Grandangolo in Radioterapia oncologica

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XXII CONGRESSO
AIRO
ROMA 2012
17-20 novembre
Ergife Palace Hotel

Androgen deprivation therapy

Dose escalation

Hypofractionation

Technique and Outcomes

Androgenic suppression combined with radiotherapy for the treatment of prostate adenocarcinoma: a systematic review

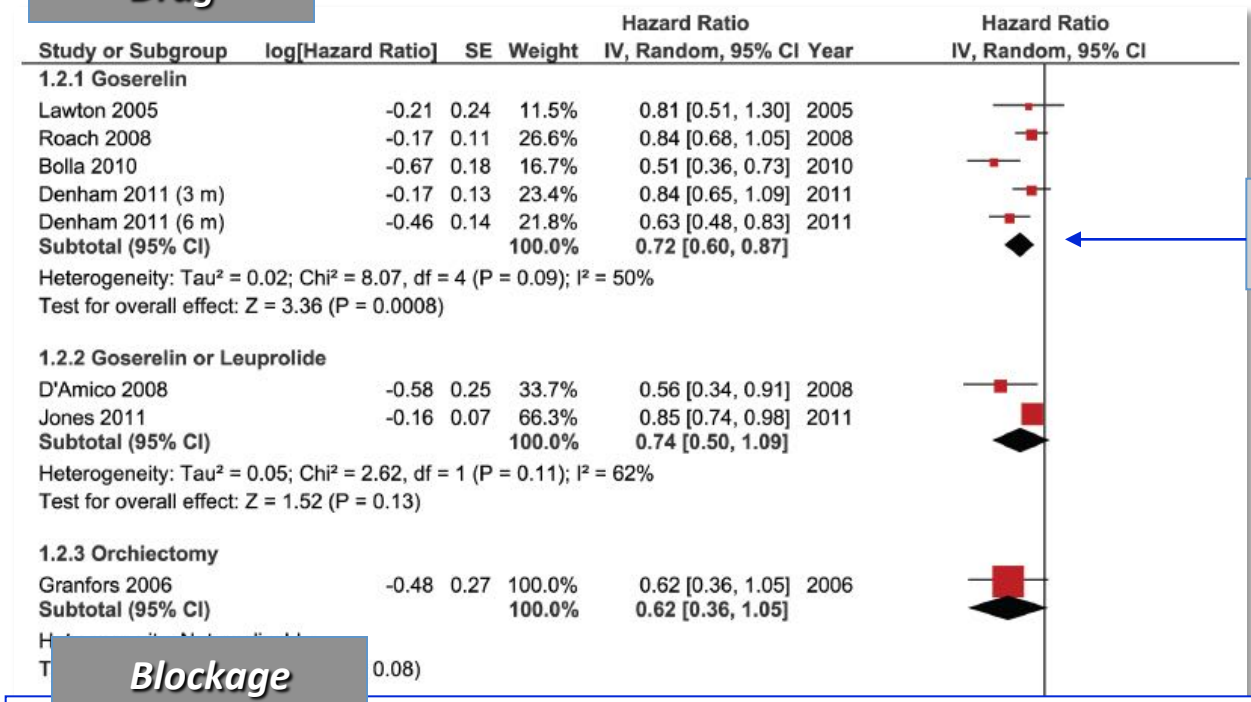
André D Sasse[1*], Elisa Sasse[2], Albertina M Carvalho[3] and Ligia T Macedo[1]

	Author	Year	Radiotherapy (dose)	Hormone Therapy	Duration	N	Median follow up
	Zagars	1988	70 Gy	Diethylstilbestrol 25 mg PO qd	Continuously	82	14.5 years
	Laverdiere	2004	64 Gy	Leuprolide 7.5 mg/month + Flutamide	3 months or 10 months	161	5 years
RTOG 85-31	Lawton	2005	65 to 70 Gy	Goserelin 3.6 mg/month	Continuously	977	6.5 years
	Granfors	2006	60 to 70 Gy	Orchiectomy	Permanent	91	9.7 years
	See	2006	NS	Bicalutamide 150 mg PO qd	Decided by investigator	1370	7.2 years
DFCI 95-096	D'Amico	2008	NS	Goserelin 3,6 mg **or** Leuprolide 7.5 mg/month + Flutamide	6 months	206	8.2 years
RTOG 86-10	Roach	2008	65 to 70 Gy	Goserelin 3.6 mg/month + Flutamide	3 months	456	11.9 years
EORTC 22863	Bolla	2010	70 Gy	Goserelin 3.6 mg/month	3 years	415	9.1 years
TROG 96-01	Denham	2011	66 Gy	Goserelin 3.6 mg/month + Flutamide	3 months or 6 months	818	10.6 years
RTOG 94-08	Jones	2011	66.6 Gy	Goserelin 3,6 mg or Leuprolide 7.5 mg/month + Flutamide	4 months	1979	9.1 years

