

Newly diagnosed early stage FL

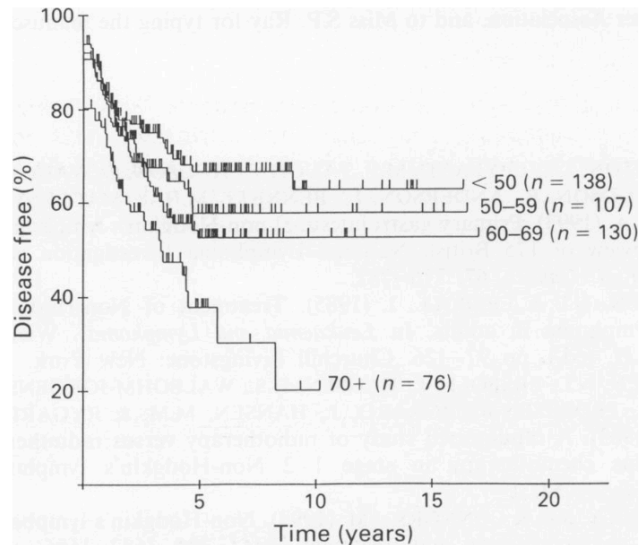
Dr Kirit Ardeshta

University College London Hospitals

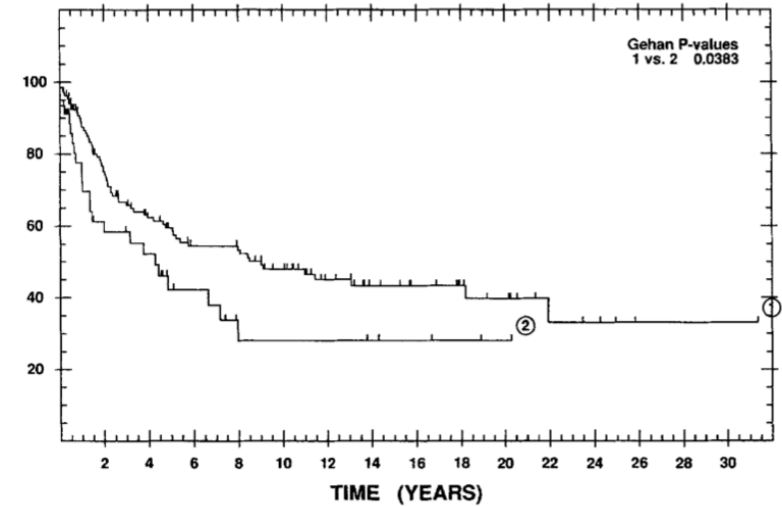
10 yr outcome following RT

Author	Pts (n)	RT Dose (Gy)	RT Vol	FU (yrs)	10y PFS	10 y OS
Vaughan Hudson 1996	208	35	NS	10	47%	CSS 71-84
MacManus 1996	177	35-44	IF EF TNI	7.7	44%	64%
Guadagnolo 2006	106	30-42	IF (EF)	12	FFTF 46%	75%
Gospodarowicz 1984	248	25-50	IF	12	53%	58%
Peterson 2004	460	16-48	IF	12.5	37%	55%

Cures are possible



DFS by age
Vaughan-Hudson et al

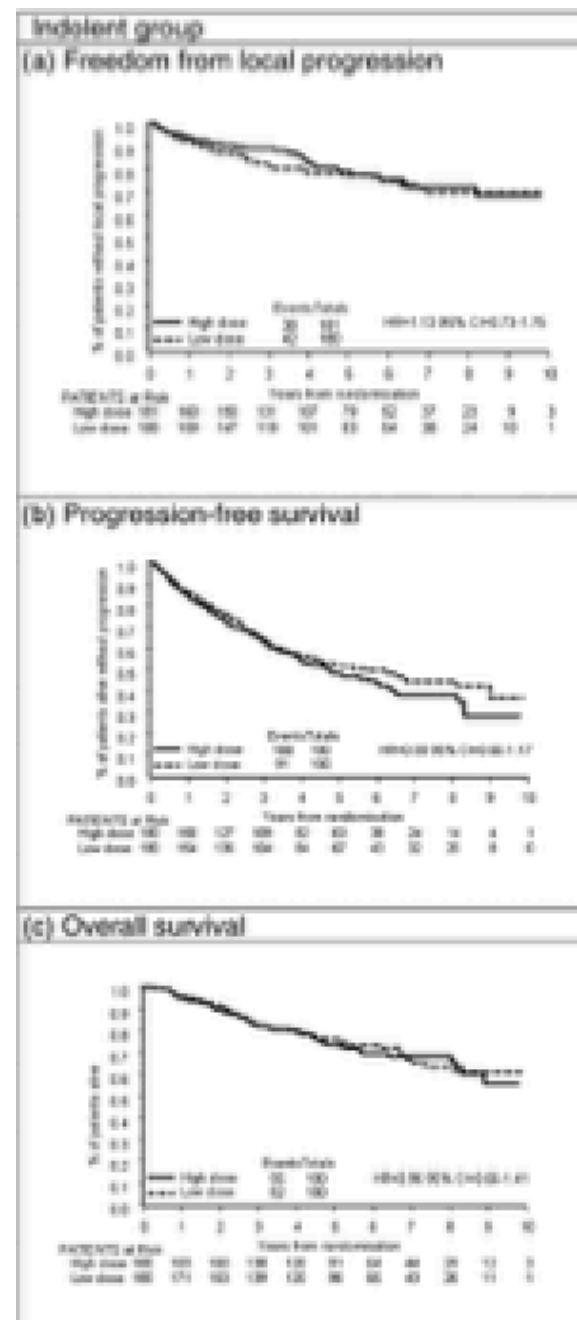


Freedom from relapse
by age
Mac Manus and Hoppe

BNLI: 24 vs 40/45Gy

361 sites of indolent NHL were randomly irradiated

Response	24 Gy	40-45 Gy
CR	145 (82%)	138 (79%)
PR	18 (10%)	24 (14%)
SD/PD	14 (8%)	12 (7%)
Death	0 (0%)	0 (0%)



