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Neoplasie del Polmone

Radioterapia ipofrazionata nel NSCLC localmente avanzato. Evidenze cliniche e prospettive.

Marco Trovò – CRO Aviano
Gruppo di Studio AIRO Polmone

DICHIARAZIONE

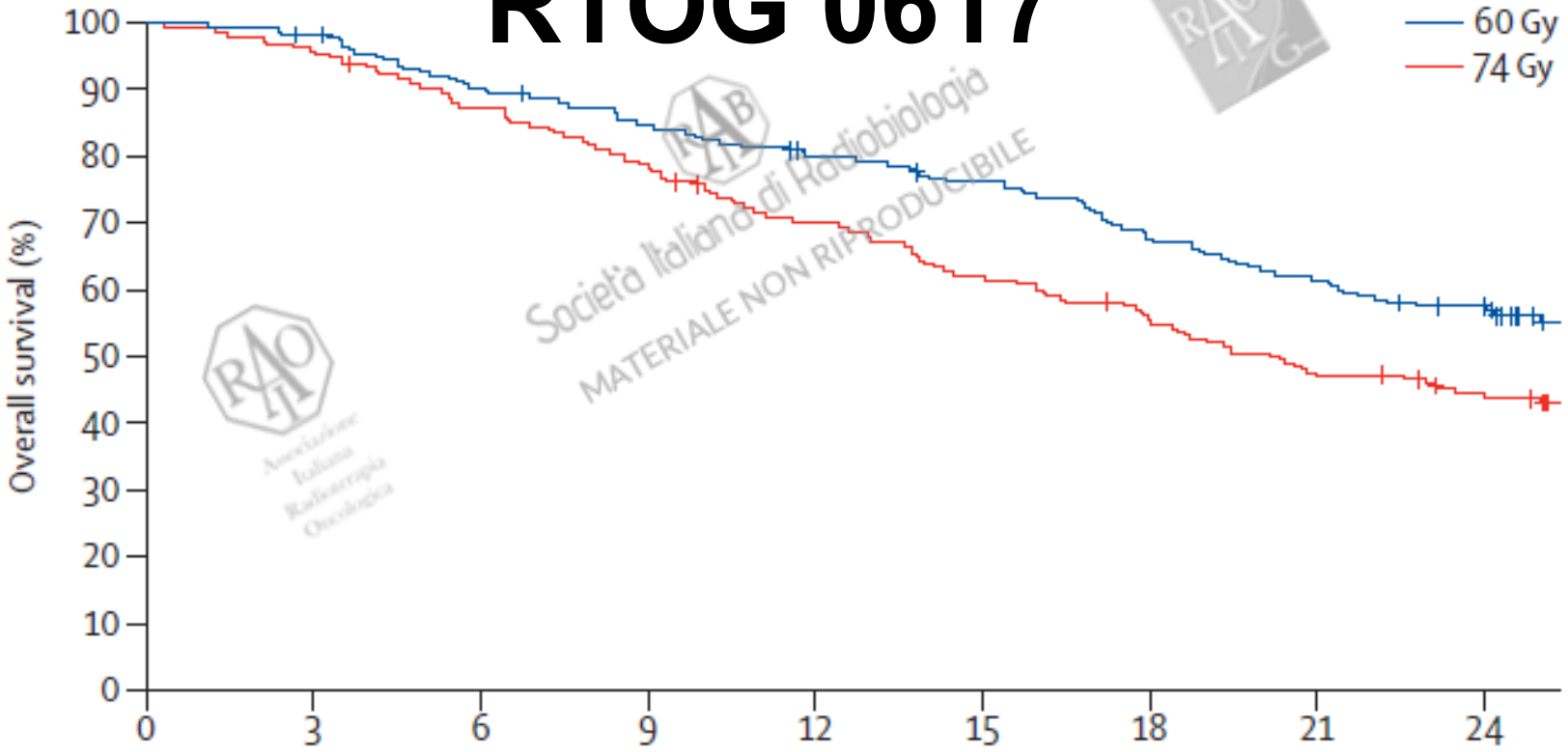
Relatore: Marco Trovò

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Consulenza ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazione ad Advisory Board **(NIENTE DA DICHIARARE)**
- Titolarietà di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**

INTRODUCTION

RTOG 0617

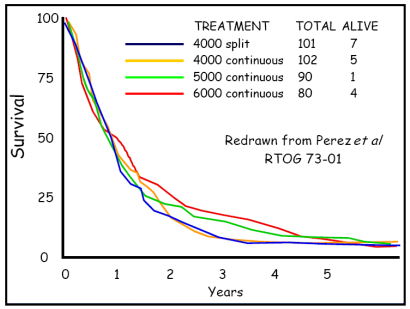


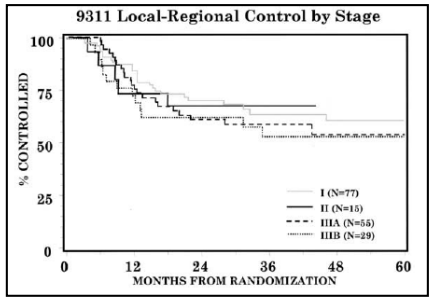
RTOG 0617

INTRODUCTION

	60 Gy (n=217)*	74 Gy (n=207)
Overall survival		
Dead	127	140
1 year	80·0% (73·9–84·7)	69·8% (63·1–75·6)
2 year	57·6% (50·6–63·9)	44·6% (37·7–51·3)
Median (months)	28·7 (24·1–36·9)	20·3 (17·7–25·0)

