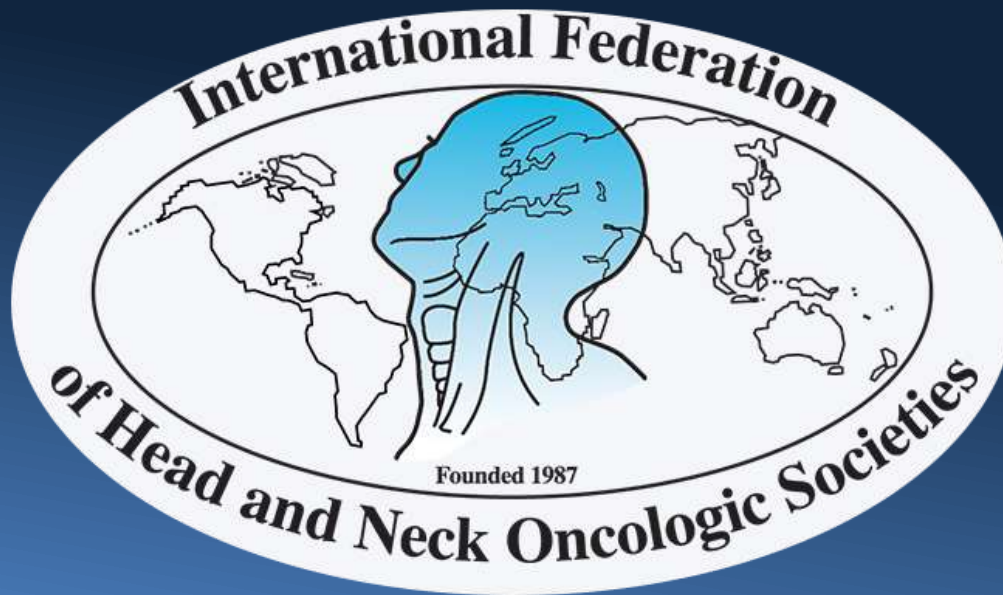




The International Federation of Head and Neck Oncologic Societies

Current Concepts in Head and Neck Surgery and Oncology 2017



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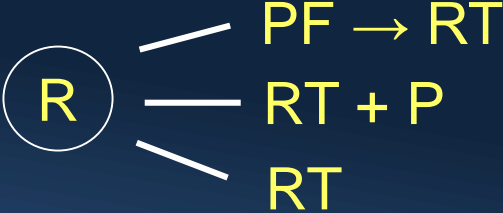
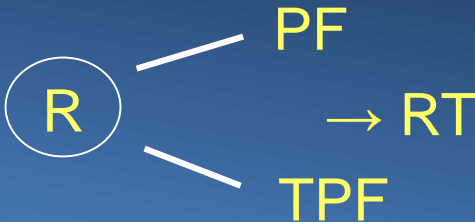
Strategies for Non-Surgical Treatment of Larynx cancer

Merrill S. Kies

Management Practices

- Radiotherapy is the core of non-surgical treatment
- CT is highly active, with accepted strategies for sequential and concomitant treatment with RT
- Modification of definitive local therapy, based on a response to CT has been studied

Induction CT / Larynx Preservation Trials

<u>Studies</u>	<u>Schema</u>	<u>Primary Objectives</u>
RTOG (Forastiere ASCO, 2006)	 <p>PF → RT RT + P RT</p>	Larynx preservation, in intermediate stage larynx cancer (N-547)
GORTEC (Pointreau JNCI, 2009)	 <p>PF → RT TPF</p>	LP, in “advanced” L and HP SCC (N-220)

RTOG 91-11 / 5 yr Outcomes (%)

	<u>% RT Compliance</u>	<u>LFS</u>	<u>LP</u>
PF → RT	84	45 (p=0.01 v RT)	71
RT + P	91	47 (p=0.01 v RT)	84 (p< 0.01 v RT)
RT alone	95	34	66

LFS – laryngectomy-free survival

LP – larynx preservation

Forastiere ASCO, 2006

RTOG 91-11 / Toxicity

- Swallow only liquids < 4 %
- Inability to swallow < 3%
- 9/515 had laryngectomy for dysfunction or necrosis