Localized + Locally advanced

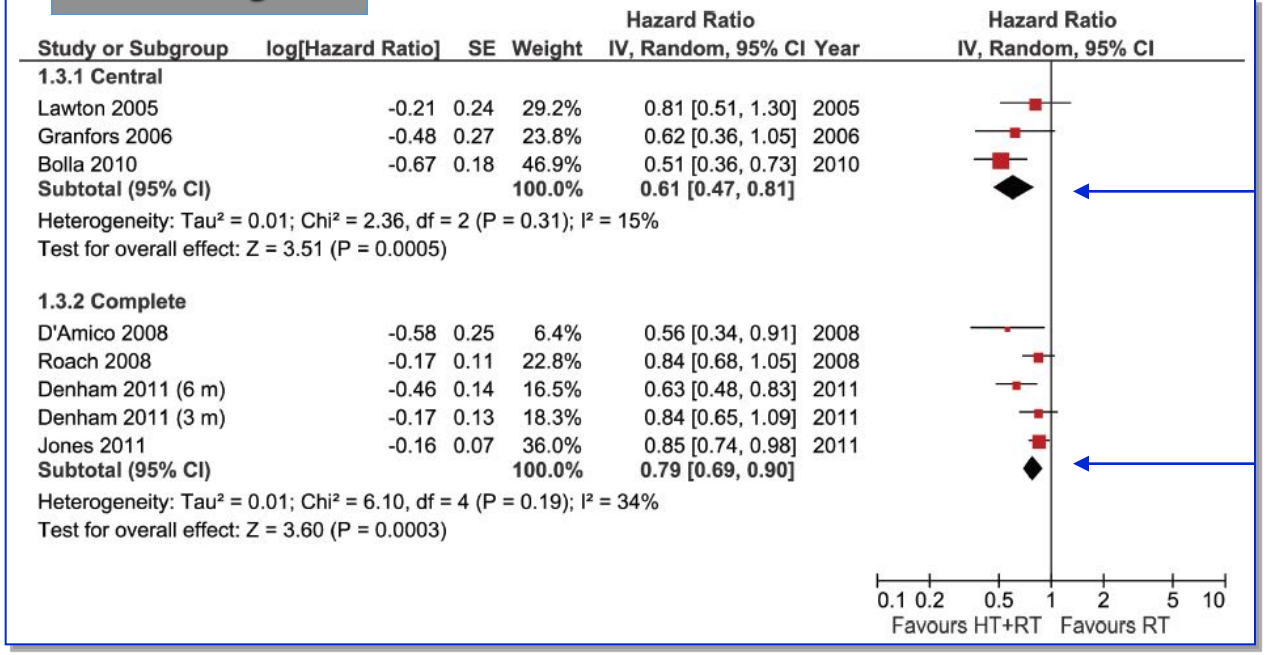
6555

Drug



Goserelin + RT
- 28% risk of death

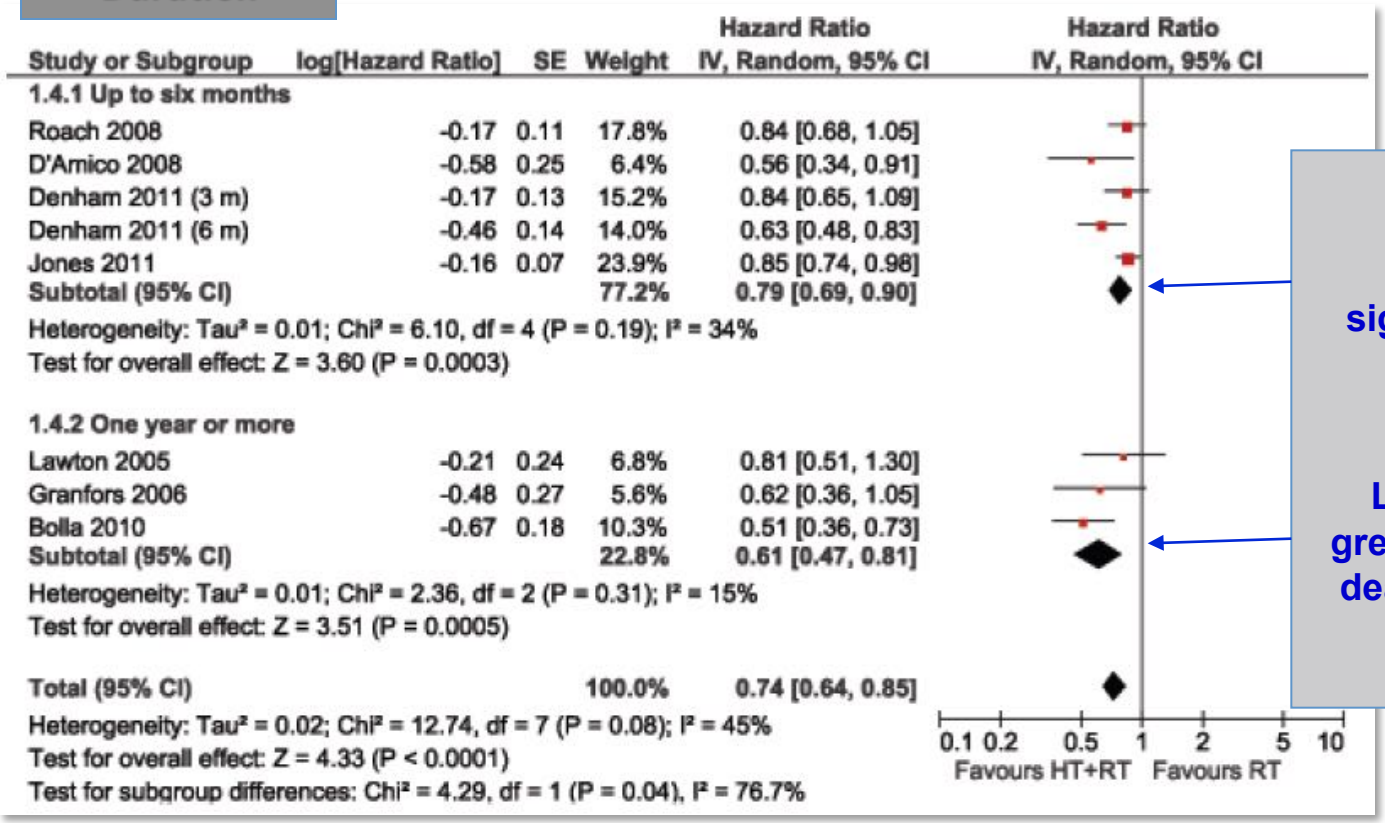
Blockage



Central blockade
- 39% risk of death

No further benefit with complete blockade

Duration



Short-term ADT + RT significantly better than RT alone

Longer duration provide greater benefits (-39% risk of death) than shorter courses

Pitfalls:

High heterogeneity in:

- **patient selection**
- **ADT schedules**
- **RT doses and volumes**

Does RT improve survival in locally advanced PC treated with ADT?

Combined androgen deprivation therapy and radiation therapy for locally advanced prostate cancer: a randomised, phase 3 trial

Padraig Warde, Malcolm Mason*, Keyue Ding, Peter Kirkbride, Michael Brundage, Richard Cowan, Mary Gospodarowicz, Karen Sanders, Edmund Kostashuk, Greg Swanson, Jim Barber, Andrea Hiltz, Mahesh K B Parmar, Jinka Sathya, John Anderson, Charles Hayter, John Hetherington, Matthew R Sydes†, Wendy Parulekar†, for the NCIC CTG PR.3/MRC UK PR07 investigators*

1205 pts.

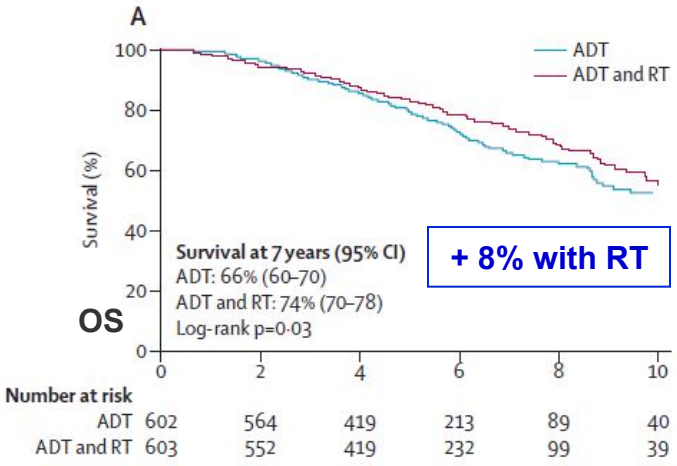
T3-4

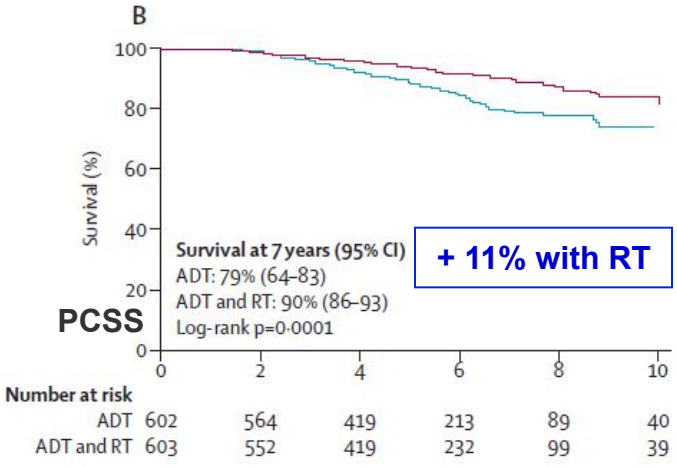
T2 (PSA >40 ng/ml)

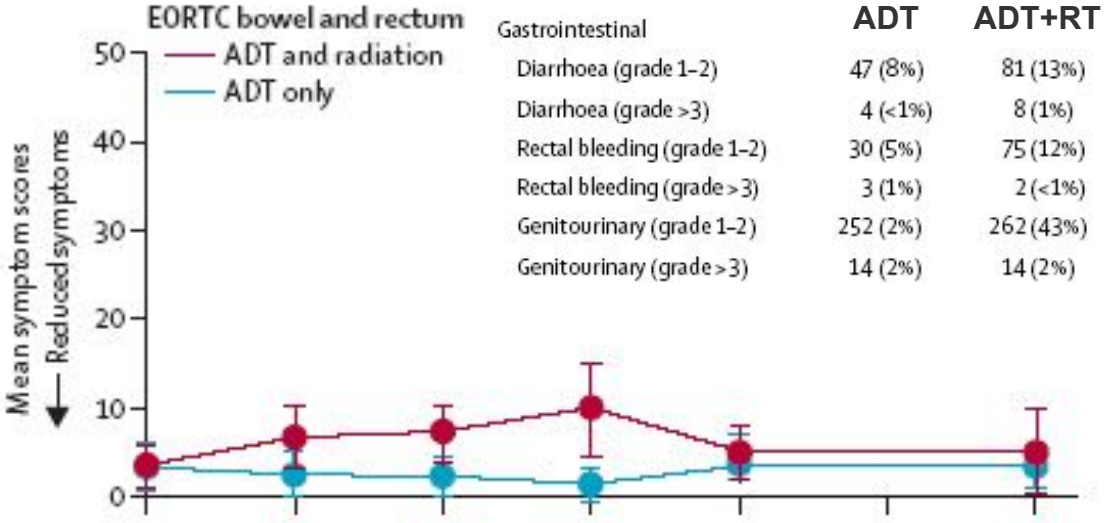
T2 (PSA >20 ng/ml + GS >7)

Lifelong ADT

Lifelong ADT
RT (45 Gy + 20-24 Gy)







Gastrointestinal	ADT	ADT+RT
Diarrhoea (grade 1–2)	47 (8%)	81 (13%)
Diarrhoea (grade >3)	4 (<1%)	8 (1%)
Rectal bleeding (grade 1–2)	30 (5%)	75 (12%)
Rectal bleeding (grade >3)	3 (1%)	2 (<1%)
Genitourinary (grade 1–2)	252 (2%)	262 (43%)
Genitourinary (grade >3)	14 (2%)	14 (2%)

Lancet 2011; 378: 2104–11

Short-term androgen deprivation therapy for patients with intermediate-risk prostate cancer undergoing dose-escalated radiotherapy: the standard of care?

