Role of Induction CT in Head and Neck Cancer

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INTRODUCTION

- Administration of chemotherapy
  - Neo-adjuvant (induction)
  - Sequential (CT followed by RT/Surgery)
  - Concurrent (CT-RT)
  - Adjuvant (RT/CTRT/Surgery- CT)

Hear No Induction – See No Induction Speak No Induction

Effect on survival of adding chemotherapy to locoregional treatment: Results from the MACH-NC 2000 analysis

Design	n of studies (n of patients)	Hazard ratio (95% CI)	p-value	Absolute survival benefit	
				2 year	5 year
Adjuvant	8 (1,854)	0.98 (0.85–1.19)	.74	1%	1%
Induction	31 (5,269)	0.95 (0.88–1.01)	.10	2%	2%
Induction with platinum and 5-FU [1, 2]	15 (2,487)	0.88 (0.79–0.97)	.01	NA	5%
Concurrent	***26 (3,727)***	***0.81 (0.76–0.88)***	***.0001***	***7%***	***8%***
Total	65 (10,850)	0.90 (0.85–0.94)	.0001	4%	4%

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16 of the 31 trials assessed for induction chemotherapy used regimens other than a platinum plus 5-FU (PF).

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When just the 15 trials using PF induction chemotherapy were analyzed, there was a statistically significant overall survival benefit of 5% at 5 years.

Effects of Chemotherapy on Survival at 5-Years From the Meta-Analysis

Trial Category	No. of Trials	No. Patients	Difference (%)	*P* value
All trials	**65**	**10,850**	**+4**	**<0.0001**
Adjuvant	8	1,854	+1	0.74
Induction	31	5,269	+2	0.10
PF	**15**	**2,487**	**+5**	**0.01**
Other Chemo	16	2,782	0	0.91
Concomitant	**26**	**3,727**	**+8**	**<0.0001**

Monnerat, et al. Annals of Oncology, *13:* 995-1006, 2002

THE EMERGENCE OF TPF IN INDUCTION CHEMOTHERAPY

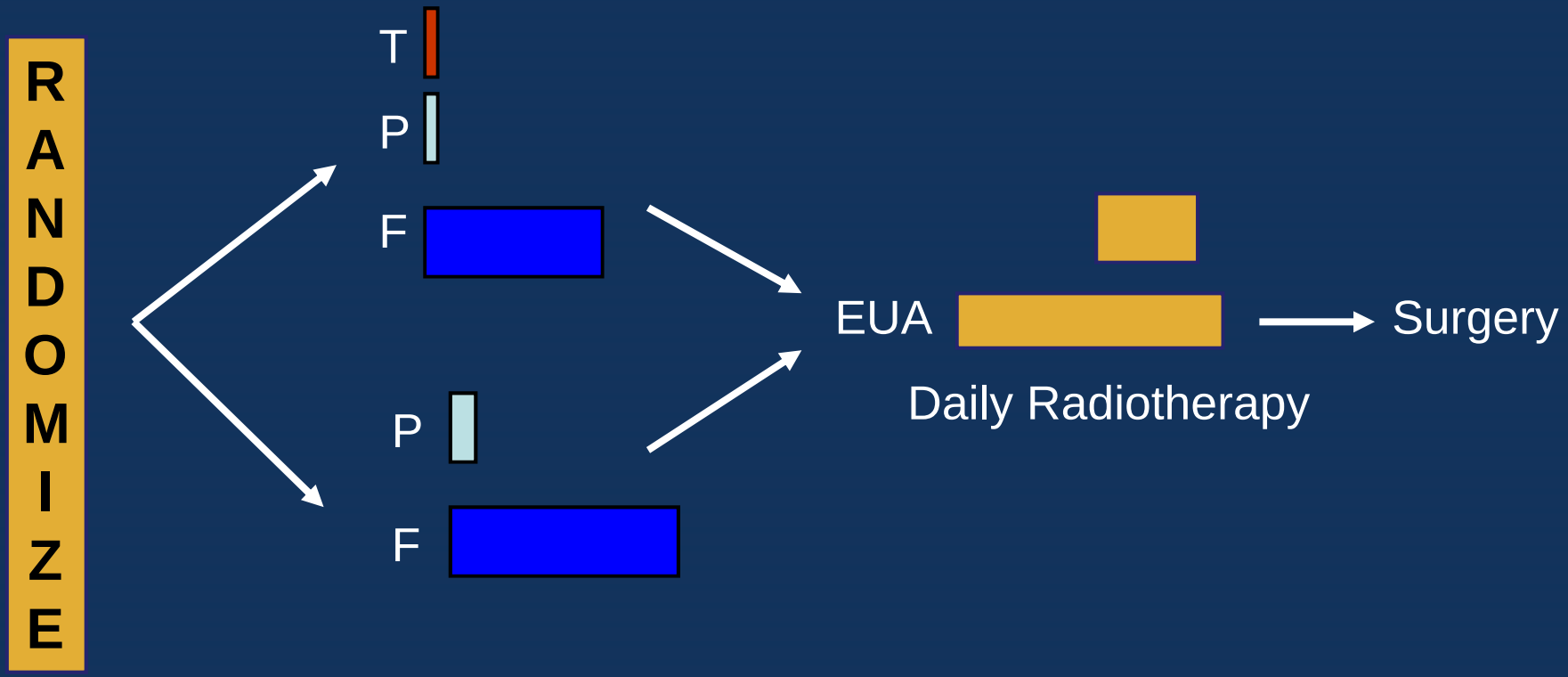
- Two phase III trials
- TAX 323
- TAX 324

Induction PF versus PF + Docetaxel (TPF) TAX 323: Eligibility Criteria

- Stage of III or IV HNSCC without metastases
- Tumors had to be considered unresectable by a multidisciplinary team
- PS 0-1

Vermorken JB, et al. N Engl J Med. 2007;357(17)1695-1704.