RTOG 0617





Study	Radiation MTD (Gy)
RTOG 0117[34]	74
NCCTG 0028[35]	74
UNC[36]	74
Wake Forest[37]	74
CALGB 30105[38]	74

RTOG 0617
60 Gy vs.74 Gy

IMRT

2D-RT

3D-CRT

Post RTOG 0617 era

‘73-‘80 ’93-’00 ’03-’05 ’06-’11

doseline

60 Gy

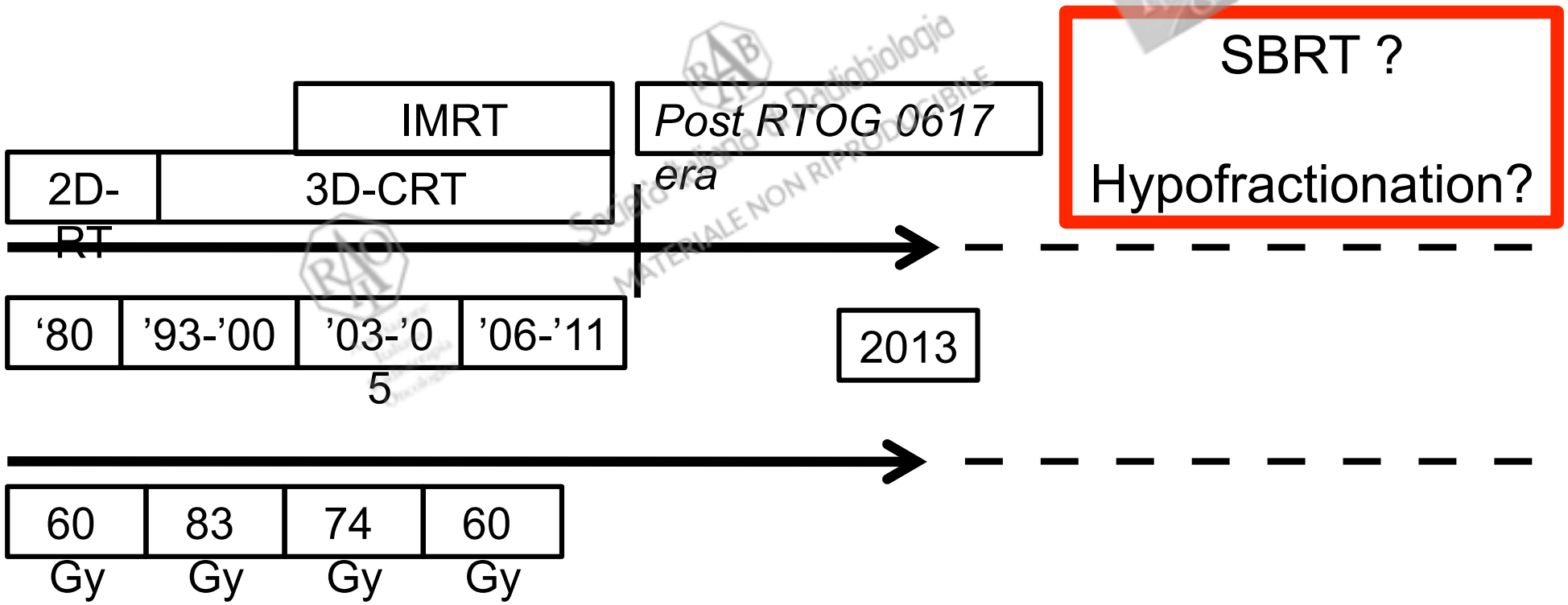
83 Gy

74 Gy

60

FDG-PET/CT

Concomitant Chemotherapy


IMRT
Post RTOG 0617 era
SBRT ?
Hypofractionation?
2D-RT
3D-CRT
'80
'93-'00
'03-'05
'06-'11
2013
60 Gy
83 Gy
74 Gy
60 Gy

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AIRO 2015
PALACONGRESSI - Rimini, 7-10 novembre

Re-irradiazione: standard clinico o ricerca?