Zachary S Zumsteg, Michael J Zelefsky

Lancet Oncol 2012; 13: e259–69

Rationale for short-term ADT + RT

- **Improvement of distant control through reduction of micrometastasis**

In high-risk PC, lower survival with short-term ADT than with longer courses

(Bolla, 2010 - EORTC 22891; Horwitz, 2008 - RTOG 9202)

No survi ***nes, NEJM 2011)***

Unfortunately, in intermediate-risk PC is unclear whether the predominant parameter for improved survival were local control, distant control or both

- **Incr**

Standard dose RT provides poor local control

(persistent PC after post-RT biopsy in 30-60%) ***(Pollak, JCO 2000)***

After neoadjuvant / concurrent ADT fewer positive post-RT biopsy

(from 39% to 20% in RTOG 9408) ***(Jones, NEJM 2011)***

Lancet Oncol 2012; 13: e259–69

	Patients (n)	Patients at intermediate risk (n)	Median follow-up (years)	Androgen deprivation therapy comparison arms	Radiotherapy dose (Gy)*	Primary endpoint	Reported outcomes with short-term androgen deprivation therapy
Jones (2011)[1]	1979	1068†	9·1	0 *vs* 4 months	63·3	Overall survival	Increased overall survival and biochemical progression-free survival, reduced prostate cancer-specific mortality and distant metastasis
D'Amico (2008)[2]	206	153†	7·6	0 *vs* 6 months	70·35	Biochemical progression-free survival	Prolonged overall survival and decreased prostate cancer-specific mortality
Denham (2011)[17]	818	130†	10·6	0 *vs* 3 *vs* 6 months	62·7	Prostate cancer-specific mortality and local control‡	Augmented overall survival and diminished prostate cancer-specific mortality and distant metastasis§
Roach (2008)[20]	456	Not reported¶	11·9–13·2	0 *vs* 4 months	61·8–66·5	Local control	Reductions in prostate cancer-specific mortality and distant metastasis, increases in biochemical progression-free survival and disease-free survival, but no improvements in overall survival or local control
Laverdière (2004)[22]	161	Not reported	5	0 *vs* 3 *vs* 10 months	64	Biochemical progression-free survival	Prolonged biochemical progression-free survival‖
Dubray (2011)[23]	366	366	3·1	0 *vs* 4 months	80	Freedom from failure**	Increased biochemical progression-free survival, non-significant rise in freedom from failure (p=0·09)

RT dose unacceptable by actual standard!

Does ADT is still necessary when dose-escalated techniques are applied?

Lancet Oncol 2012; 13: e259–69

	Patients (n)	Patients at intermediate risk (n)	Median follow-up (years)	Radiotherapy dose (Gy) comparison arms*	Androgen deprivation therapy	Primary endpoint	Outcomes with dose escalation
Dearnaley (2007)[24]	843	264†	10	74 vs 64	3–6 months in 100%	Biochemical progression-free survival, local control, distant metastasis-free survival, overall survival, late toxic effects	Prolonged biochemical progression-free survival but not overall survival
Al-Mamgani (2008)[25]	669	182†	5·8	74·1 vs 64·6	6 months or 3 years in 21%	Freedom from failure (combined clinical and biochemical failure)	Rise in freedom from failure but not overall survival
Zietman (2010)[26]	393	144‡	8·9	79·2 vs 70·2	None	Biochemical progression-free survival	Increased biochemical progression-free survival but not overall survival
Kuban (2008)[27]	301	139§	8·7	74·1 vs 66·5	None	Freedom from failure (combined clinical and biochemical failure)	Augmented freedom from failure but not overall survival; distant metastasis-free survival and prostate cancer-specific mortality saw non-significant improvement
Beckendorf (2011)[28]	306	218‡	5·1	70 vs 80	None	Biochemical recurrence	Decreased biochemical recurrence¶, overall survival not reported

No mature results of high-dose RT +/- short-term ADT !

- **MRC-RT01**

ADT + HD-RT (64 vs. 74 Gy)

Increased Bio-PFS

No difference in: Local progression, Metastasis-free survival, Overall survival

- **GETUG 14** **(366 IR pts.) → 80 Gy +/- ADT**

Closed; poor accrual

Increased Bio-PFS… → Final Analysis expected for 2013 (Dubray et al. ASCO 2011)

Lancet Oncol 2012; 13: e259–69

In the meantime…

Risk-adaptive strategy

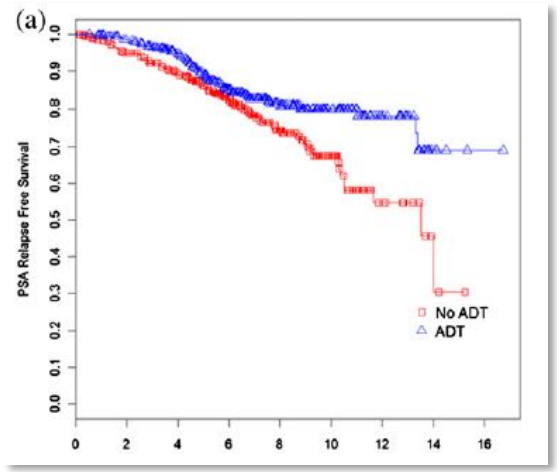
	Favourable intermediate-risk prostate cancer*	Unfavourable intermediate-risk prostate cancer†
Clinical characteristics	One intermediate risk factor Gleason score of 3+4=7 or less <50% positive biopsy cores	Several intermediate risk factors[57] Gleason score of 4+3=7[14] ≥50% positive biopsy cores[11]
Recommended radiation options	Dose-escalated external beam radiotherapy alone Brachytherapy alone in select cases (eg, ≤3 positive cores, none with >50% involvement)	Dose-escalated external beam radiotherapy and short-term androgen deprivation therapy Combined brachytherapy and external beam radiotherapy with or without short-term androgen deprivation therapy

*All these criteria are required. †Any of these criteria can be met.

Although…

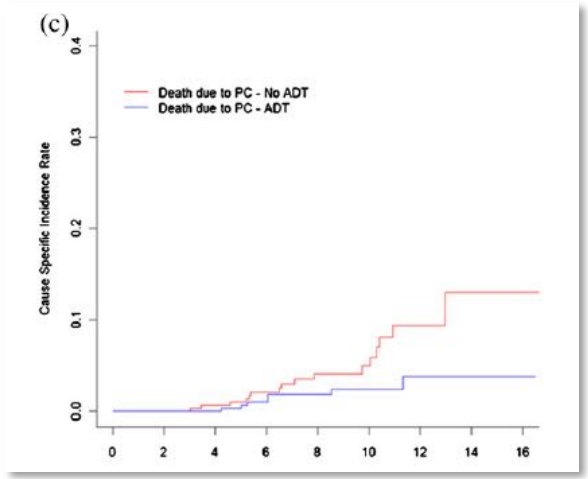
Short-term Androgen-Deprivation Therapy Improves Prostate Cancer-Specific Mortality in Intermediate-Risk Prostate Cancer Patients Undergoing Dose-Escalated External Beam Radiation Therapy

***Retrospective:* 710 IR-PC, receiving HD-RT (> 80 Gy) +/- short ADT (357 pts.)**



Increased Bio-PFS

HR 0.59



Increased PCSS

HR 0.38

The issue of ADT toxicity

Table 1. Causes of Death for All Men and Men With No or Minimal vs Moderate or Severe ACE-27 Defined Comorbidity Score at Randomization Stratified by Treatment Group[a]

	RT			RT and AST		
Cause of Death	All	No or Minimal Comorbidity	Moderate or Severe Comorbidity	All	No or Minimal Comorbidity	Moderate or Severe Comorbidity
Prostate cancer	14	14	0	4	3	1
Myocardial infarction	13	7	6	13	2	11
Second cancer	9	5	4	9	5	4
Other[b]	8	5	3	4	1	3
Total	**44**	**31**	**13**	**30**	**11**	**19**

JAMA. 2008;299(3):289-295

- ***ADT use → shorter time to fatal MI in men > 65 yrs***

  (D'amico, JAMA 2008)

- ***SEER-Database: GnRH agonist → + 16% risk of CAD / + 11% risk of MI***

  (Keating, JCO 2006)

Does the survival benefit of ADT might be counterbalanced by excessive cardiovascular risk?

