

Immunotherapy Updates in Head and Neck Cancer

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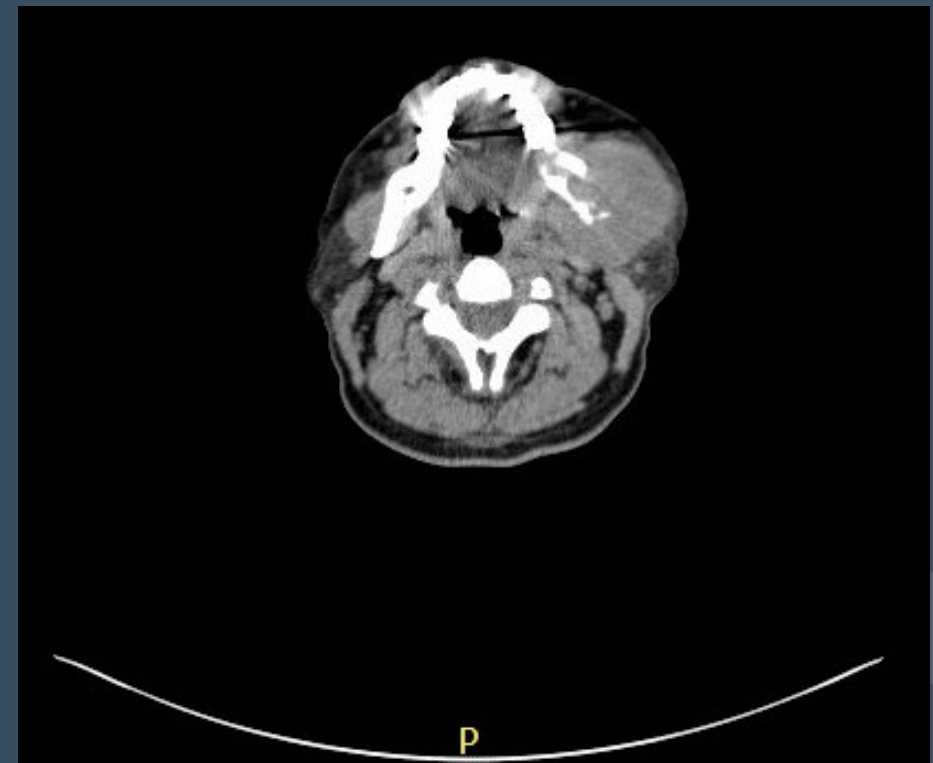
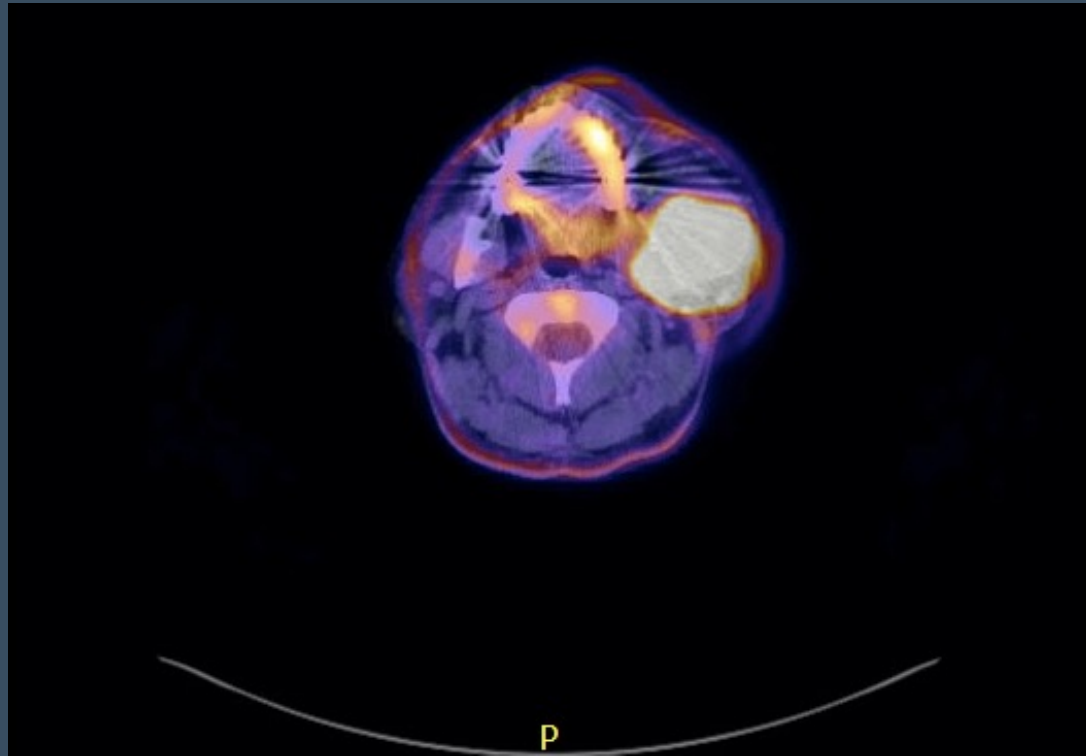


Immunotherapy in HNC – Case Approach

- 51 year old male presented with progressive left dental, jaw, and facial pain.
- 10 pack-years smoking; chewing tobacco “decades” but quit in his 40s.
- Had wisdom tooth removed and intraoral biopsy of erythematous and edematous tissue
 - Invasive SCC moderately differentiated, p16 negative (HPV negative) of the oral cavity

Oral Cavity SCC

cT4b N2b M0 SCC left mandible



Oral Cavity SCC

- Standard of care
 - Oncologic resection followed by pathology-driven adjuvant therapy¹
 - Consider induction chemotherapy (“chemoselection”) in borderline resectable disease or patient-specific factors
 - What is the role for immunotherapy in the curative treatment for head and neck cancer?

HNC: Immunotherapy in Curative Setting

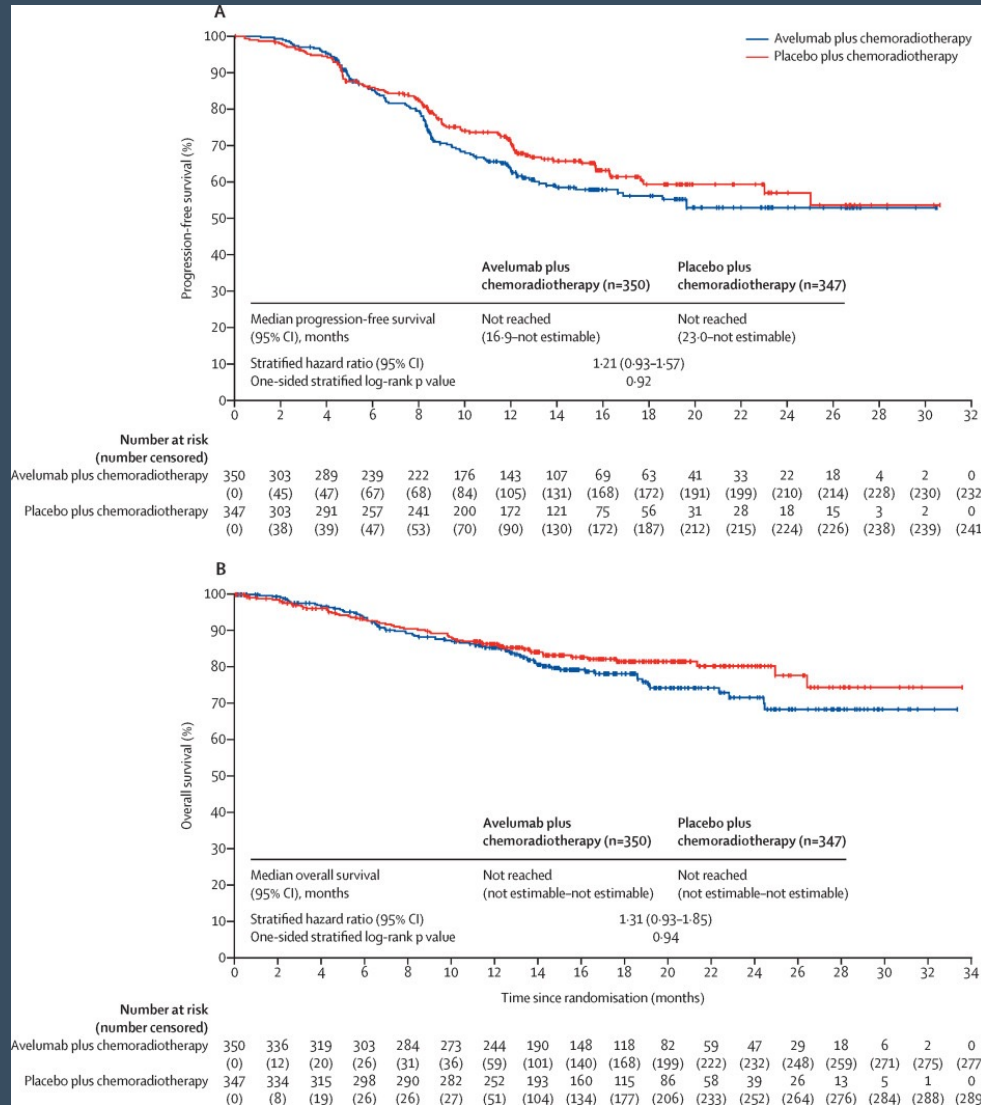
- Neoadjuvant therapy
 - KN689
- Definitive RT-based therapy (unresected)
 - JAVELIN
- Adjuvant therapy
 - IMvoke010
 - RTOG 1216



