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TOBACCO AS A PROGNOSTIC FACTOR IN HPV + PATIENTS

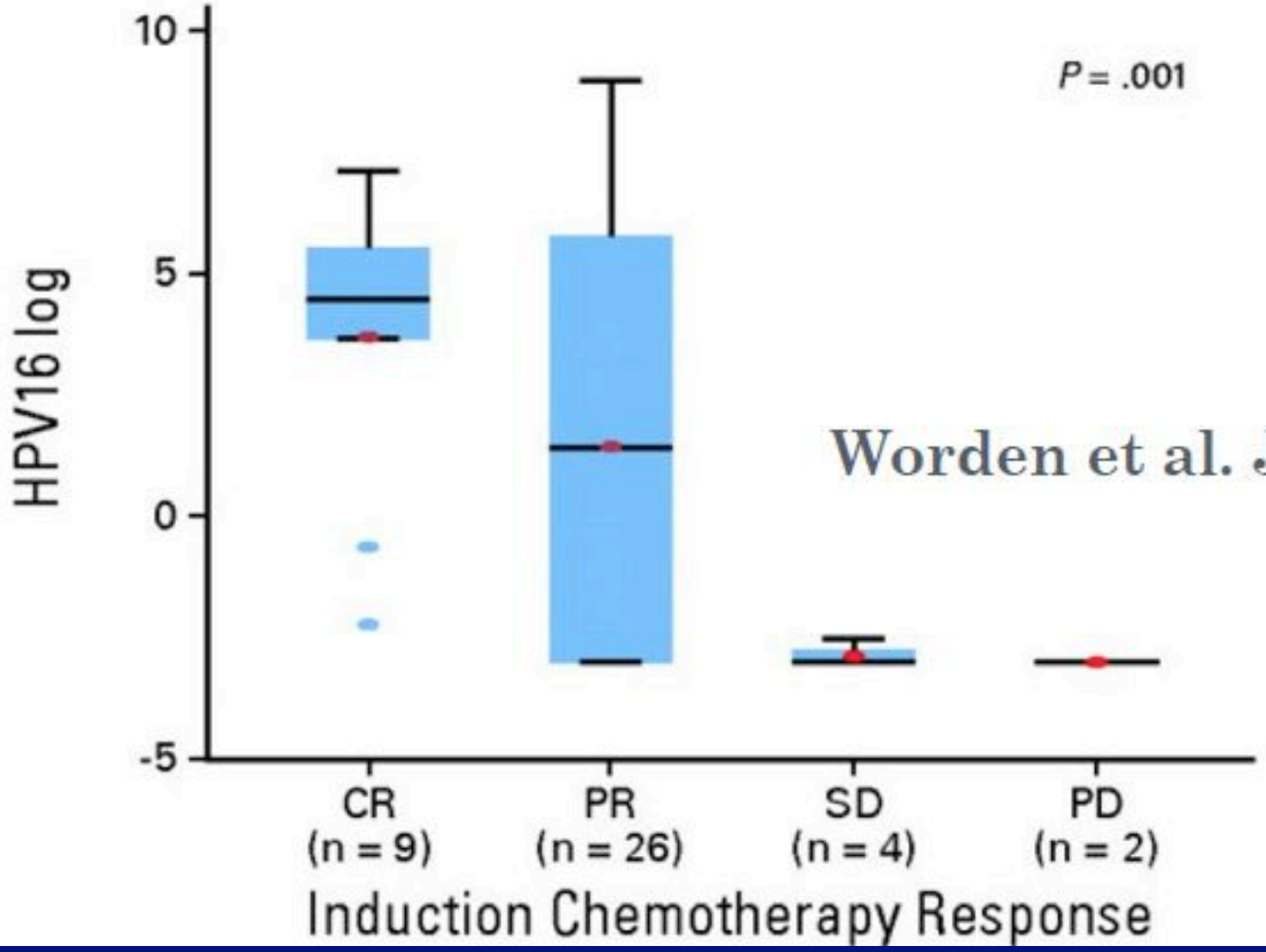
Ang et al. NEJM 2010

	HR	95% CI	2 yr Survival
HPV +, <20py	1.0		95%
HPV +, >20py	1.91	1.2-3.05	80%
HPV -, <20py	2.25	1.44-3.5	71%
HPV -, >20py	4.30	2.4-7.71	63%

Py = pack/years =≥ *20* cigarettes/day.