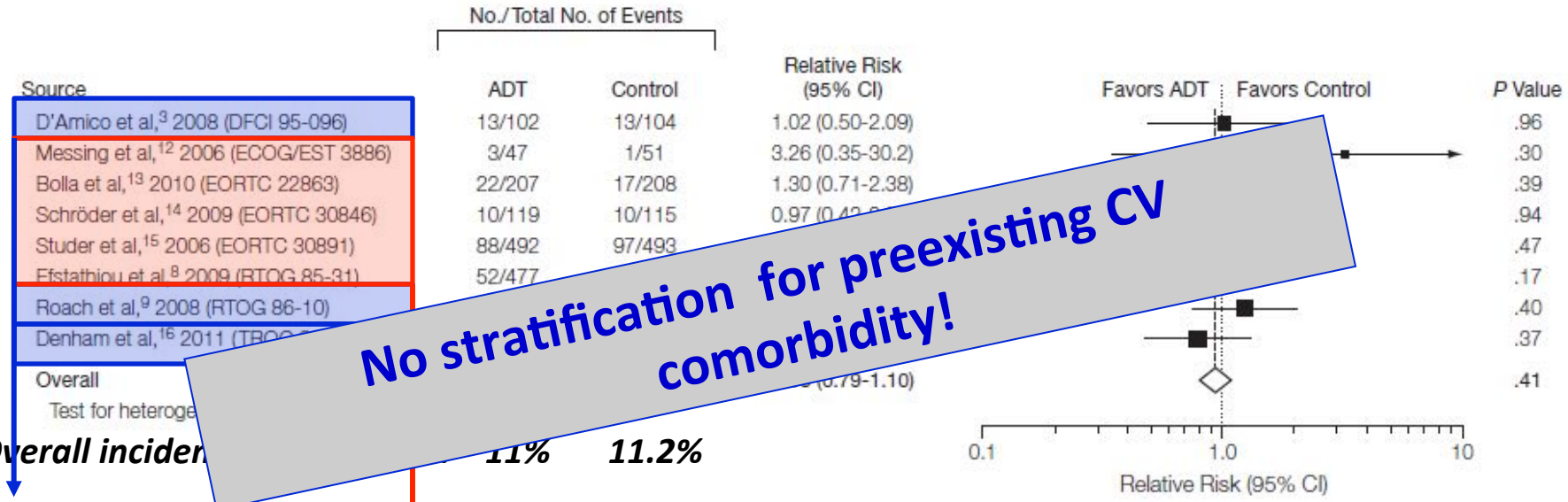
Association of Androgen Deprivation Therapy With Cardiovascular Death in Patients With Prostate Cancer

A Meta-analysis of Randomized Trials *JAMA. 2011;306(21):2359-2366*

4.141 patients 8 Randomized Clinical Trials

Non-metastatic disease; immediate ADT; follow-up > 1 year

Adequate informations on cardiovascular deaths !



No stratification for preexisting CV comorbidity!

Overall incider ***11%*** ***11.2%***

Short-course ADT: ***10.5%*** ***10.3%*** ***RR 1.0; p: ns***

Long-course ADT: ***11.5%*** ***11.5%*** ***RR 0.91; p: ns***

Androgen deprivation therapy

Dose escalation

Hypofractionation

Technique and Outcomes

High-dose RT is superior to conventional RT in preventing biochemical failure regardless of risk status

Viani et al. IJROPB 2009

So far, no evidence of survival benefit due to HDRT, exists

High-Dose Conformal Radiotherapy Reduces Prostate Cancer—Specific Mortality: Results of a Meta-analysis

Gustavo Arruda Viani, M.D., Lucas Godói Bernardes da Silva, M.D., and Eduardo Jose Stefano, M.D.

2.508 patients **5 Randomized Clinical Trials**

- ✓ *"pure" Dose-escalation (i.e. ≥ 74 Gy)*
- ✓ *No Hypofractionation*
- ✓ *EBRT only (i.e. no Brachytherapy boost)*
- ✓ *Median Follow-up 7 years*

Study (reference), patient number, and risk groups	Treatment modality	PTV, CTV, and setup	Biochemical failure definition	Total dose and ADT
Zietman *et al.* (9) HDRT: 197 CDRT: 196	Conformal radiotherapy was given with photons and Phase II with protons.	CTV = Prostate, with 5-mm margin. PTV = CTV + 7–10 mm. Setup: Error was minimized by obtaining daily portal images throughout the first phase; portal images were obtained weekly during the second phase.	Defined using the American Society for Radiation Oncology criteria of three successive increases in PSA level.	Total dose: HDRT: 79.2 GyE CDRT: 70.2 GyE ADT: Not permitted
Dutch (5) HDRT: 333 CDRT: 331	Conformal radiotherapy with photons.	CTV = prostate + SV + 10 mm ± 5 mm (except toward the rectum, 0 mm) for the last 10 Gy in the high-dose arm.	Biochemical failure was defined according to the definition of the American Society for Radiation Oncology and was considered three consecutive increases in PSA level after a nadir.	Total dose: HDRT: 78 Gy CDRT:68 Gy ADT: Permitted
MRC RT01 (7) HDRT: 422 CDRT: 422	Conformal radiotherapy with photons.	CTV = GTV plus a 0–5-cm margin. PTV = 0.5–1.0 cm. Setup: Not reported.	PSA failure was defined as an increase in PSA concentration greater than the nadir by at least 50% and greater than 2 ng/mL 6 mo or more after the start of radiotherapy.	Total dose: HDRT: 74 Gy CDRT: 64 Gy ADT: Permitted
MDACC (2) HDRT: 151 CDRT: 150	Conventional four boxes and conformal radiation in the Phase II after the first 46 Gy.	Phase I = field sizes 11 × 11 cm for the anterior and posterior fields and 11 × 9 cm for the lateral fields. Phase II CTV = prostate and SV. PTV = CTV + 1.25–1.5 cm in the anterior and inferior dimensions and 0.75–1.0 cm in the posterior. Setup: Not reported.	The nadir + 2 ng/mL failure definition was used to define PSA failure.	Total dose: HDRT: 78 Gy CDRT: 70 Gy ADT: Not permitted
GETUG (8) HDRT: 153 CDRT: 153	Conformal radiotherapy with photons.	CTV = Prostate + SV + 10 mm ± 5 mm (except toward the rectum). Setup: First-day port films or portal images of each field were required. Orthogonal images were verified on Days 2 and 3 and thereafter (weekly rectum, 5 mm).	The nadir + 2 ng/mL failure definition was used to define PSA failure, or three successive increases in PSA level.	Total dose: HDRT: 80 Gy CDRT: 70 Gy ADT: Not permitted