Re-irradiazione neoplasie toraciche

Marco Trovò

Rimini, 9 Novembre 2015

Hypofractionation

- Rationale
- Clinical data
- Points of discussion
- Future directions

Hypofractionation

- Rationale
- Clinical data
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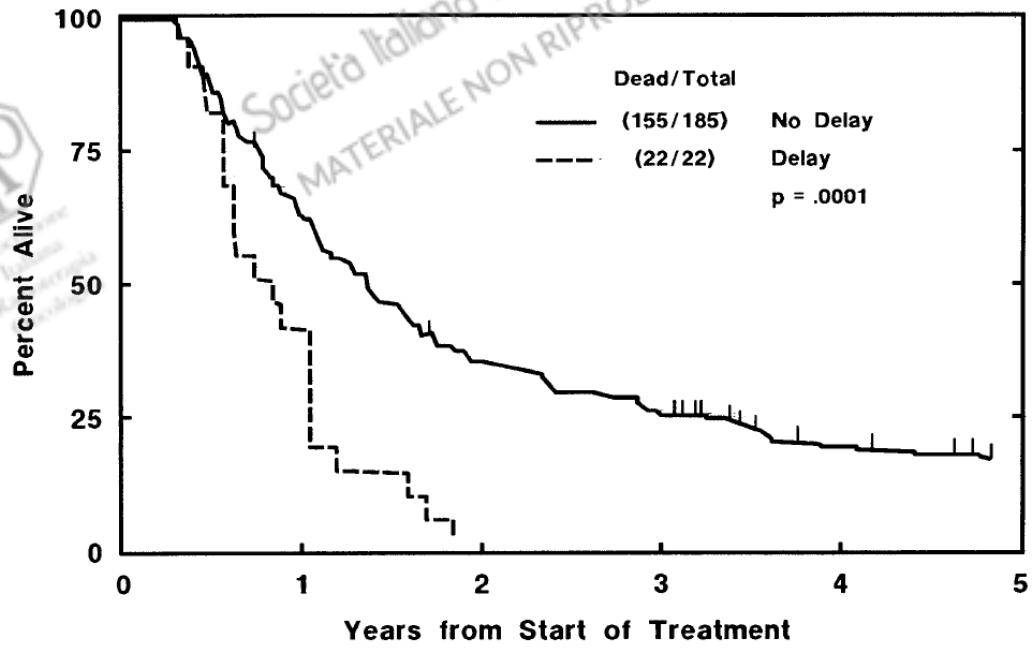
- Future directions

INTERRUPTIONS OF HIGH-DOSE RADIATION THERAPY DECREASE LONG-TERM SURVIVAL OF FAVORABLE PATIENTS WITH UNRESECTABLE NON-SMALL CELL CARCINOMA OF THE LUNG: ANALYSIS OF 1244 CASES FROM 3 RADIATION THERAPY ONCOLOGY GROUP (RTOG) TRIALS

JAMES D. COX, M.D.,[1] THOMAS F. PAJAK, PH.D.,[2] SUCHA ASBELL, M.D.,[3] ANTHONY H. RUSSELL, M.D.,[4] JOHN PEDERSON, M.D.,[5] ROGER W. BYHARDT, M.D.,[6] BAHMAN EMAMI, M.D.[7] AND MACK ROACH III[8]



ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 63, No. 3, pp. 667–671, 2005

0360-3016/05/$–see front matter

doi:10.1016/j.ijrobp.2005.03.037

CLINICAL INVESTIGATION **Lung**

EFFECT OF OVERALL TREATMENT TIME ON OUTCOMES AFTER CONCURRENT CHEMORADIATION FOR LOCALLY ADVANCED NON–SMALL-CELL LUNG CARCINOMA: ANALYSIS OF THE RADIATION THERAPY ONCOLOGY GROUP (RTOG) EXPERIENCE

MITCHELL MACHTAY, M.D.,* CHUANCHIEH HSU, PH.D.,† RITSUKO KOMAKI, M.D.,‡ WILLIAM T. SAUSE, M.D.,§ R. SUZANNE SWANN, PH.D.,† COREY J. LANGER, M.D.,‖ ROGER W. BYHARDT, M.D.,¶ AND WALTER J. CURRAN, M.D.*

Rationale for Hypofractionation

1. Radiation fraction size

   α/β is not favorable in lung cancer!

   Tumors might be heterogeneous, with clones which respond more like late-responding tissue.

Rationale for Hypofractionation

2. Repopulation

It might be benefitial to employ shortened regimen

Rationale for Hypofractionation

3. Volume effect

n: effect/volume parameter

- n → 0: serial organ (ex. cord): toxicity related to “dose effect”
- n → 1: parallel organ (ex. lung): toxicity related to “volume effect”

Tumori. 1992 Oct 31;78(5):305-10.

Unfavorable experience with hypofractionated radiotherapy in unresectable lung cancer.

Pirtoli L[1], Bindi M, Bellezza A, Pepi F, Tucci E.

The use of a reduced number of large-sized fractions in radiotherapy (hypofractionation) is usually associated with poor therapeutic results and severe adverse effects, in accord with radiobiologic concepts. However by some authors unresectable lung cancer patients have been treated with hypofractionated radiotherapy with the main aim of "convenience". Result and damage rates are reported to be comparable to those of conventional treatment. In our experience, based on palliative irradiation of 86 advanced-stage, nonmicrocytoma patients, objective remission rates, subjective and performance status improvement, and survival overall were as poor as could be expected in this kind of presentation, with no striking impact of this treatment modality. Severe adverse effects were shown by a large proportion of cases involving skin and soft tissues of the chest wall (40%) and lungs (55.5%). The incidence of severe damage was in agreement with BED (biologic effective dose) values, differently from other experiences of radiotherapeutic management of advanced lung cancer with large fractions.

