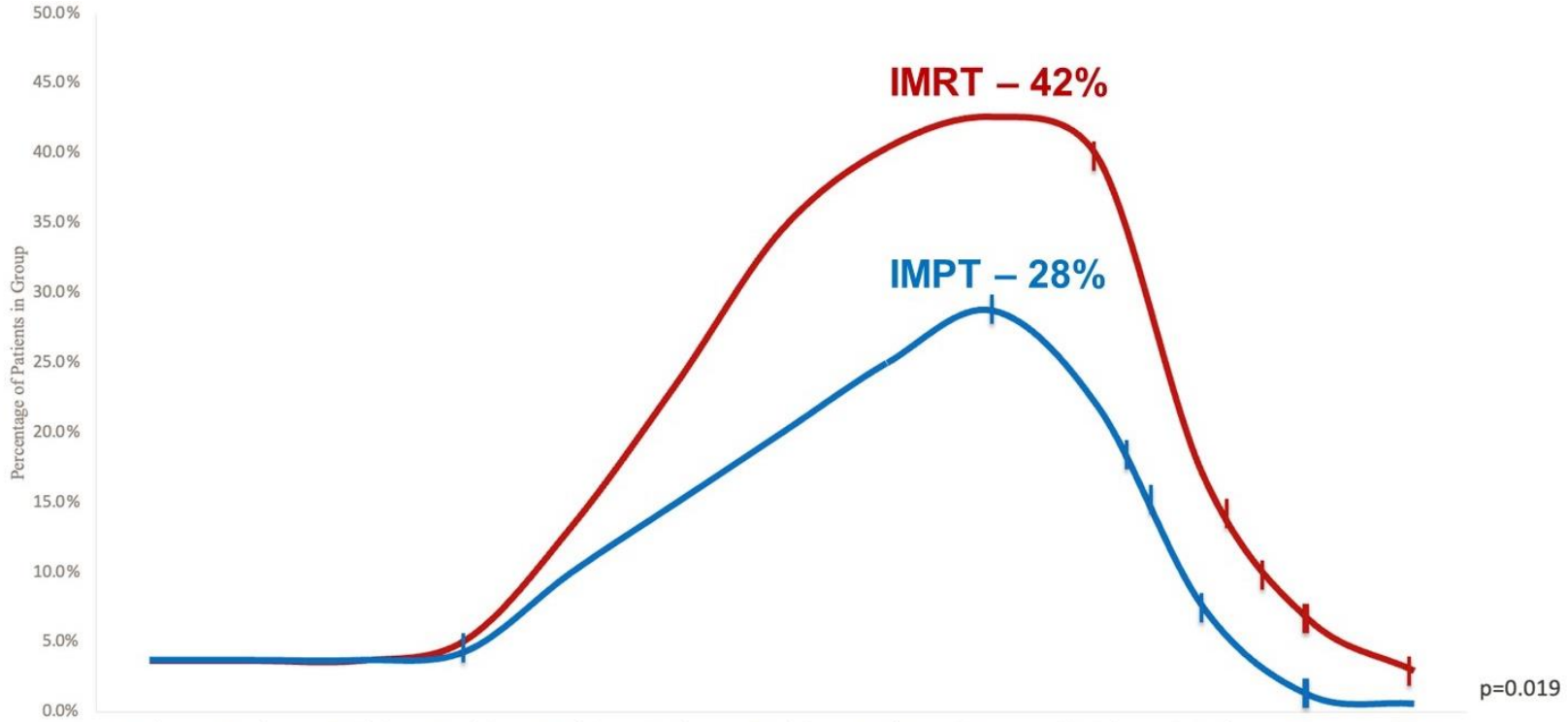


Number at risk

IMPT (E/N=21/221)	221	(7)	178	(4)	159	(3)	115	(0)	81	(1)	67	(2)	51	(2)	41	(1)	32	(0)	21	(1)	0	(0)
IMRT (E/N=32/219)	219	(8)	184	(4)	163	(5)	119	(4)	88	(4)	64	(1)	48	(2)	39	(0)	28	(3)	12	(1)	0	(0)

Frank et al, Abstract #6006, ASCO 2024

Secondary Endpoint: Gastrostomy Tube Dependence



Number of evaluable patients without FT	Baseline	Tx Wk 1	Tx Wk 2	Tx Wk 3	Tx Wk 4	Tx Wk 5	Tx Wk 6	Tx Wk 7	Recovery Period	First Follow Up	6 Month	1 Year	2 Year
Group 1 - IMRT	131	131	131	129	118	104	89	81	78	77	76	76	76
Group 2 - IMPT	154	154	154	152	143	135	127	119	112	111	111	111	111

Frank et al, Abstract #6006, ASCO 2024

Summary

- Efficacious combinations are under study for R/M disease
- Toxicity impacts survival benefit
- Immune check point inhibitors are being introduced in curative intent setting
- Evidence supporting proton radiation therapy is emerging

The Head and Neck Oncology Program











THANK YOU!

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