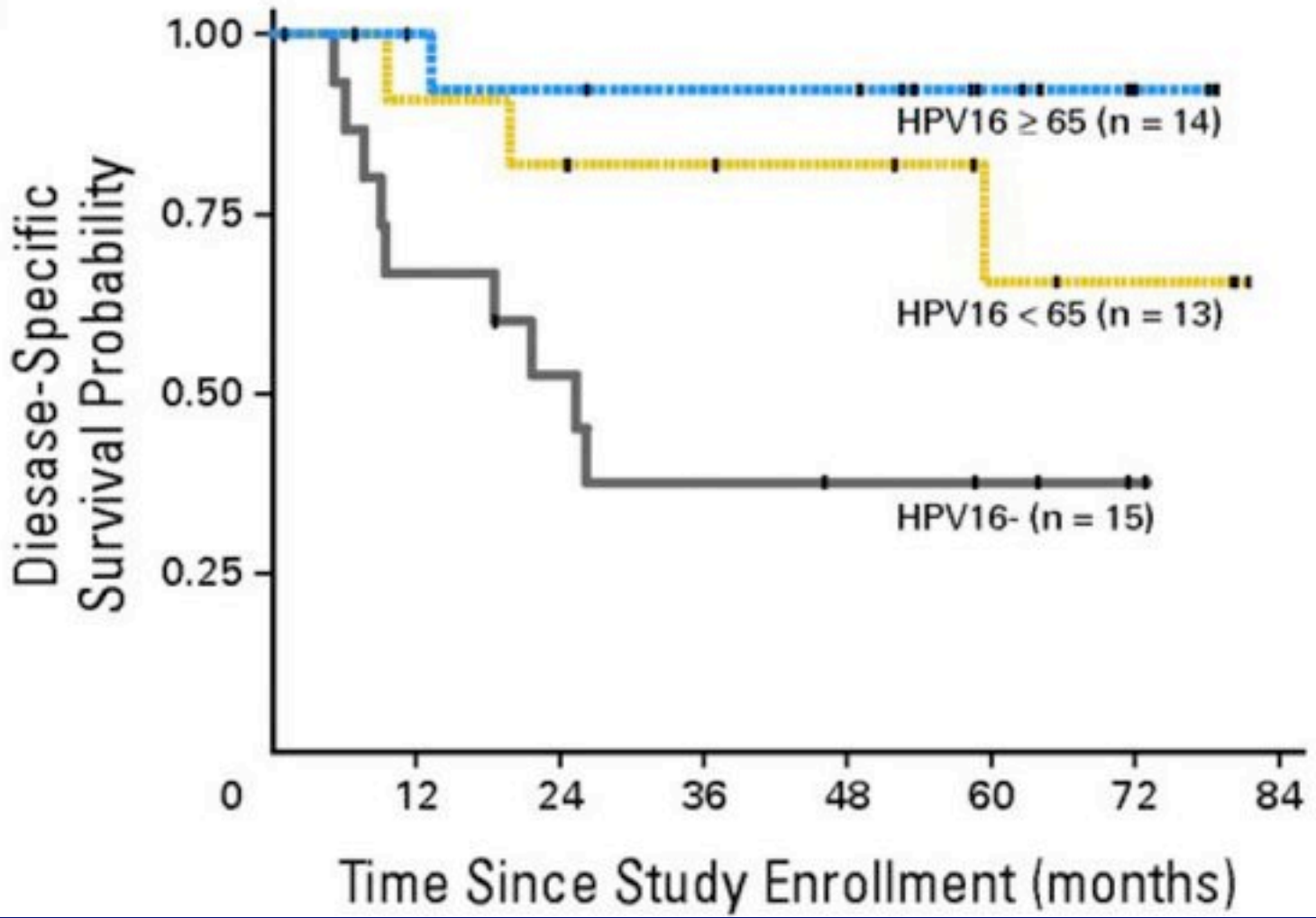
ARE THERE ADDITIONAL BIOMARKERS THAT MAY HELP FURTHER PREDICT OUTCOMES?