Neoadjuvant Immunotherapy – KN689

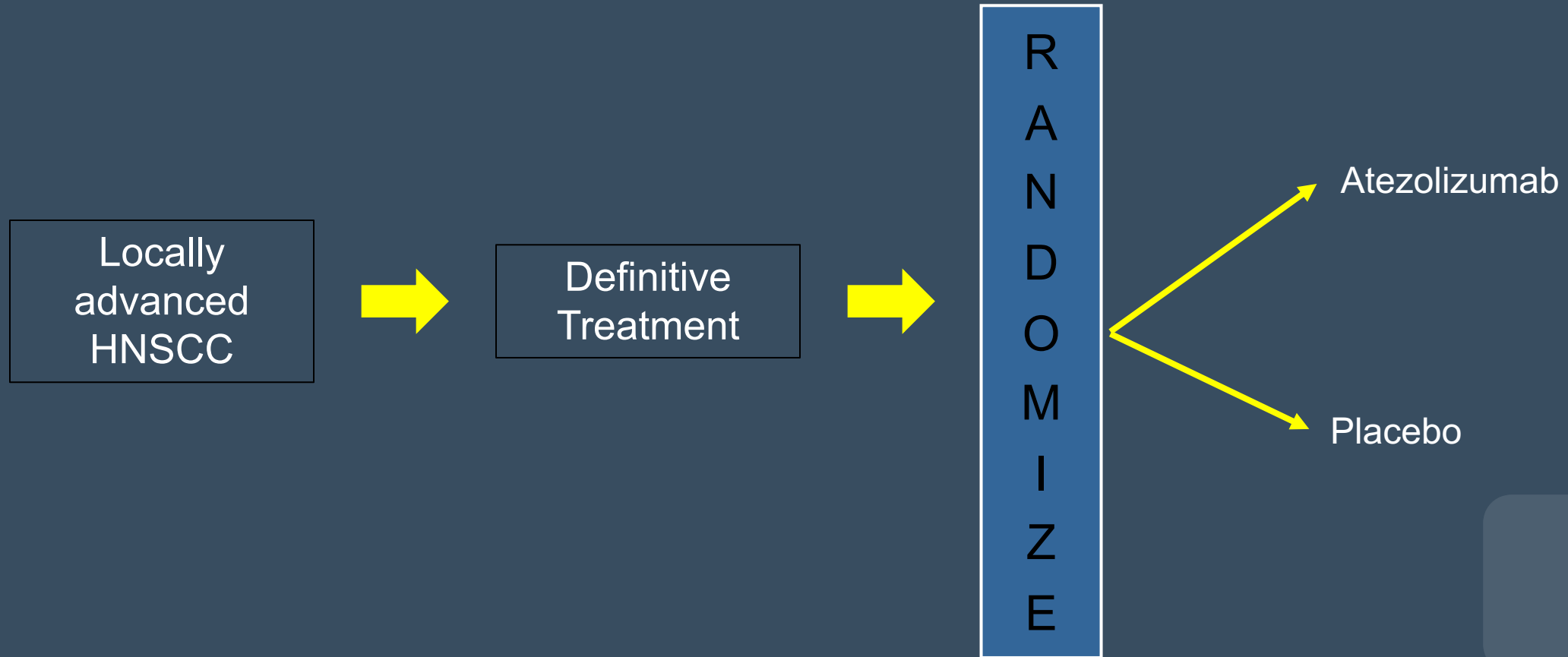
- Phase III, randomized, open-label pembrolizumab prior to surgery, and in combination with standard post-operative RT (+/- cisplatin) in locally advanced, resectable HNSCC
 - 704 pts
 - Estimated completion 9/2026

Combination of Checkpoint Inhibitor with Definitive Chemoradiotherapy - JAVELIN



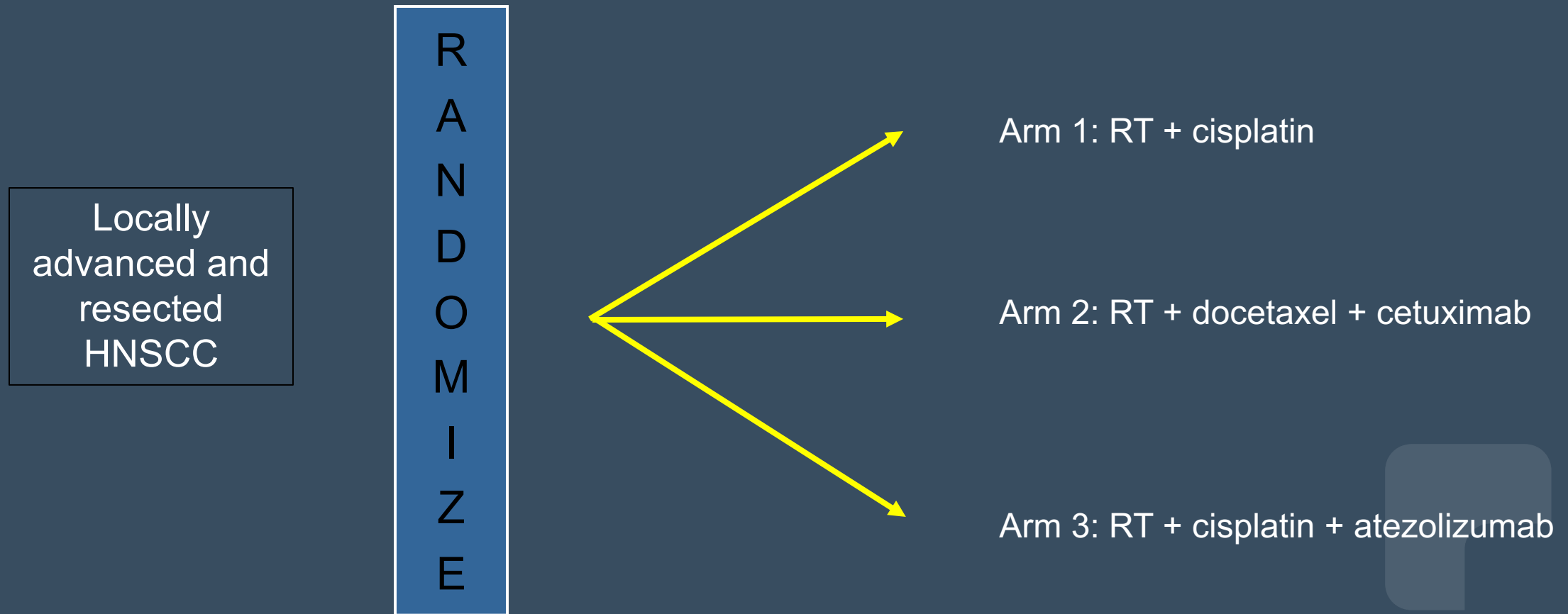
Avelumab+chemoradiation vs chemoradiation

