

De-intensification for HPV-OPSCC: Why is it NOT Standard of Care Yet?

39th Annual F. Johnson Putney
Lectureship in Head and Neck Cancer



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Hollings Cancer Center
An NCI-Designated Cancer Center

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Disclosures

Medical University of South Carolina
› Employment

Co-inventor of intellectual property held by University of North Carolina regarding the ctHPVDNA detection methodology (US Patent 11,168,373)

Scientific advisor with ownership interest in Naveris, Inc, a company that has licensed ctHPVDNA technology from University of North Carolina for commercialization

The presenter has no relevant nonfinancial relationship to disclose



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Objective

To discuss why de-intensification is not yet standard of care.



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UNC/UF Paradigm (1st generation, LCCC 1120)

Phase 2 Trial of De-intensified Chemoradiation Therapy for Favorable-Risk Human Papillomavirus–Associated Oropharyngeal Squamous Cell Carcinoma

N=44
Median f/u = 34 months (88% ≥ 2 years)

Primary endpoint (IJROBP 2015):
pCR rate = 86%

Secondary endpoints (Cancer 2018):
3 year PFS = 100%
3 year OS = 95%
Global QoL returned to baseline
Swallowing returned to baseline
Dry mouth continues to improve > 1 year

All patients had biopsy of primary site and supraseductive neck dissection

• **De-intensified Chemoradiotherapy**
– 60 Gy at 2 Gy/fx, daily, 6 weeks (IMRT)
– Cisplatin 30mg/m², 6 weekly doses

Int J Radiation Oncol Biol Phys. Vol. 93, No. 5, pp. 976–985, 2015

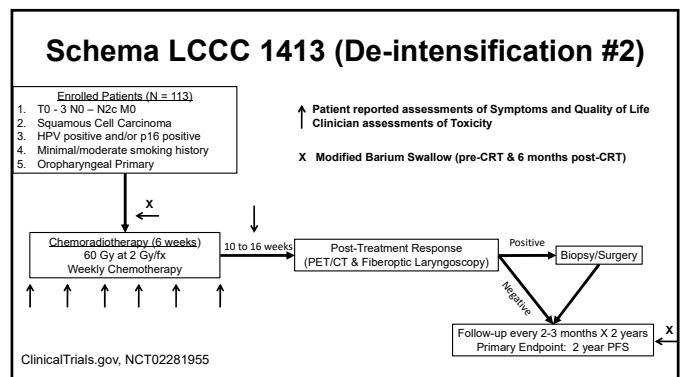
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Phase II Trial of De-Intensified Chemoradiotherapy for Human Papillomavirus–Associated Oropharyngeal Squamous Cell Carcinoma