ASTRO

ASTRO

PHOENIX

PHOENIX

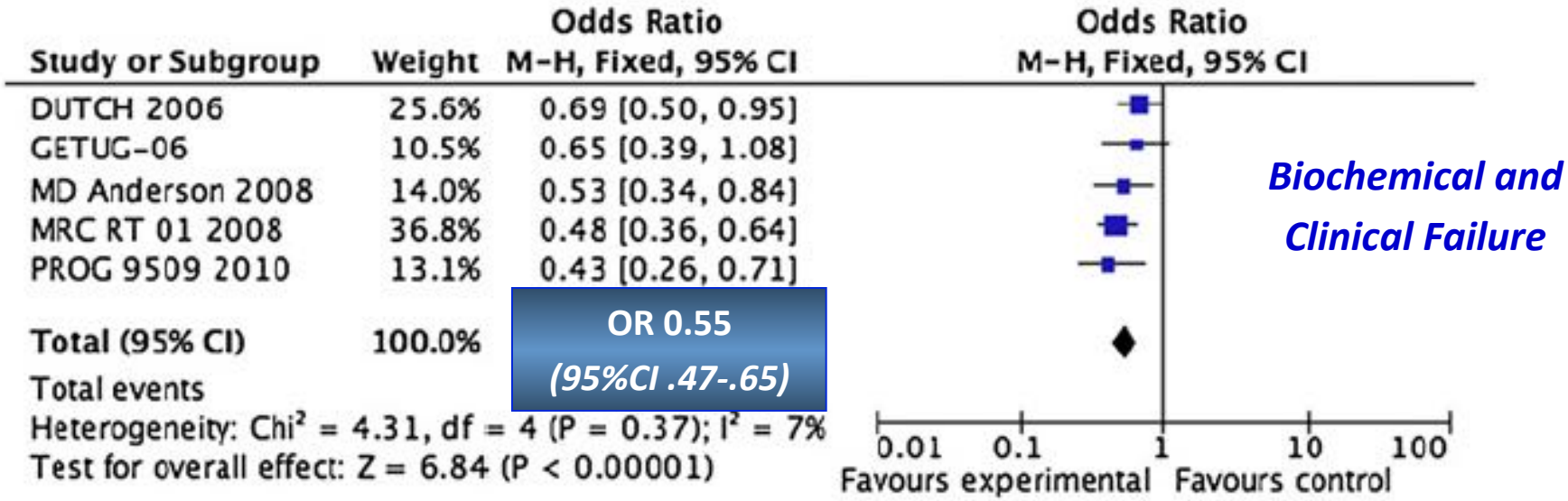
PHOENIX

No elective node irradiation

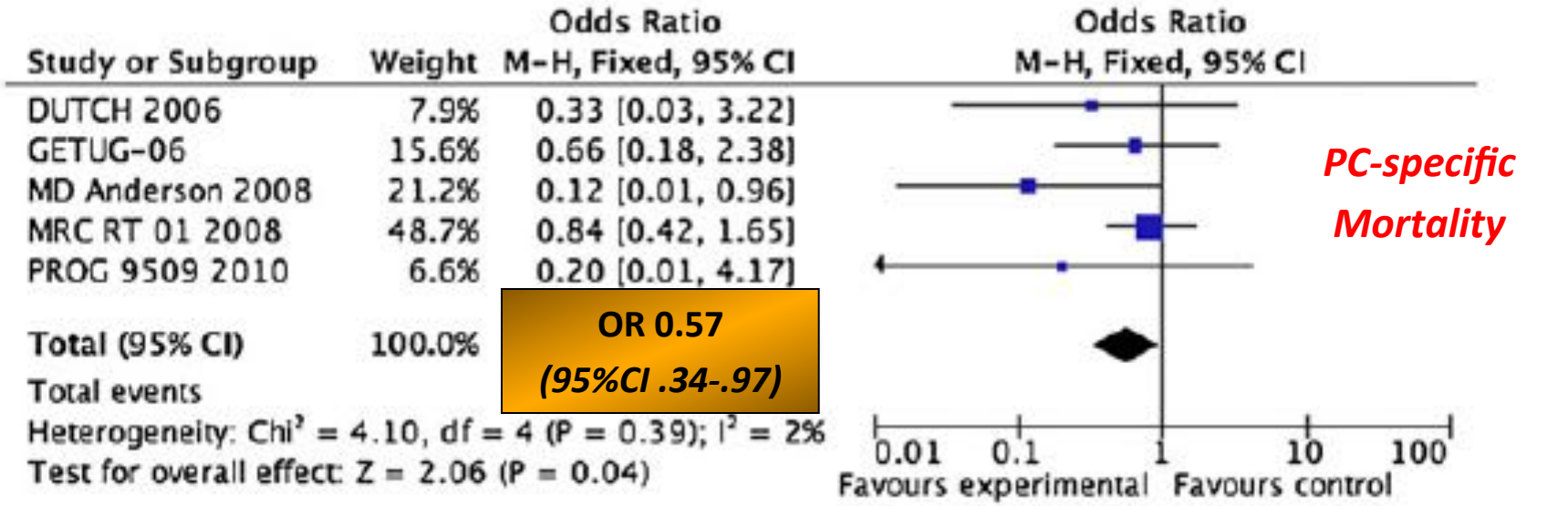
ADT optional

HDRT: 74-80 Gy
CDRT: 64-70.2 Gy

Viani et al. IJROPB 2009



5 years absolute risk reduction of 12.6% with High-dose RT



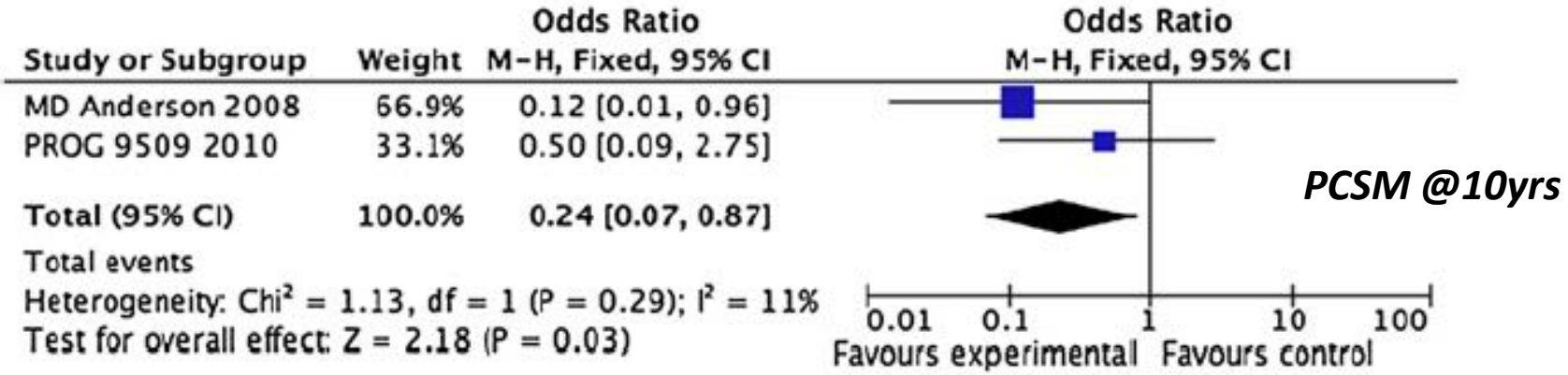
5 years absolute risk reduction of 1.7% with High-dose RT

Viani et al. IJROPB 2009

High-dose RT is superior to conventional RT in preventing biochemical failure and prostate cancer-specific survival (no conclusions for risk groups)

So far, no improvement in Overall survival *… more deaths for other causes…*

- ✓ **is follow-up long enough?**
- ✓ **does HDRT reduce or simply delay relapse?**



PCSM @10yrs

Gain in absolute risk reduction: 2.3%

Viani et al. IJROPB 2009

Androgen deprivation therapy

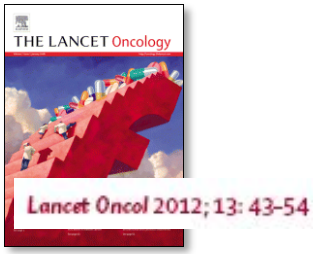
Dose escalation

Hypofractionation

Technique and Outcomes

Conventional versus hypofractionated high-dose intensity-modulated radiotherapy for prostate cancer: preliminary safety results from the CHHiP randomised controlled trial

David Dearnaley, Isabel Syndikus, Georges Sumo, Margaret Bidmead, David Bloomfield, Catharine Clark, Annie Gao, Shama Hassan, Alan Horwich, Robert Huddart, Vincent Khoo, Peter Kirkbride, Helen Mayles, Philip Mayles, Olivia Naismith, Chris Parker, Helen Patterson, Martin Russell, Christopher Scrase, Chris South, John Staffurth, Emma Hall



T1b-T3a
PSA <30 ng/ml
N+ risk < 30%
GS < 8

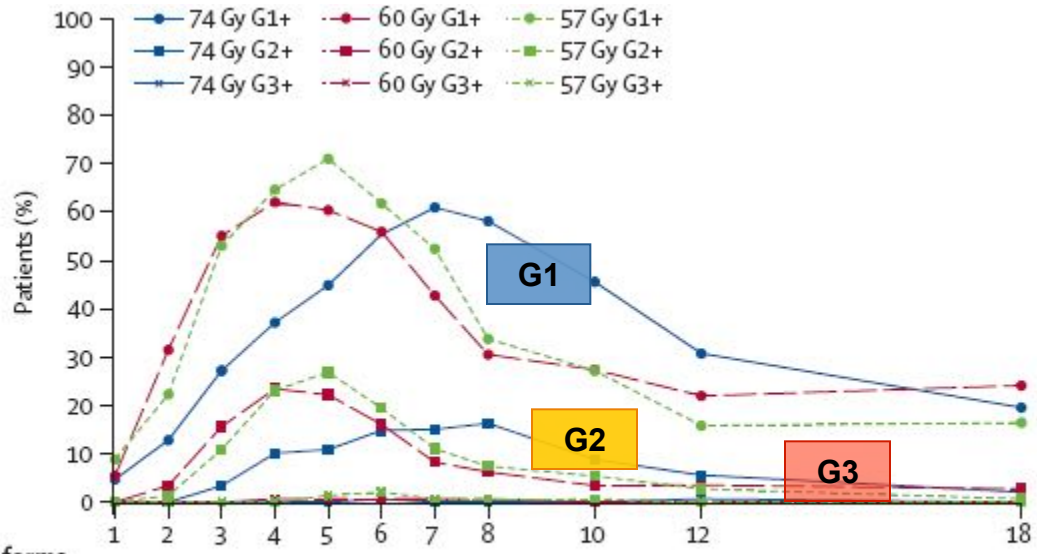
- 74 Gy; 2 Gy/fr.
- 57 Gy; 3 Gy/fr.
- 60 Gy; 3 Gy/fr.