Freedom from local progression

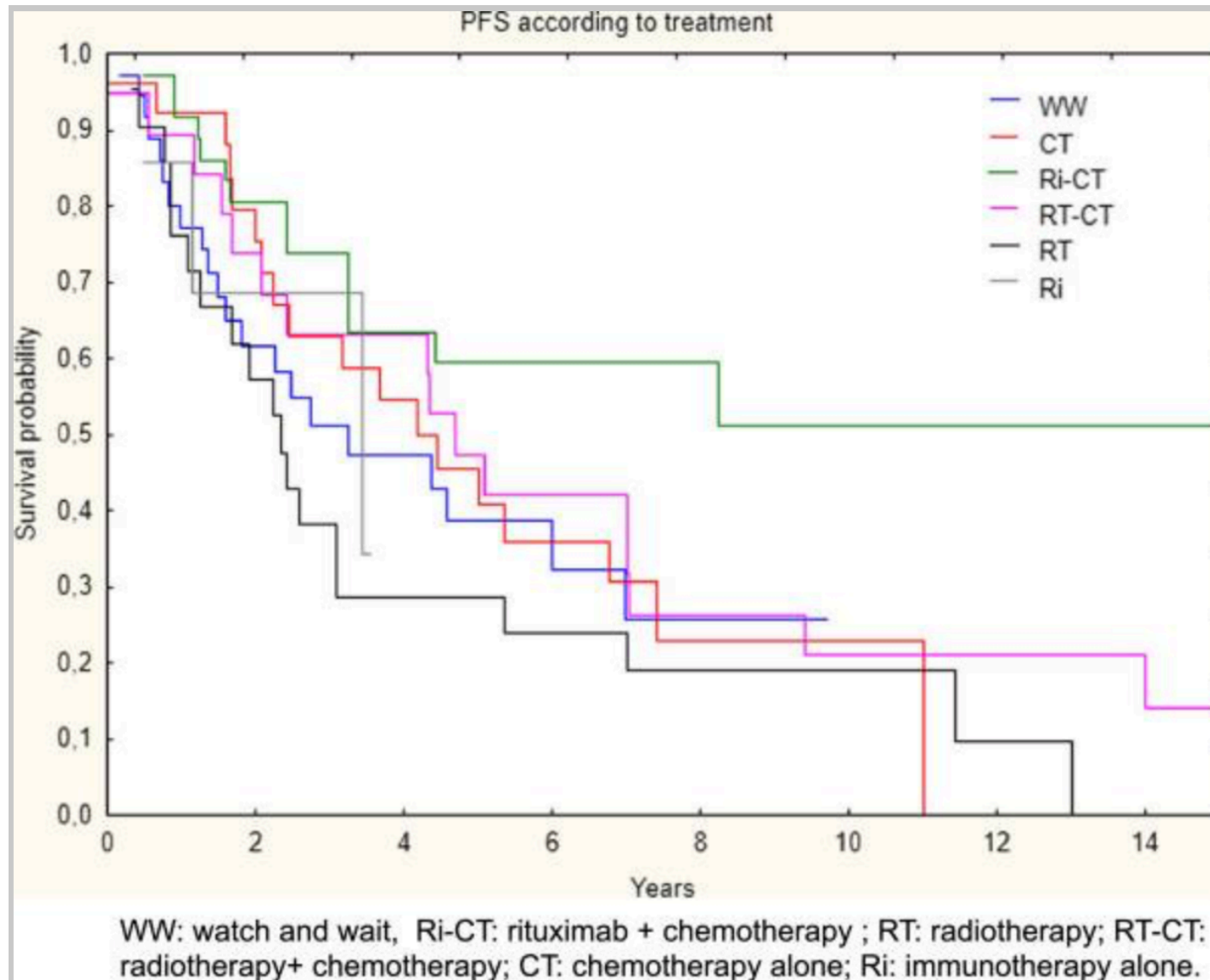
PFS

OS

Watch and Wait

- No randomised studies of W&W vs RT
- Retrospective 43 pts - stage 1a (11) & 2a (32)
- Median FU 7yr
- 16 (37%) required treatment after median 22mo
- 27 (63%) not received any therapy
- Estimated 10 yr OS= 86% (not inferior to RT)

Watch and Wait

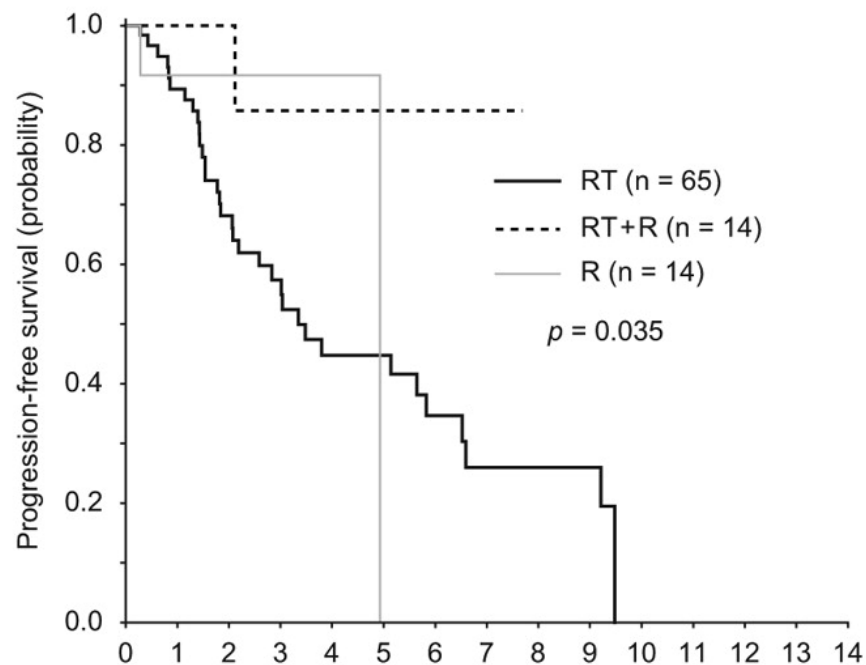


Fully excised

- 26 pts
- Median FU 4.6yr
- 13 had not relapsed
- 6 relapsed same site -median 4.2yr (0.6-9yr)
- 7 relapsed different site –median 1yr (0.5-5.5yr)
- 5yr OS=82.5%

