University of Colorado
Anschutz Medical Campus

Head and Neck Cancer

Jessica McDermott, MD MSCS

Evolving Treatments for the Oncology Practice

September 24, 2022

Agenda

- Updates on Definitive Therapy for Locally Advanced HNSCC
- Updates on Therapy for Metastatic HNSCC
- Updates on Nasopharyngeal Carcinoma

Locally Advanced HNSCC

Concurrent Chemoradiation – Cisplatin Dosing

- Prior studies: TATA Memorial and JCOG1008

Weekly Cisplatin Arms	Tata Memorial	JCOG 1008
Non-OP (%)	90.7	89.4
5 year OS (%)	--	70.0
2 year LRC (%)	58.5	70.0
2 year PFS (%)	52.0	70.0
2 year OS (%)	55.0	80.0
Cumulative Cisplatin dose (mg/m2)	210, IQR (180-210)	239, IQR(199-277)

ConCERT Trial

- Non-inferiority RCT as definitive therapy for non-nasopharynx HNSCC
- 59.6% oropharynx, 17.5% larynx, 11.6% hypopharynx, 11.6% oral cavity
- Randomized:
  - Cisplatin 100 mg/m2 q3weeks x 3
  - Cisplatin 40 mg/m2 weekly x 7
- 2-year Locoregional Control 52.6% (weekly) vs 47.4% (bolus) (p=0.426)
- Bolus dosing with significantly more: treatment interruptions, hospitalizations, mucositis, myelosuppression, renal toxicity, vomiting
- No significant difference in median time to loco-regional failure, overall survival, progression free survival

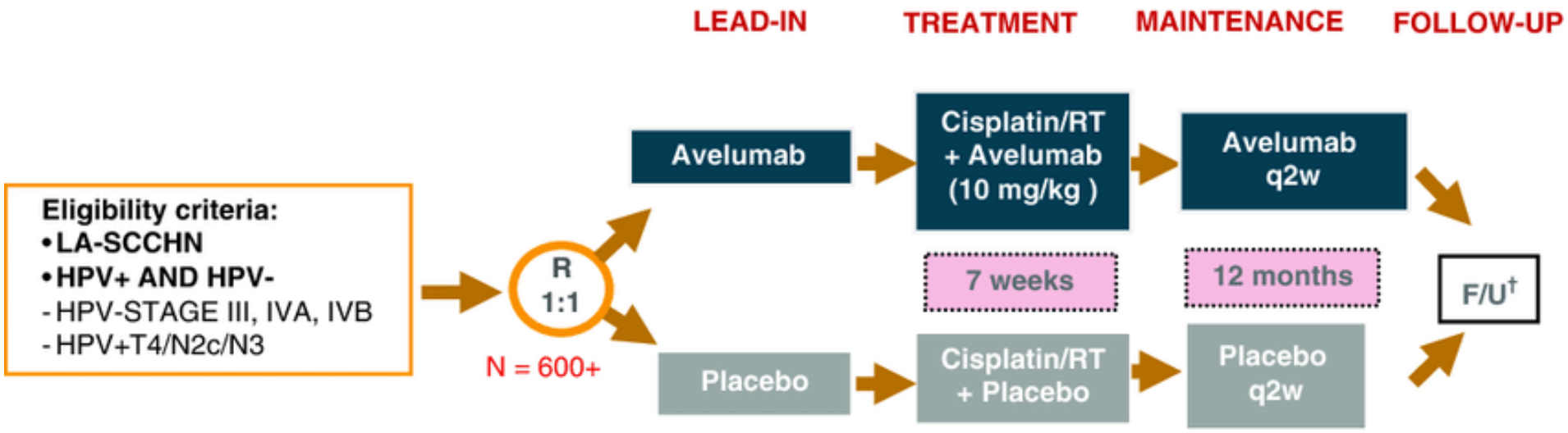
Sharma A, et al. Journal of Clinical Oncology 2022 40:16_suppl, 6004-6004