3DCRT / IMRT
Short-course ADT (option for LR)

Stage 1	Stage 2	Stage 3
50	~ 135	
50	~ 135	+ 2700 pts.
50	~ 135	

457 patients

Primary end-point: 2y RTOG tox. G ≥ 2



Lancet Oncol 2012; 13: 189–95

Acute toxicity peak sooner in the exp… …tal arms

Acute RTOG bowel toxicity

More data needed to increase the evidence in terms of oncologic outcome

Late toxicity

	Total events	60 Gy vs 74 Gy		57 Gy vs 74 Gy		…tion of events at 2 years					
						…(n=149)		60 Gy (n=147)		57 Gy (n=148)	
						Events	% (95% CI)	Events	% (95% CI)	Events	% (95% CI)
Bowel											
RTOG											
Grade 1 or worse	150	0·76 (0·52–1·12)	0·169	0·72 (0·48–1·06)	0·091	45	30·6% (23·8–38·7)	40	27·6% (21·1–35·6)	37	25·2% (18·9–33·0)
Grade 2 or worse	36	0·93 (0·44–1·97)	0·845	0·62 (0·27–1·44)	0·270	11	7·6% (4·3–13·2)	10	6·9% (3·8–12·5)	7	4·8% (2·3–9·7)
Grade 3 or worse	4	0·99 (0·06–15·76)	0·992	1·94 (0·18–21·44)	0·587	0	..	1	0·7% (0·1–4·7)	1	0·7% (0·1–4·7)
Bladder											
RTOG											
Grade 1 or worse	82	1·15 (0·69–1·93)	0·597	0·85 (0·49–1·47)	0·553	18	12·3% (7·9–18·8)	25	17·4% (12·1–24·6)	16	10·9% (6·8–17·1)
Grade 2 or worse	37	1·74 (0·79–3·79)	0·167	0·99 (0·41–2·37)	0·978	5	3·5% (1·5–8·1)	13	9·0% (5·4–15·1)	7	4·8% (2·3–9·8)
Grade 3 or worse	14	2·62 (0·70–9·91)	0·155	0·97 (0·20–4·80)	0·969	2	1·4% (0·4–5·4)	6	4·2% (1·9–9·0)	1	0·7% (0·1–4·7)

No significant differences among groups

Contents lists available at SciVerse ScienceDirect

Clinical Oncology

journal homepage: www.clinicaloncologyonline.net

Guidelines

Intensity-modulated Radiotherapy in the Treatment of Prostate Cancer

G. Bauman *, R.B. Rumble †, J. Chen ‡, A. Loblaw §, P. Warde ¶ and Members of the IMRT Indications Expert Panel

* *The University of Western Ontario, London, Ontario, Canada*
† *Cancer Care Ontario's Program in Evidence-based Care, Hamilton, Ontario, Canada*
‡ *London Regional Cancer Centre, London, Ontario, Canada*
§ *Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada*
¶ *Radiation Treatment Program, Cancer Care Ontario, Toronto, Ontario, Canada*

Review – Prostate Cancer

Functional Outcomes and Complications Following Radiation Therapy for Prostate Cancer: A Critical Analysis of the Literature

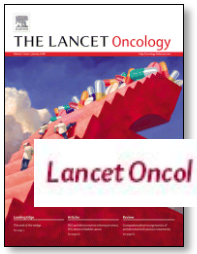
Lars Budäus [a,], Michel Bolla [b], Alberto Bossi [c], Cesare Cozzarini [d], Juanita Crook [e], Anders Widmark [f], Thomas Wiegel [g]*

Radiochemotherapy

Unconventional irradiation

Outcomes and toxicity

Concomitant chemoradiotherapy versus acceleration of radiotherapy with or without concomitant chemotherapy in locally advanced head and neck carcinoma (GORTEC 99-02): an open-label phase 3 randomised trial



Lancet Oncol 2012; 13: 145–53

Jean Bourhis, Christian Sire, Pierre Graff, Vincent Grégoire, Philippe Maingon, Gilles Calais, Bernard Gery, Laurent Martin, Marc Alfonsi, Patrick Desprez, Thierry Pignon, Etienne Bardet, Michel Rives, Lionel Geoffrois, Nicolas Daly-Schveitzer, Sok Sen, Claude Tuchais, Olivier Dupuis, Stéphane Guerif, Michel Lapeyre, Véronique Favrel, Marc Hamoir, Antoine Lusinchi, Stéphane Temam, Antonella Pinna, Yun Gan Tao, Pierre Blanchard, Anne Aupérin

Stage III-IV SSC
(oral c., oropharynx, hypopharynx, larynx)
ECOG 0-2

3DCRT (NO IMRT)

70 Gy (7 wks) + CT (CBDCA+5FU x 3)

70 Gy (6 wks) + CT (CBDCA+5FU x 2)

64.8 Gy (3.5 wks; BID)

840 patients

Primary end-point: **Progression-free survival**

Hypothesis: +15% in PFS from RT acceleration

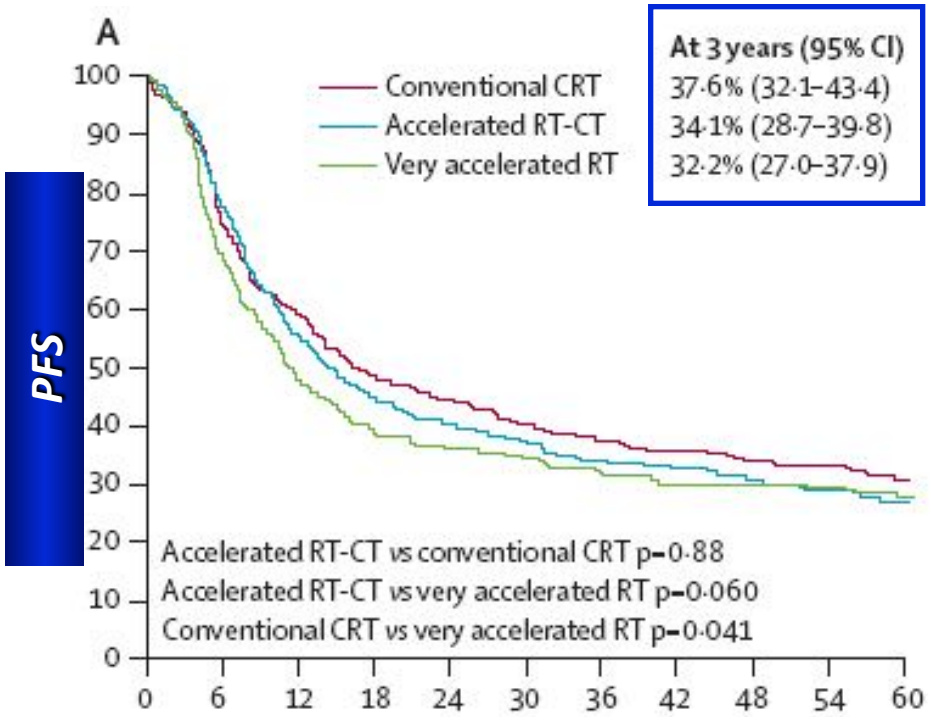
Median FU: 5.2 yrs

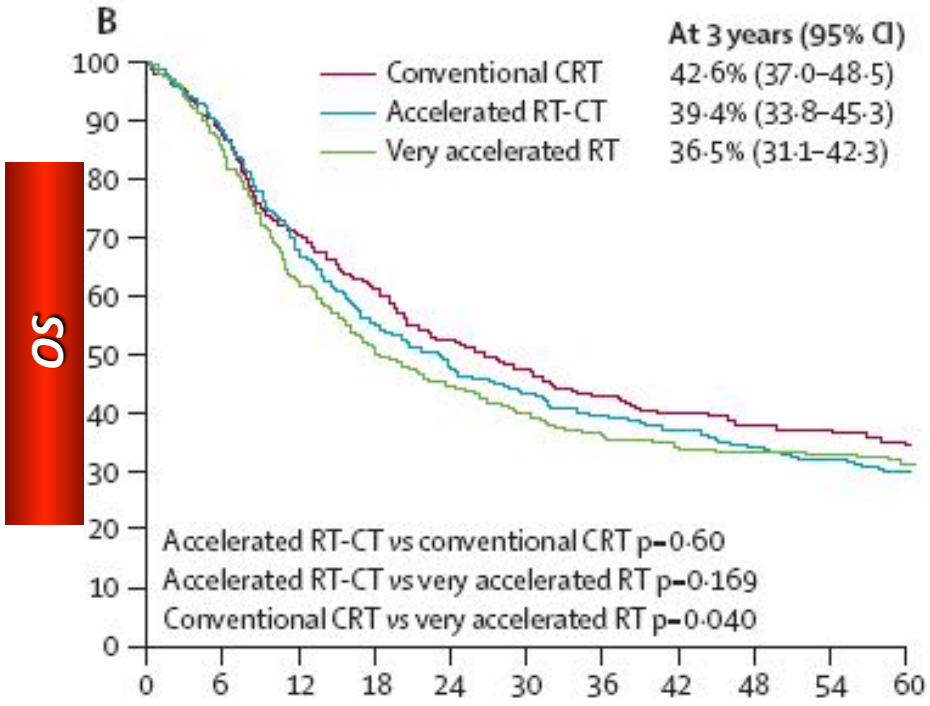
	Progression-free survival		Overall survival		Locoregional failure		Distant metastases	
	HR (95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value
Accelerated RT-CT *vs* conventional CRT	1·02 (0·84–1·23)	0·88						
Accelerated RT-CT *vs* very accelerated CRT	0·83 (0·69–1·01)	0·060						
Conventional RT-CT *vs* very accelerated CRT	0·82 (0·67–0·99)	0·041						

No difference between Acc. RTCT and Conv. RTCT

Acc. RTCT seemed to improve PFS vs. Very Acc. RT

Conv. RTCT improved PFS vs. Very Acc. RT





Lancet Oncol 2012; 13: 145–53

Chemotherapy has a main effect on the outcome.
RT acceleration does not compensate for the absence or reduction of concomitant CT
Very intense acceleration is unable to increase the outcome, if RT is given alone.
Treatment-related toxicity is increased from RT intensification.