Forastiere HN, JCO 2010

RTOG 91-11/ 10-year f/u

LFS: RT+ ICT 28.9 %; RT-CT 23.5 %

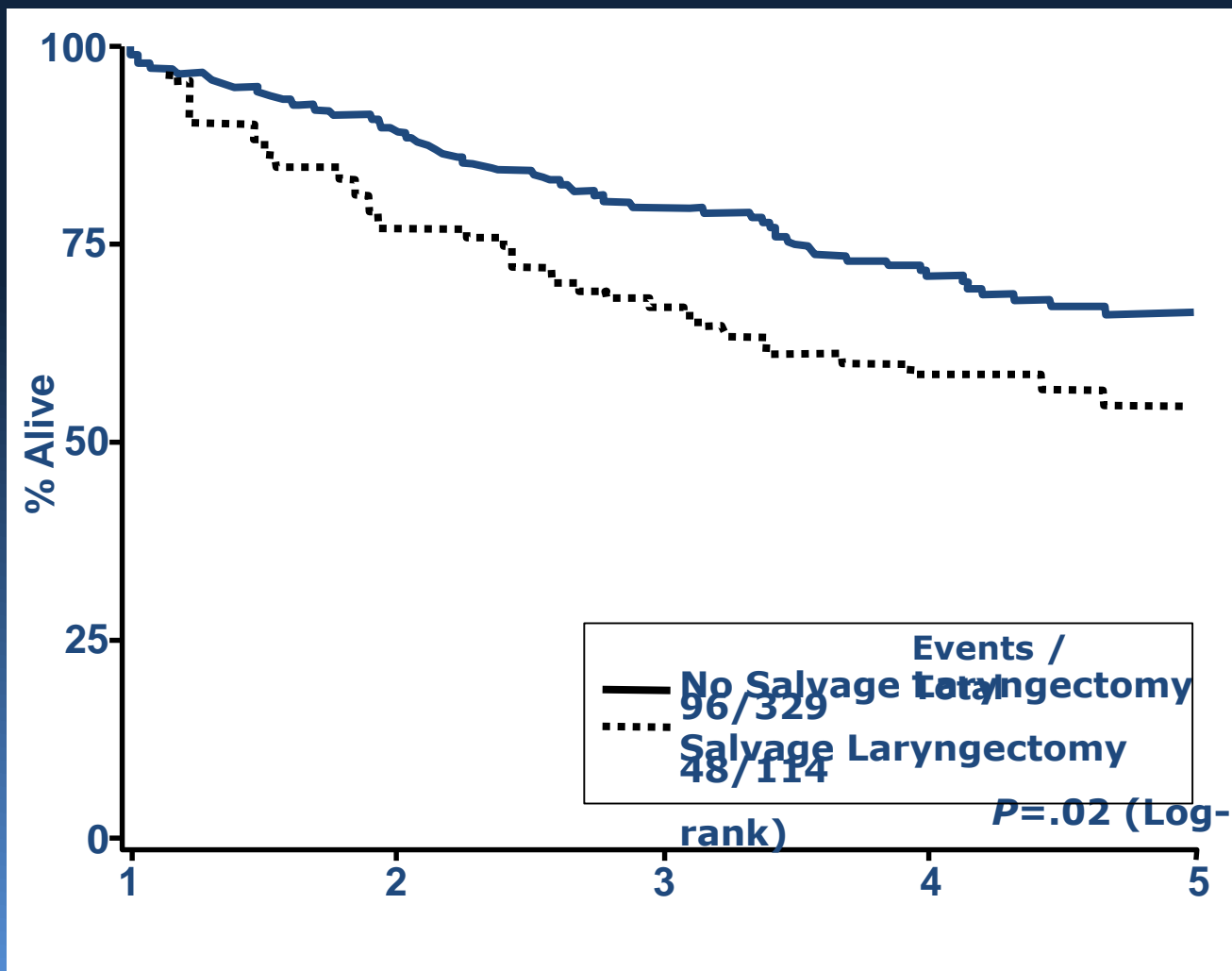
Long term function: Swallow only liquids < 4 % all groups; Moderate speech impairment < 10 % all groups