Docetaxel in Cisplatin ineligible

- Patients deemed Cisplatin ineligible receiving adjuvant or definitive CRT
- Randomized:
  - Radiation alone
  - Docetaxel/Radiation (15 mg/m2 x 7 weeks)
- 2-year Disease free survival: 30.3% vs 42% (p=0.002)
- Median OS 15.3 months vs 25.5 months (p=0.035)
- Grade 3+ AE: 58% vs 81.6% (p=0.000)

Patil VM, et al. Journal of Clinical Oncology 2022 40:17_suppl

JAVELIN Head and Neck

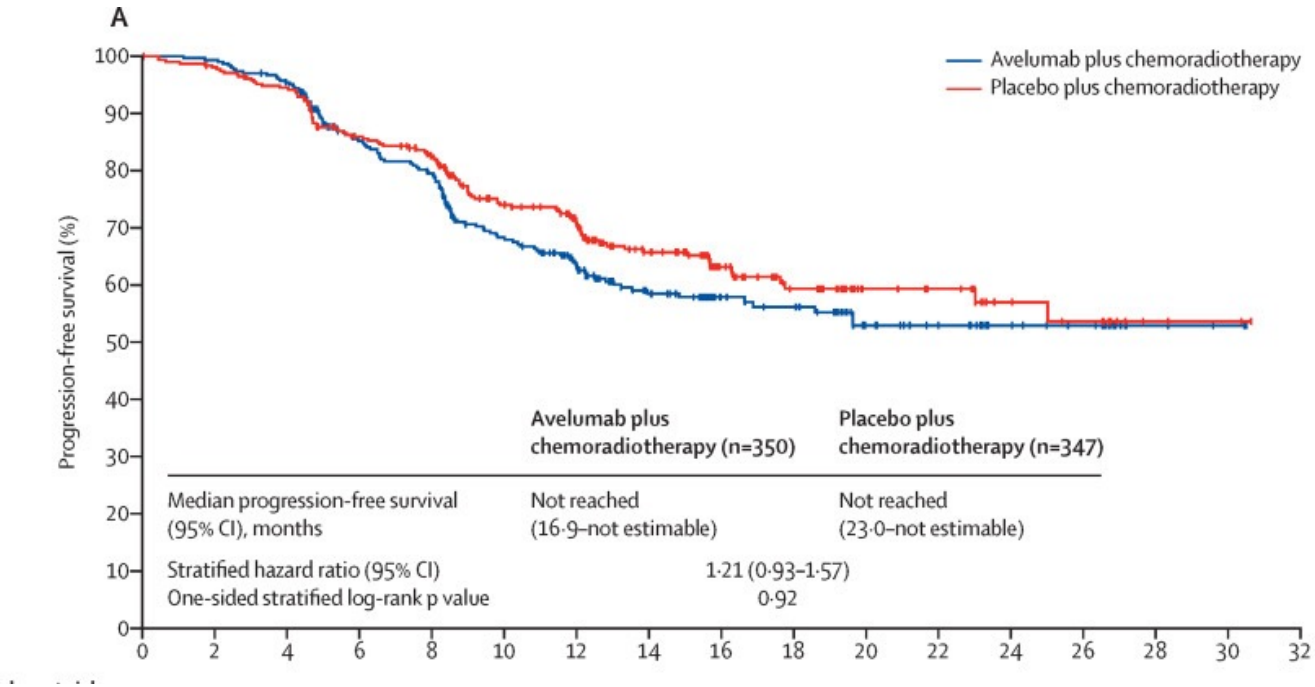


Key: F/U – follow-up; HPV – human papillomavirus; LA-SCCHN – locally-advanced squamous cell cancer of the head and neck; q2w – every 2 weeks; R – randomisation; RT - radiotherapy