TAX 323: TPF vs. PF Followed by Radiotherapy
A Phase III Study in Unresectable SCCHN



TPF: Docetaxel 75_{D1} + Cisplatin 75_{D1} + 5-FU $750_{Cl- D1-5}$ Q 3 weeks x4
PF: Cisplatin 100_{D1} + 5-FU $1000_{Cl-D1-5}$ Q 3 weeks x 4

Remenar, ASCO, 2006

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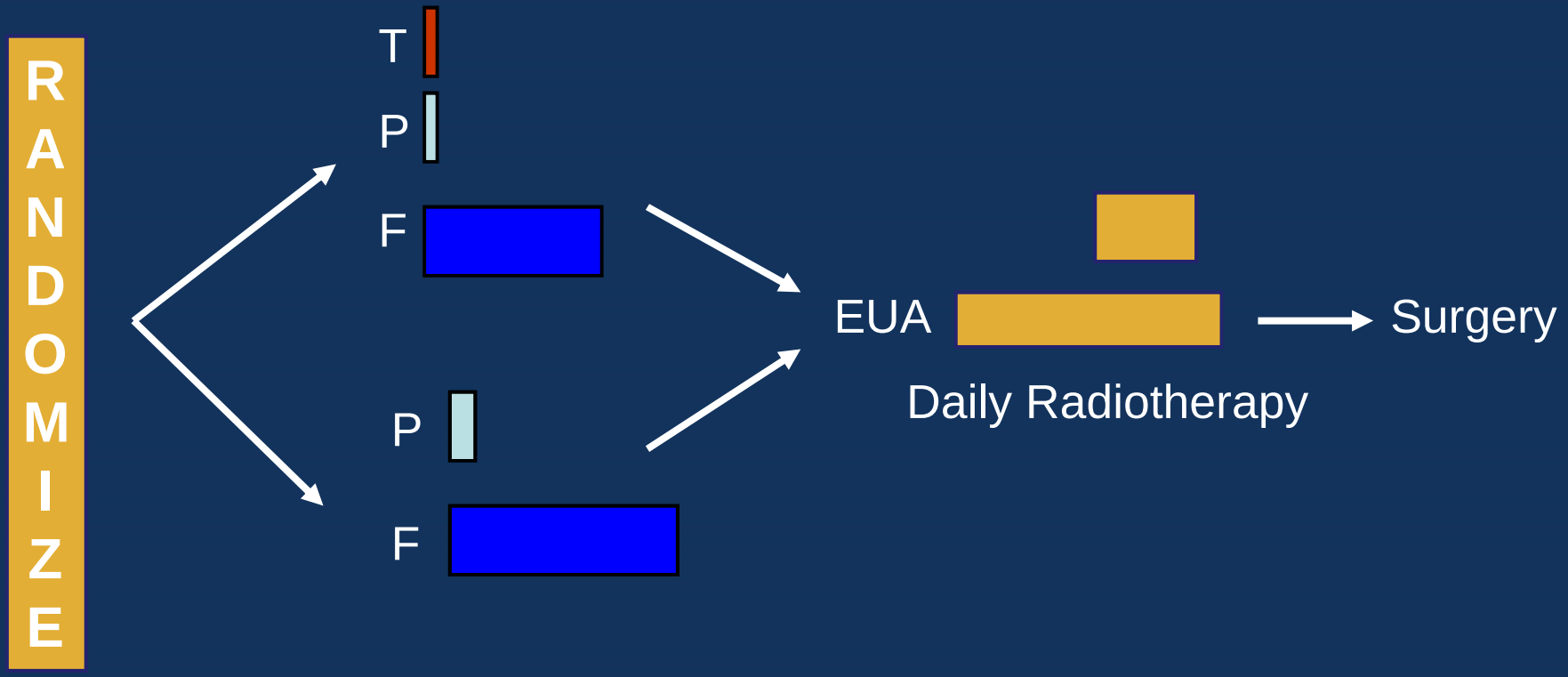