Adjuvant Immunotherapy Following Definitive Local Therapy – IMvoker010



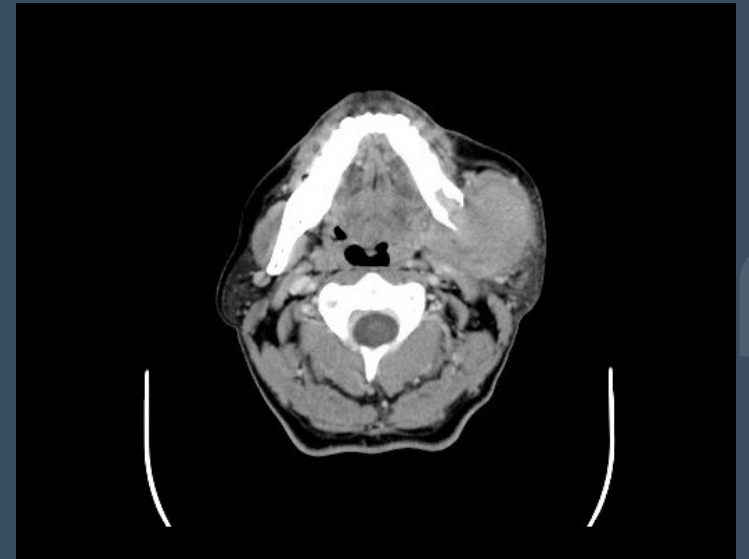
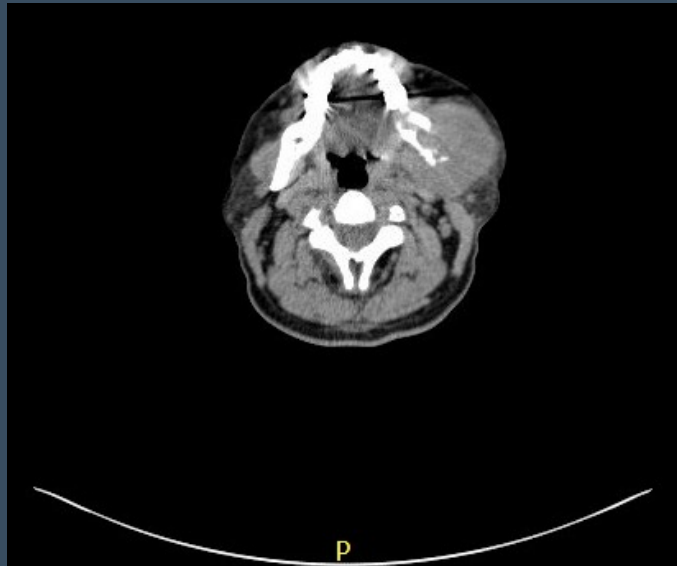
Phase III; 406 patients
Early termination, did not meet endpoint of EFS

Adjuvant Immunotherapy in High-Risk Resected HNSCC – RTOG 1216



Case

- The patient was treated with platinum doublet chemotherapy x 2 cycles with response to therapy, and proceeded to resection



Case

- The patient underwent left radical mandibulectomy, left radical parotidectomy with resection lower division of facial nerve, infratemporal fossa resection and resection of tumor involving skull base, left SND levels 1-4 followed by reconstruction
 - Pathology: 7.0 cm SCC poor diff, invasive, extensive invasion of mandibular bone and soft tissues, SM+ at left proximal V3, total 1/47 LN+, no ENE.
 - Stage: cT4b N2b M0 → ypT4b N1 M0

Adjuvant Therapy

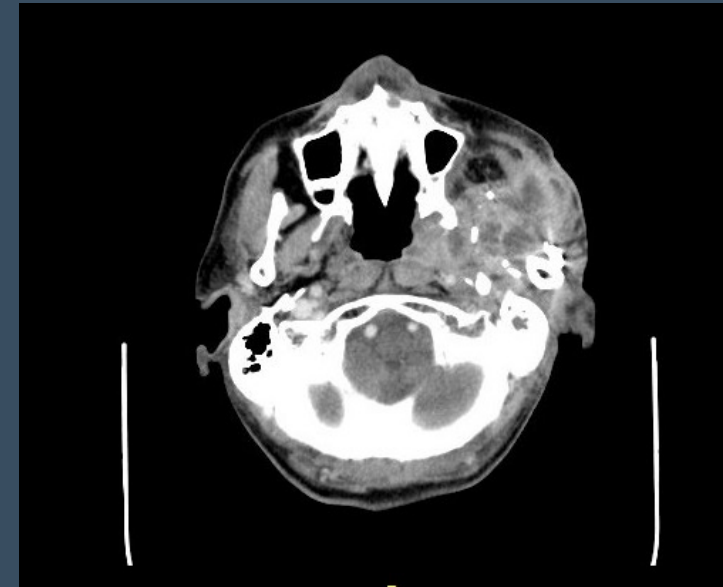
- RTOG 1216
 - Patient ineligible given upfront chemotherapy prior to resection
- Adjuvant immunotherapy trial closed to accrual
 - IMvoke010



Case

- The patient was treated with standard of care cisplatin-based adjuvant chemoradiotherapy
 - Positive surgical margin
 - Completed adjuvant CRT 5/3/2023

- Restaging imaging:
 - Rapid recurrence
 - Biopsy +SCC



Recurrent/Metastatic HNSCC:

First Checkpoint Inhibitor Approvals in Head and Neck Cancers

CHECKMATE-141

Nivolumab for Recurrent Squamous-Cell Carcinoma of the Head and Neck

R.L. Ferris, G. Blumenschein, Jr., J. Fayette, J. Guigay, A.D. Colevas, L. Licitra, K. Harrington, S. Kasper, E.E. Vokes, C. Even, F. Worden, N.F. Saba, L.C. Iglesias Docampo, R. Haddad, T. Rordorf, N. Kiyota, M. Tahara, M. Monga, M. Lynch, W.J. Geese, J. Kopit, J.W. Shaw, and M.L. Gillison
N ENGL J MED 375:19 NEJM.ORG NOVEMBER 10, 2016

KEYNOTE-012/KEYNOTE-040

Safety and clinical activity of pembrolizumab for treatment of recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-012): an open-label, multicentre, phase 1b trial

Tangy Y Seiwert, Barbara Burtness, Raneeh Mehra, Jared Weiss, Raanan Berger, Joseph Paul Eder, Karl Heath, Terrill McClanahan, Jared Lunceford, Christine Gause, Jonathan D Cheng, Laura Q Chow

Lancet Oncol 2016; 17: 956-65

Pembrolizumab versus methotrexate, docetaxel, or cetuximab for recurrent or metastatic head-and-neck squamous cell carcinoma (KEYNOTE-040): a randomised, open-label, phase 3 study

Ezra E W Cohen, Denis Soulières, Christophe Le Tourneau, José Dinis, Lisa Licitra, Myung-Ju Ahn, Ainara Soria, Jean-Pascal Machiels, Nicolas Mach, Raneeh Mehra, Barbara Burtness, Pingye Zhang, Jonathan Cheng, Ramona F Swaby, Kevin J Harrington, on behalf of the KEYNOTE-040 investigators*