Lee NY, et al. Lancet Oncol. 2021 Arp;22(40:450-462

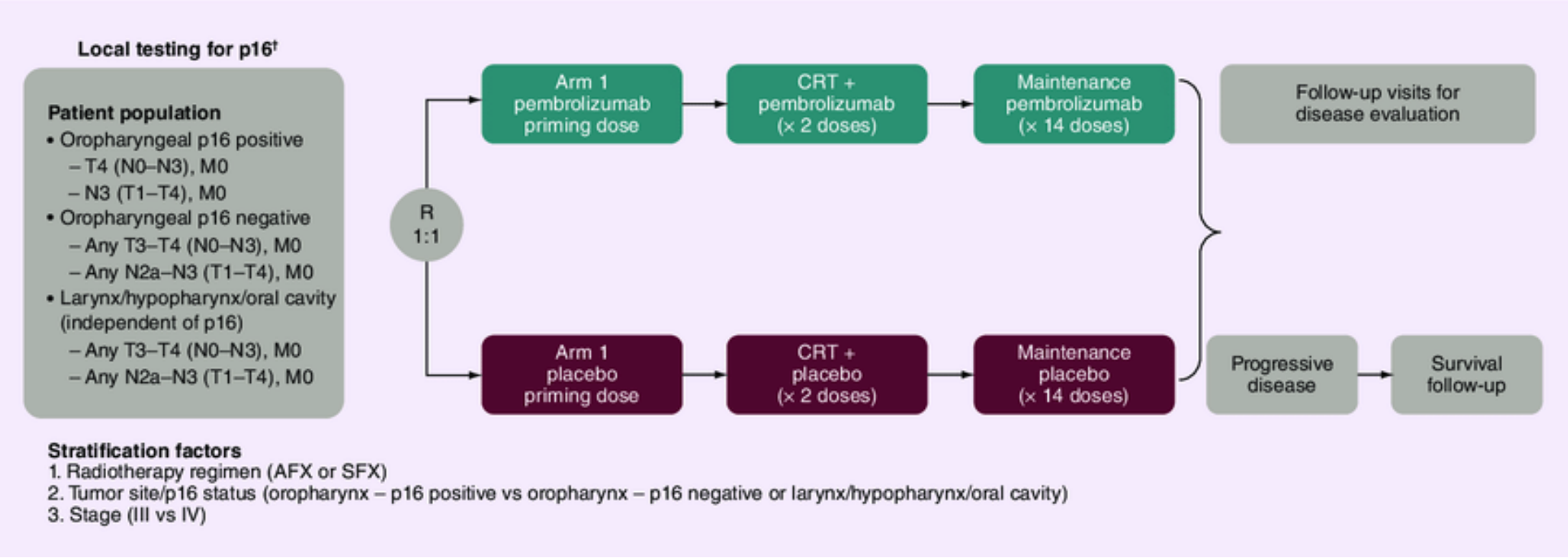
JAVELIN Head and Neck

- Primary endpoint of PFS difference not met (
  - Median follow-up 14.8 months
  - Median PFS not met with either treatment group
- Trial terminated on the basis of futility at preplanned interim analysis