HPV COPY NUMBER
INDUCTION CHEMOTHERAPY RESPONSE



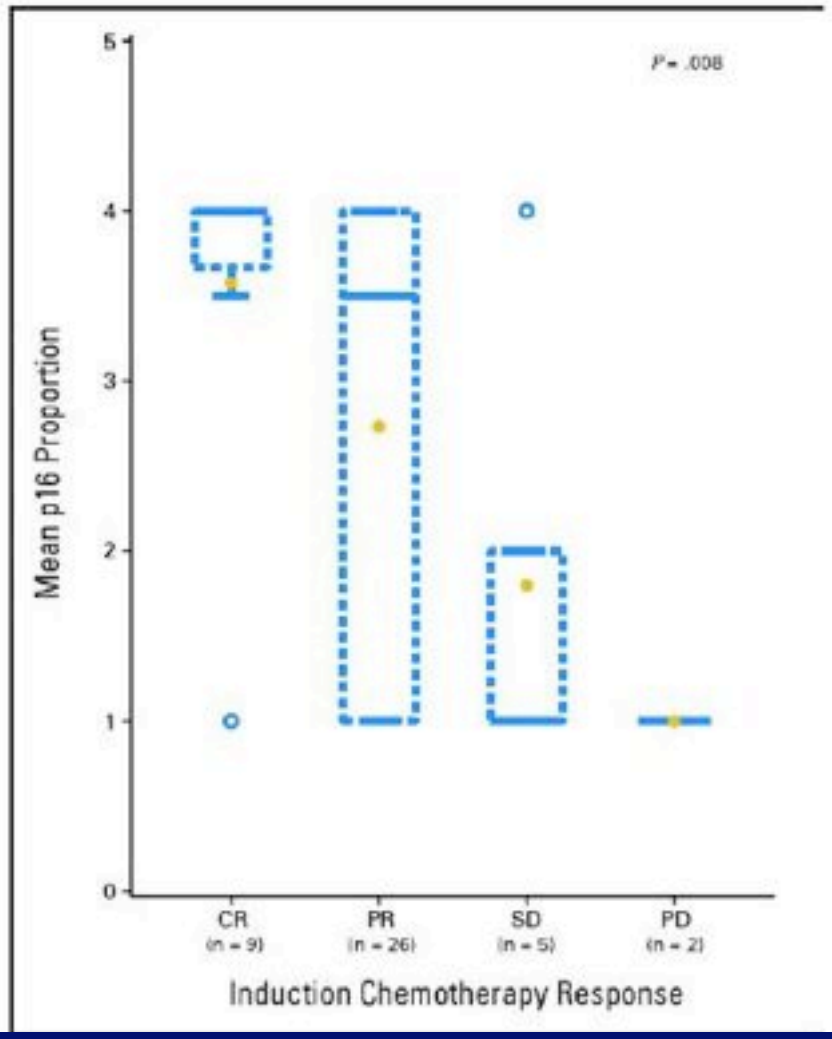
Worden et al. JCO 2008

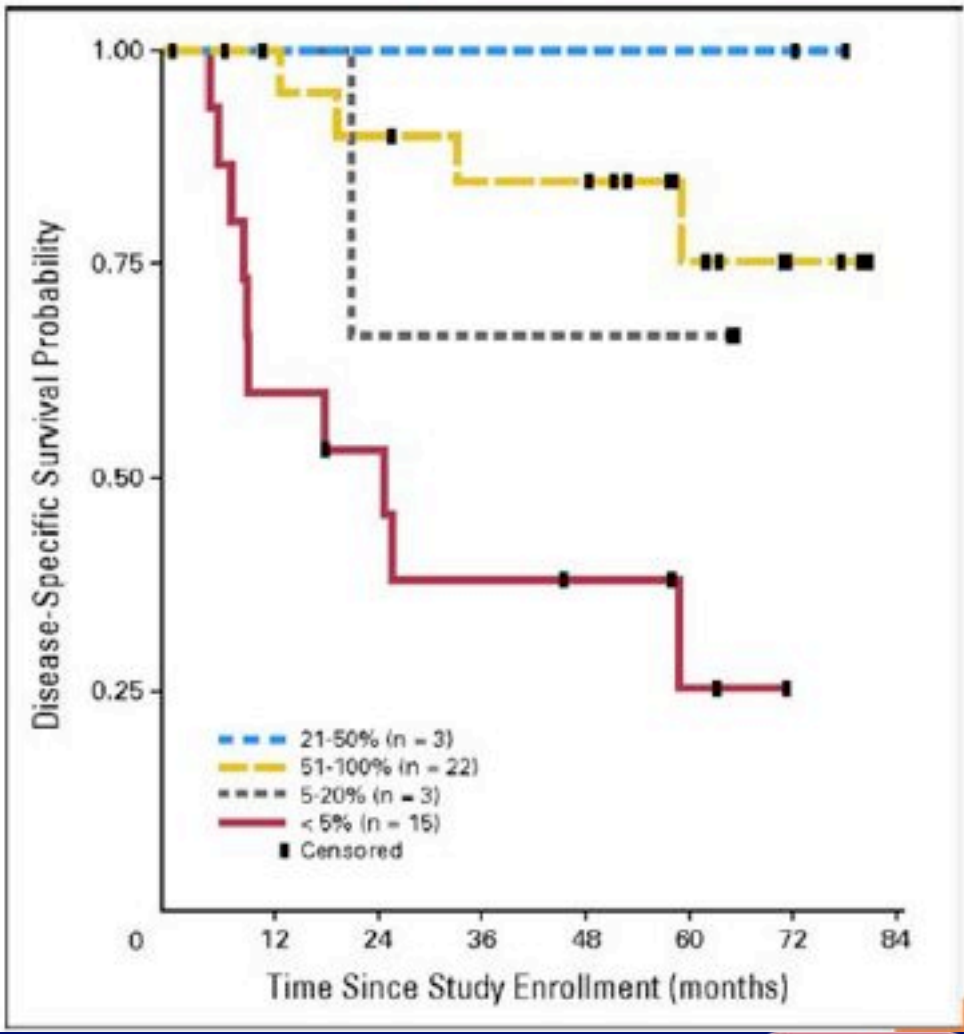
HPV COPY NUMBER
SURVIVAL



Worden et al. JCO 2008

P16

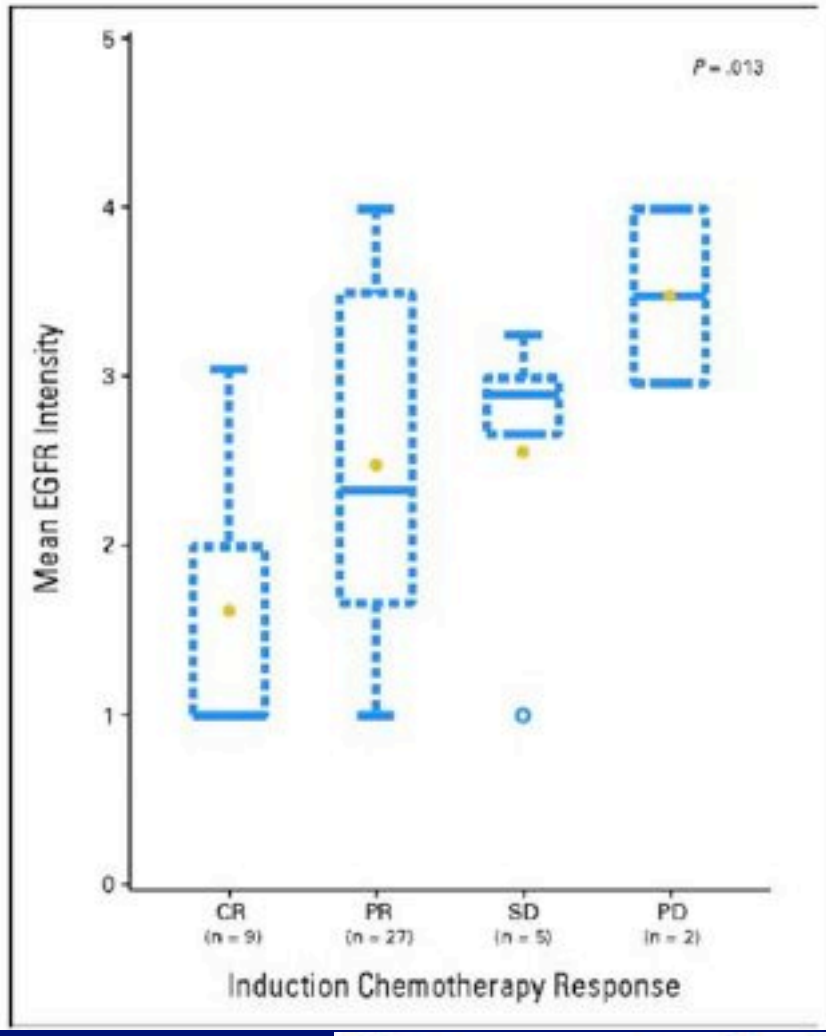


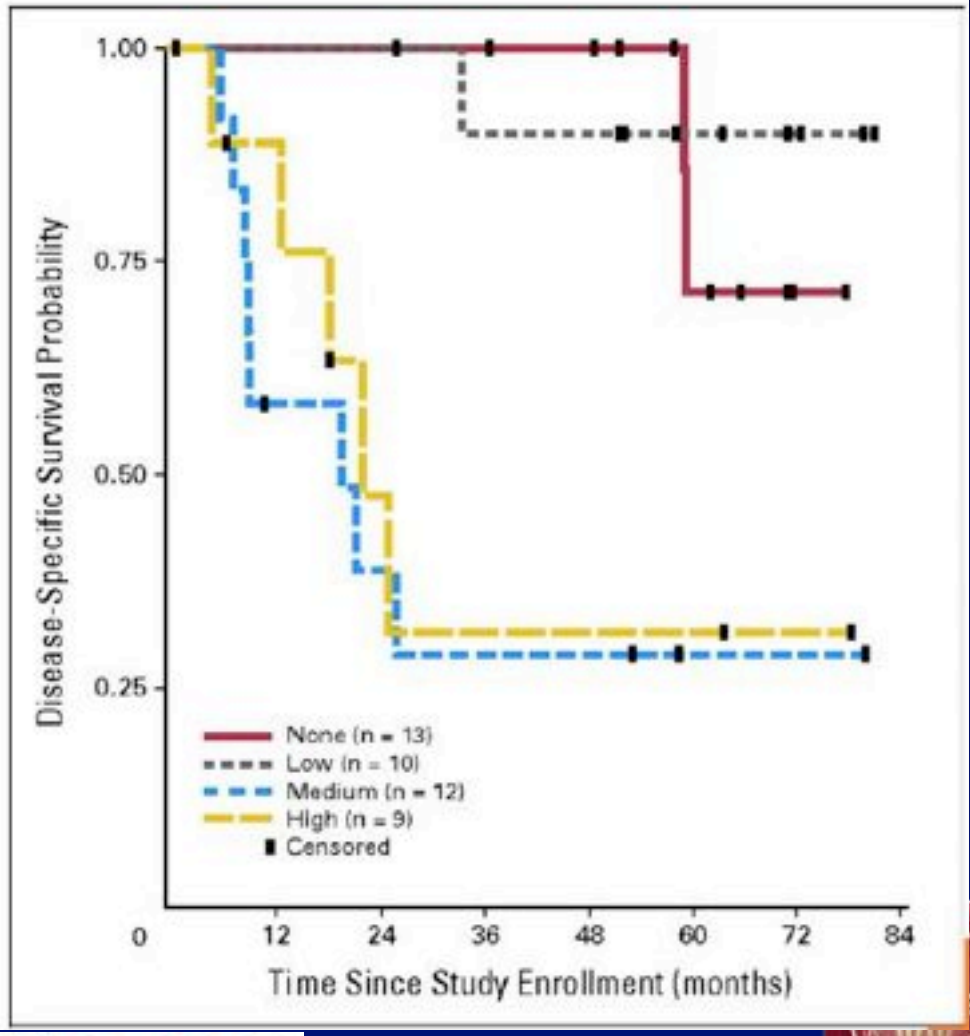


Kumar et al. JCO 2008

EGFR

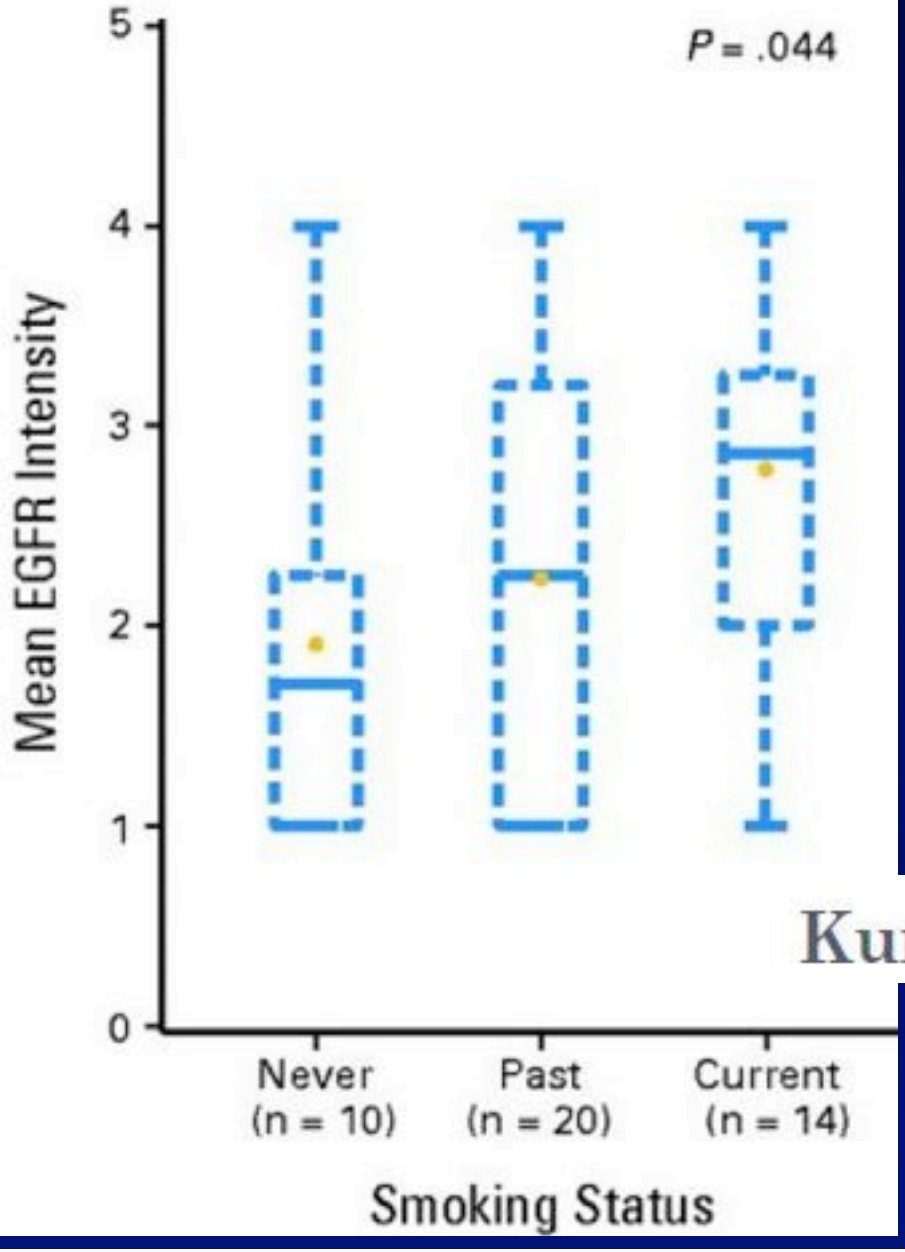
INDUCTION CHEMOTHERAPY RESPONSE AND SURVIVAL