OS: RT + ICT 39 %; RT-CT 28 %

Forastiere HN et al, JCO 2010

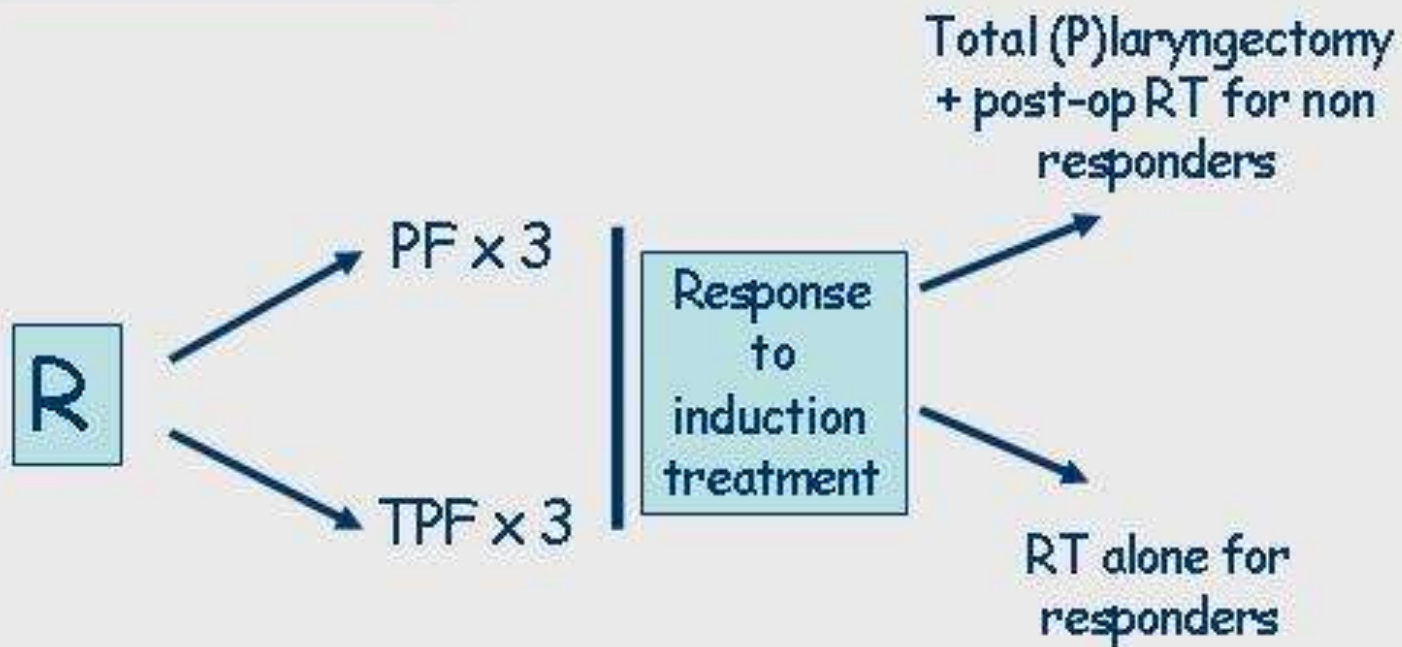
RTOG 91-11

Overall survival of patients surviving at least 1 year



French HN Onc Trial TPF vs PF

Study Design

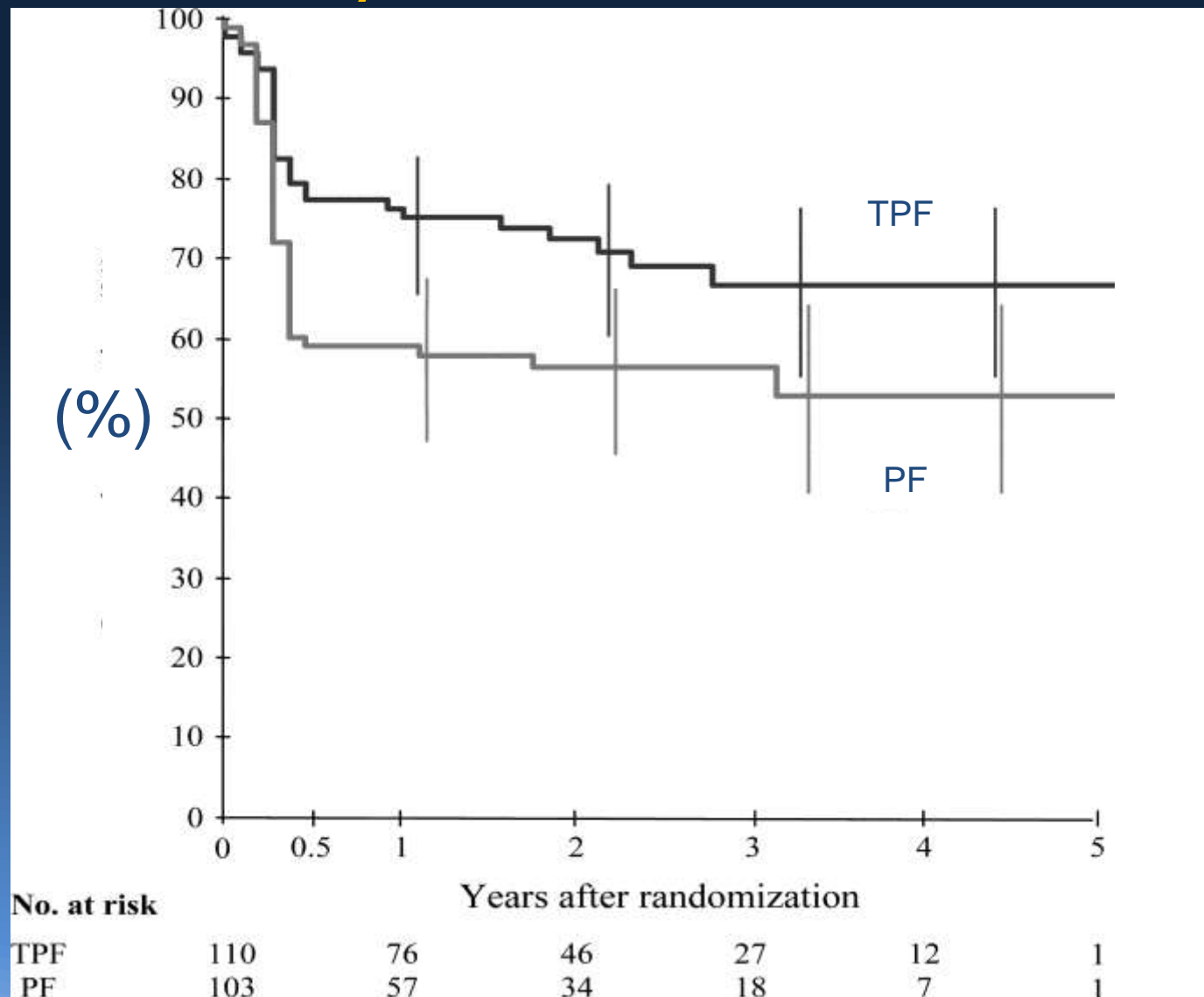


Tumor Response to Chemotherapy

	<u>TPF</u>	<u>PF</u>
CR	42%	30%
PR	38%	29%
R=0	12%	35%
Progression	3%	6%
<hr/>		
CR + PR →	80%	59%
p=0.0024		