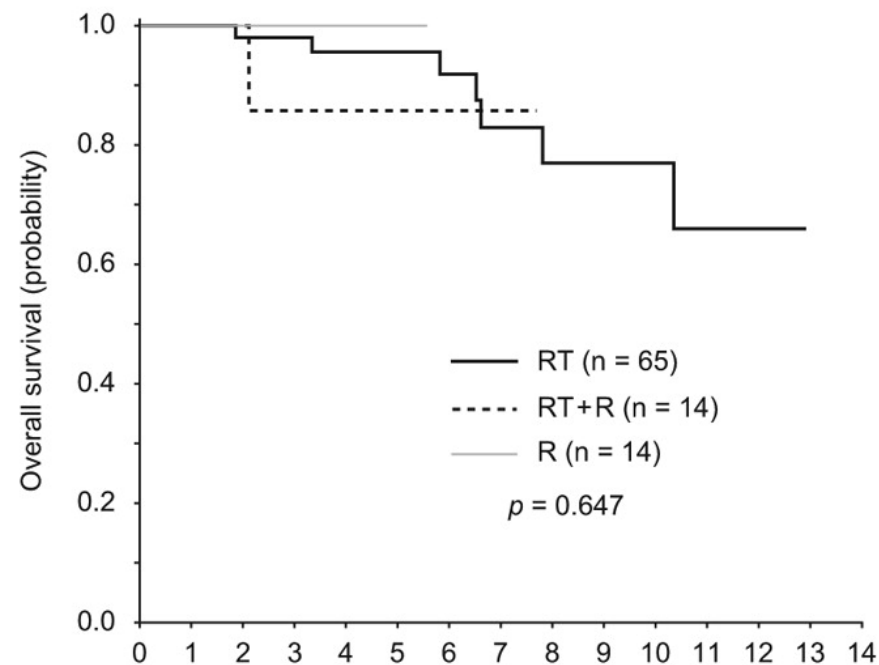
Rituximab & IFRT

(A)



No. at risk	Time (years)														
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
RT:	65	49	33	23	16	15	10	5	4	4	0	0	0	0	0
RT+R:	14	11	8	5	4	3	1	1	0	0	0	0	0	0	0
R:	14	11	7	5	1	0	0	0	0	0	0	0	0	0	0

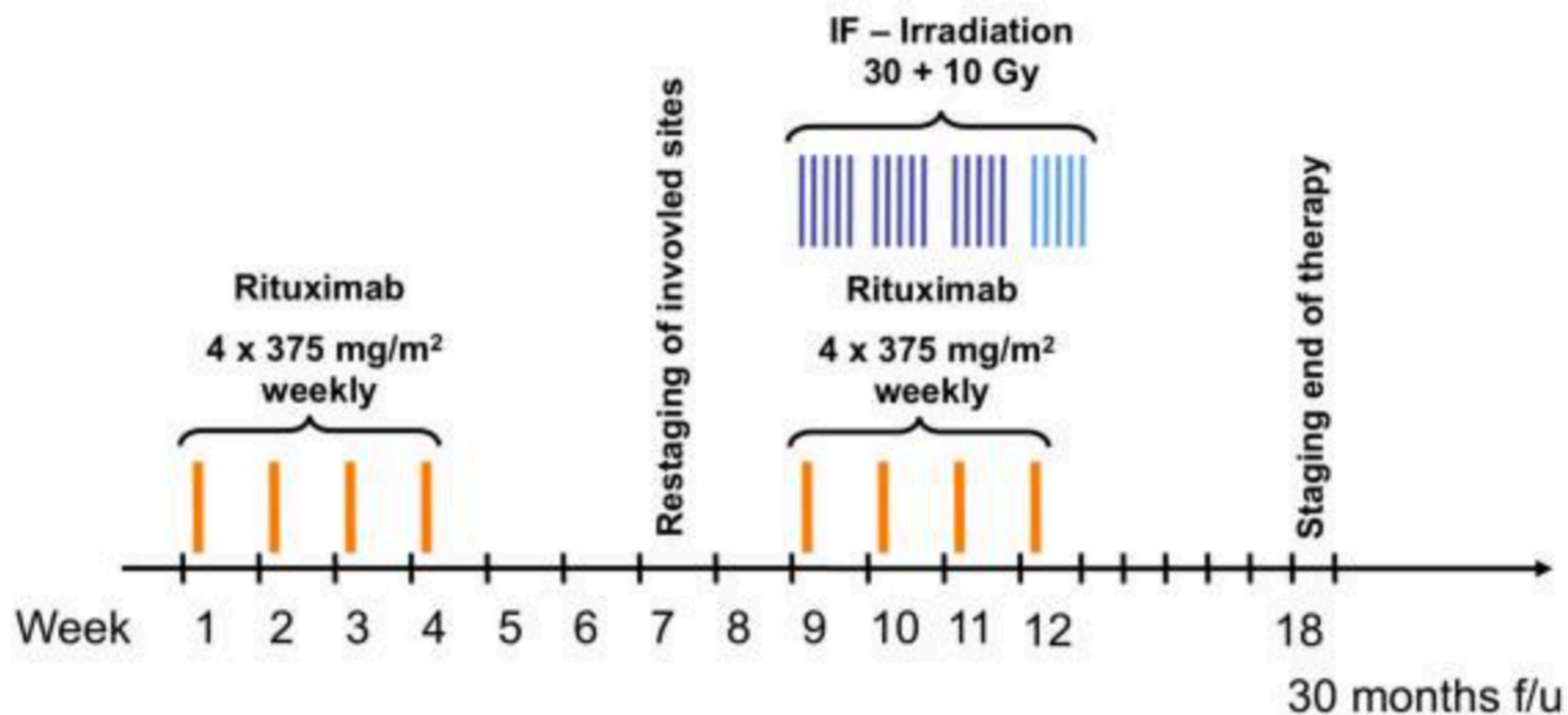
(B)



No. at risk	Time (years)														
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
RT:	65	55	46	40	36	32	25	17	13	12	7	3	1	0	0
RT+R:	14	11	8	5	4	3	1	1	0	0	0	0	0	0	0
R:	14	12	8	6	2	1	0	0	0	0	0	0	0	0	0