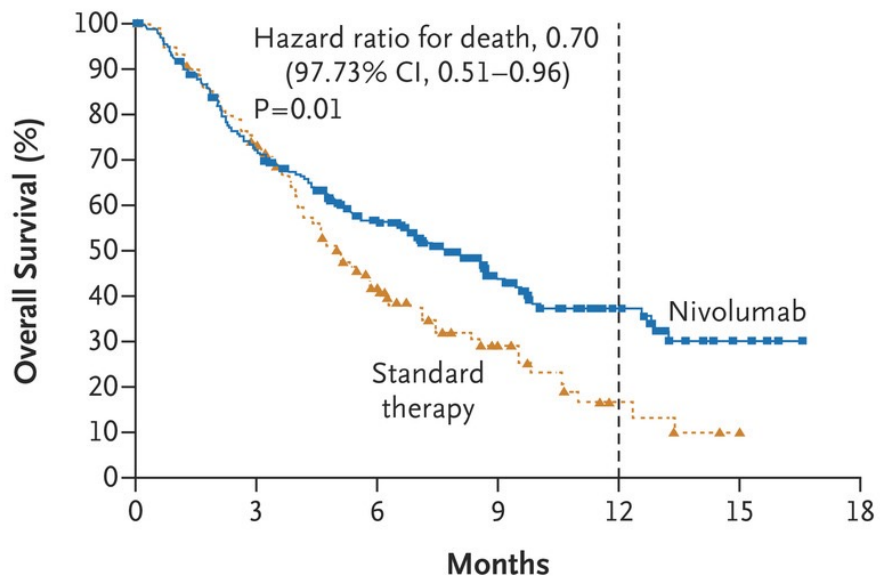
Lancet 2019; 393: 156-67

Checkpoint Inhibitors in Platinum Refractory Head & Neck Cancers

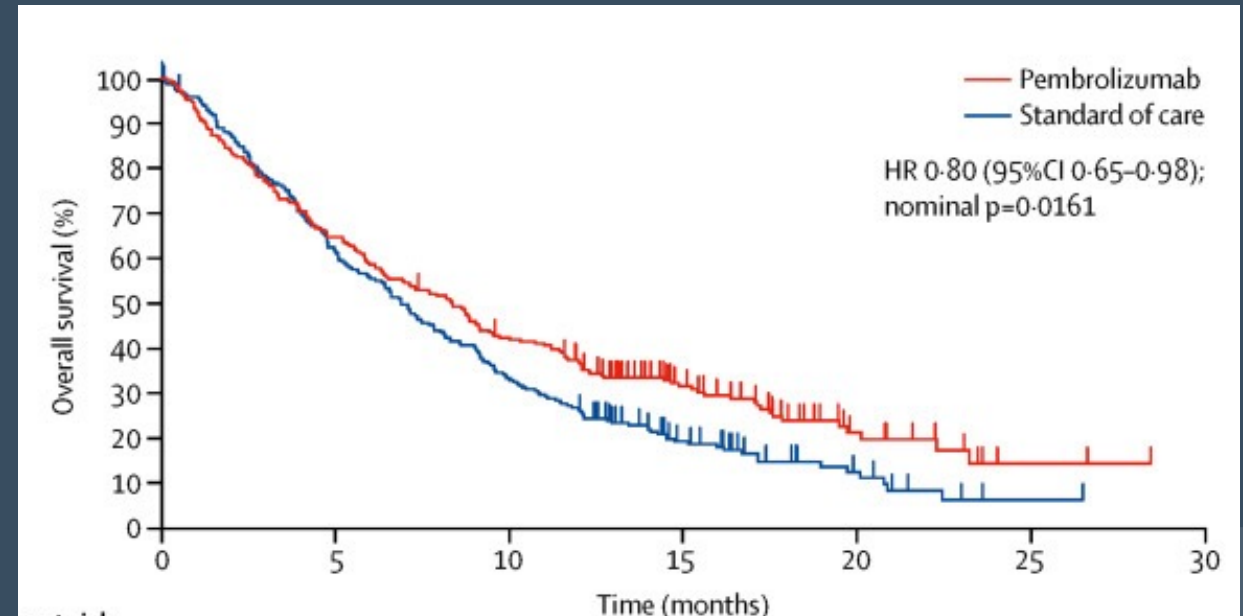
CHECKMATE-141

A Overall Survival

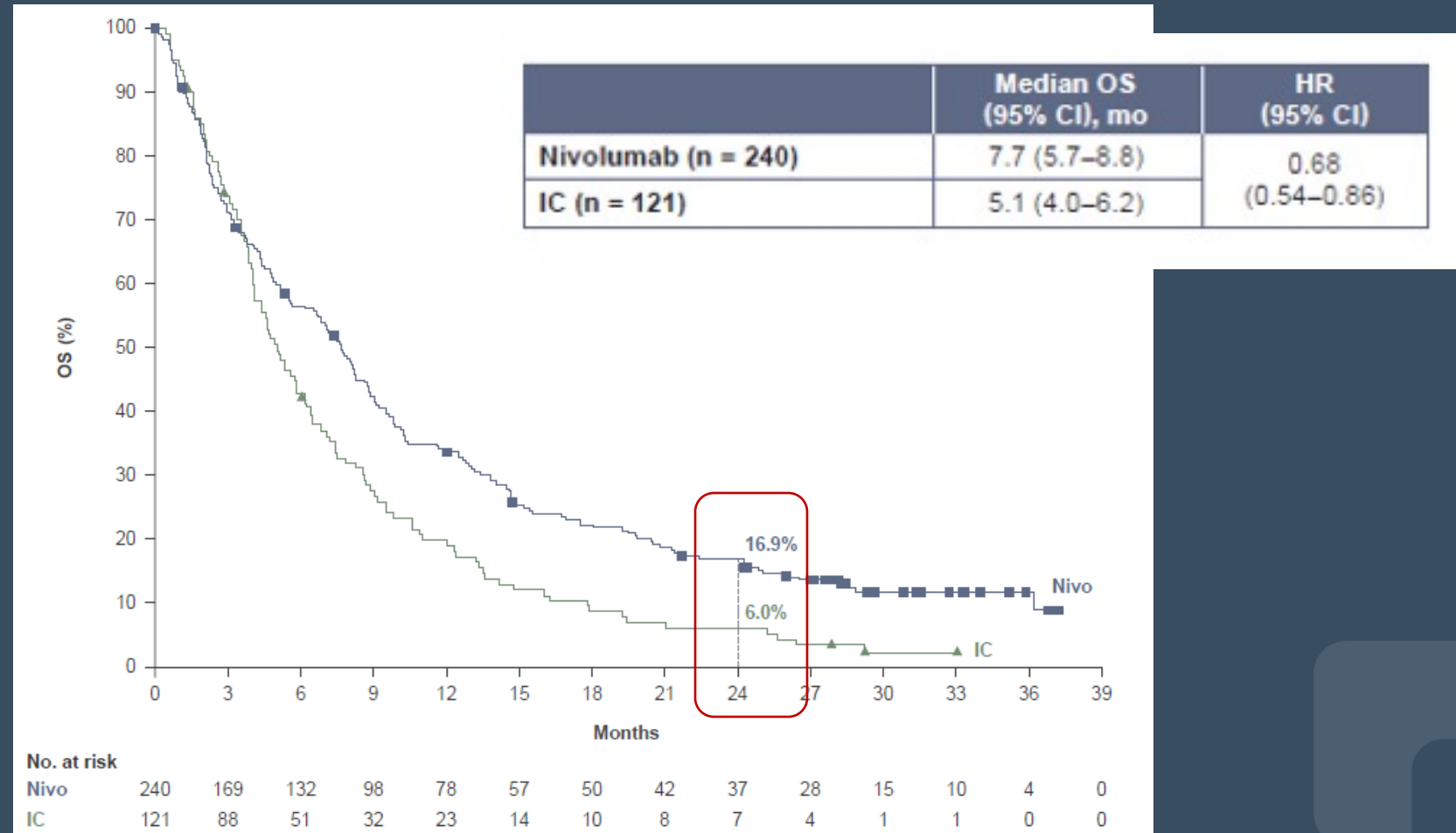
	No. of Patients	No. of Deaths	1-Yr Overall Survival Rate % (95% CI)	Median Overall Survival mo (95% CI)
Nivolumab	240	133	36.0 (28.5–43.4)	7.5 (5.5–9.1)
Standard Therapy	121	85	16.6 (8.6–26.8)	5.1 (4.0–6.0)