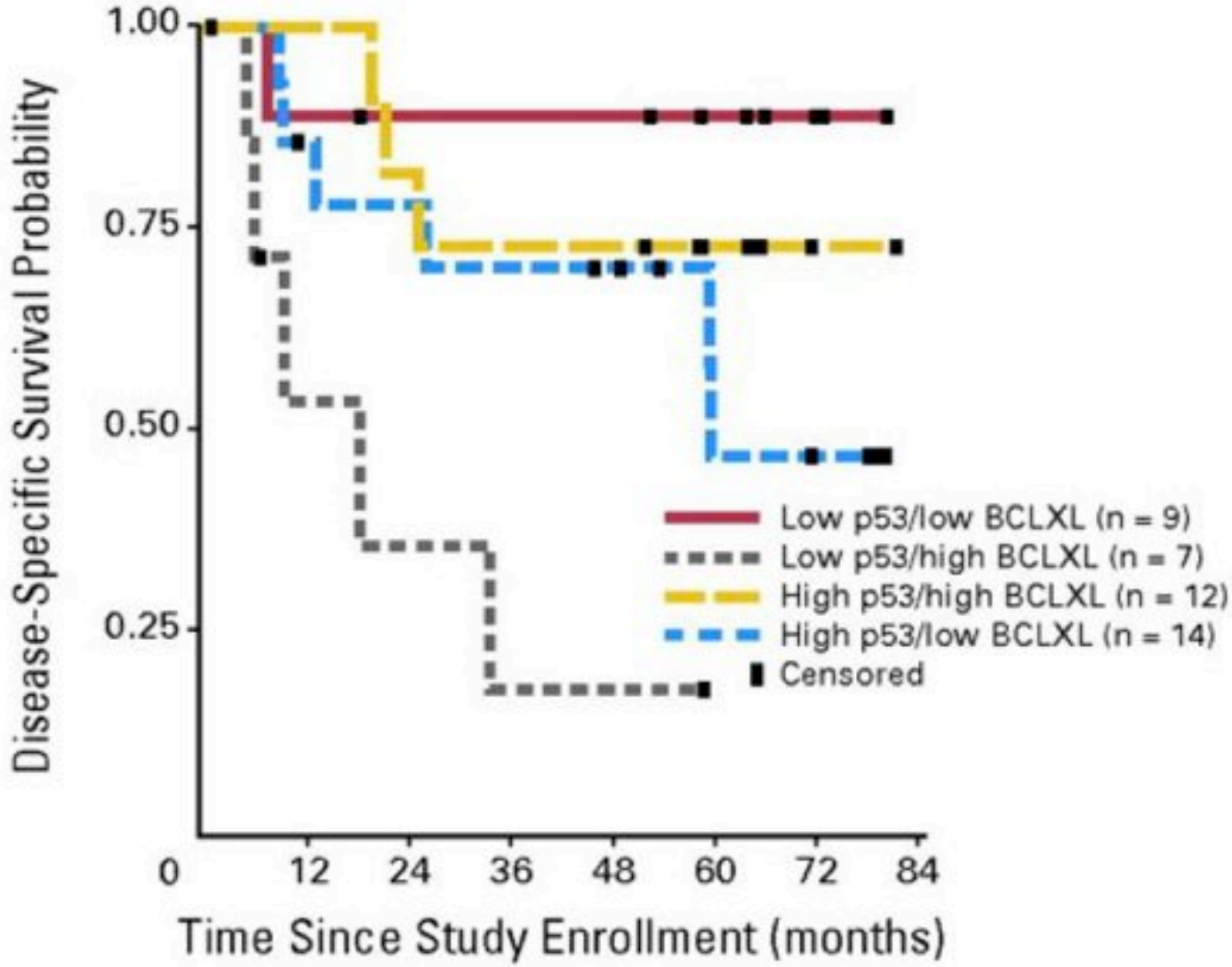
Kumar et al. JCO 2008

EGFR AND TOBACCO



Kumar et al. JCO 2008

P53 AND BCLXL



Kumar et al. JCO 2008

HPV COPY NUMBER, P16, EGFR, P53, AND BCLXL MAY HELP TO PREDICT SURVIVAL AND GUIDE TREATMENT STRATEGIES

IF HPV + PATIENTS HAVE BETTER SURVIVAL, CAN WE DECREASE INTENSITY OF TX?

RTOG TRIAL

- Modest dose reductions of chemotherapy = 33%
- RT dose reduction = 14%