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Remenar, ASCO, 2006

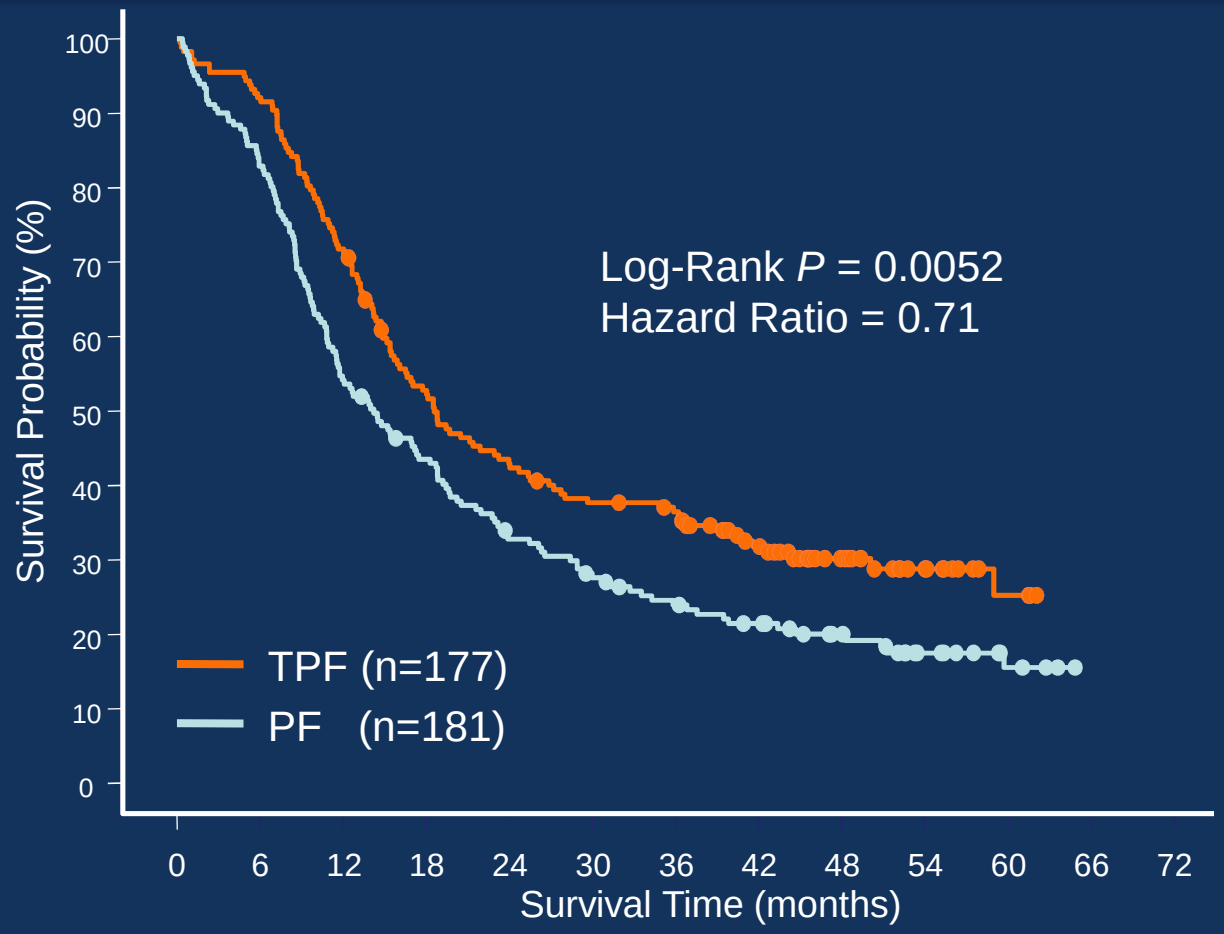
TN Stage of Primary

Stage	T1	T2	T3	T4	Total
N0		1 (<1)	12 (3)	29 (8)	42 (12)
N1		4 (1)	13 (4)	39 (11)	56 (16)
N2	1 (<1)	13 (4)	38 (11)	153 (43)	205 (57)
N3	3 (1)	7 (2)	11 (3)	31 (9)	52 (15)
Total	4 (1)	25 (7)	77* (22)	252 (70)	358

** 3 patients were T3Nx*

Vermoken, ASCO, 2004

TAX 323: Survival Update



Patients at Risk

TPF:	177	163	127	91	74	64	60	43	26	16	7
PF:	181	150	98	77	57	47	39	33	25	15	8	4

Remenar, ASCO, 2006

TAX 323: Severe Adverse Events
Chemotherapy

Toxicity ≥ 3% of pts	PF (n=179) N (%)	TPF (n=174) N (%)
Alopecia	0	20 (11.5)
Stomatitis/oral	20 (11.2)	8 (4.6)
Infection	13 (7.3)	15 (8.6)
Nausea	13 (7.3)	1 (0.6)
Vomiting	9 (5.0)	1 (0.6)
Diarrhea	8 (4.5)	5 (2.9)
Dyspnea	8 (4.5)	6 (3.4)
Dysphagia	5 (2.8)	6 (3.4)
Pain	7 (3.9)	11 (6.3)
Death	*12 (6.6)*	*6 (3.4)*