Are the results robust enough?

Strengths

- ***Largest RCT to assess potential benefit of different strategies (840 patients, FU > 7 years)***

Weakness

- ***No stratification on HPV status***
- ***No IMRT contemplated***
- ***"Old" CT scheme (no Taxanes, no induction, no biologic drugs)***

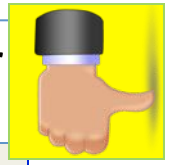
DECIDE: a phase III randomized trial of docetaxel, cisplatin, 5-fluorouracil (TPF) induction chemotherapy in patients with N2/N3 locally advanced head and neck squamous cell carcinoma

... High survival rates were observed in both arms. Further analysis and follow-up may provide insights into why significant decrease in distant failures did not translate into improved overall survival...

PARADIGM: a phase III study comparing sequential therapy to concurrent chemoradiotherapy in locally advanced head and neck cancer

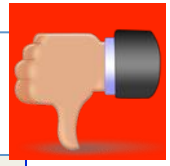
... results suggest no survival differences... excellent results observed in both arms.

NCT01086826: Cetuximab /radiotherapy vs. concomitant chemoradiotherapy with or without induction TPF in LAHNSCC: preliminary results on toxicity.



... No advantage for CET+RT over cCHT+RT was oserved regarding G3-G4 in-field toxicities...patients are still being followed-up to access OS.

Efficacy of concurrent cetuximab vs. 5-FU/CBDCA or CDDP with intensity-modulated radiation therapy for LAHNSCC



... No significant difference in OS and LCFS between 5FU/CBDCA and high-dose CDDP, but Cet/RT resulted in significantly inferior OS and LCFS.

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JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Accelerated Radiotherapy With Carbogen and Nicotinamide for Laryngeal Cancer: Results of a Phase III Randomized Trial

Geert O. Janssens, Saskia E. Rademakers, Chris H. Terhaard, Patricia A. Doornaert, Hendrik P. Bijl, Piet van den Ende, Alim Chin, Henri A. Marres, Remco de Bree, Albert J. van der Kogel, Ilse J. Hoogsteen, Johannes Bussink, Paul N. Span, and Johannes H. Kaanders

345 pts.

T2 glottic (impair. mobility, subglottic ext.)

T2 supraglottic (oro-hypopharynx. ext.)

T3-4 glottic - supraglottic

A-RT 68 Gy (38 days)

A-RT 64 Gy + Carbogen inhal. / Nicotinamide

3DCRT

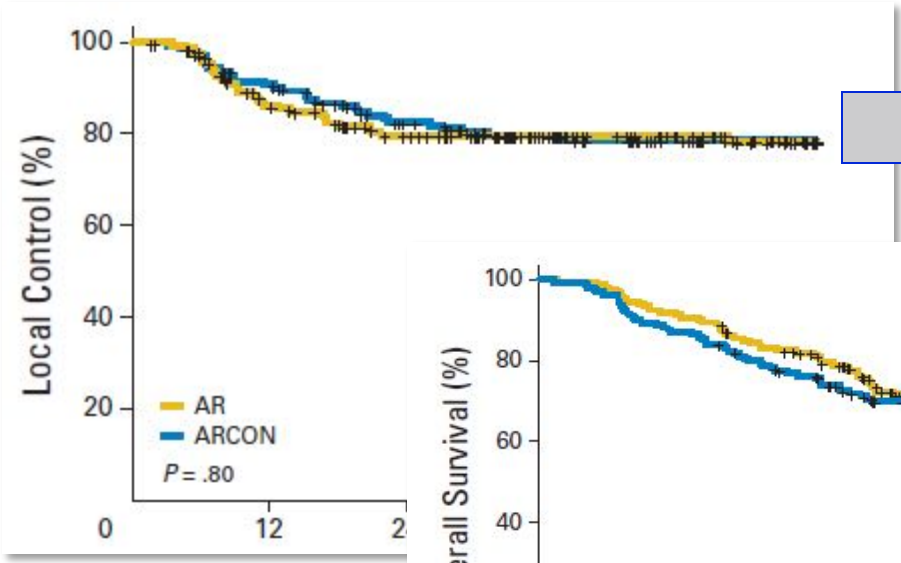
No prior concomitant treatments

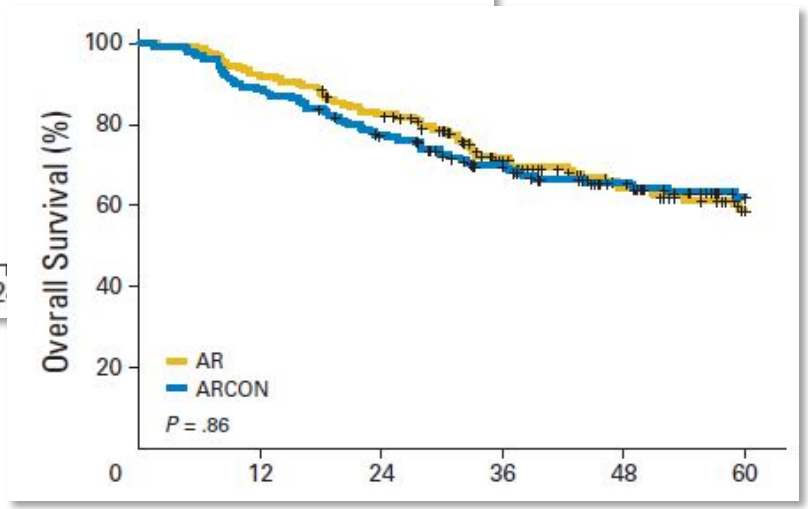
Primary end-point: - local control

Secondary end-points: - larynx preservation

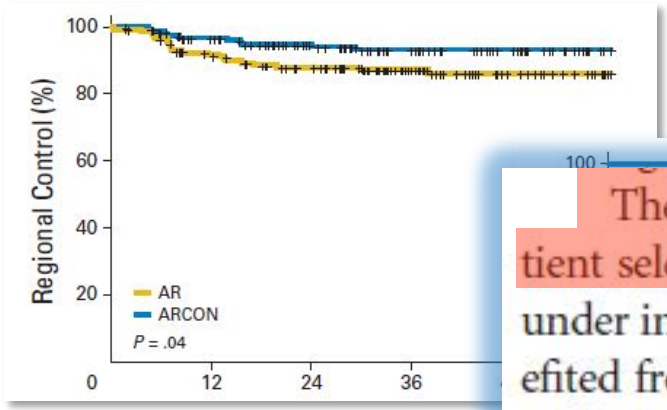
- toxicity, QoL

- DFS, OS





No difference between AR and ARCON



Better regional control with ARCON, especially in hypoxic tumors

The present study demonstrates the importance of proper patient selection that is based on the mode of action of the treatment under investigation, because only patients with hypoxic tumors benefited from ARCON therapy and no gain was seen in patients with well-oxygenated tumors. This finding strongly supports the notion

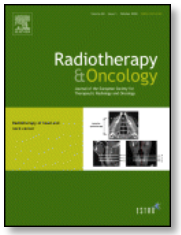
… suggestions

- Conventional RT + concomitant platinum-based CT as the actual SoC in LAHNSCC
- Variations to SoC (new drugs, target-therapies) are not completely validated
- Knowledge of HPV-status drives for personalized treatment strategies
- Treatment intensification does not automatically lead to better outcome

- *Treatment de-intensification may be considered in good-prognosis patients*
- *Closer attention to QoL and long-term toxicity should be considered*
- *A better definition of treatment-related toxicity is warranted*
- *Organ preservation does not automatically mean function preservation*