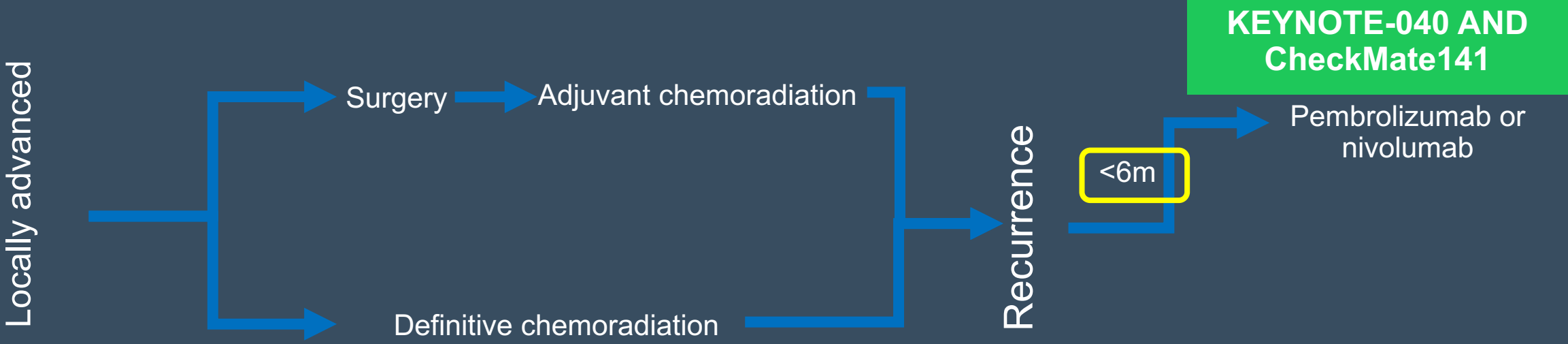
KEYNOTE-040



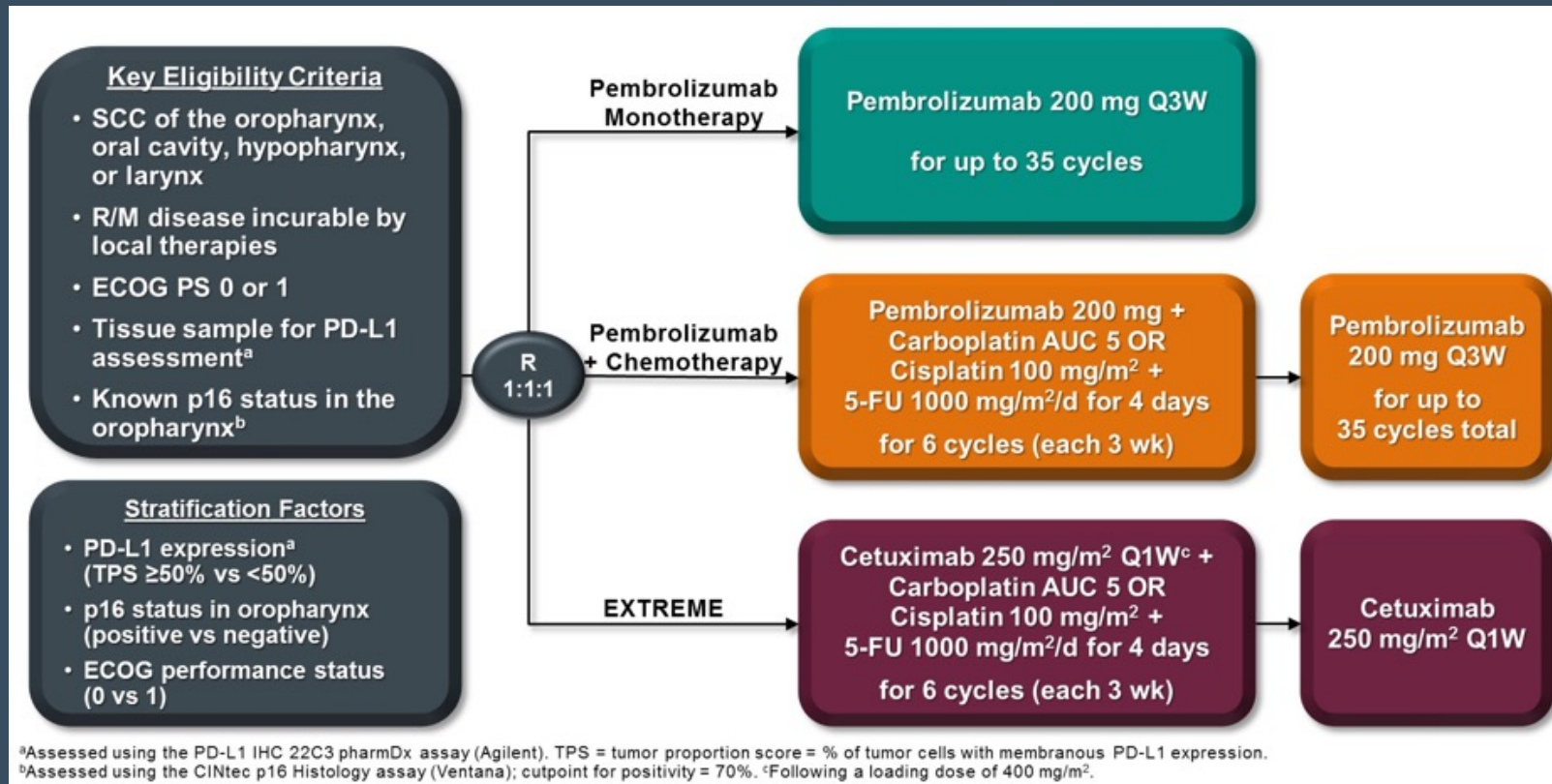
Checkmate 141: 2-year OS update



Checkpoint Inhibitors in Head & Neck Cancers



Protocol-Specified Final Results of the KEYNOTE-048 Trial of Pembrolizumab as First-Line Therapy for Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma (R/M HNSCC)



KEYNOTE-048

- Overlapping patient populations
 - CPS ≥ 20
 - CPS ≥ 1
 - Total patient population
- Multiple endpoints
 - Overall survival
 - Response rate
 - Toxicity



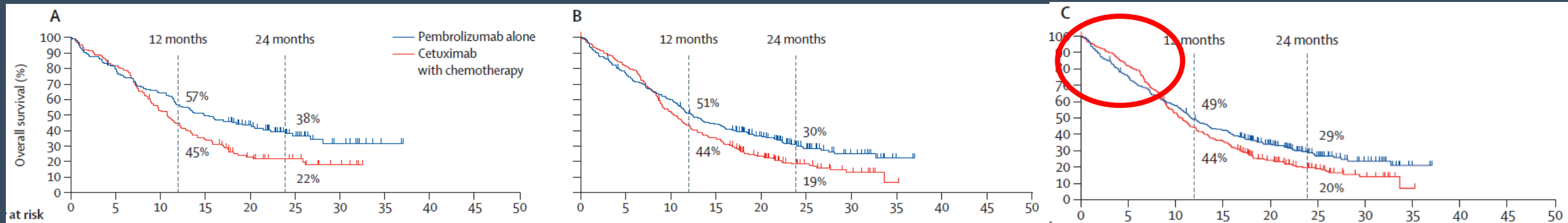
Checkpoint inhibitor in first-line treatment of R/M HNSCC