Larynx Preservation

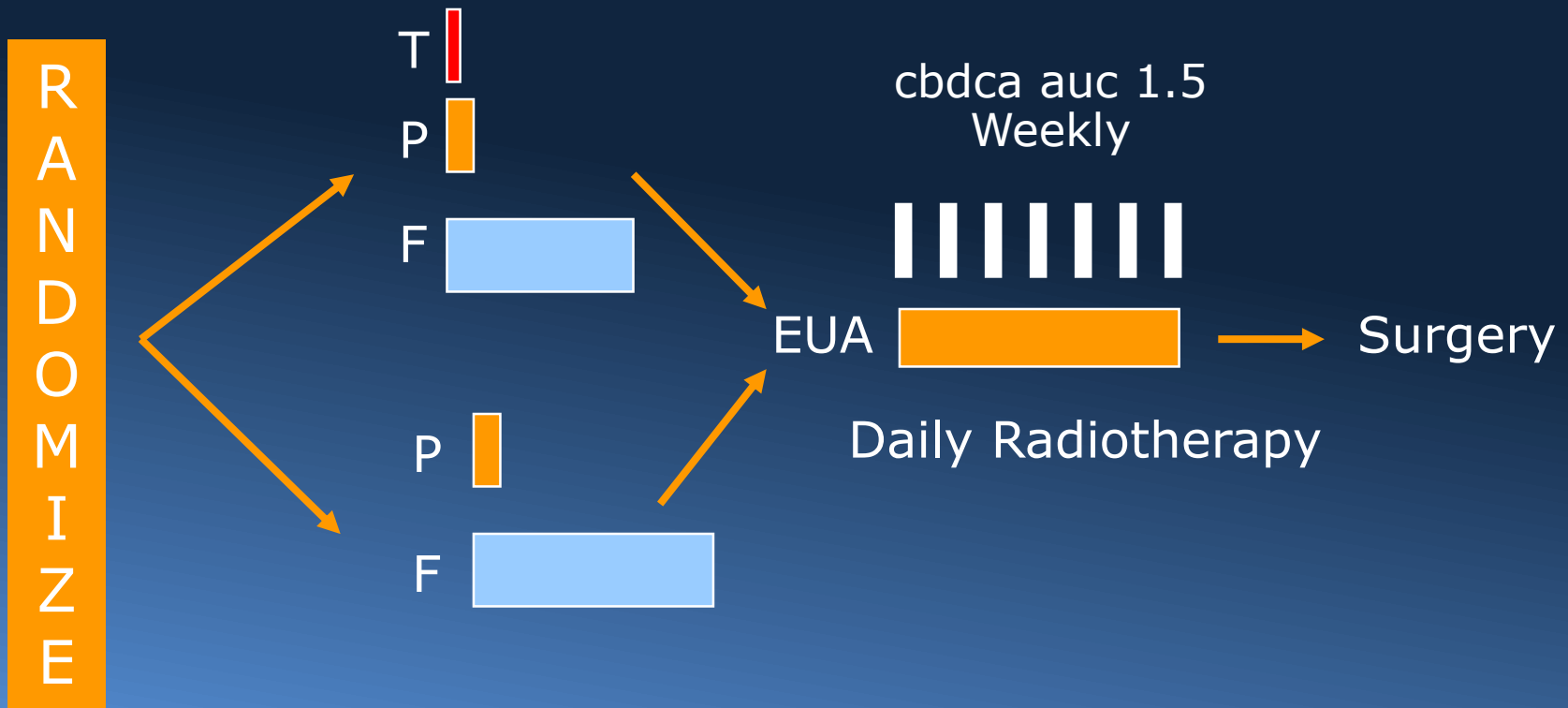


Pointreau Y et al, JNCI 2009

Sequential Combined Modality Therapy

A Phase III Study: TAX 324

TPF vs PF Followed by Chemoradiotherapy



TPF: Docetaxel 75_{D1} + Cisplatin 100_{D1} + 5-FU 1000_{CI-D1-4} Q 3 weeks x3

PF: Cisplatin 100_{D1} + 5-FU 1000_{CI-D1-5} Q 3 weeks x 3

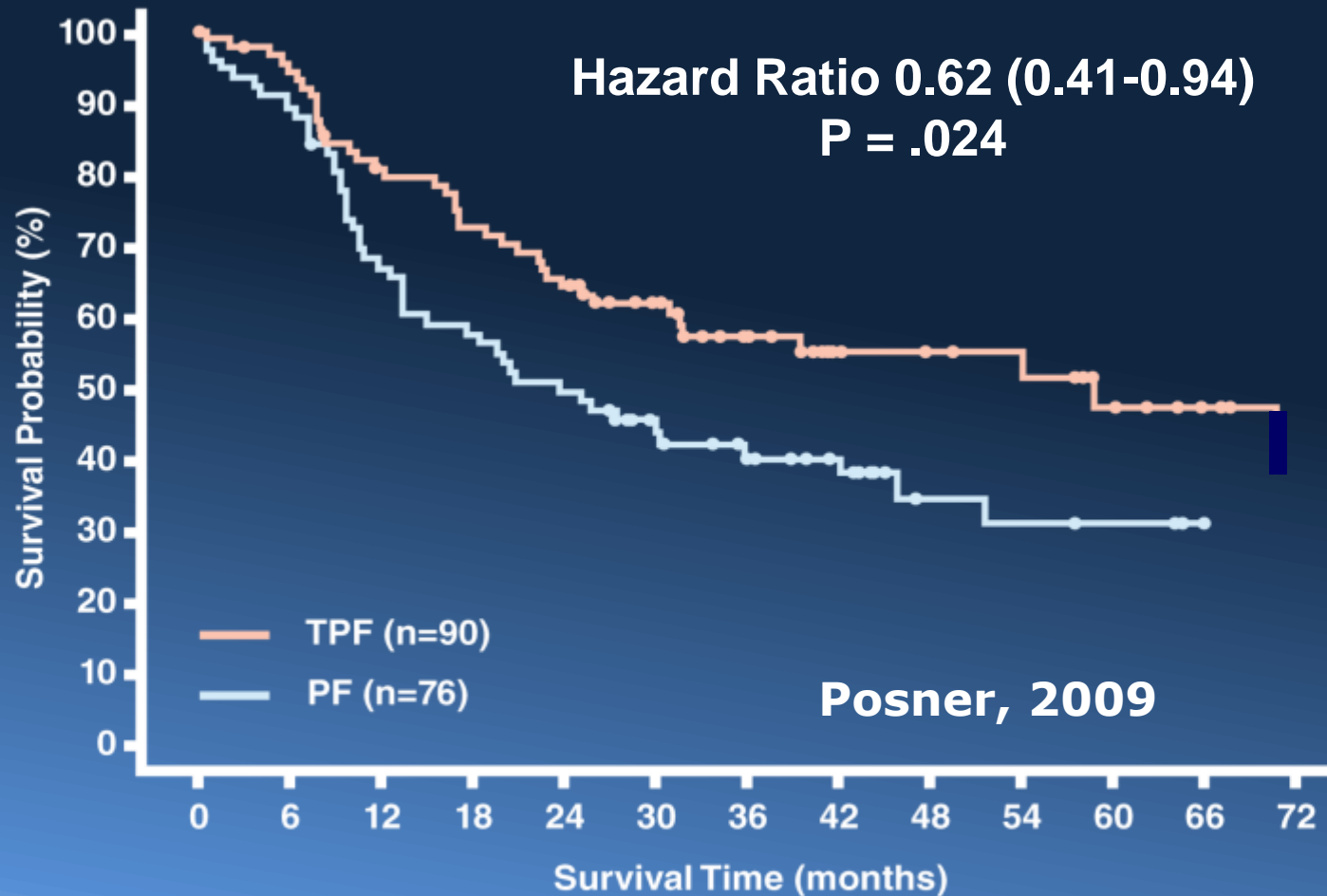
Characteristics of Hypopharynx and Larynx Cases Treated On TAX 324