PFS (A) and OS (B) from first-line treatment initiation: RT vs. RT + R vs. R

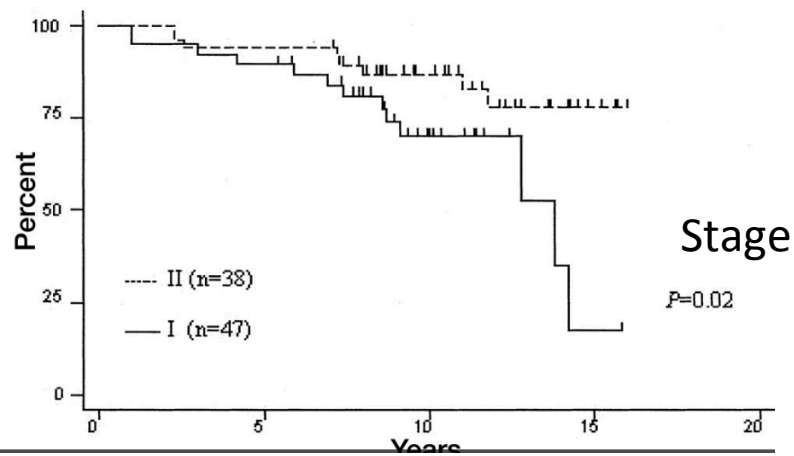
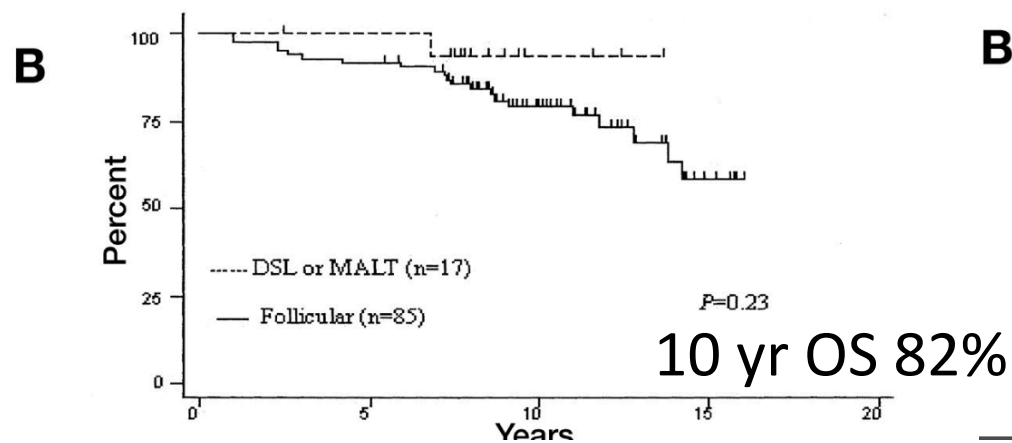
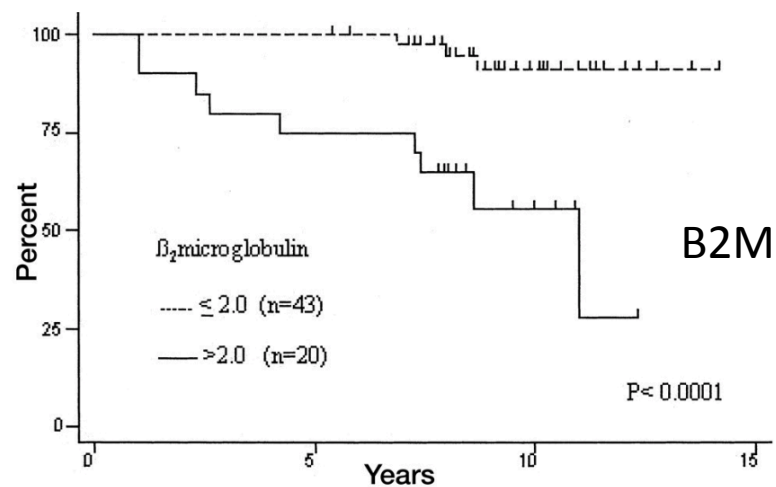
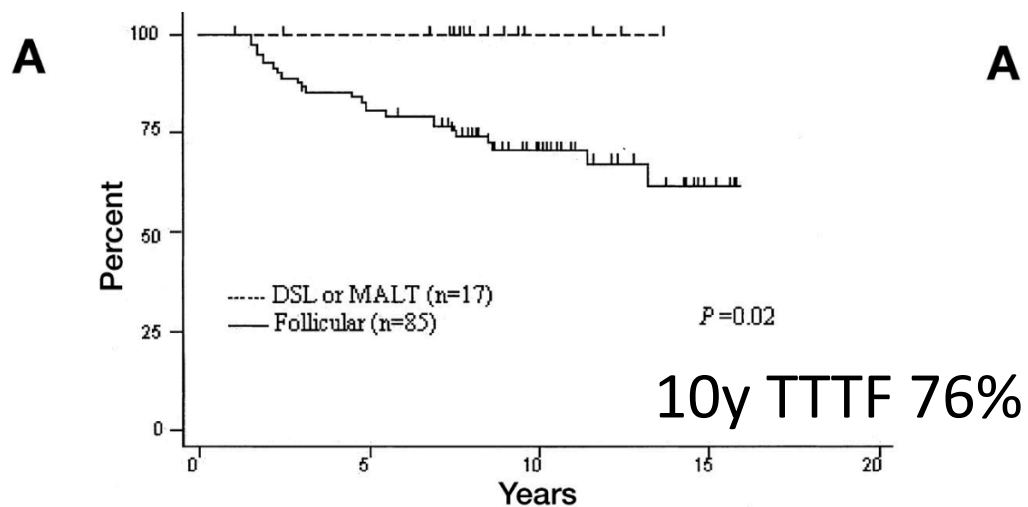
Rituximab & IFRT



Combined modality

- 102 pts 1984-1992
- Stage 1-2 LGNHL
- C(H)OP-Bleo x 10 + IFRT concurrently
 - Median age 56 (28-77)
 - FL 83%, Bulky >5cm 24%, Stage 2 52%
 - Median 10yr FU
 - 21% of cycles N<0.5
 - 8.8% of cycles resulted in admission
 - No deaths