Pembrolizumab

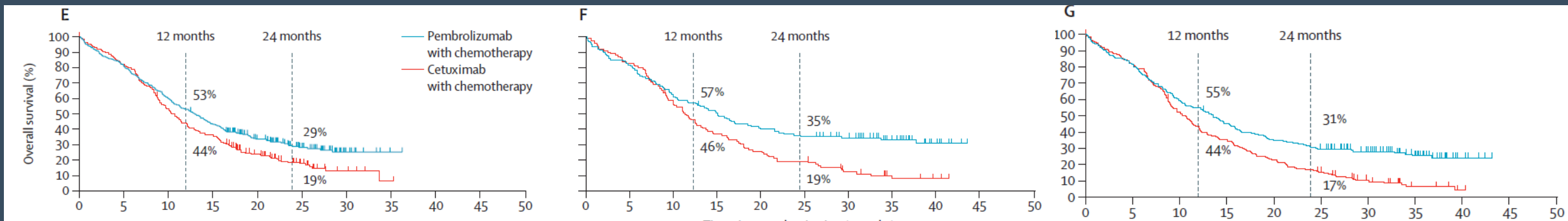
CPS ≥ 20

CPS ≥ 1

Total

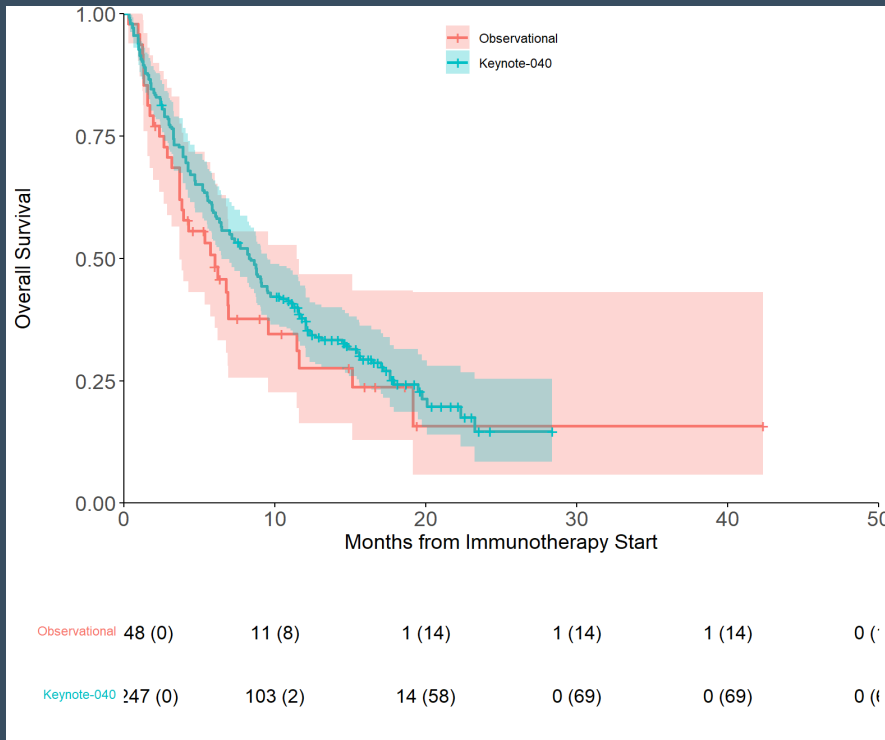


Pembrolizumab with chemotherapy

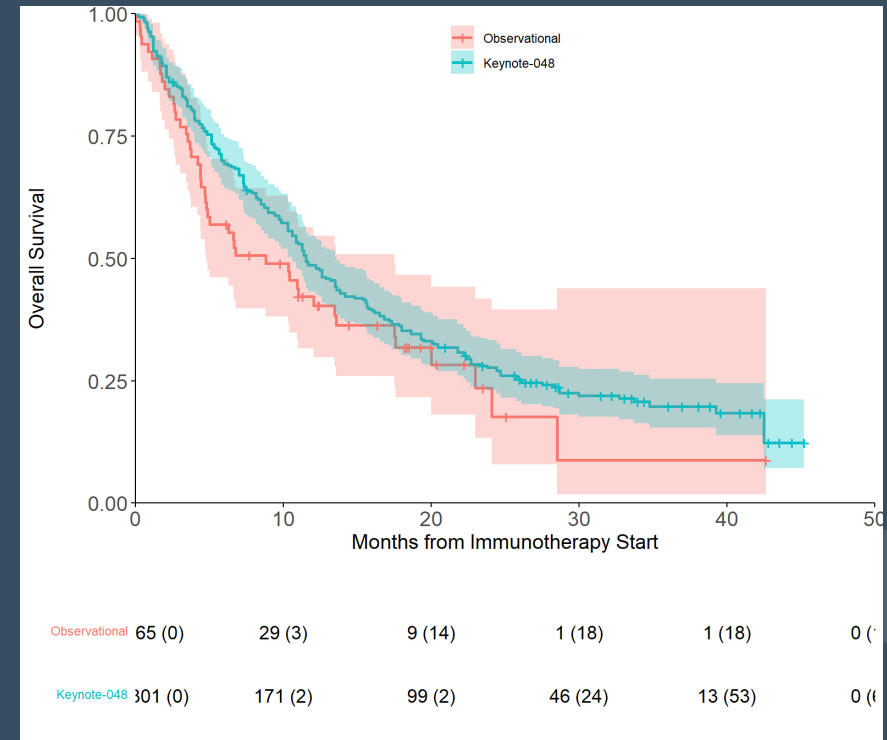


Real-World Experience of Checkpoint Inhibitors at Cleveland Clinic

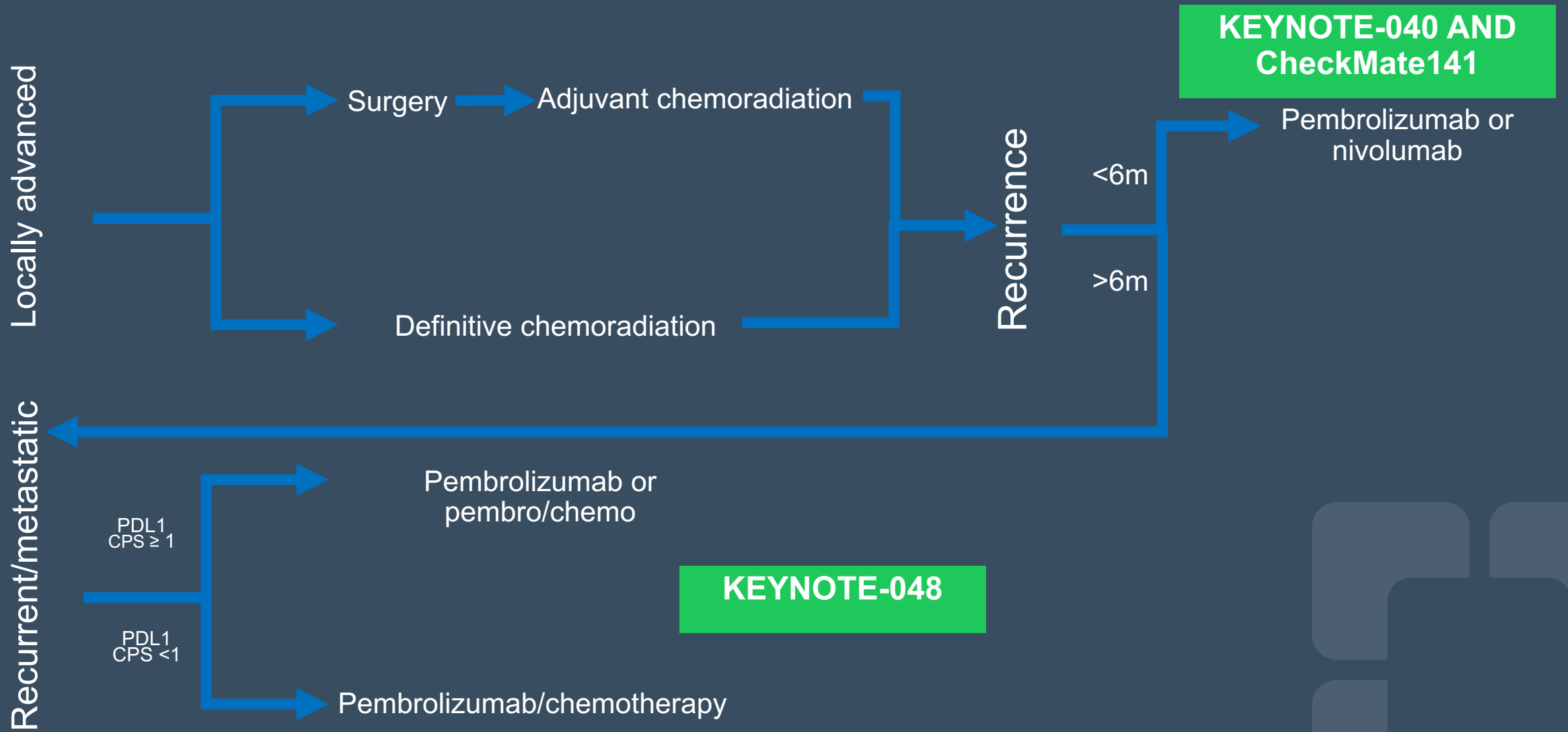
Single agent immunotherapy in Keynote-40 population