Hypofractionation

- Rationale
- Clinical data
- Points of discussion
- Future directions

Table 2 Studies With Nonconcurrent Chemoradiotherapy

Study	Dose	Fraction	Dose/fx	Acute BED	Late BED	3 Year OS (%)	1 Year OS (%)	AE (%)	AP (%)	LE (%)	LP (%)
Schuster-Uitterhoeve (1993)[35]	60	20	3	78.0	120.0		57	0	6	NR	NR
Graham (1995)[36]	75	28	2.68	95.2	142.1	18	41	5	0	NR	NR
Bernier (1999)[37]	55	20	2.75	70.1	105.4			6	9	3	6
Nguyen (1999)[38]	45	15	3	58.5	90.0			NR	NR	NR	NR
Sun (2000)[39]	65	26	2.5	81.3	119.2			0	0	NR	NR
Holloway (2004)[40]	84	35	2.4	104.2	151.2			NR	NR	NR	NR
Lester (2004)[41]	55	20	2.75	70.1	105.4	22	57	0	0	0	0
Thirion (2004)[42]	72	24	3	93.6	144.0		68	8	4	0	0
Kepka (2009)[43]	56.7-60.9	21	2.7-2.9	72.0-78.5	107.7-119.8	19	69	7	0	0	6
Pemberton (2009)[12]	55	20	2.75	70.1	105.4	7	65	NR	NR	NR	NR
Bral (2010)[44]	70.5	30	2.35	87.1	125.7	18	65	NR	NR	0	16
Zhu (2011)[45]	65-68	25-26	2.6	81.9-85.8	121.3-127.3	32	68	6	3	NR	NR
Monaco (2012)[46]	67.5	30	2.25	82.7	118.1			0	0	NR	NR
Amini (2012)[47]	45	15	3	58.5	90.0	12	53	NR	NR	NR	NR
Din (2013)[13]	55	20	2.75	70.1	105.4			0	0	NR	NR
McPartlin (2013)[48]	55	20	2.75	70.1	105.4			NR	NR	NR	NR
Osti (2013)[49]	60	20	3	78.0	120.0		75	7	3	3	7
Cannon (2013)[18]	57-85.5	25	2.28-3.42	70.0-114.7	100.3-183.0	29		0	0	0	0
Belderbos (2007)[22,b]	66	24	2.75	84.2	126.5	22	69	5	8	4	13
Uitterhoeve (2007)[23,b]	66	24	2.75	84.2	126.5	19	53	NR	NR	5[a]	18[a]
Donato (2013)[32,b]	68.4	30	2.28	82.7	118.1		77[a]	0	10[a]	0[a]	5[a]
Maguire (2012)[17,b]	55	20	2.75	70.1	105.4	27	83	NR	NR	NR	NR

Kaster TS. Clin Lung Cancer 2015

Table 1 Studies With Concurrent Chemoradiotherapy

Study	Dose	Fraction	Dose/fx	Acute BED	Late BED	3 Year OS (%)	1 Year OS (%)	AE (%)	AP (%)	LE (%)	LP (%)
Machtay (2005)[21]	60	20	3	78.0	120.0			0	0	0	25
Belderbos (2007)[22]	66	24	2.75	84.2	126.5	29	56	17	9	5	18
Uitterhoeve (2007)[23]	66	24	2.75	84.2	126.5	31	57	NR	NR	5[a]	18[a]
Tsoutsou (2008)[24]	52.5	15	3.5	70.9	113.8		28	0	0	NR	NR
Bral (2010)[25]	67.2	30	2.24	82.3	117.4			NR	NR	NR	NR
Matsuura (2009)[26]	65	26	2.5	81.3	119.2	44	90	0	0	0	0
Casas (2011)[27]	61.6	23	2.68	78.2	116.7	34	59	6.	3	0	0
Carruthers (2011)[28]	55	20	2.75	70.1	105.4			13	3	NR	NR
Maguire (2012)[17]	55	20	2.75	70.1	105.4	38	73	NR	NR	NR	NR
Lin (2013)[29]	69	22-24	3	85.8	132.0			15	8	NR	NR
Liu (2013)[30]	75	25	3	78.0	120.0		61	15	8	8	0
Chen (2013)[31]	55	20	2.75	70.1	105.4		69	22	NR	11	NR
Donato (2013)[32]	68.4	30	2.28	82.7	118.1		77[a]	7	10[a]	0[a]	5[a]
van Den Heuvel (2013)[33]	66	24	2.75	84.2	126.5		80	NR	NR	NR	NR
Bearz (2013)[34]	60	25	2.4	74.4	108.0	24	80	3	0	0	0

Kaster TS. Clin Lung Cancer 2015

Main Limitations:

- No robust and reliable toxicity data
- Palliative treatments
- ENI
- No PET or IMRT
- Retrospective studies
- Prospective although observational studies

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Radiotherapy Alone.