- Mantain tumor control and rate of distant metastases
- Better QoL < toxicity

COME DEFINIRE I PZ A BASSO RISCHIO?

- Orofaringe HPV 16 +
- < 10p/y
  - T2 –N2a/N3
  - T3-T4 any N
- > 10 p/y
  - Non N3

Adottare una strategia adattiva?

- Chemioterapia di induzione → valutazione risposta T e N
- Dose della RT scelta sulla base della risposta (DFCI Trial)
- Protocolli basati sulla riposta a una RT/CT verificata a metà trattamento

DFCI TRIAL

- Concept: use response to induction to stratify dose de-escalation candidates
- Eligibility: HPV 16 and p16+, Stage III/IV without distant mets
- Treatment Plan:
  - TPF (docetaxel, cisplatin, 5-FU) induction x 3 cycles
  - Clinical/radiographic response assessment
  - Concurrent XRT/Carboplatin/Cetuximab

***Radiation dose determined by response to induction

DFCI TRIAL

- Response Assessment:
  - If CR of primary and neck disease, reduce dosing
  - If PR at either site, need to analyze further
    - Primary: no residual mass, distorted anatomy accepted
    - Nodes: PET, size criteria
- Radiation Dosing (with concurrent Carbo/Cetuximab)
  - Standard: 70 Gy "GTV", 64/60 CTV (35 Fx)
  - Reduced: 60 Gy "GTV", 60/54 CTV (30 Fx) with reduction in normal tissue dose contraints