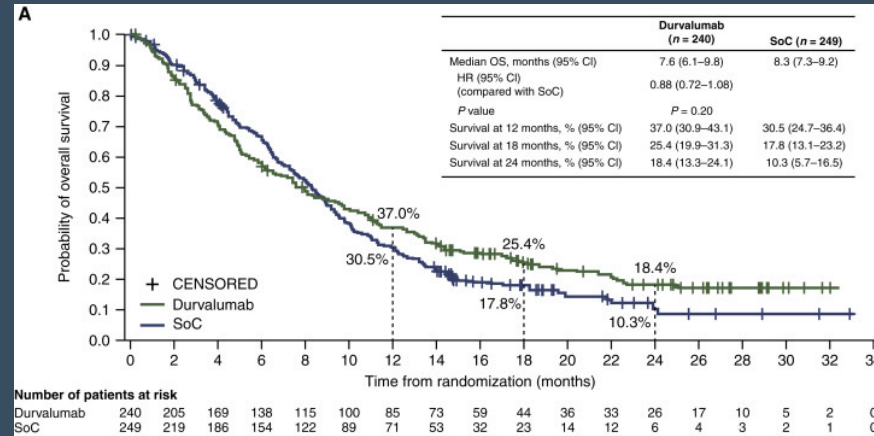
Single agent immunotherapy in Keynote-48 population



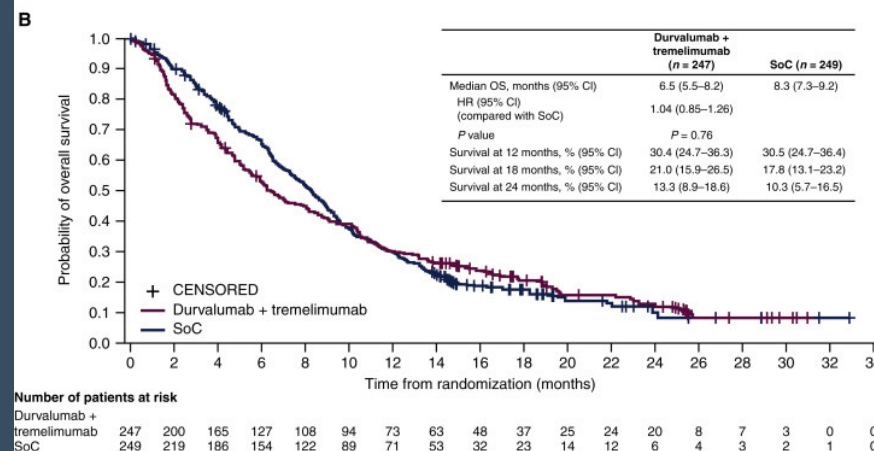
Checkpoint Inhibitors in Head & Neck Cancers



PD-L1 and CTLA-4 Combination in Platinum Refractory Head & Neck Cancer

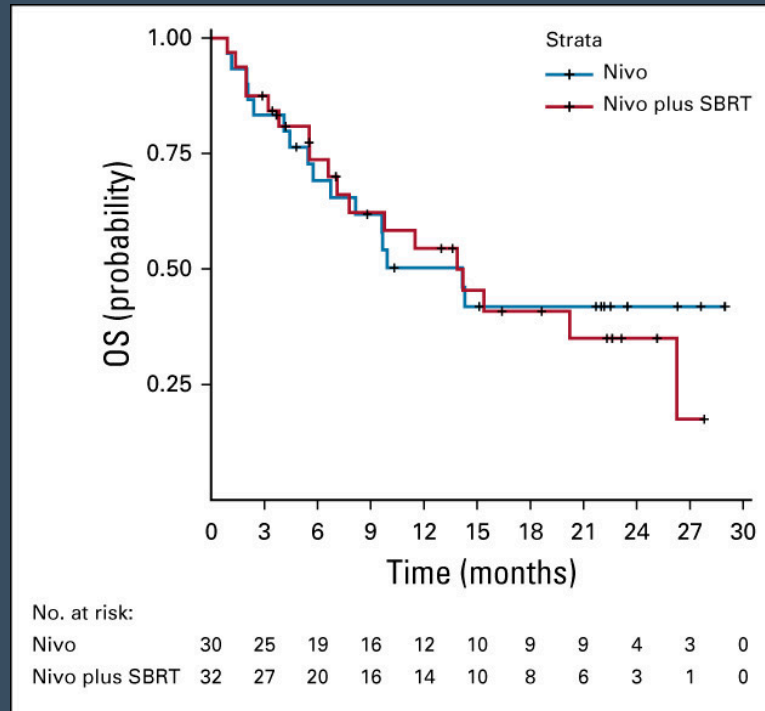


Durvalumab vs SoC



Durvalumab+Tremelimumab vs SoC

Checkpoint Inhibitor and SBRT combination in R/M HNSCC



Primary endpoint – ORR in non-irradiated lesions

TABLE 3. Overall Response Rate of Eligible Patients (n = 60)

Treatment Arm	PR or CR, No. (%)	SD or PD, No. (%)	P
Nivolumab (n = 29)	10 (34.5)	19 (65.5)	.86
Nivolumab + SBRT (n = 31)	9 (29.0)	22 (71.0)	

Abbreviations: CR, complete response; PD, progressive disease; PR, partial response; SBRT, stereotactic body radiotherapy; SD, stable disease.

TABLE 4. Multivariable Logistic Model With Objective Response Rate as the Outcome

Variable	OR (95% CI)	P
PD-L1 status	3.08 (0.94 to 10.04)	.06
Viral status	2.70 (0.81 to 9.02)	.11
Treatment arm	0.80 (0.24 to 2.61)	.71

Abbreviations: OR, odds ratio; PD-L1, programmed death-ligand 1.

RTOG 3507: SBRT +/- pembrolizumab for regional recurrent HNSCC

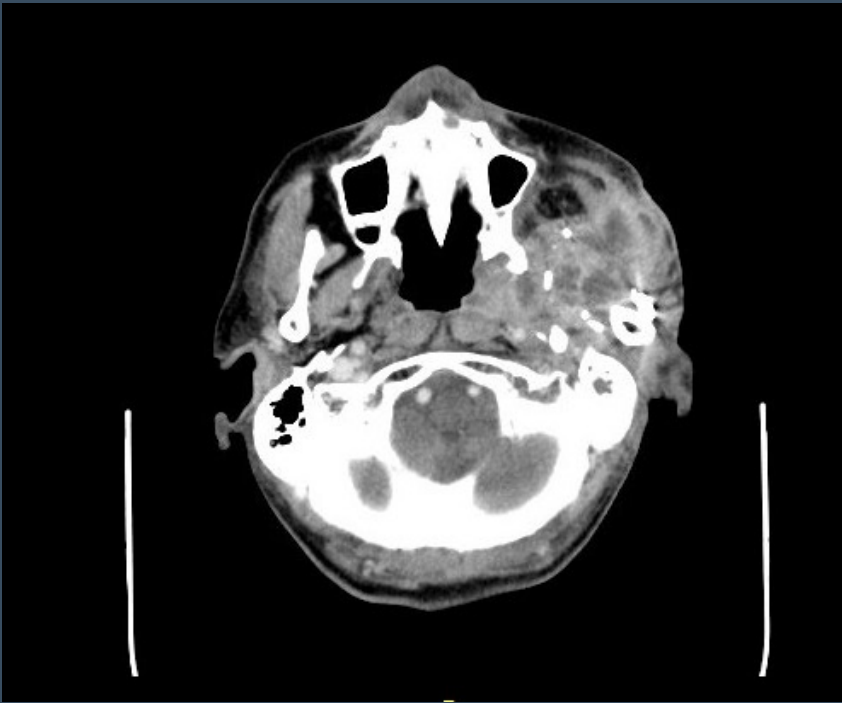
Case

- The patient just completed platinum-based CRT
- PD-L1 CPS 100
- Initiated pembrolizumab monotherapy, 6/28/2023