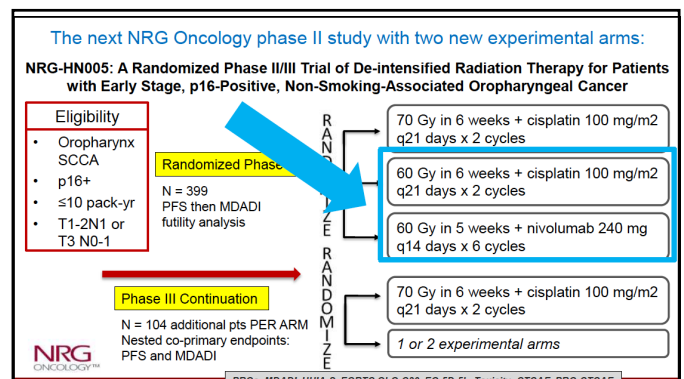
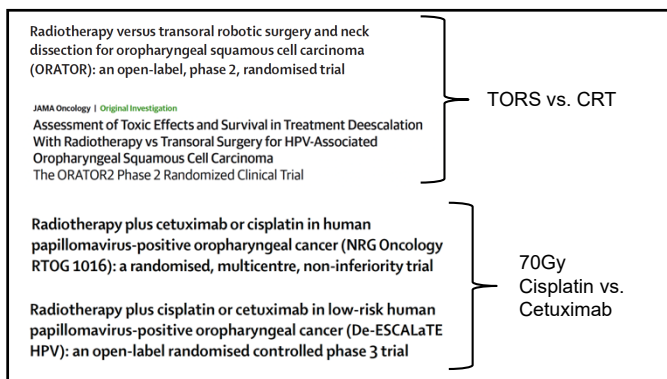
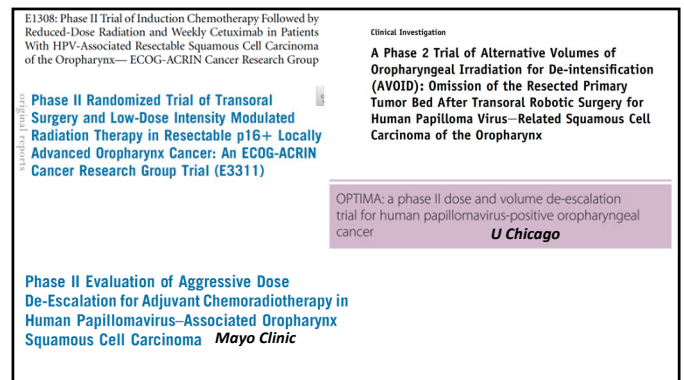
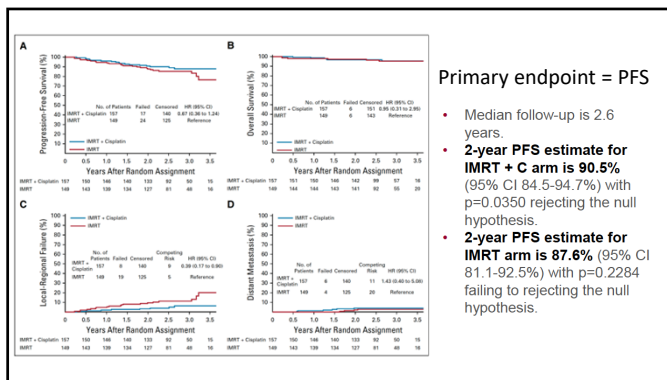
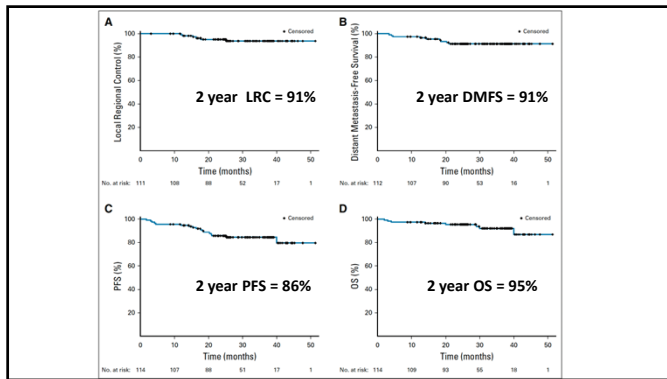
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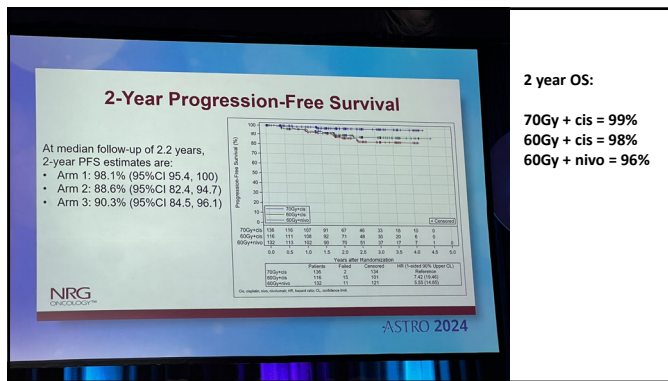
Journal of Clinical Oncology

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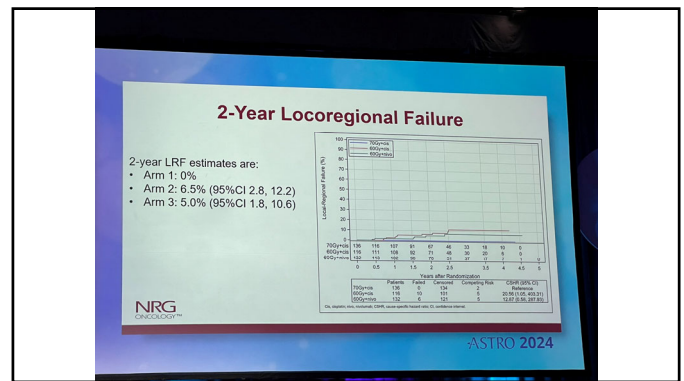
2 year OS:

70Gy + cis = 99%

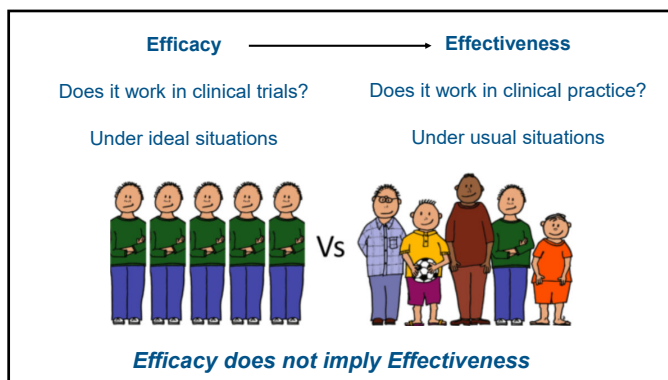
60Gy + cis = 98%

60Gy + nivo = 96%

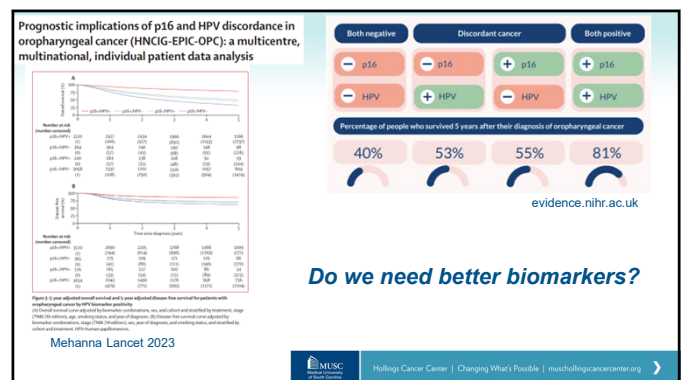
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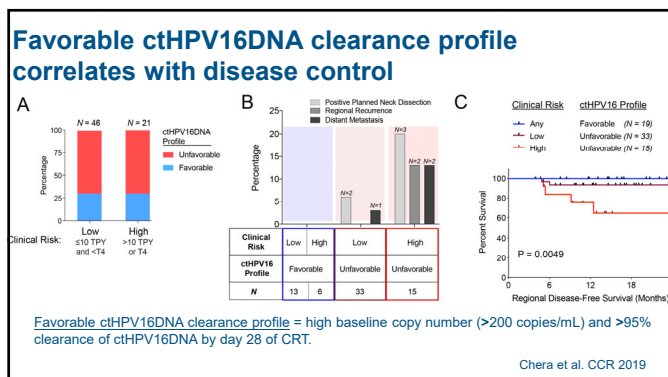
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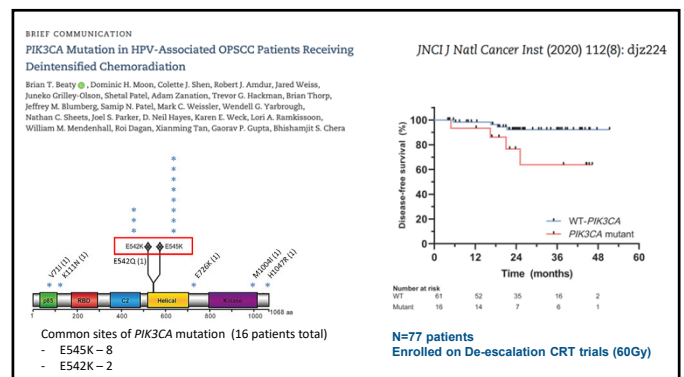
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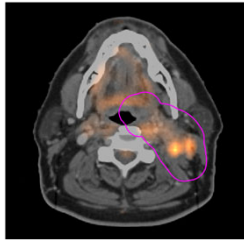


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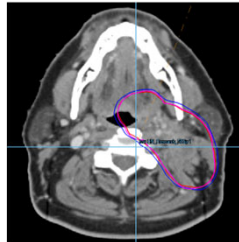


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3 month post-treatment PET fused to CT sim