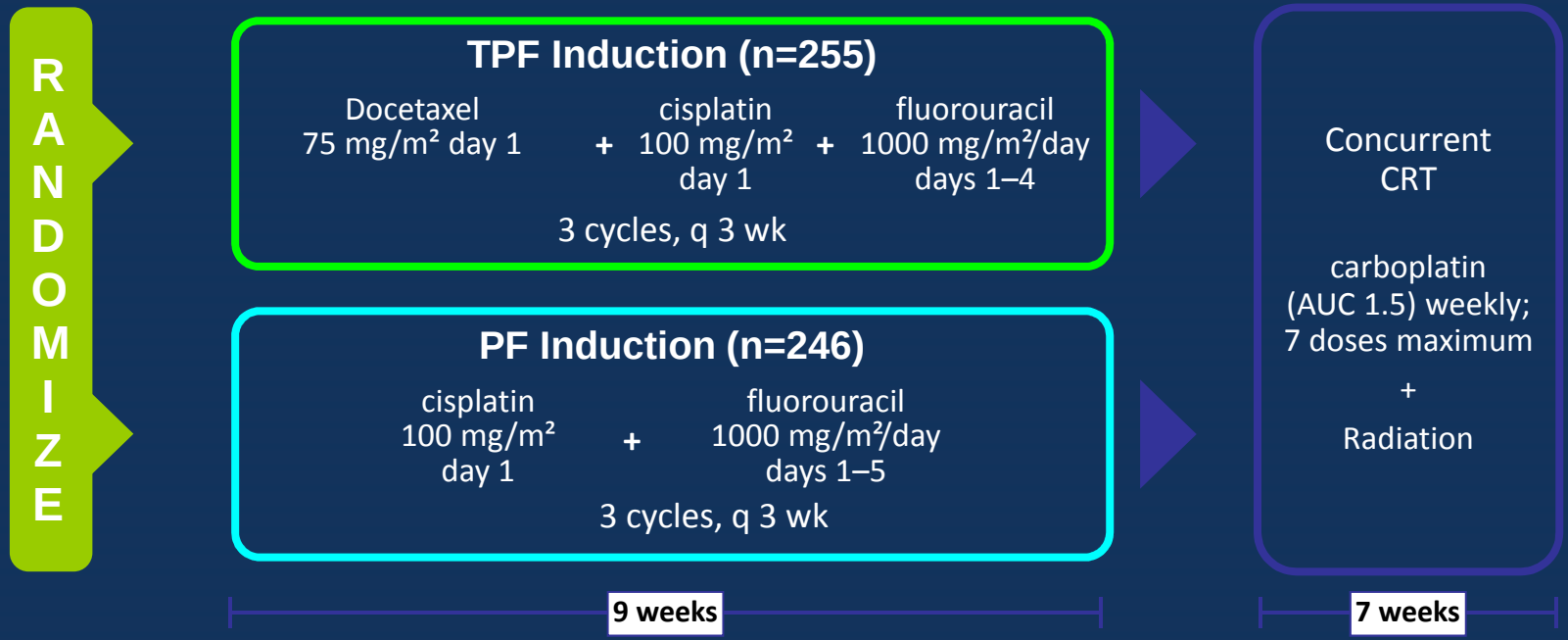
Vermoken, ASCO, 2004

Induction PF versus PF + Docetaxel (TPF) TAX 324: Eligibility Criteria

- Stage III, IVA, IVB HNSCC unresectable or potentially resectable
  - Low surgical curability (advanced T or N)
  - Goal of organ preservation
- PS 0-1

Posner MR, et al. N Engl J Med. 2007;357(17):1705-1715.