Lee NY, et al. Lancet Oncol. 2021 Arp;22(40:450-462

Keynote 412



Machiels JP, et al. ESMO Congress 2022

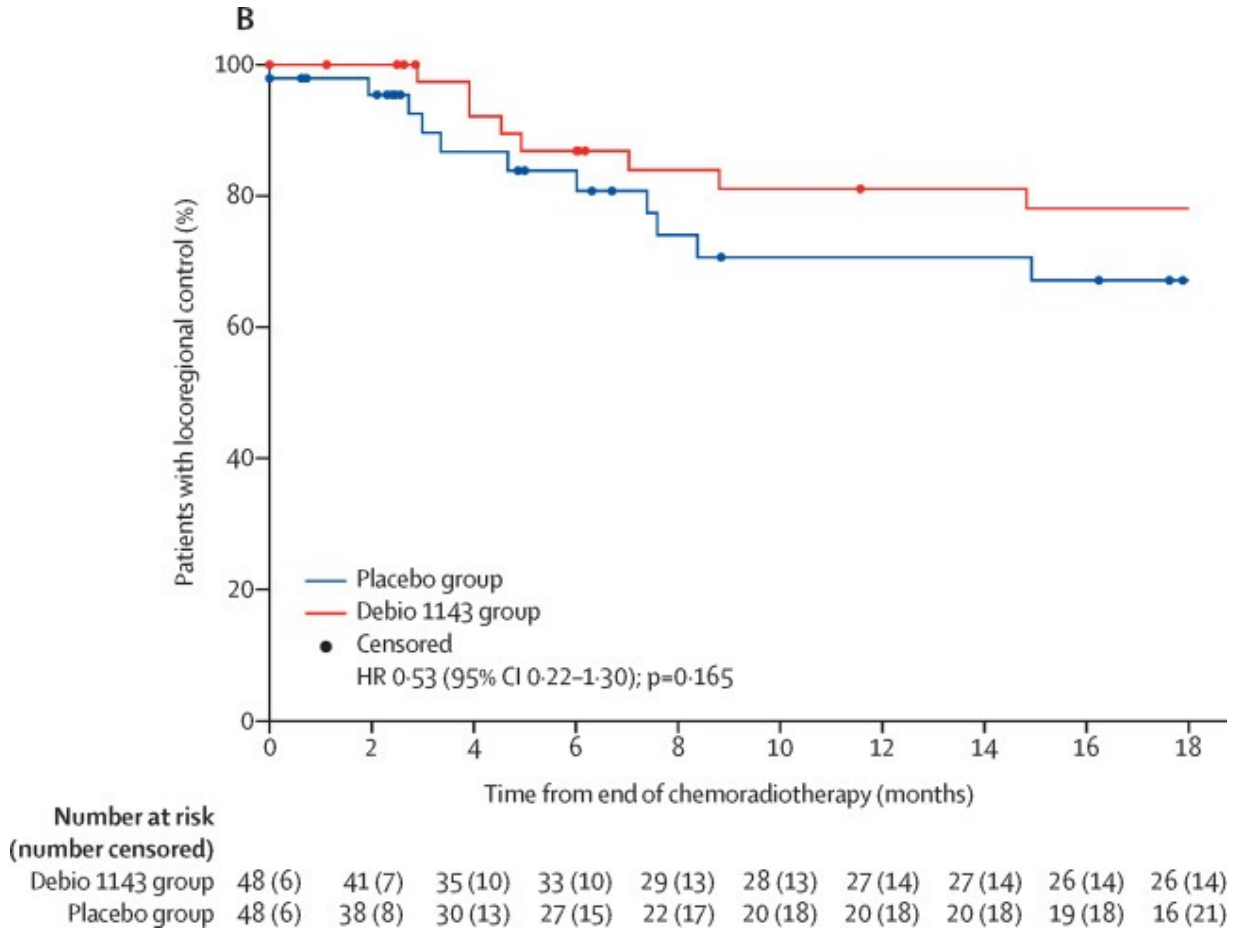
Keynote 412

- Presented at ESMO 2022
- Randomized, double-blind Phase 3 Trial
- Primary endpoint Event Free Survival (EFS)
  - Median EFS not reached vs 46.6 months (p=0.429 not meeting superiority threshold of 0.0242)
  - 36-month EFS 57.4% vs 52.1%
- Overall survival at 36-months: 71.9% vs 70.1%
- Post-hoc analysis showed greater benefit with PD-L1 CPS >=20

Machiels JP, et al. ESMO Congress 2022

Debio 1143

- Oral antagonist of inhibitor of apoptosis proteins
- Cisplatin/RT +/- Debio 1143
- Phase 2 data:
  - LRC 54% vs 33% (p=0.026)
  - No significant difference in AEs (63% vs 60%)
- Currently in Phase 3