Radiotherapy and Oncology 109 (2013) 8–12

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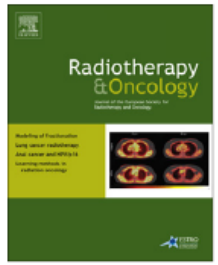

Hypofraction in lung cancer

Accelerated hypo-fractionated radiotherapy for non small cell lung cancer: Results from 4 UK centres

Omar S. Din [a], Susan V. Harden [b], Emma Hudson [c], Nazia Mohammed [d], Laura S. Pemberton [a], Jason F. Lester [c], Debashis Biswas [b], Lavinia Magee [b], Aisha Tufail [d], Ross Carruthers [d], Ghazia Sheikh [d], David Gilligan [b], Matthew Q.F. Hatton [a,*]

[a] Dept. of Clinical Oncology, Weston Park Hospital, Sheffield; [b] Dept. of Oncology, Addenbrookes Hospital, Cambridge; [c] Dept. of Clinical Oncology, Velindre Hospital, Cardiff; and [d] Dept. of Clinical Oncology, Beatson West of Scotland Cancer Centre, Glasgow, UK

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609 patients
55 Gy in 20 fr @2.75 Gy/fr

OS:
-median: 24 mo
-2-year: 50%

Grade II pneumonitis: 20%

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Considerations:

- 200 patients were stage I
- GTV-PTV margin: 15-20 mm
- No PET
- Toxicity recorded in 378 patients
- No Grade ≥3 Toxicity

International Journal of Radiation Oncology biology • physics
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Clinical Investigation: Thoracic Cancer

Image Guided Hypofractionated 3-Dimensional Radiation Therapy in Patients With Inoperable Advanced Stage Non-Small Cell Lung Cancer

Mattia Falchetto Osti, MD, Linda Agolli, MD, Maurizio Valeriani, MD, Teresa Falco, MD, Stefano Bracci, MD, Vitaliana De Sanctis, MD, and Riccardo Maurizi Enrici, MD

Institute of Radiation Oncology, La Sapienza University, Sant'Andrea Hospital, Rome, Italy

Received Aug 16, 2012, and in revised form Oct 1, 2012. Accepted for publication Oct 8, 2012

Image Guided Hypofractionated 3-Dimensional Radiation Therapy in Patients With Inoperable Advanced Stage Non-Small Cell Lung Cancer

Mattia Falchetto Osti, MD, Linda Agolli, MD, Maurizio Valeriani, MD, Teresa Falco, MD, Stefano Bracci, MD, Vitaliana De Sanctis, MD, and Riccardo Maurizi Enrici, MD

30 patients (stage III 77%; stage IV 23%)
60 Gy @3Gy/fr
Induction chemo 80%
Median PTV: 335 cc (range 73-682)

LRR: 37%
2-Y OS: 38%.

Table 3 Treatment-related toxicities based on RTOG radiation scales of acute and late morbidity

	Grade 1		Grade 2		Grade 3		Grade 4		Total	
Toxicity	No.	%	No.	%	No.	%	No.	%	No.	%
Acute										
Erythema	2	7	0	0	0	0	0	0	2	7
Esophagitis	3	10	9	30	1	3	0	0	13	43
Cough	3	10	3	10	0	0	0	0	6	20
Odynophagia	1	3	2	7	0	0	0	0	3	10
Pneumonitis	3	10	3	10	2	7	0	0	8	27
Hematological toxicity	4	14	1	3	1	3	0	0	6	20
Late										
Esophagitis	0	0	1	3	1	3	0	0	2	7
Pneumonitis	2	7	6	20	2	7	0	0	10	33

Ren *et al. BMC Cancer* (2016) 16:288
DOI 10.1186/s12885-016-2314-1

BMC Cancer

RESEARCH ARTICLE Open Access

Accelerated hypofractionated three-dimensional conformal radiation therapy (3 Gy/fraction) combined with concurrent chemotherapy for patients with unresectable stage III non-small cell lung cancer: preliminary results of an early terminated phase II trial

Xiao-Cang Ren[1], Quan-Yu Wang[1], Rui Zhang[1], Xue-Ji Chen[1], Na Wang[1], Yue-E Liu[1], Jie Zong[1], Zhi-Jun Guo[2], Dong-Ying Wang[3] and Qiang Lin[1*]

Radiotherapy + Chemotherapy.

European Journal of Cancer (2014) 50, 2939–2949

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Available at www.sciencedirect.com

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journal homepage: www.ejcancer.com

SOCCAR: A randomised phase II trial comparing sequential versus concurrent chemotherapy and radical hypofractionated radiotherapy in patients with inoperable stage III Non-Small Cell Lung Cancer and good performance status

J. Maguire [a,*], I. Khan [b], R. McMenemin [c], N. O'Rourke [d], S. McNee [d], V. Kelly [a], C. Peedell [e], M. Snee [f]

SOCCAR: A randomised phase II trial comparing sequential versus concurrent chemotherapy and radical hypofractionated radiotherapy in patients with inoperable stage III Non-Small Cell Lung Cancer and good performance status