		TPF	PF	P
Number		90	76	
Hypopharynx		43 (48%)	34 (45%)	
Larynx		47 (52%)	42 (55%)	
Median Age (Range)		56 (39-82)	59 (37-80)	P=.21
T Stage	T1/2	15 (17%)	17 (22%)	P=.37
	T3	35 (39%)	33 (43%)	
	T4	40 (44%)	26 (34%)	
Nodal Stage	N0/1	43 (47%)	33 (46%)	P=.81
	N2	35 (39%)	31 (40%)	
	N3	12 (13%)	12 (15%)	
Clinical Stage	III	22 (24%)	22 (29%)	P= .60
	IV	68 (76%)	54 (71%)	

Larynx and Hypopharynx Survival and Progression Free Survival

	TPF	PF	P
Number	90	76	
Overall Survival			
Median, mo (range)	59 (31-NR)	24 (13-42)	
2 Year	64% (54-74%)	50% (38-61%)	
3 Year	57% (46-68%)	40% (29-52%)	
Hazard ratio			
	0.62 (0.41-0.94)		.024
PFS (Equivalent to LFS)			
Median, mo (range)	21 (12-59)	11 (8-14)	
2 Year	48% (37-58%)	33% (22-43%)	
3 Year	43% (32-54%)	29% (19-40%)	
Hazard ratio			
	0.66 (0.45-0.97)		.032

Larynx and Hypopharynx - Overall Survival



Number of patients at risk

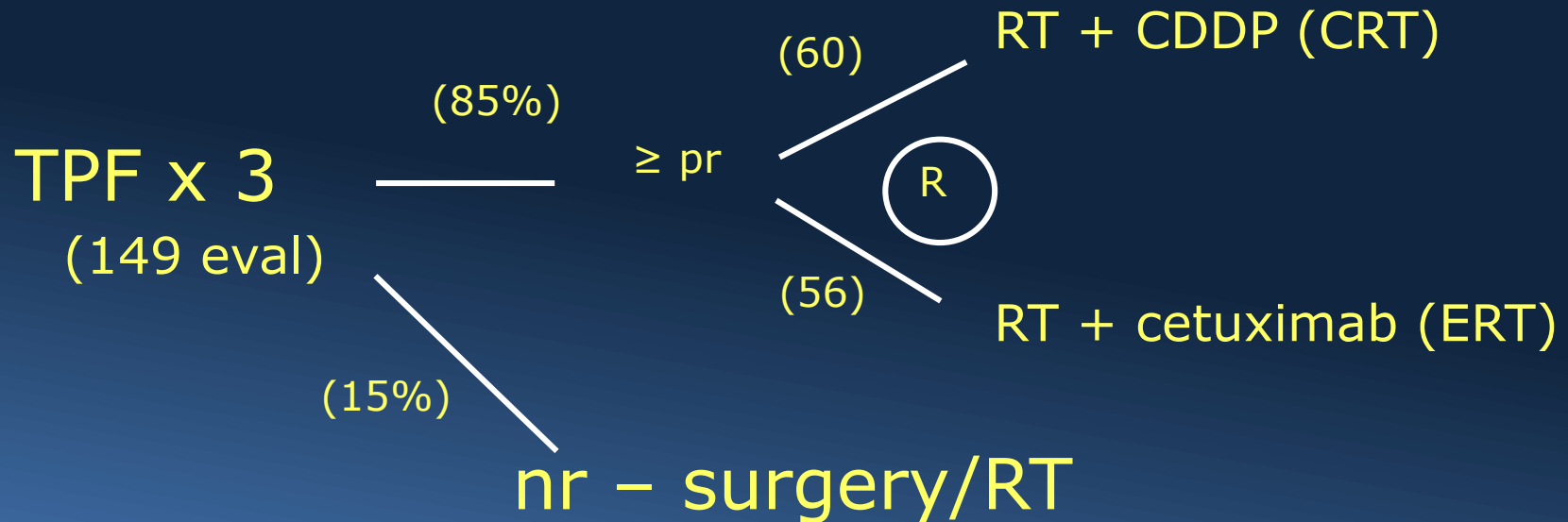
TPF:	90	83	69	62	55	44	29	20	17	15	11	7	
PF:	76	68	50	43	37	27	21	16	9	8	7	4	2

