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CLINICAL PRACTICE GUIDELINES

European Lung Cancer Working Party Clinical Practice Guidelines Non-small Cell Lung Cancer: II. Unresectable Non-metastatic Stages

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ABSTRACT

The present guidelines on the management of unresectable non-metastatic non-small cell lung cancer (NSCLC) were formulated by the ELCWP in October 2005. They are designed to answer the following eight questions: 1) Is chest irradiation curative for NSCLC? 2) What are the contra-indications (anatomical or functional) to chest irradiation? 3) Does the addition of chemotherapy add an advantage to radiotherapy? 4) Does the addition of radiotherapy add an advantage to chemotherapy? 5) Is irradiation as effective as surgery for marginally resectable stage III? 6) How to best combine chemotherapy with radiotherapy: sequentially, concomitantly, as consolidation, as induction, as radiosensitiser? 7) In case of too advanced locoregional disease, is there a role for consolidation (salvage) local treatment (surgery or radiotherapy) after induction chemotherapy? 8) In 2005, what are the technical characteristics of an adequate radiotherapy?

INTRODUCTION

This is the second of a series of five articles, reporting clinical practice guidelines for lung cancer, formulated by the European Lung Cancer Working Party (ELCWP). The articles will consecutively present the recommended treatment of early (resectable) stages of non-small cell lung cancer (NSCLC), locoregionally advanced NSCLC, metastatic NSCLC and small-cell lung cancer (SCLC) of limited and extensive stage. The rationale of the reasons and methodology used for those guidelines has been previously reported.

After an extensive discussion, a consensus was reached among members of the Group to formulate the guidelines of treatment of the unresectable non-metastatic stages of non-small lung cancer on the basis of eight predefined essential questions: 1) Is chest irradiation curative for NSCLC? 2) What are the contra-indications (anatomical or functional) to chest irradiation? 3) Does the addition of chemotherapy

add an advantage to radiotherapy? 4) Does the addition of radiotherapy add an advantage to chemotherapy? 5) Is irradiation as effective as surgery for marginally resectable stage III? 6) How to best combine chemotherapy with radiotherapy: sequentially, concomitantly, as consolidation, as induction, as radiosensitiser? 7) In case of too advanced locoregional disease, is there a role for consolidation (salvage) local treatment (surgery or radiotherapy) after induction chemotherapy? 8) In 2005, what are the technical characteristics of an adequate radiotherapy?

Those questions have been extensively discussed during a meeting organised in April 2005 in Brussels, in Belgium. The present consensus has been definitively approved by the Group in a final meeting in Bruges, in October 2005.

METHODOLOGY

Guidelines were established on the basis of the various data published in the literature: clinical trials, systematic reviews and meta-analyses, guidelines from medical societies or groups. Literature was identified and analysed by the evidence-based medicine group of the ELCWP. The quality of the published guidelines was assessed with the use of the AGREE instrument [1,2], allowing elimination of the worst ones and use of the best available ones for the establishment of our own guidelines. The following guidelines were selected: ASCO (American Society of Clinical Oncology) [3,4], BTS (British Thoracic Society) [5], Cancer Care Ontario Practice Guidelines [6], Royal College of Radiologists [7], American College of Chest Physicians (ACCP) [8] and FNCLCC (Fédération Nationale des Centres de Lutte contre le Cancer) [9]. Selection was based on the previous assessment of the literature performed by the ACCP [10], and it was completed by the analysis using AGREE instrument of other guidelines that had not been taken into consideration. This approach allowed the addition of the FNCLCC and ACCP guidelines to the list.

QUESTION 1: IS CHEST IRRADIATION CURATIVE FOR NSCLC?

There is no published series of patients with unresectable locoregional NSCLC, treated with elective chest irradiation alone for which cure (more than 5-year disease-free survival) was documented. Evidence is indirect, mainly obtained from the control arms of randomised trials treated with irradiation alone or by extrapolation from series of inoperable patients with resectable NSCLC (stages I and II).