Phase III randomised trial

Predictors of severe late radiotherapy-related toxicity after hyperfractionated radiotherapy with or without concomitant cisplatin in locally advanced head and neck cancer. Secondary retrospective analysis of a randomized phase III trial (SAKK 10/94)



Pirus Ghadjar[a,*], Mathew Simcock[b], Frank Zimmermann[c], Michael Betz[d], Stephan Bodis[e], Jacques Bernier[f], Gabriela Studer[g], Daniel M. Aebersold[a], on behalf of the Swiss Group for Clinical Cancer Research (SAKK)

Radiotherapy and Oncology 104 (2012) 213–218

No IMRT

Variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*p*-value	HR (95% CI)	*p*-Value
Age: ⩾55 vs. <55 years old	0.77 (0.50, 1.18)	0.23	–	–
Gender: Male vs. Female	0.99 (0.56, 1.79)	0.98	–	–
Performance status: WHO 1-2 vs. 0	1.46 (0.95, 2.24)	0.09	–	–
Site: Hypopharynx & Larynx vs. Other	0.66 (0.42, 1.03)	0.07	–	–
Tumor classification: cT3-4 vs. cT1-2	1.13 (0.65, 1.99)	0.66	–	–
Nodal classification: cN2-3 vs. cN0-1	2.25 (1.42, 3.57)	<0.001	1.96 (1.21, 3.19)	0.007
Technically resectable: No vs. Yes	1.58 (1.02, 2.46)	0.04	1.64 (1.02, 2.62)	0.04
Weight loss ratio: <0.97 vs. ⩾0.97	2.00 (1.27, 3.16)	0.003	1.77 (1.10, 2.83)	0.02
Hemoglobin: ⩾14 vs. <14 g/dl	1.15 (0.74, 1.79)	0.53	–	–
Radiotherapy total dose: ⩾74.4 vs. <74.4 Gy	0.91 (0.44, 1.88)	0.79	–	–
Total cisplatin (mg/m^2)	1.00 (1.00, 1.00)	0.96	–	–
Supportive measures used: Yes vs. No	1.96 (1.18, 3.25)	0.009	1.23 (0.60, 2.52)	0.57
Salvage neck dissection: Yes vs. No	1.22 (0.49, 3.02)	0.67	–	–
Acute dysphagia: Grade ⩾ 3 vs. other	2.21 (1.38, 3.56)	0.001	2.44 (1.28, 4.69)	0.007

What “severe late toxicity” does mean?

Emerging understanding of dosimetric factors impacting on dysphagia and nutrition following radiotherapy for oropharyngeal cancer

Bena Cartmill, BSpPath, Hons, PhD,[1] Petrea Cornwell, BSpPath Hons, PhD,[2] Elizabeth Ward, BSpThy Hons Grad Cert Ed, PhD,[3] Wendy Davidson, BSc, Grad Dip Nutr Diet, Master Appl Sc Res,[4] Rebecca Nund, BSpPath Hons,[5] Catherine Bettington, BSc, MBBS,[6] Reza Masoud Rahbari, BSc, MBBS,[7] Michael Poulsen, MBBS, FRANZCR, MD,[6] Sandro Porceddu, BSc, MBBS, FRANZCR, MD[6,8]

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Cancer Treatment Reviews

journal homepage: www.elsevierhealth.com/journals/ctrv

General and Supportive Care

Swallowing dysfunction in head and neck cancer patients treated by radiotherapy: Review and recommendations of the supportive task group of the Italian Association of Radiation Oncology

Elvio G. Russi [a,*], Renzo Corvò [b], Anna Merlotti [c], Daniela Alterio [d], Pierfrancesco Franco [e], Stefano Pergolizzi [f], Vitaliana De Sanctis [g], Maria Grazia Ruo Redda [h], Umberto Ricardi [i], Fabiola Paiar [j], Pierluigi Bonomo [k], Marco C. Merlano [l], Valeria Zurlo [m], Fausto Chiesa [m], Giuseppe Sanguineti [n], Jacques Bernier [o]

SCREEN

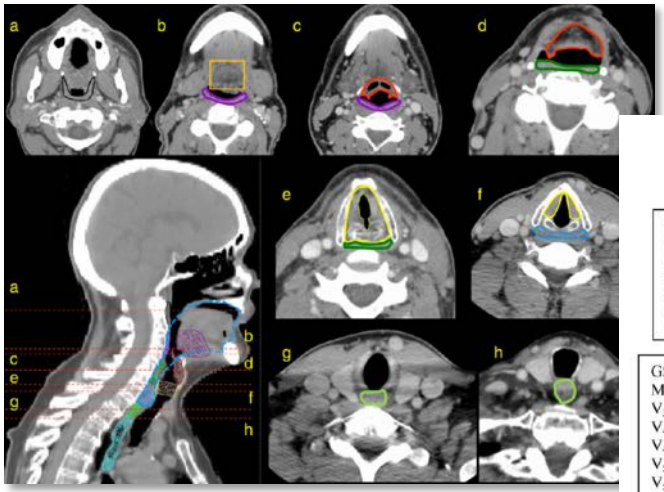
Triggers for dysphagia evaluation.[26]

- Inability to control food liquids or saliva within the oral cavity
- Pocketing of food in cheek
- Excessive chewing
- Drooling
- Coughing choking or throat clearing before during or after swallowing
- Abnormal vocal quality after swallowing; "wet" or "gurgly" voice
- Build-up or congestion after a meal
- Complaint of difficulty swallowing
- Complaint of food "sticking" in throat
- Nasal regurgitation
- Weight loss

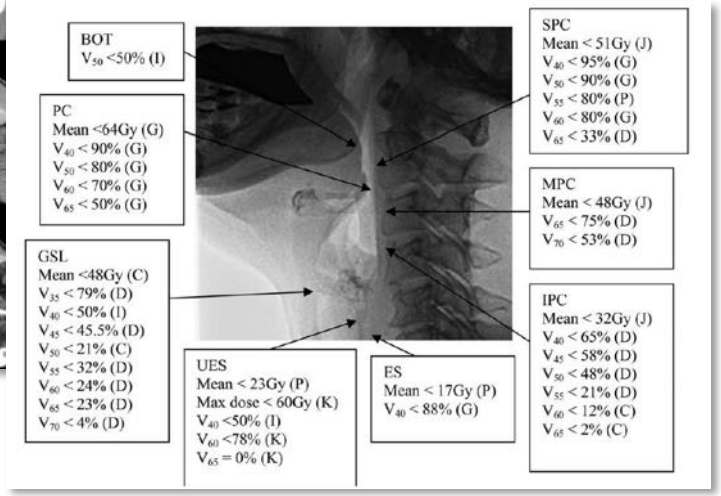
SCORE

Bedside test	Scale denomination
Trial swallowing using water	The Swallowing Questionnaire QoL Questionnaire
Trial swallow using different	
	MD Anderson Dysphagia Inventory
Oxygen desaturation[33,34,36]	European Organization for Research and Treatment of Cancer (Global QoL Scale
Swallow test combining water desaturation[33,34]	
Combination of clinical condit	European Organization for Research and Treatment of Cancer (Head and Neck Module)

PREVENT



Russi et al.



Cartmil et al.

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Clinical Oncology

journal homepage: www.clinicaloncologyonline.net

Guidelines

Intensity-modulated Radiotherapy in the Treatment of Head and Neck Cancer

B. O'Sullivan *, R.B. Rumble †, P. Warde ‡ and Members of the IMRT Indications Expert Panel

* *Princess Margaret Hospital, Toronto, ON, Canada*
† *Cancer Care Ontario's Program in Evidence-based Care, Hamilton, ON, Canada*
‡ *Provincial Head, Radiation Treatment Program, Cancer Care Ontario, Toronto, ON, Canada*

Clinical Oncology 24 (2012) 474–487

sites, including head and neck cancer. This systematic review examined the evidence for IMRT compared with two-dimensional external beam radiotherapy (EBRT) in the treatment of head and neck cancer in order to quantify the potential benefits of this new technology and made recommendations for radiation treatment programmes considering adopting this technique. Findings were in favour of IMRT compared with two-dimensional EBRT where avoidance of the adverse outcomes xerostomia, osteoradionecrosis and blindness are the main outcomes of interest, based on a review of 15 papers including 1555 patients. There are insufficient data to recommend IMRT over two-dimensional EBRT if treatment-related outcomes are the main outcomes of interest. Future research should focus on additional normal tissue preservation, and the role of IMRT in the treatment of recurrent head and neck cancer, as well as its use in combination with surgery, chemotherapy and/or brachytherapy.