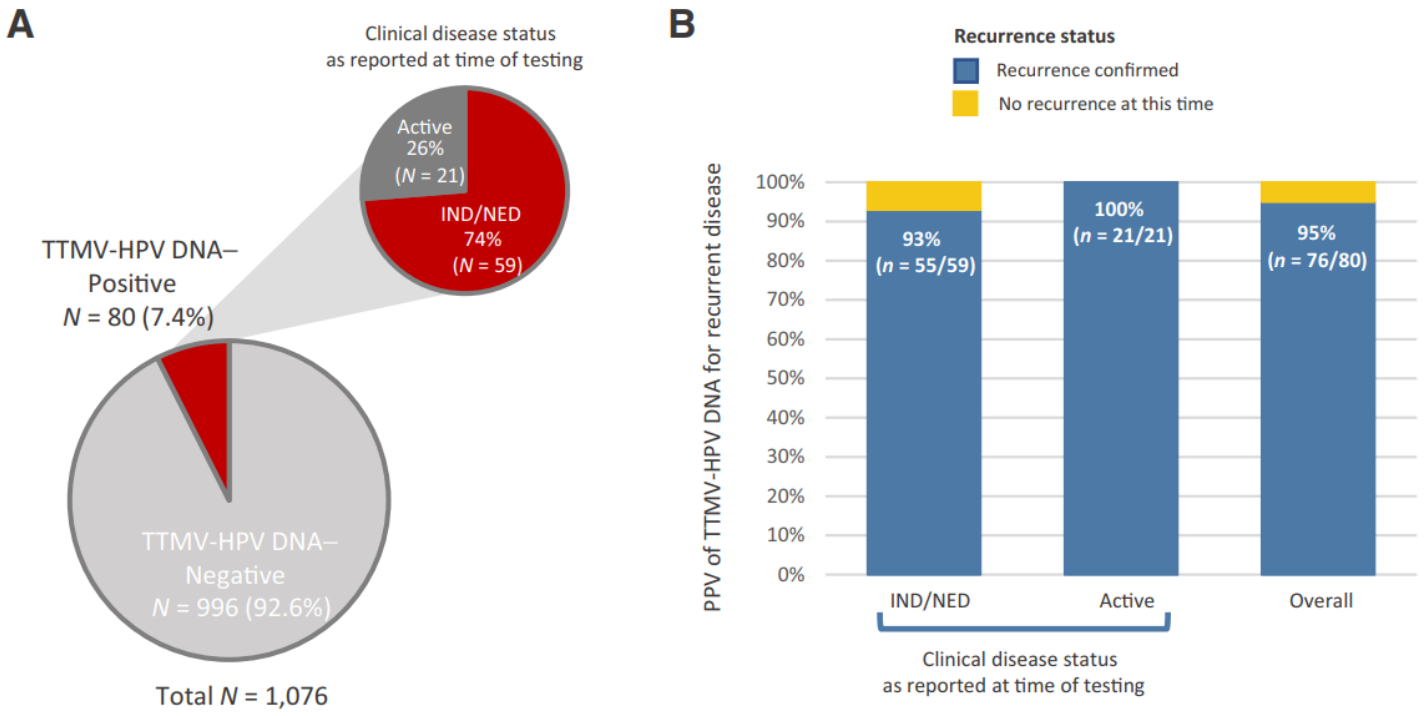
Sun XS, et al. The Lancet Oncologyl 2020, Vo.21(9), p.1173-1187

HPV Biomarker surveillance

- Circulating tumor tissue modified viral (TTMV)-HPV DNA Assay
- Prospectively designed, retrospective consecutive clinical case series
- Patients treated for non-metastatic HPV-driven oropharyngeal SCC
- 7.4% (80) had positive TTMV-HPV DNA
  - 21/80 (26%) had known recurrence
  - 59 unknown, 55/59 (93%) had subsequent recurrence
- Overall PPV = 95%, Overall NPV = 95%

Berger BM, Hanna GJ, et al. Clin Cancer Res 2022.