Combined modality



2 MDS and 12 second cancers

Seymour JCO 2003 21 p2115

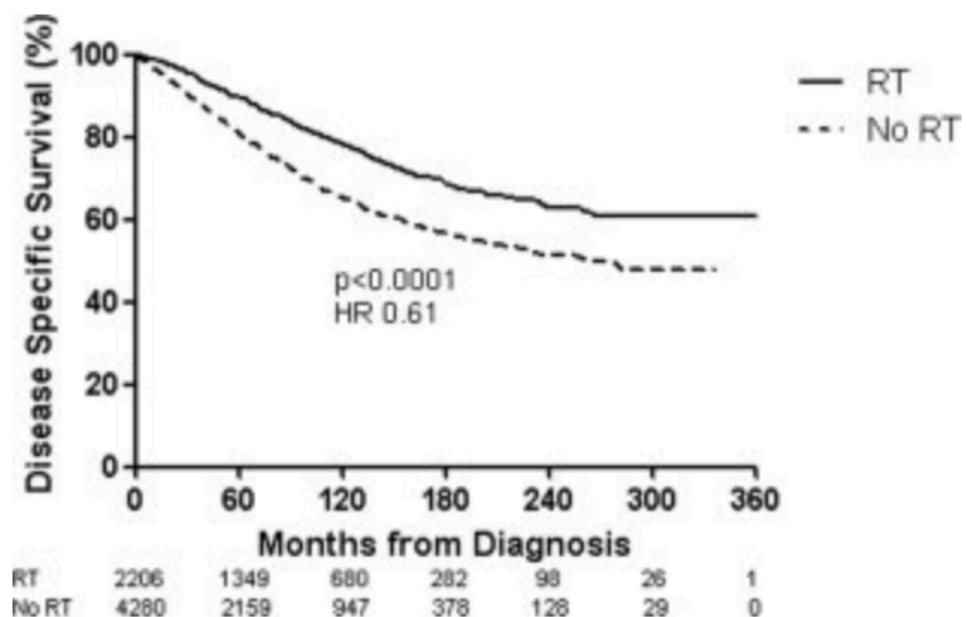
Role of PET in staging

- Retrospective 1997-2006
- 42 pts early stage FL by CT
- PET
 - 97% avid
 - Change in management 19/42 (45%)
 - 13 (31%) stage 3-4
 - 6 (14%) involved field enlarged (4 upstaged from 1 to 2)

SEER

- 1973-2004
- 6568 pts with grade 1 or 2, stage 1&2 FL
- Median age 63
- Median FU 66 mo
- Upfront RT in 2222pts (34%)
 - More likely if <60, stage 1, grade 1, no extranodal

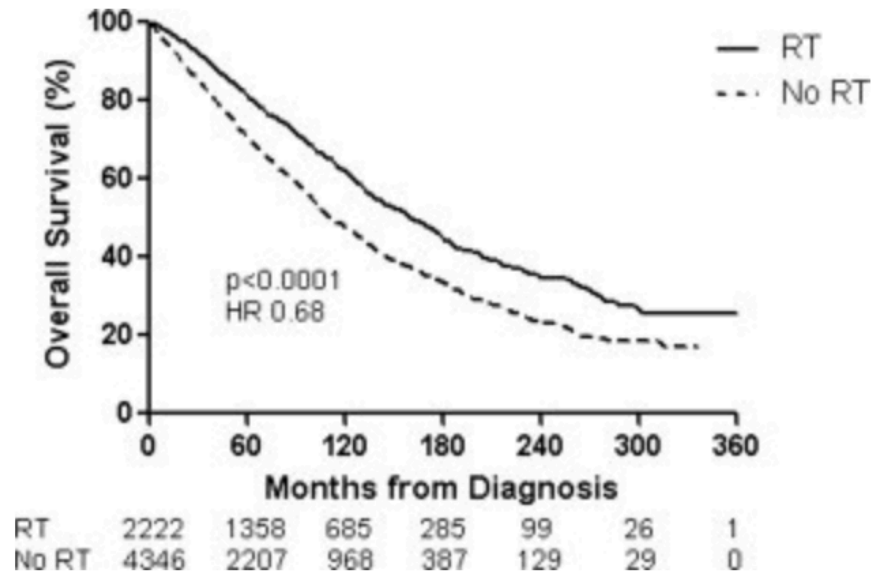
SEER-Disease specific survival



10 yr DSS with RT 79% vs without RT 65% $p < 0.0001$

Multivariate: Improved DSS if , Stage 1, <60y, no extranodal

SEER-Overall Survival



10 yr OS with RT 62% vs without RT 48% $p < 0.0001$

Multivariate: Improved OS if , upfront RT Stage 1

SEER

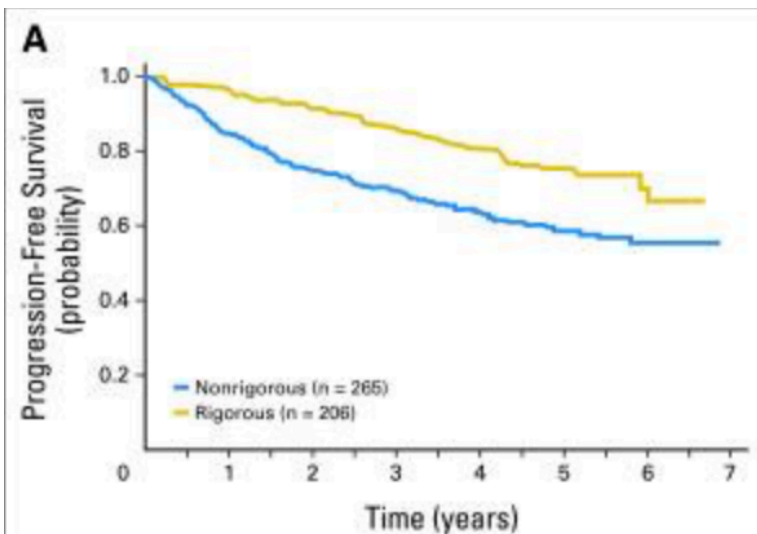
- RT utilisation
 - 34% -static over 3 decades
- Deaths
 - 52% due to NHL
- Conclusions
 - Upfront RT reduces risk of death
 - from NHL at 10y by 13.1%
 - From any cause at 10yr by 14.2%
 - Benefit of RT seen in all subgroups
 - Age, stage, grade, sex, extranodal
 - Not non-white (small nos)