Michigan Data for Treatment Selection Based on CT Response (N 97)

- Stages III / IV with T4 33%
- PF x 1
 - \geq pr \rightarrow CT-RT \rightarrow PF x 2
 - $<$ pr \rightarrow laryngectomy
- Larynx preservation in 70%
- 3 year OS 85%

Urba S et al, JCO, 2006

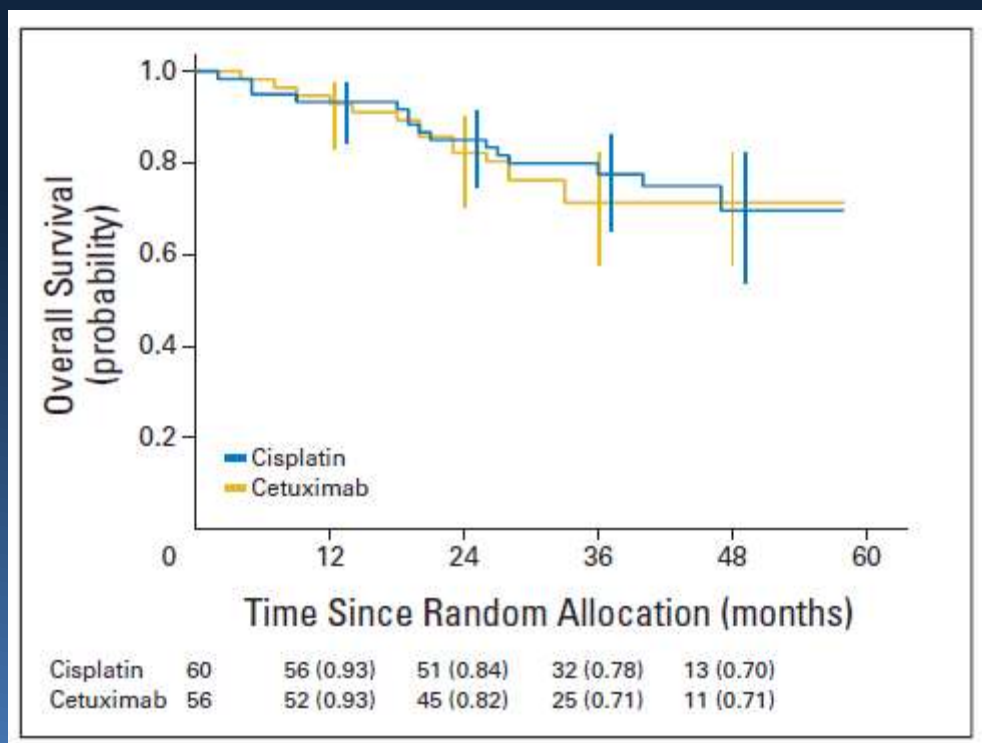
Phase II TREMPLIN Study for Larynx / Hypopharynx SCC (N=156)



Results:

- Larynx preservation @ 3 mos: 95% (CRT) vs 93%
- Received allocated rx: 58 (CRT) and 56 (ERT)

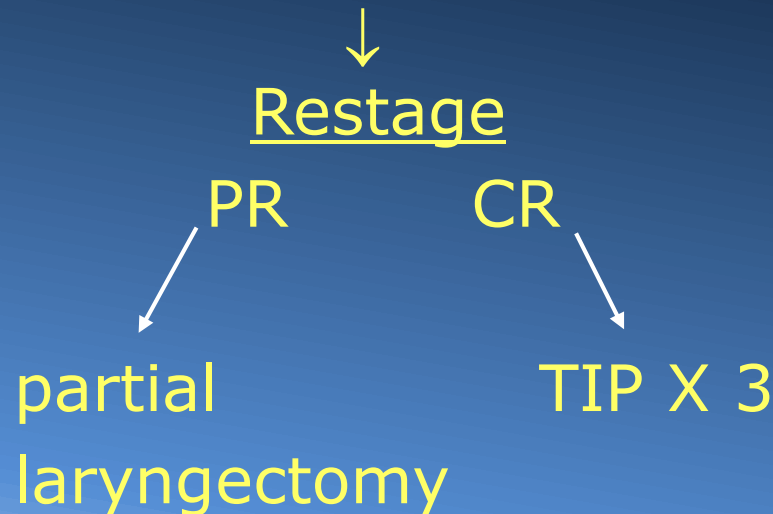
Overall Survival



TIP → Larynx Schema

Intermediate stage scc of the glottic and supraglottic larynx

Paclitaxel	175 mg/m ² d1	}	q 21 d x 3
Ifosfamide	1000 mg/m ² d1-3		
Cisplatin	60 mg/m ² d1		
(TIP)			



Histologic Response to TIP chemotherapy

Response to Chemotherapy			
<u>Site and T Stage</u>	<u>Response</u>		
	<u>CR</u>	<u>PR</u>	<u>N</u>
Glottic larynx	4	10	14
T2	3	9	12
T3	0	1	1
T4	1	0	1
Supraglottic larynx	7	9	16
T2	5	4	9
T3	1	4	9
T4	1	1	2

Scc of the larynx may be cured after chemotherapy - Pt #21, of the TIP-Larynx study