J. Maguire [a,*], I. Khan [b], R. McMenemin [c], N. O'Rourke [d], S. McNee [d], V. Kelly [a], C. Peedell [e], M. Snee [f]

130 Stage III NSCLC pt.

R

→ VNB+CDDPx4 → 55Gy/20 fr (2.75 Gy/fr)

→ VNB+CDDP + 55Gy/20 fr

RT details:

- Lung V20 < 35%
- PET + disease (no ENI)
- GTV→PTV 1.5 cm
- No IMRT

SOCCAR	Concomitant	Sequential
Compliance to RT	95%	78%
Grade 3-5 toxicity	34%	41%
Mortality	2.9%	1.7%
Grade 3 pneumonitis	3%	5%
Median OS	24 mo	18 mo

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Radiotherapy and Oncology 118 (2016) 442–446

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Phase III random

Additional v
in locally ac
outcomes o

Michel M. van
Joachim Aerts [d]
Edith Dieleman

[a] Department of Thoracic
Amphia Ziekenhuis Breda
Amsterdam; [g] Pulmonary
Amsterdam, The Netherla

Phase II randomised trial

Long-term follow-up of patients with locally advanced non-small cell lung cancer receiving concurrent hypofractionated chemoradiotherapy with or without cetuximab

Iris Walraven [a], Michel van den Heuvel [b], Judi van Diessen [a], Eva Schaake [a], Wilma Uyterlinde [b], Joachim Aerts [c,d], Frederieke Koppe [e], Henk Codrington [f], Peter Kunst [g], Edith Dieleman [h], Paul van de Vaart [i], Marcel Verheij [a], Jose Belderbos [a,*]

[a] Department of Radiation Oncology; [b] Department of Thoracic Oncology, The Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital, Amsterdam; [c] Department of Pulmonary Medicine, Amphia Hospital, Breda; [d] Department of Pulmonary Medicine, Erasmus Medical Center, Rotterdam; [e] Department of Radiation Oncology, Verbeeten Institute, Tilburg; [f] Department of Pulmonary Medicine, Haga Hospital, The Hague; [g] Department of Pulmonary Medicine; [h] Department of Radiation Oncology, Academic Medical Center, Amsterdam; and [i] Department of Radiation Oncology, MC Haaglanden, The Hague, The Netherlands

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102 Stage
II-III NSCLC

R

66 Gy/24fr (2.75Gy/fr) + daily CDDP

66 Gy/24fr + daily CDDP + Cetuximab

RT details:

- MLD< 20 Gy
- PET + disease (no ENI)
- GTV→PTV 1.2 cm
- IMRT 75%
- IGRT

Results:

- Compliance to RT: 84%-88%.
- Grade 3-5 tox: 45% - 65%
- Grade 3 Pneumonitis: 0% - 6%
- Median OS: 31 mo (no difference)
- 2y OS = 60%; 5-y OS 37%

Hypofractionation

- Rationale
- Clinical data
- Points of discussion
- Future directions

Which fractionations to use with or without chemo?

Any evidence of Dose Limiting Toxicity?

Which fractionations to use with or without chemo?

A. No chemo. British Fractionation: 55 Gy in 20 fractions @ 2.75 Gy/fr.

B. Concomitant chemo.
   - SOCCAR Trial: 55 Gy in 20 fr. + CDDP-VNBx2
   - RADITUX Trial: 66 Gy in 24 fr + Daily CDDP

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Any evidence of Dose Limiting Toxicity?

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Clinical Investigation

IDEAL-CRT: A Phase 1/2 Trial of Isotoxic Dose-Escalated Radiation Therapy and Concurrent Chemotherapy in Patients With Stage II/III Non-Small Cell Lung Cancer

David B. Landau, MRCP,* Laura Hughes, NDipSc,† Angela Baker, MSc,‡

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IDEAL-CRT: A Phase 1/2 Trial of Isotoxic Dose-Escalated Radiation Therapy and Concurrent Chemotherapy in Patients With Stage II/III Non-Small Cell Lung Cancer

David B. Landau, MRCP,* Laura Hughes, NDipSc,† Angela Baker, MSc,‡

Isotoxic dose escaltion
63 Gy →73 Gy in 30 fr.
Concurrent CDDP+VNB x 2

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IDEAL-CRT: A Phase 1/2 Trial of Isotoxic Dose-Escalated Radiation Therapy and Concurrent Chemotherapy in Patients With Stage II/III Non-Small Cell Lung Cancer

Table 1 Summary of the radiation therapy planning and dose prescription process

	Process steps			
Tumor coverage aim				
PTV	90% isodose to cover 98% of PTV			
Tumor dose prescribed to the ICRU reference point initially selected to achieve				
Lung	EQD_{2mean} 18.2 Gy			
Prescribed tumor dose reduced by 10%, and further if needed to meet the following limits				
Heart	$D_{100\%}$ <45 Gy, $D_{67\%}$ <53 Gy, $D_{33\%}$ <60 Gy			
Spinal cord	$D_{0.1cc} \leq 47$ Gy			
Brachial plexus	$D_{30\%} \leq 60$ Gy, $D_{0.1cc} \leq 65$ Gy			
Esophagus	Dose to 1 cm^3 = 65 Gy	Dose to 1 cm^3 = 68 Gy	Dose to 1 cm^3 = 71 Gy	Dose to 1 cm^3 ≤63 Gy*
Limit for	Group 1: cohort 1	Group 1: cohort 2	Group 1: cohort 3	Group 2

Abbreviations: EQD_{2mean} = equivalent dose in 2-Gy fractions averaged across lung, excluding gross tumor volume (GTV); ICRU = International Commission on Radiation Units and Measurements; PTV = planning target volume.