Induction PF versus PF + Docetaxel (TPF)
TAX 324: Trial Design

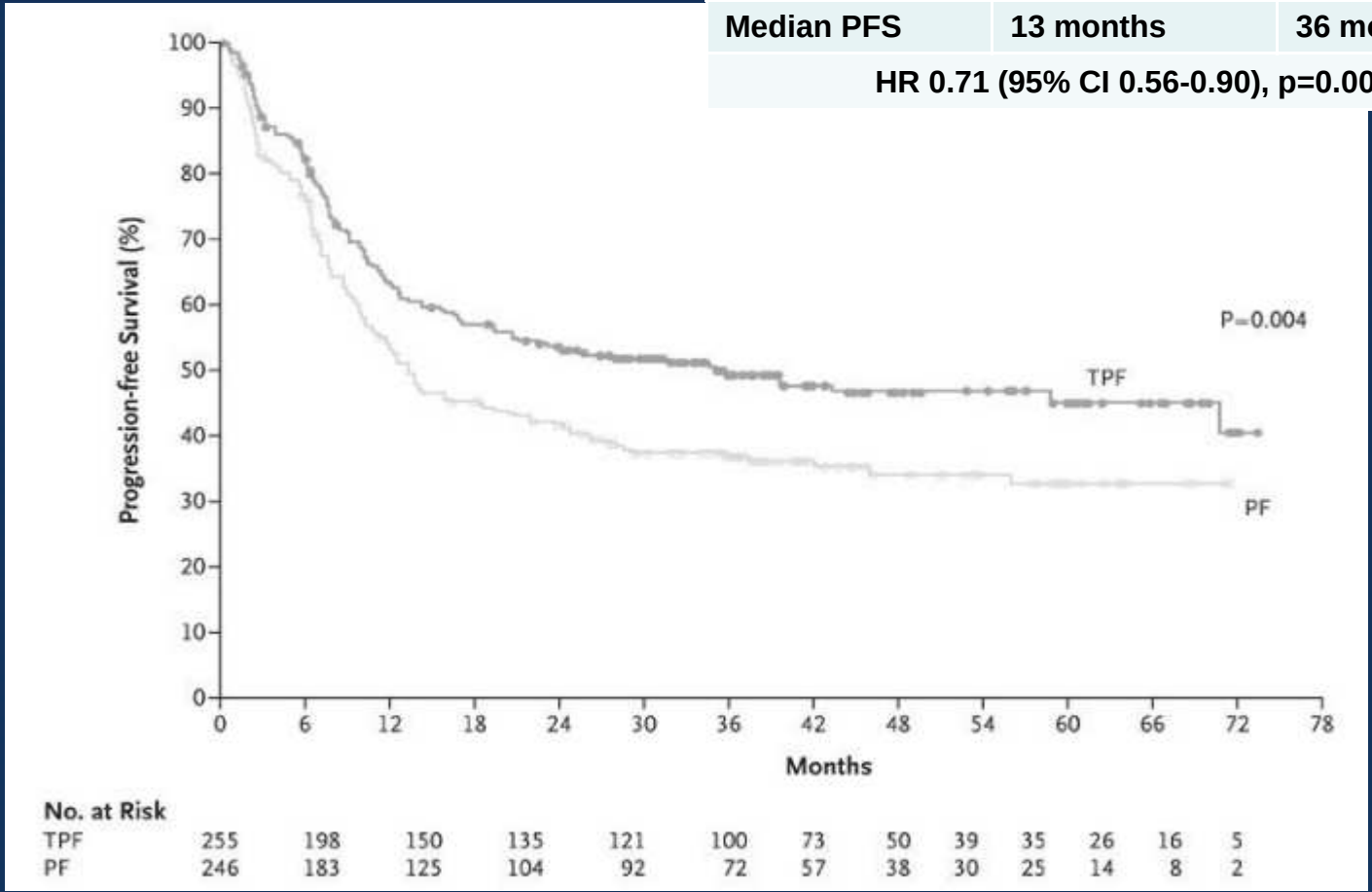


Primary endpoint: overall survival

Posner MR, et al. N Engl J Med. 2007;357(17):1705-1715.

Induction PF versus PF + Docetaxel (TPF) TAX 324: PFS

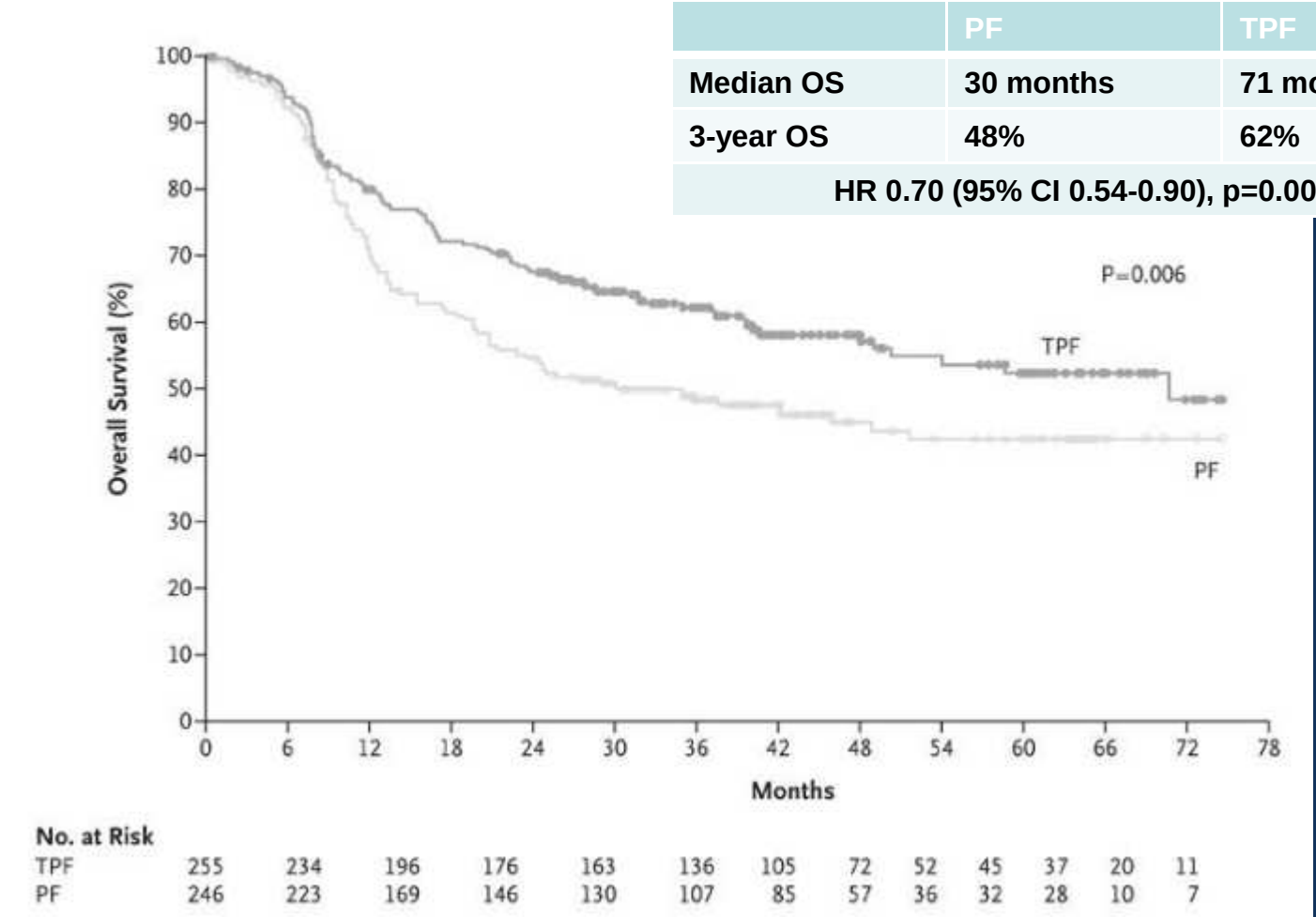
	PF	TPF
Median PFS	**13 months**	**36 months**
HR 0.71 (95% CI 0.56-0.90), p=0.004		



Posner MR, et al. N Engl J Med. 2007;357(17):1705-1715.