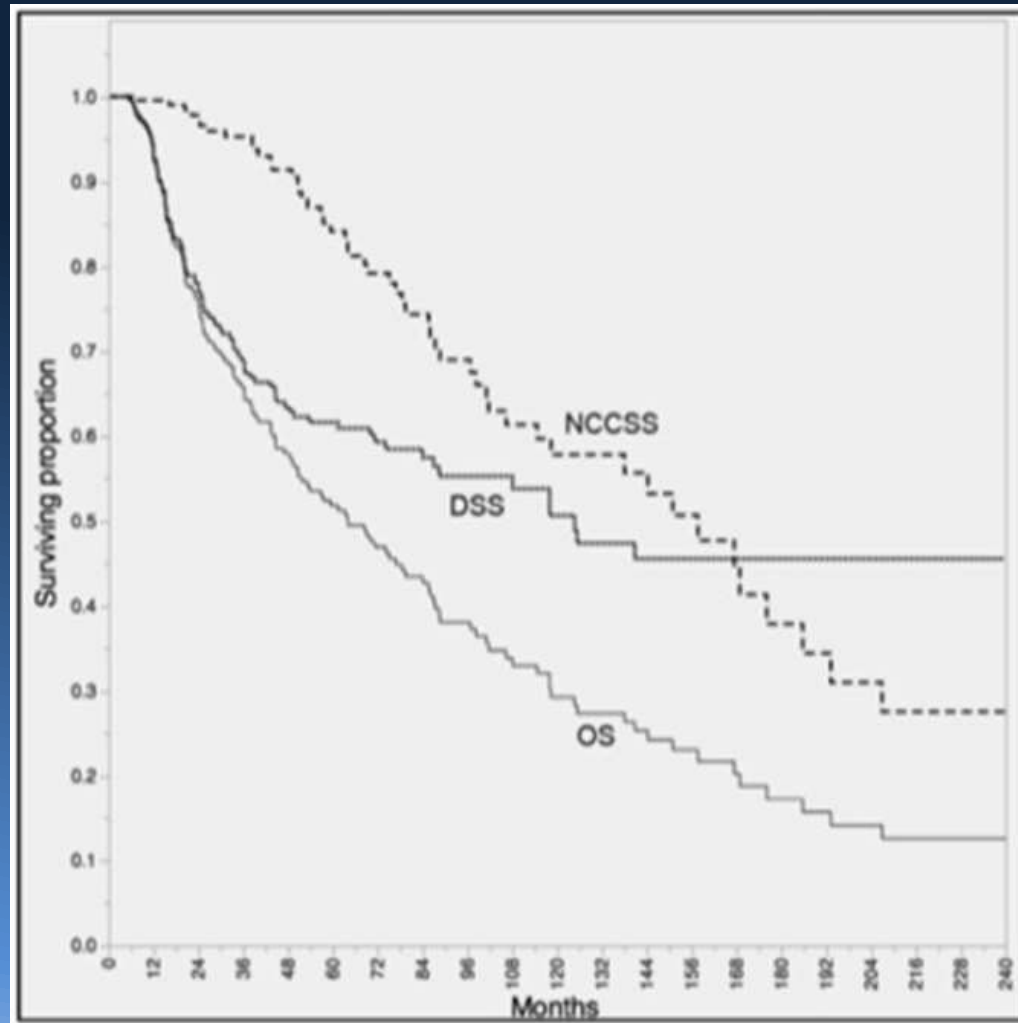


Pre-Treatment
5/18/01



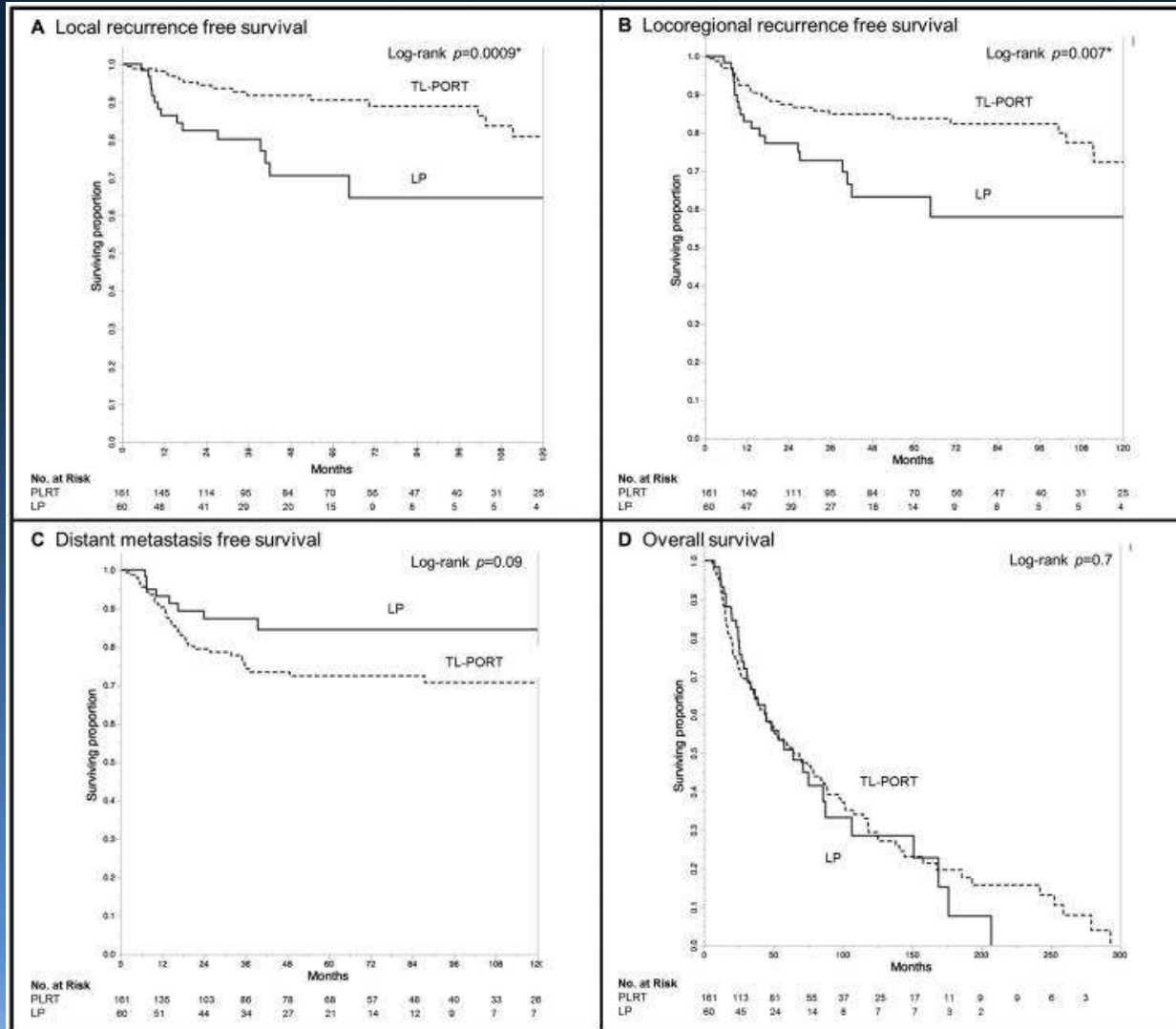
Post Chemotherapy
08/29/01

MDA Review: Long-term Outcomes in T4 SCC/Larynx (N 221)

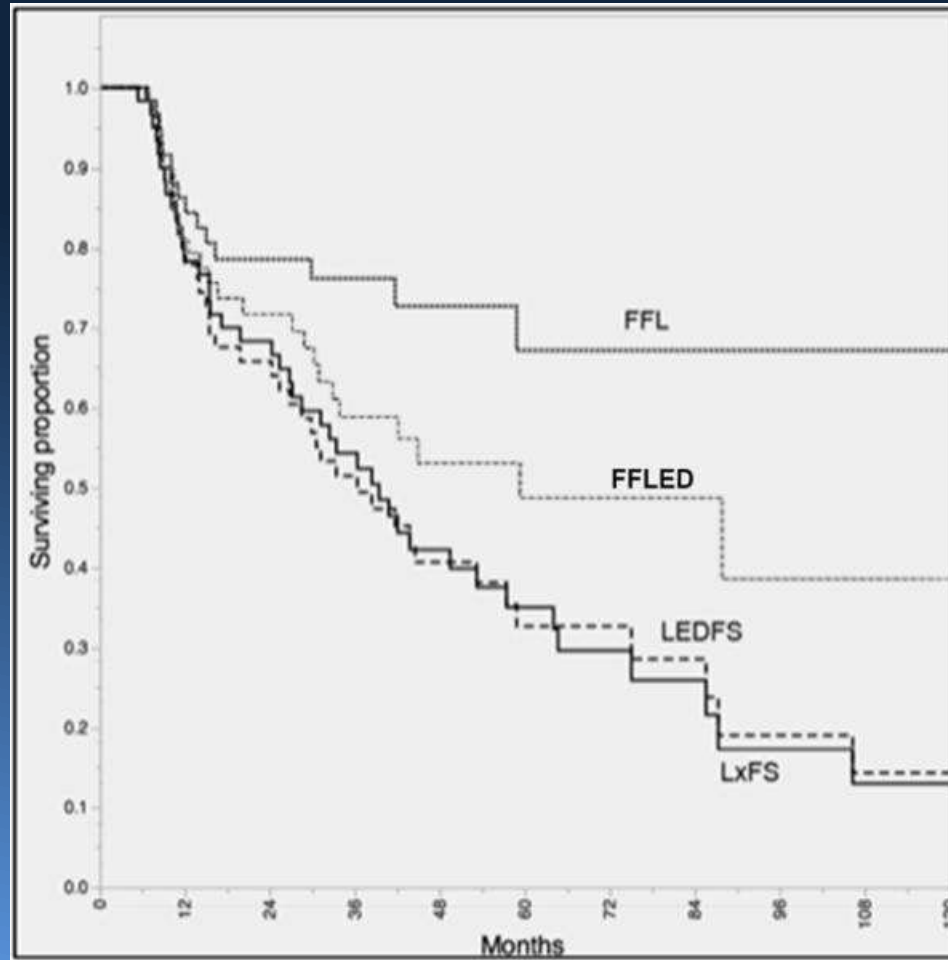


Rosenthal D et al, Cancer 2015

Long-Term Survival



Larynx Preservation / Dysfunction



Rosenthal D et al, Cancer 2015

CT-RT for Squamous Cancer of the Larynx

- Treatment goals are OS, PFS, and Preservation of Laryngeal/Esophageal Function
- Concomitant cisplatin and RT is an established paradigm for T3 and selected T4 disease
- Deeply invasive T4 ds management is surgical
- Induction CT in sequence with RT is an option for non-surgical management
 - may compromise definitive RT (+ / - CT)
 - prompts modification of local/definitive therapy
- A focus of current research is to develop molecular markers for improved selection of systemic and local rx