Lymphocare

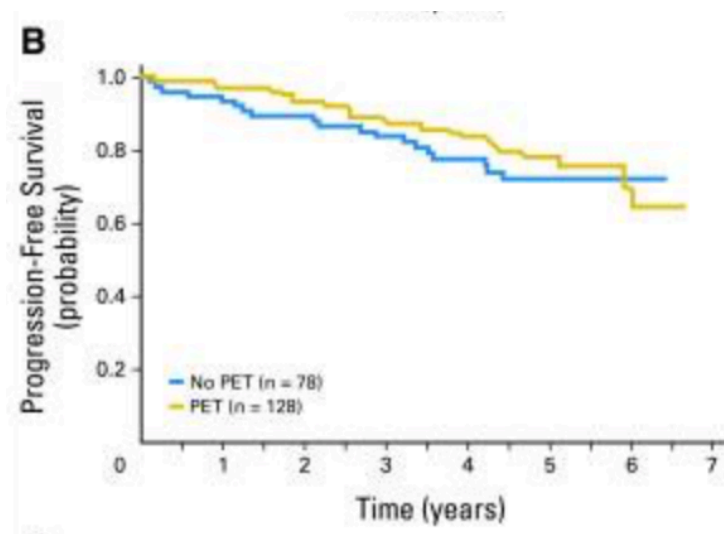
- 471 stage 1 FL
- Staging
 - Rigorous in 206pt: BM plus CT and/or PET
 - community 42% vs academic 52% p=NS
 - PET in 128/206pt (community 66% vs academic 48% p=0.026)
 - Rig vs NonRig no diff: Hb, LDH FLIPI grade 3, B sympt
 - More NonRig
 - > 60y (64% vs 52% p=0.08)
 - Undergo W&W (39% vs 17% p<0.001)
 - More Rig receive
 - R-Chemo (28% vs 17% p<0.001)
 - Systemic plus RT (13% vs 6% p<0.001)

Lymphocare

- Treatment selection
 - Amongst Rig
 - Varied according to LDH, grade 3, B symptoms
- Outcomes



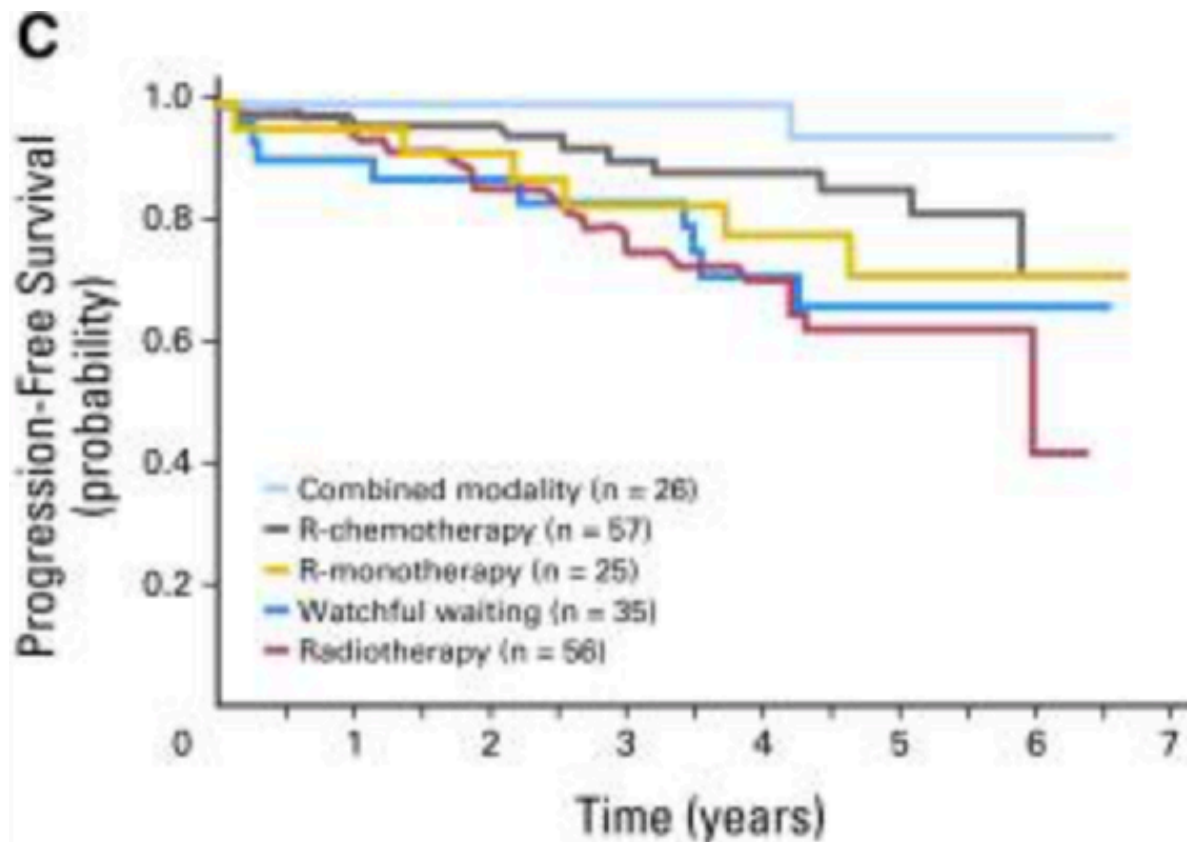
PFS :***Rig vs Non rig*** HR 0.63 CI 0.44-0.92
OS –No diff