Induction PF versus PF + Docetaxel (TPF) TAX 324: OS

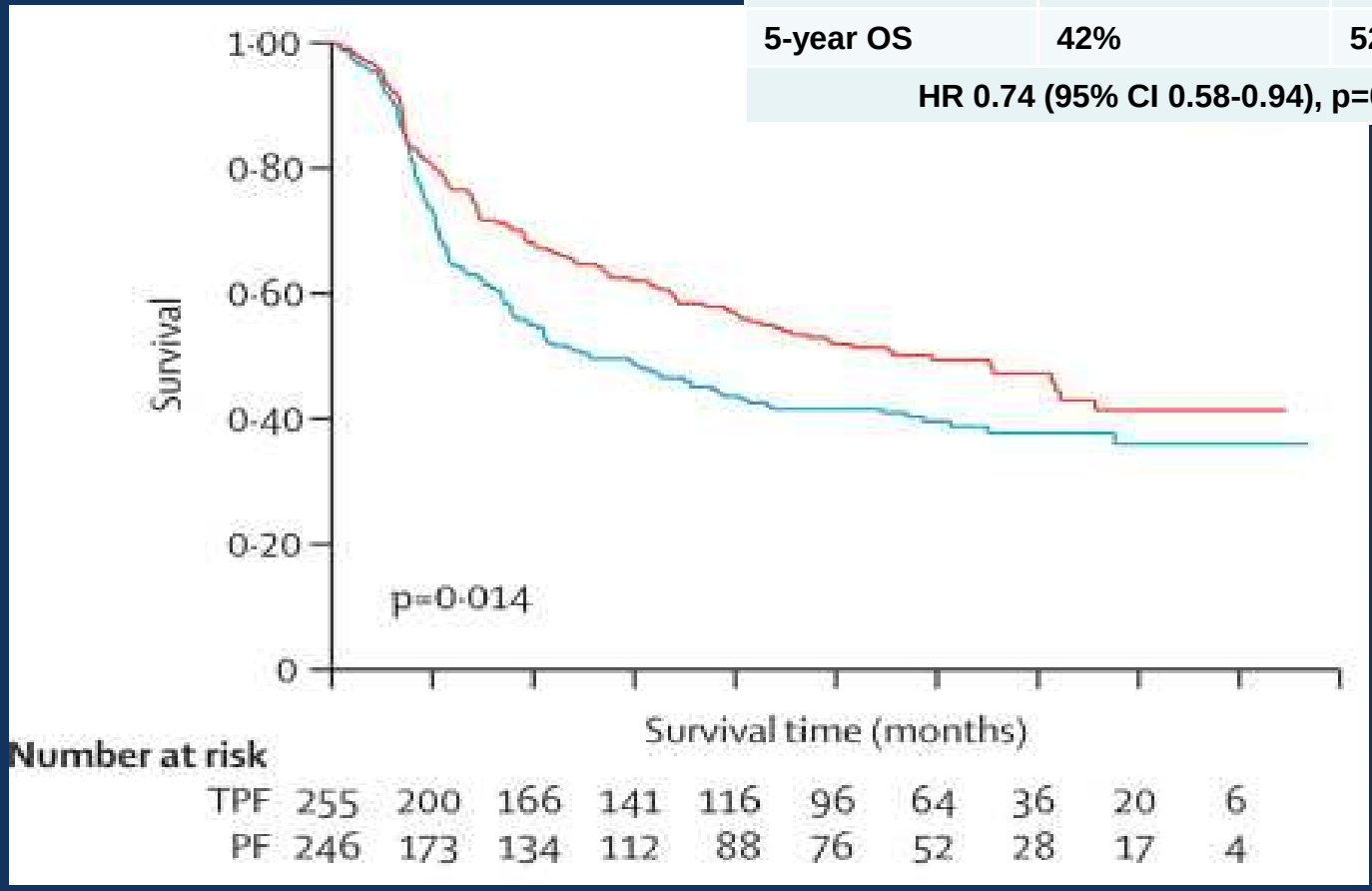
	PF	TPF
Median OS	**30 months**	**71 months**
3-year OS	**48%**	**62%**
HR 0.70 (95% CI 0.54-0.90), p=0.006		



Posner MR, et al. N Engl J Med. 2007;357(17):1705-1715.