HPV Biomarker surveillance



Berger BM, Hanna GJ, et al. Clin Cancer Res 2022.

Metastatic HNSCC

Keynote-048

- Combined Positive Score (CPS) = (# of PD-L1 positive cells (tumor, lymphocytes, macrophages) / total # of cells) x 100
- Analysis stratified patient into CPS of 1 or more and CPS of 20 or more
- Patients randomized 1:1:1 to:
  - Pembrolizumab alone
  - Pembrolizumab + Chemotherapy (platinum + 5-FU)
  - Cetuximab + Platinum + 5-FU

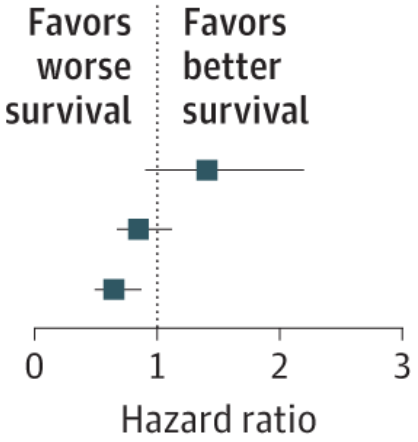
Burtness et al. Lancet. 2019 nov;394(10212):1915-1928

KEYNOTE-048 Updates

A Pembro vs cetuximab + chemo, OS

CPS	Hazard ratio (95% CI)
CPS, <1	1.40 (0.89-2.20)
CPS, 1-19	0.86 (0.66-1.12)
CPS, ≥20	0.64 (0.48-0.85)

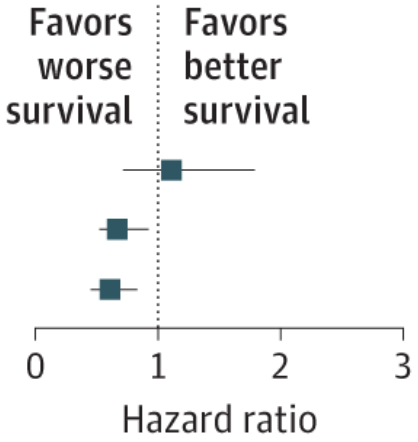
Trend test for interaction, $P = .003$



B Pembro + chemo vs cetuximab + chemo, OS

CPS	Hazard ratio (95% CI)
CPS, <1	1.13 (0.71-1.80)
CPS, 1-19	0.69 (0.52-0.91)
CPS, ≥20	0.62 (0.46-0.83)

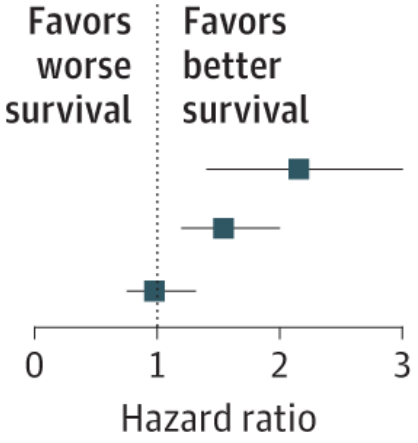
Trend test for interaction, $P = .03$



C Pembro vs cetuximab + chemo, PFS

CPS	Hazard ratio (95% CI)
CPS, <1	2.17 (1.38-3.42)
CPS, 1-19	1.55 (1.20-2.01)
CPS, ≥20	0.99 (0.75-1.31)