Prescribed tumor dose finally limited to 63-73 Gy, patients being ineligible for the trial if this causes lung V_{20Gy} (the volume of lung excluding GTV receiving more than 20 Gy) or $EQD2_{mean}$ to exceed 35% or 19.3 Gy, respectively.

* This dose level increased to 65 Gy, and then 68 Gy as safety data became available from group 1.

IDEAL-CRT: A Phase 1/2 Trial of Isotoxic Dose-Escalated Radiation Therapy and Concurrent Chemotherapy in Patients With Stage II/III Non-Small Cell Lung Cancer

David B. Landau, MRCP,* Laura Hughes, NDipSc,† Angela Baker, MSc,‡

Esophageal MTD = 68 Gy in 30 fr. @ 2.26 Gy/fr

- Grade 3 esophagitis < 6 %

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frontiers in ONCOLOGY

ORIGINAL RESEARCH ARTICLE
published: 18 November 2013
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Moderately escalated hypofractionated (chemo) radiotherapy delivered with helical intensity-modulated technique in stage III unresectable non-small cell lung cancer

Vittorio Donato[1], Stefano Arcangeli[1]*, Alessia Monaco[1], Cristina Caruso[1], Michele Cianciulli[1], Genoveva Boboc[1], Cinzia Chiostrini[1], Roberta Rauco[2] and Maria Cristina Pressello[2]

[1] Department of Radiotherapy, Azienda Ospedaliera S.Camillo-Forlanini, Rome, Italy
[2] Department of Medical Physics, Azienda Ospedaliera S. Camillo-Forlanini, Rome, Italy

Points of Discussion

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ORIGINAL REPORT

Dose-Limiting Toxicity After Hypofractionated Dose-Escalated Radiotherapy in Non–Small-Cell Lung Cancer

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57 Gy→85.5 Gy in 25 daily fractions
57Gy;63Gy;69Gy;75Gy;80Gy
No concurrent chemo
MTD: <20% risk of severe toxicity

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MTD = 63.25 Gy in 25 fractions !

= 70 Gy at 2Gy/fr

Grade 4-5 toxicity: 1.8% vs. 31% p=0.0036

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Table A3. Univariate Analysis of Grade 2 Radiation Pneumonitis

Variable	Coefficient	*P*
Chemotherapy, any	0.77	.35
Chemotherapy, adjuvant	1.49	.052
Age	0.013	.69
Bin	0.12	.66
Total dose delivered	−0.05	.30
PTV, cm^3	0.004	.028*
Lung dosimetry		
V5	4.4	.026
V10	4.9	.016
V20	3.7	.37
V30	11.4	.14
Mean	0.23	.027*

Table 2. Patients With Grade 4-5 Toxicity

Age (years)	Sex	Stage	Bin	Dose (Gy)*	Grade	Interval (months)†	Toxicity
69	M	IIIB	3	63.25	5	1.2	HSV/CMV pneumonitis; history of pre-RT low-dose methotrexate
66	F	IIA	1	85.5	5	55	Fatal hemoptysis
58	M	IIIB	3	75	5	7.9	Fatal hemoptysis
63	M	IIIB	1	75	5	1.6	Lung abscess
62	M	IIIA	3	75	5	8.1	Fatal hemoptysis and abscess
61	F	IV	3	75	4	10.3	Lung abscess, bronchocavitary fistula, tracheoesophageal fistula