PTV 60 got 50Gy per protocol



PTV 60 (magenta), 100% IDL (red), 95% IDL (blue)

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Pathology and NGS from 2/21/25 salvage neck surgery

Final Diagnosis

- A. LYMPH NODE, LABELED AS "LEFT LEVEL 4 NECK DISSECTION", REGIONAL RESECTION:
- THREE BENIGN LYMPH NODES (0/3)
- B. LYMPH NODE, LABELED AS "LEFT LEVEL 3 NECK DISSECTION", REGIONAL RESECTION:
- FIVE BENIGN LYMPH NODES
 - BENIGN NERVE
 - CHANGES SUGGESTIVE OF PRIOR SURGICAL SITE WITH DYSTROPHIC CALCIFICATIONS
- C. LYMPH NODE, LABELED AS "LEFT LEVEL 2 NECK DISSECTION", BIOPSY:
- METASTATIC SQUAMOUS CARCINOMA INVOLVING 1/4
 - SIZE OF LARGEST METASTATIC DEPOSIT: AT LEAST 1.8 CM
 - EXTRANODAL EXTENSION PRESENT, INCLUDING DIRECT EXTENSION
 - DISTANCE OF EXTENSION: 0.2 CM
 - LYMPHOVASCULAR INVASION: ABSENT
 - PERINEURAL INVASION: PRESENT
 - DYSTROPHIC CALCIFICATIONS
 - IMMUNOHISTOCHEMICAL STAIN
 - CK5/6 POSITIVE
 - HPV HR: POSITIVE

Results with Therapy Associations

Association	Outcome	Significance	Notes
HPV HR	HR	0.0001	HPV HR
CK5/6	HR	0.0001	CK5/6

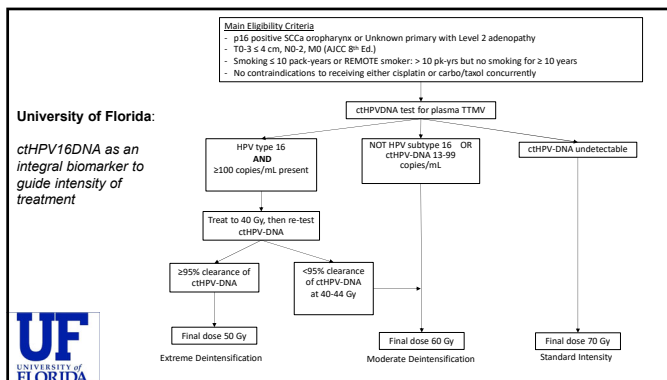
Important Note

The present report is part of the preclinical studies for the HPV HR and CK5/6 assays. The present report is not intended to be used for clinical decision making. The present report is not intended to be used for clinical decision making. The present report is not intended to be used for clinical decision making.

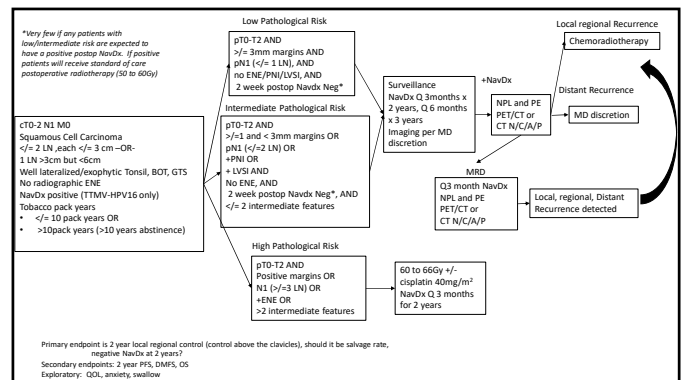
Cancer-Type Relevant Biomarkers

Marker	Result	Interpretation	Notes
HPV HR	HR	0.0001	HPV HR
CK5/6	HR	0.0001	CK5/6

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Conclusions and Final Thoughts

- I personally do not have equipoise → I think we should be de-intensifying
- Maybe PFS is the wrong endpoint since OS is >95%
 - Salvage treatment more efficacious?
 - Would patients accept a lower cancer control in favor of less toxicity?
- ctHPV-DNA →
 - Better "window" into tumor biology
 - Is it a better biomarker that can be used for more precise patient selection?



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