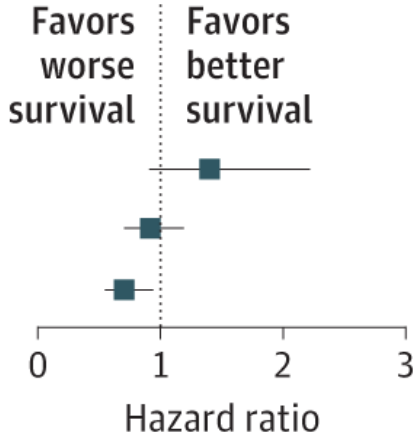
Trend test for interaction, $P < .001$



D Pembro + chemo vs cetuximab + chemo, PFS

CPS	Hazard ratio (95% CI)
CPS, <1	1.42 (0.91-2.23)
CPS, 1-19	0.92 (0.71-1.19)
CPS, ≥20	0.71 (0.53-0.94)

Trend test for interaction, $P = .01$



Yu Y, et al. JAMA Oncol. 2022; 8(8):1216-1218

KEYNOTE B10

- Phase 4, R/M HNSCC
- Patients treated with pembrolizumab (200mg), carboplatin (AUC5), and paclitaxel (175 mg/m2) IV q 3 weeks x 6 followed by maintenance pembrolizumab
- Data cutoff 3/2022, 92% patients enrolled
- ORR 43%
- Median OS 12.1 months
- May be comparable to historical 1L SOC

Dzienis M, et al. Annals of Oncology (2022) 33 (suppl_7): S295-S322.

Pembrolizumab + cabozantinib

- Phase II, single arm, multicenter study
- R/M HNSCC, immunotherapy naïve, PD-L1 CPS >1
- Pembrolizumab 200 mg/m2 every 3 weeks, Cabozantinib 40 mg po daily
- ORR 45.2%
- 1 yr OS 67.7%, 1 yr PFS 51.8%