Hypofractionation

- Rationale
- Clinical data
- Points of discussion
- Future directions

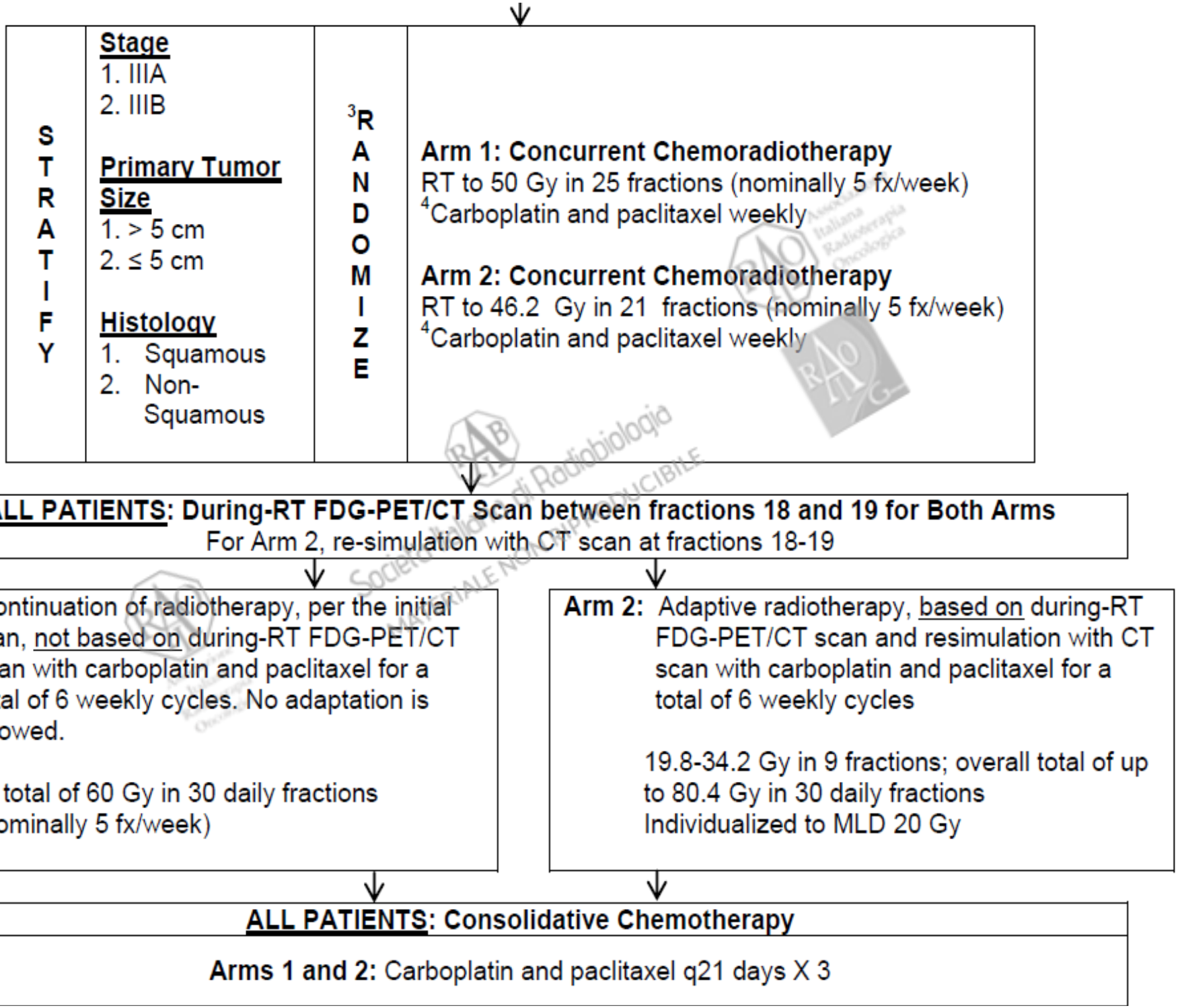
Società Italiana di Radiobiologia

XXVI CONGRESSO NAZIONALE AIRO
XXX CONGRESSO NAZIONALE AIRB
IX CONGRESSO NAZIONALE AIRO GIOVANI

NRG ONCOLOGY
ECOG-ACRIN

RTOG 1106/ACRIN 6697

RANDOMIZED PHASE II TRIAL OF INDIVIDUALIZED ADAPTIVE RADIOTHERAPY USING DURING-TREATMENT FDG-PET/CT AND MODERN TECHNOLOGY IN LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC) (1/26/16)


STRATIFY
Stage
1. IIIA
2. IIIB
Primary Tumor Size
1. > 5 cm
2. ≤ 5 cm
Histology
1. Squamous
2. Non-Squamous
[3]RANDOMIZE
Arm 1: Concurrent Chemoradiotherapy
RT to 50 Gy in 25 fractions (nominally 5 fx/week)
[4]Carboplatin and paclitaxel weekly
Arm 2: Concurrent Chemoradiotherapy
RT to 46.2 Gy in 21 fractions (nominally 5 fx/week)
[4]Carboplatin and paclitaxel weekly
ALL PATIENTS: During-RT FDG-PET/CT Scan between fractions 18 and 19 for Both Arms
For Arm 2, re-simulation with CT scan at fractions 18-19
Arm 1: Continuation of radiotherapy, per the initial plan, not based on during-RT FDG-PET/CT scan with carboplatin and paclitaxel for a total of 6 weekly cycles. No adaptation is allowed.
A total of 60 Gy in 30 daily fractions (nominally 5 fx/week)
Arm 2: Adaptive radiotherapy, based on during-RT FDG-PET/CT scan and resimulation with CT scan with carboplatin and paclitaxel for a total of 6 weekly cycles
19.8-34.2 Gy in 9 fractions; overall total of up to 80.4 Gy in 30 daily fractions
Individualized to MLD 20 Gy
ALL PATIENTS: Consolidative Chemotherapy
Arms 1 and 2: Carboplatin and paclitaxel q21 days X 3

Conclusions:

- No randomized data on conventional vs. hypofractionated RT
- Caution: DLTs exist!
- Encouraging results are published
- Future trials are justified

Thank you for your attention!

marco.trovo@cro.it