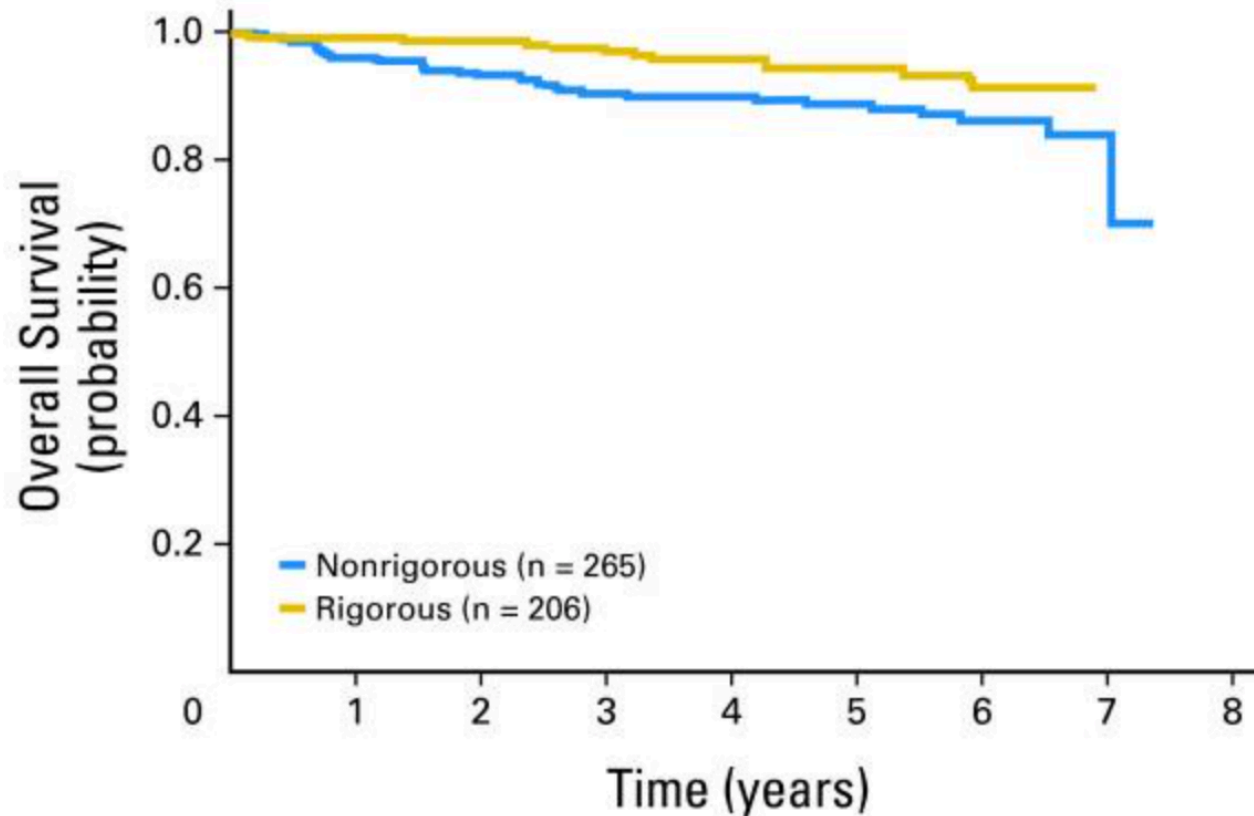
PFS :***PET vs no PET*** HR 0.87 CI 0.47-1.62

Lymphocare

- PFS according to treatment- Rig staged- median FU 57m
 - R-Chemo vs RT alone HR 0.36 (CI 0.16-0.82)
 - Systemic+RT vs RT alone HR0.11 (CI 0.01 to 0.83)



Lymphocare

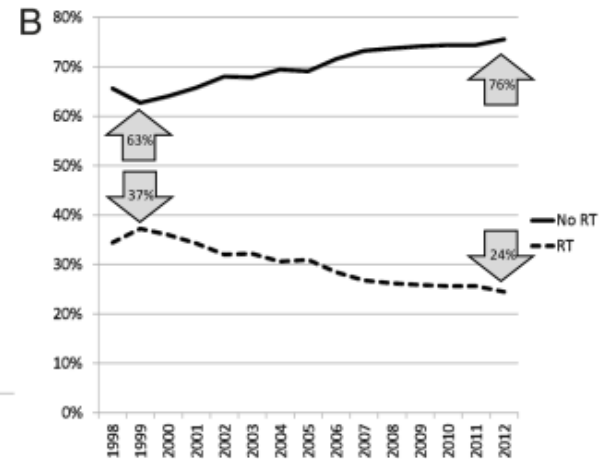
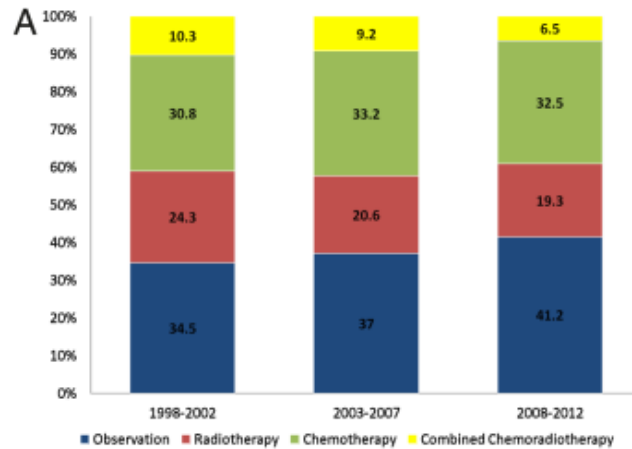


No. at risk	0	1	2	3	4	5	6	7	8							
Nonrigorous	265	259	248	236	226	217	202	194	185	160	128	105	75	44	1	0
Rigorous	206	204	202	196	187	178	172	165	141	105	68	34	9	0		

National Cancer Database

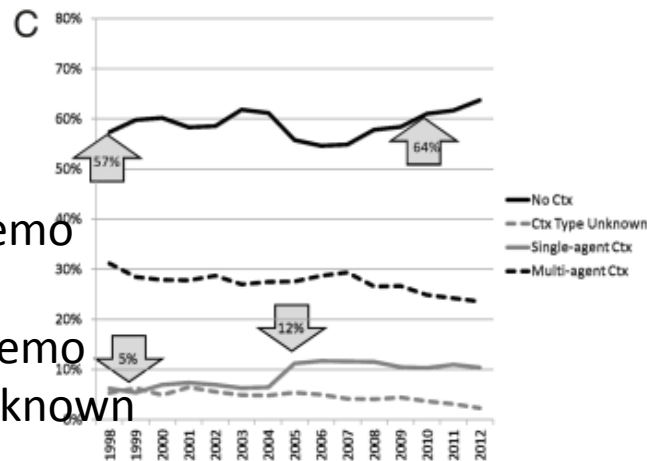
- 1998-2012
- 35,961 grade 1-2 FL pts stage 1 or 2
- Median FU 64 mo