Future Prospective

Management of HPV-related Oropharyngeal Cancer

De-escalation Regimens

Advancement in Surgery

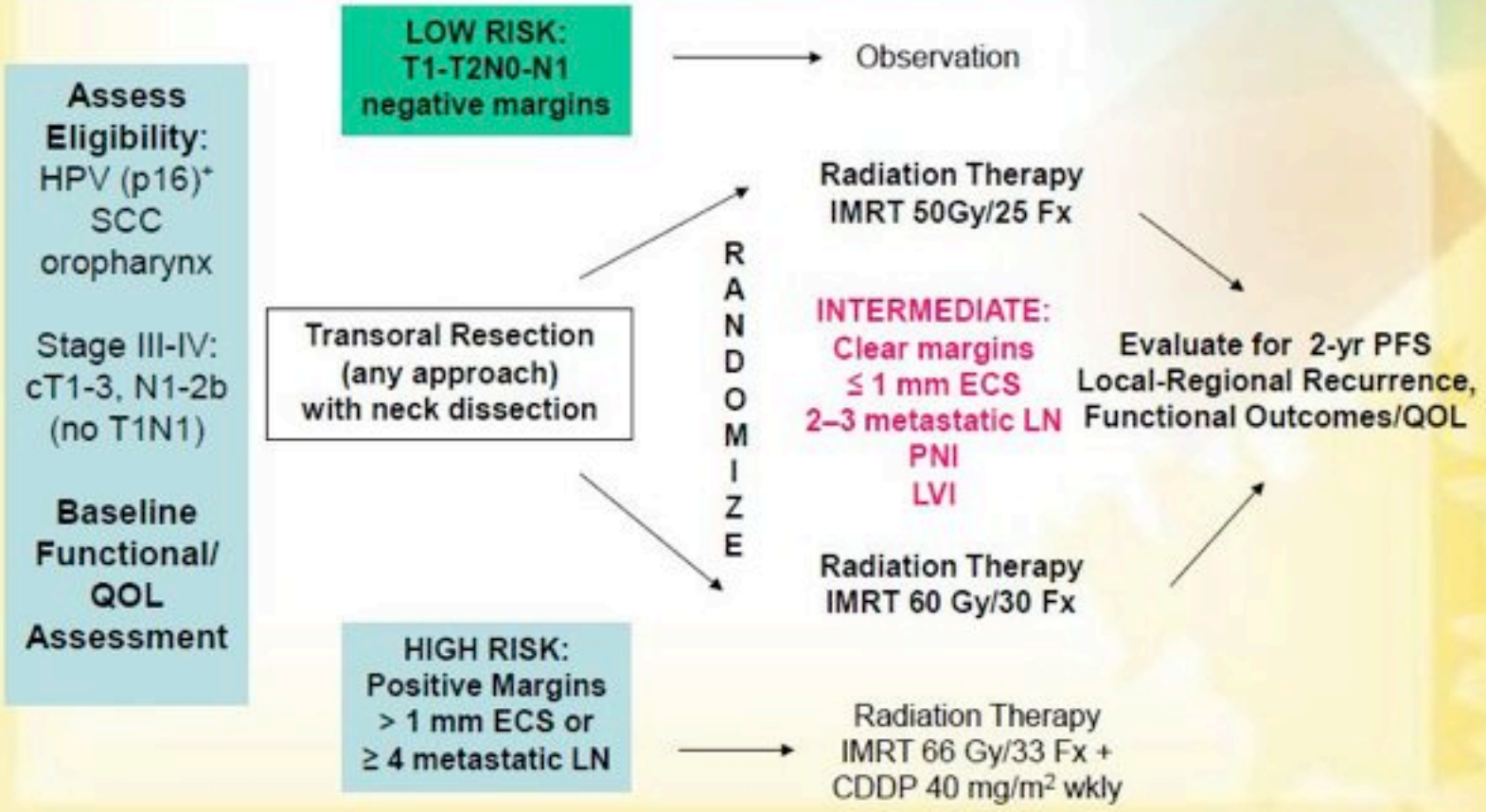
- Historical surgeries for OPC were open resections
- Advent of minimally invasive transoral techniques
  - TLM – transoral laser microsurgery
  - TORS – transoral robotic surgery

Minimally Invasive Surgery

First author, year	Patient number	Surgery	T1 – 2 (%) / N2c(%)	XRT / Chemo-XRT	LRC
Moore, 2012	66	TORS +ND	90% /12%	21% / 42%	97% LC/94% RC
Genden, 2009	20	TORS +ND	100% / 0%	35% / 15%	ND
Weinstein, 2012	30	TORS +ND	83% / 0%	0%/ 0%	97% LC
Weinstein, 2010	47	TORS +ND	76% / 4%	28% / 57%	98% LC/96% RC
White, 2010	89	TORS +/- ND	80% / 13%	63% / ND	89%
Haughey, 2011	204	TLM +ND	66% / 8%	54% / 25%	93%

Courtesy of Dr. Garden

ECOG 3311 P16+ Trial – Low Risk OPSCC: Personalized Adjuvant Therapy Based on Pathologic Staging of Surgically Excised HPV+ Oropharynx Cancer



ECS= extracapsular spread
PNI =Perineural Invasion
LVI =Lymphovascular invasion