Saba NF, et al. Journal of Clinical Oncology 2022 40:16_suppl, 6008-6008

Nasopharyngeal Carcinoma

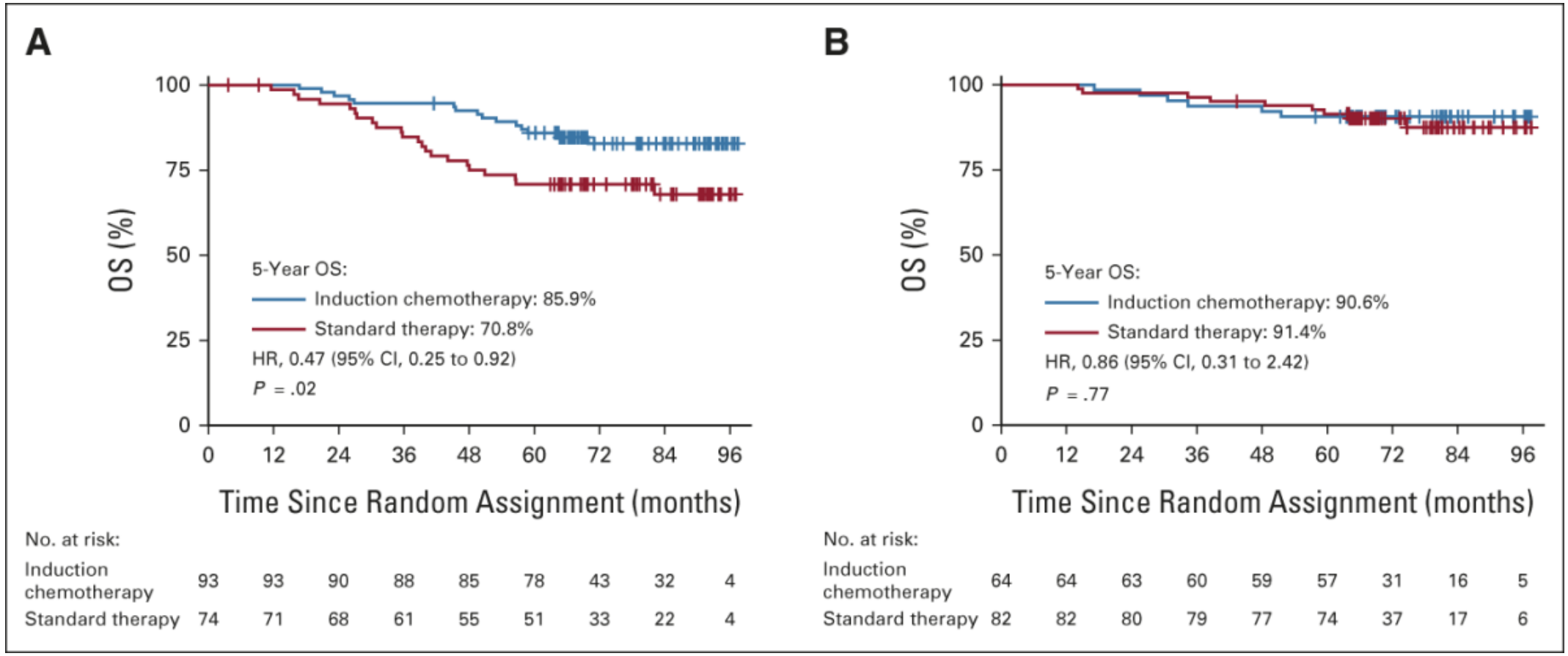
NPC Induction Chemotherapy

- Final Survival Analysis of Phase III Cisplatin/Gemcitabine Induction in NPC
- Phase III randomized to CRT +/- induction chemotherapy for stage III/IV NPC
  - 3 cycles gemcitabine (1 g/m2 days 1, 8) and cisplatin (80 mg/m2 day1) q 3wks
  - Concurrent chemoradiation with cisplatin
- 5-year OS 87.9% vs 78.8% (p=0.001)
- Similar risk of late toxicities (11.3% vs 11.4%)

Zhang Y, et al. J Clin Oncol. 2022 Aug 1;40(22):2420-2425

NPC Induction Chemotherapy

- Low pre-treatment EBV virus DNA load may receive less benefit
  - 5 yr OS 90.6% vs 91.4% (p=0.777)



Zhang Y, et al. J Clin Oncol. 2022 Aug 1;40(22):2420-2425

Rationale 309 Study

- Tislelizumab = humanized immunoglobulin G4 PD-1 mAb
- Phase III randomized study chemotherapy +/- tislelizumab
  - Gemcitabine 1g/m2 IV day 1,8, cisplatin 80 mg/m2 day 1 q 3 weeks)
- 1st line treatment R/M Nasopharyngeal Cancer
- Updated Data cut-off (9/2021) – median follow-up 15.5 months
  - Significant improvement in PFS (9.6 vs 7.4 months)
  - Overall survival: Not reached vs 23 months

Zhang L, et al. Journal of Clinical Oncology 2022 40:36_suppl, 384950-384950

JUPITER - 02

- Toripalimab = humanized IgG4K anti-PD-1 mAB
- Phase III, randomized, placebo controlled, 1st line R/M NPC
- Chemotherapy +/-Toripalimab (240 mg q 3 weeks)
  - Gemcitabine 1g/m2 Days 1,8, cisplatin 80 mg/m2 Day 1
- Median PFS 12 vs 8 months (p=0.0003)
- ORR 77% vs 66%
- OS similar, but ongoing

Mai HG, et al. Nat Med. 2021;27(9):1536. Epub 2021 Aug 2.

CAPTAIN-1st

- Camrelizumab = PD-1 inhbitor
- Phase III, randomized, placebo-controlled. 1st line R/M NPC
- Chemotherapy +/- Camrelizumab (200 mg IV q 3 weeks)
  - Gemcitabine 1g/m2 days 1,8 and cisplatin 80 mg/m2 day 1
- PFS 9.7 months vs 6.9 moths (p=0.0002)
- OS data are immature

Lancet Oncol. 2021;22(8):1162. Epub 2021 Jun 23.

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Thank You!