National Cancer Database



No RT

RT

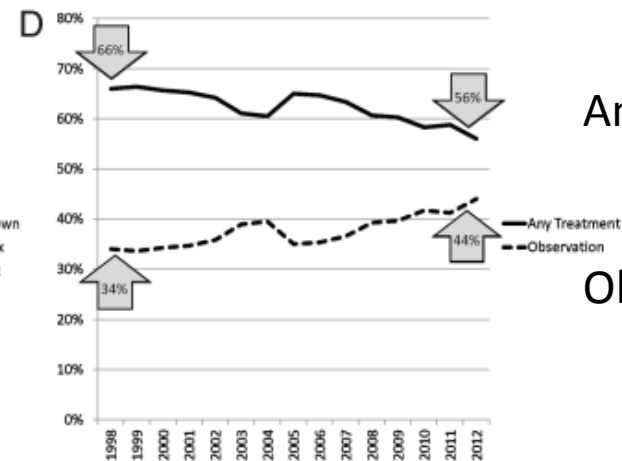


No Chemo

Multi agent chemo

Single agent chemo

Chemo type unknown

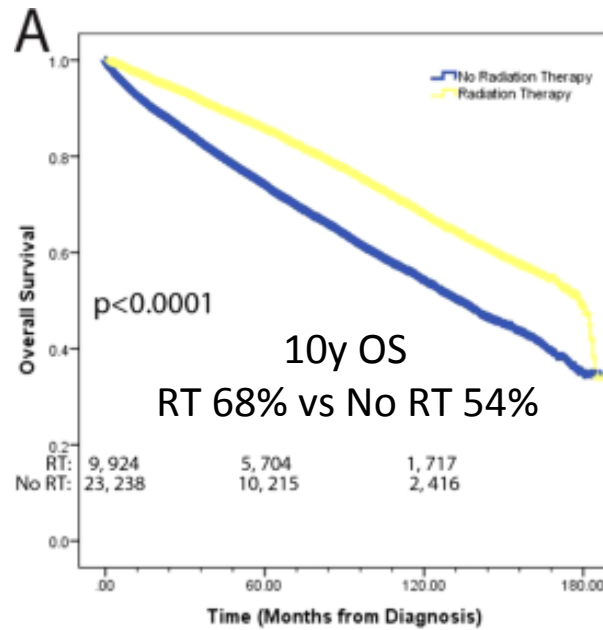


Any treatment

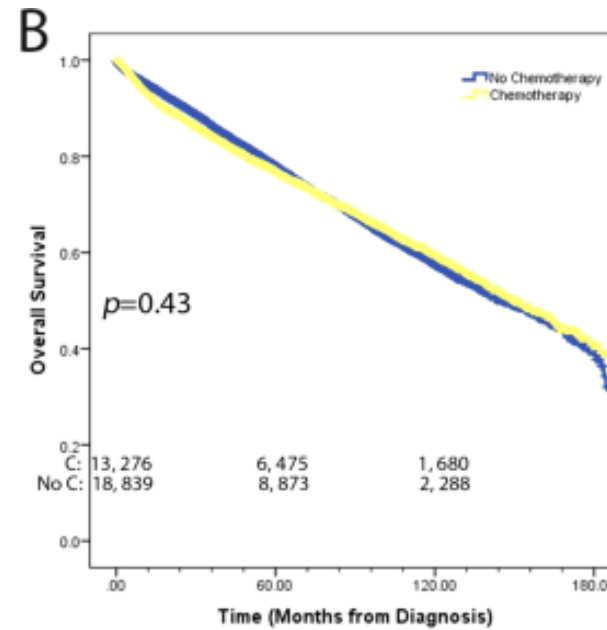
Observation

National Cancer Database

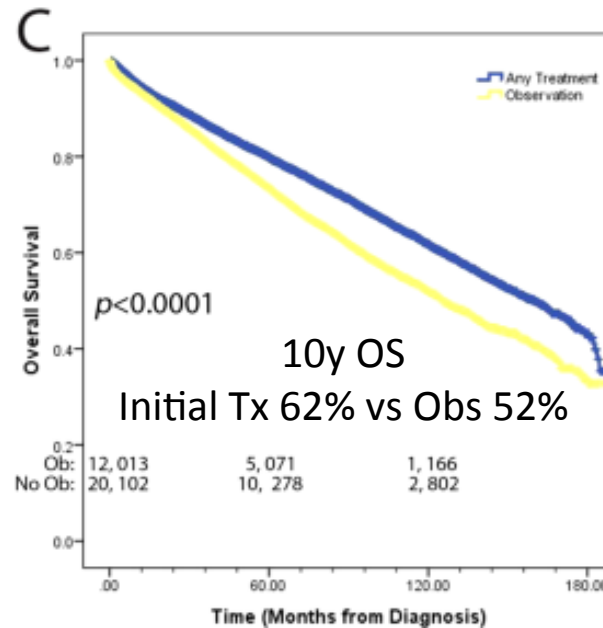
RT vs No RT



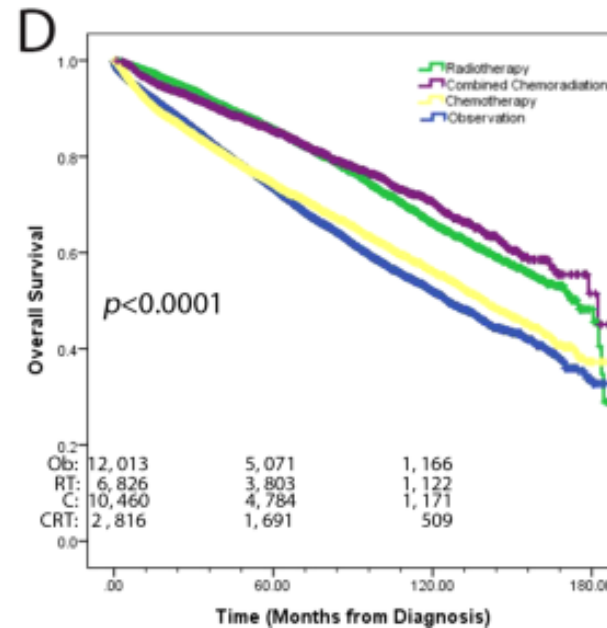
Chemo
vs
no chemo



Initial therapy
vs observation



RT alone
vs
Chemo radiation
vs
Chemo
vs
Observation



Combined modality therapy

- 2002-2012
- Stage 1&2 FL grades 1,2,3a
- CT and BM staged (PET optional)
- 150 pts randomised to
 - IFRT =Arm A
 - IFRT followed by 6x(R)CVP=Arm B
- Median FU 9.6 yr

Combined modality therapy

- PFS superior arm B
 - **RCVP and CVP 10 yr PFS 59% vs 41%**
 - HR 0.57 (95% CI 0.34-0.95) p0.033
 - **If RCVP**
 - HR 0.26 (95% CI 0.07-0.97) p0.045
- OS 95% vs 87% p=0.4
- Grade 2+ toxicity greater in Arm B

My approach

- Stage 1 and contiguous stage 2 FL 1,2 3a
- Confirmed by CT, BM and PET
- For IFRT 24Gy
 - If funded, Rx4 IF-RT with concurrent Rx4
- Non contiguous stage 2 or RT contraindicated
 - As per advanced disease