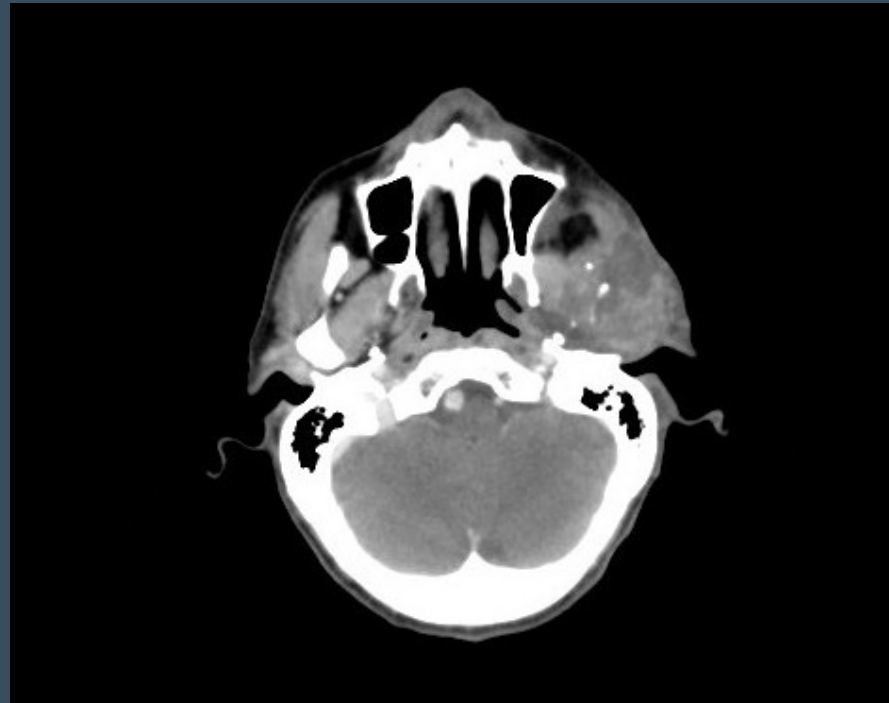


Case

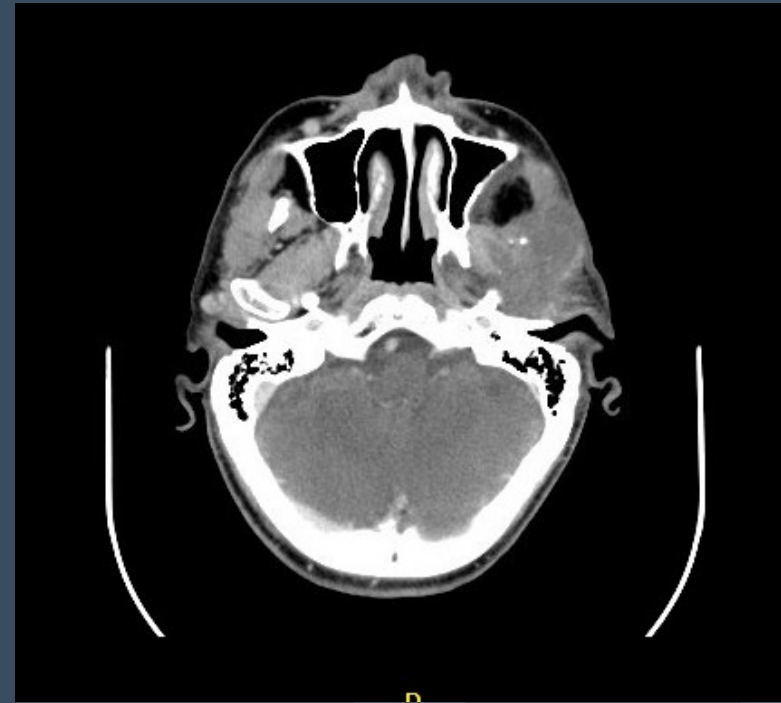
June 14, 2023



September 21, 2023

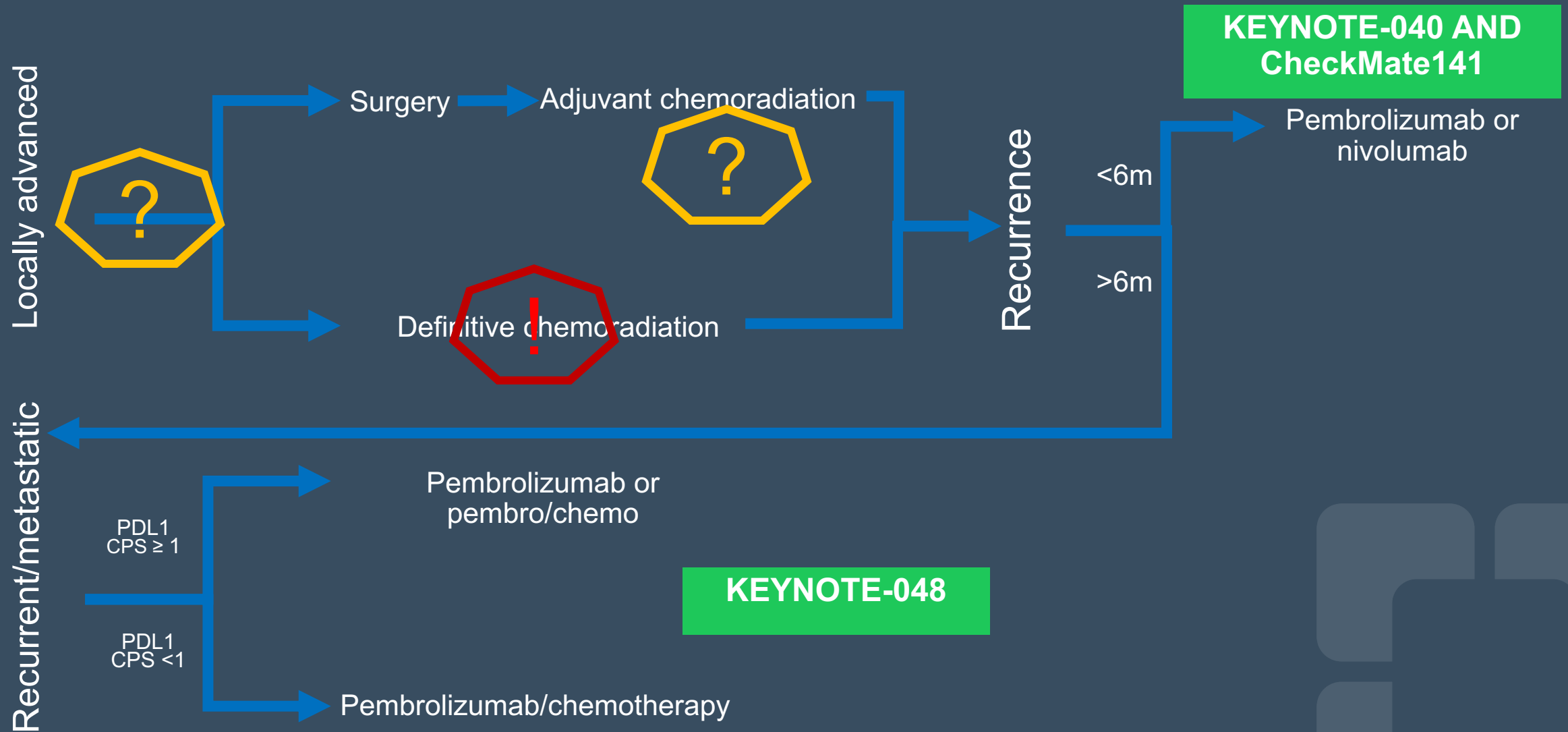


November 28, 2023



Pembrolizumab initiated ^

Checkpoint Inhibitors in Head & Neck Cancers



Immunotherapy in HNSCC

- Unclear role for immunotherapy in the curative setting
 - Patient selection, biomarkers needed
- Checkpoint inhibitors should be used in the frontline R/M setting (monotherapy vs chemoimmunotherapy)
- Post-immunotherapy failure in R/M setting: unmet need

THANK YOU

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