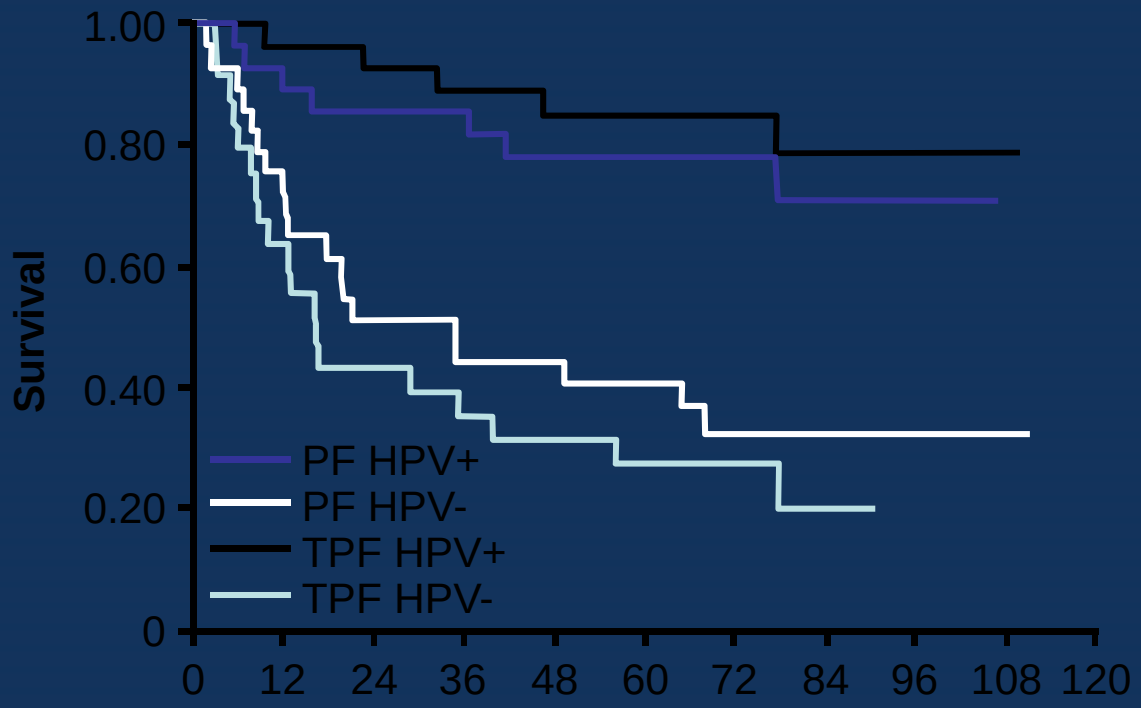
Induction PF versus PF + Docetaxel (TPF) TAX 324: Long-term OS

	PF	TPF
Median OS	**34.8 months**	**70.6 months**
5-year OS	**42%**	**52%**
HR 0.74 (95% CI 0.58-0.94), p=0.014		



Lorch JH, et al. Lancet Oncol. 2011 Feb;12(2):153-9

Survival According to HPV Status and Treatment Arm in TAX 324



Pts at Risk, n										
PF HPV+	28	25	24	24	19	18	15	9	5	
PF HPV-	29	21	15	13	13	12	5	3	2	1
TPF HPV+	28	27	26	24	22	21	19	10	7	2
TPF HPV-	26	16	11	9	8	7	4	2		

Posner MR, et al. Ann Oncol. 2011;22:1071-1077

Induction PF versus PF + Docetaxel (TPF) TAX 323 and 324: Patterns of Failure

Response Rates

	TPF	PF	*P*
TAX 323	**68%**	**54%**	***0.006***
TAX 324	**72%**	**64%**	***0.07***

Locoregional Failure

	TPF	PF	*P*
TAX 323	*81 to 85% of the first relapses were locoregional*		
TAX 324	**30%**	**38%**	***0.04***

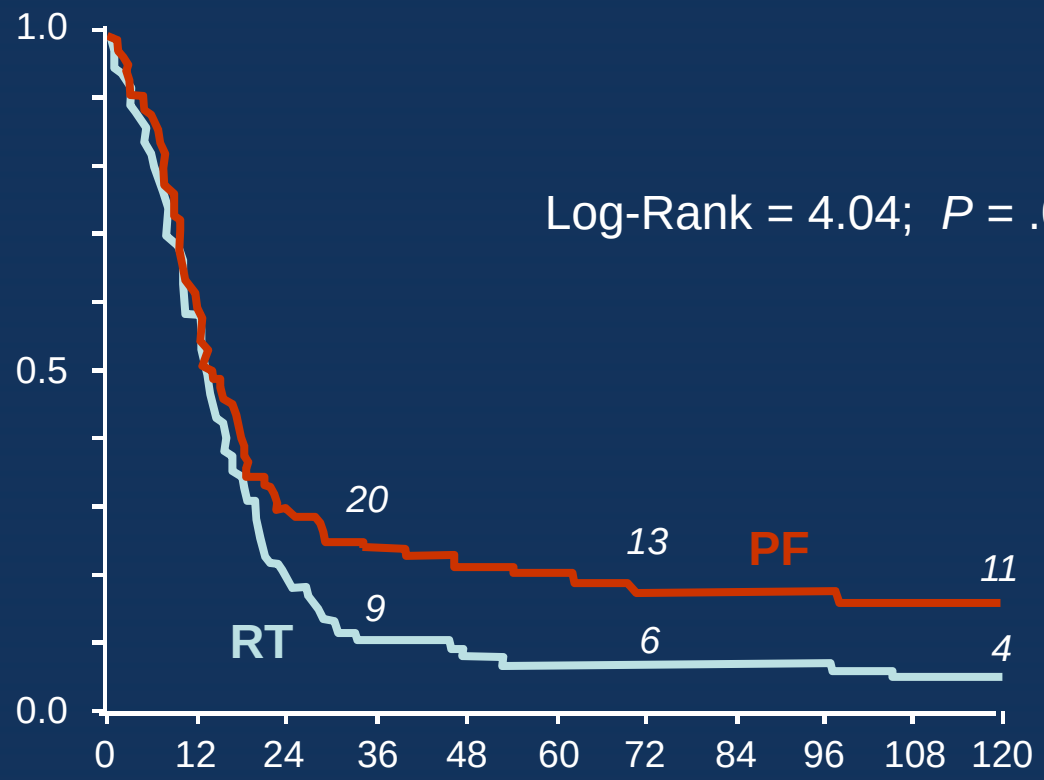
Distant Metastases

	TPF	PF	*P*
TAX 323	**13%**	**10%**	***N/A***
TAX 324	**5%**	**9%**	***0.14***

TAX 323 and TAX 324: Summary

- Response rates to induction chemotherapy are higher with TPF compared to PF
- Induction chemotherapy with TPF improves survival compared to PF, primarily due to increased locoregional control
- Rate of distant failure is low with both TPF and PF
- It is unknown whether induction chemotherapy is superior to upfront chemoXRT
- It is unknown whether the improved survival with TPF would be observed in the setting of definitive treatment with concurrent cisplatin / XRT

Can TPF Improve Overall Survival?



Log-Rank = 4.04; *P* = .04

Zorat JNCI 2004

Induction Chemotherapy

- Pros
  - High dose treatment, systemic exposure, transient toxicity
  - Improved nutrition and PS
  - Reduced tumor volume
    - Better preparation for definitive radiotherapy and IMRT planning
    - Improved function
  - Established efficacy in resectable disease and organ preservation
  - Improved survival
  - Intermediate assessment of response/prognosis
    - Adjusted intensity of post-induction therapy
- Cons
  - Systemic toxicity increased
  - Survival improvement may be site and stage related
  - Increased duration of therapy, change in tumor biology
  - No improvement in local/regional dose intensity
  - Cisplatin-based PF was the only effective chemotherapy regimen

CONCLUSION

- Induction chemotherapy
  - High response rates, organ preservation, improved survival, systemic treatment
  - Reduced tumor volume, improved functional outcome
  - An intermediate assessment of response

CONCLUSION

- ***INDUCTION CHEMOTHERAPY***
- Has not withstood its test.

- Still fighting !!!

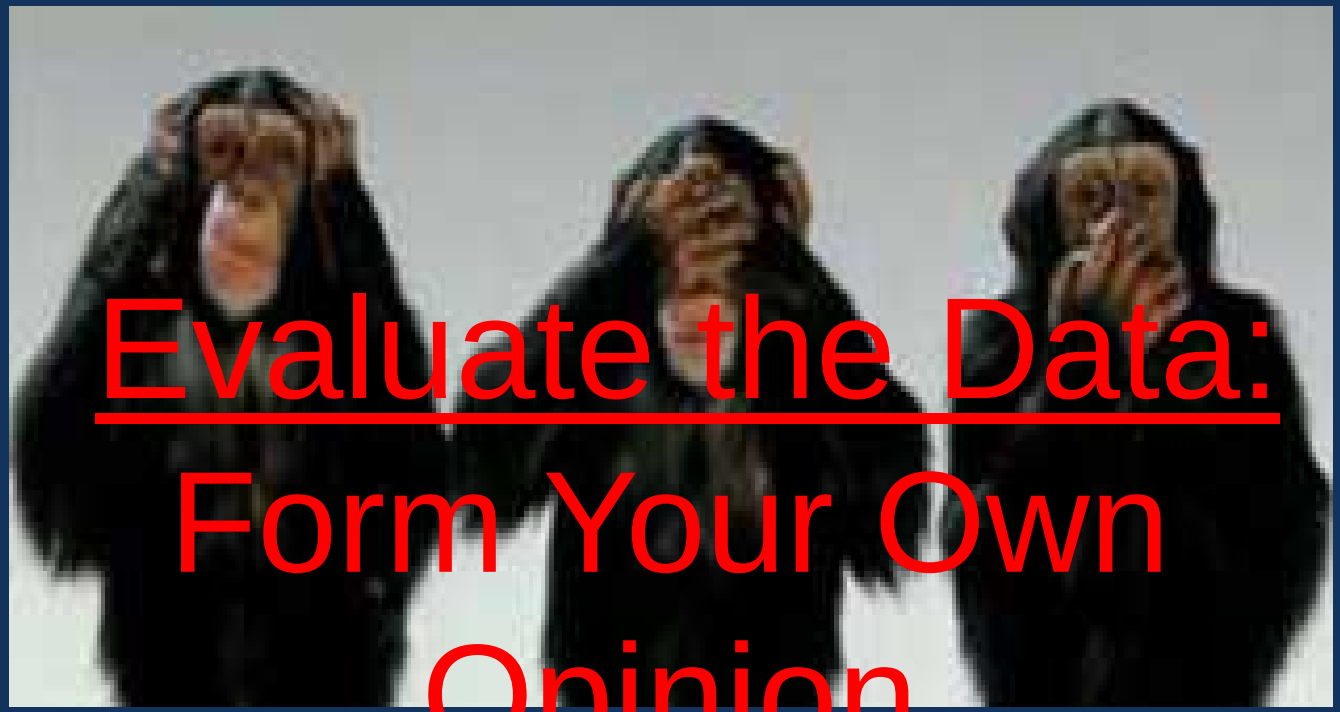
- In selected cases

Hear No Induction – See No Induction – Speak No Induction

Hear About The Data

Think About The Data

Speak About The Data



Evaluate the Data:

Form Your Own Opinion

THANKS