From the historical point of view, the first report of lung cancer treated with irradiation (low energy x-ray) was presented in 1915 by Cole from the Memorial Sloan Kettering Cancer Centre in New-York [11]. In 1942, Leddy at the Mayo Clinic in Rochester obtained a 4% 5-year survival in a series of 125 patients treated with irradiation (135-200 kV energy). Megavoltage irradiation was introduced in Canada in the late forties; in 1968, data from the Memorial Center of the period 1949 to 1960 were reviewed. A total of 1047 patients were treated with external irradiation and only two five-year survivors were observed .

In the meta-analysis of the NSCLC Collaborative Group [12], there was a total of 893 patients in the control arms of the trials testing irradiation with or without chemotherapy. Twenty- five patients were alive and followed up at 5 years but no information is available about their cancer status and the concomitant administration of other treatments. In a review of the literature about the curative role of radiotherapy, Damstrup and Poulsen identified many uncontrolled studies of patients with inoperable or unresectable tumours, showing a 1-year survival rate ranging from 29 to 58% and a 5-year survival rate ranging 4-10% [13]. The data were not analysed by disease stage. A systematic review of radical radiotherapy for stage I/II NSCLC in patients not sufficiently fit for or declining surgery (medically inoperable) was performed by Rowell and Williams [14]. The authors identified two randomised (including the CHART trial [15] comparing two radiotherapy fractionation schedules) and 35 non- randomised trials, with more than two thousands patients. Overall 5-year survival ranged from 0 to 42%. These data were fully analysed in the guidelines of the FNCLCC [16] for the management of stage I and II NSCLC treated by radiotherapy alone.

Recommendation: the curative role of radiotherapy for unresectable stage III NSCLC is not fully demonstrated. Chest radiotherapy can probably cure less than 5% of those patients (level of evidence: uncontrolled series of patients). Chest irradiation should, in this situation, be combined with chemotherapy.

QUESTION 2: WHAT ARE THE CONTRA-INDICATIONS (ANATOMICAL OR FUNCTIONAL)TO CHEST IRRADIATION?

ASCO, ACCP, FNCLCC and Ontario Cancer Care Practice provide evidence of some contra-indications to chest irradiation without mentioning data supporting their recommendations.

These contra-indications to radical radiotherapy include poor performance status (ECOG 2-3), weight loss >5-10%, inadequate pulmonary function and metastatic disease confined to the thorax. In fact, some contra-indications are relative and others absolute. They are related to the general condition of the patient and the existence of comorbidities, the presence of pulmonary diseases compromising lung function and the extent of the tumour. A prerequisite for the administration of radical radiotherapy is the possibility to treat all the disease in a single irradiation field (including the primary tumour and lymph nodes involved). Presence of extrathoracic or intrathoracic (including pleural involvement)

metastases is considered as an absolute contra-indication for curative irradiation. The size of the field is limited by the potential risk of lung toxicity, namely radiation pneumonitis. Various attempts have been made to define parameters derived from the dose-volume histogram to predict toxicity and define the ability to perform chest irradiation [17]. These parameters include the Vdose (percentage of CT-defined total lung volume receiving greater or equal than a threshold dose like 20, 25 or 30 Gy), the mean lung dose (MLP) or the normal time complication probability (NTCP). Despite the fact that they are related to the risk of developing radiation pneumonitis, their precision is insufficient to recommend their routine use.

Recommendation: Radical radiotherapy should be limited to non- metastatic tumours that can be treated within a single field, provided that there is adequate pulmonary function, lack of severe comorbidity and an acceptable general medical condition. All these parameters should be assessed by an experienced radiotherapist (level of evidence: experts opinion).

QUESTION 3: DOES THE ADDITION OF CHEMOTHERAPY ADD AN ADVANTAGE TO RADIOTHERAPY?

Today, none of the guidelines of other scientific societies - ASCO, ACCP, FNCLCC, Ontario Cancer Care Practice – recommend radical chest irradiation alone. Instead they recommend combined administration of radiotherapy and platinum-based chemotherapy.

The evidence that chemotherapy adds an advantage to radical chest irradiation comes from multiple randomised trials (Tables I and II) and meta-analyses (Table III). Randomised studies have compared radiotherapy alone with induction chemotherapy followed by irradiation or with radiosensitisation using cytotoxic drugs, mainly platinum derivatives. There are 12 "modern" trials having tested induction chemotherapy in this indication [18-32]. They are summarised in table I. Five have resulted in a statistically significant improvement in survival, confirmed by a specific meta-analysis [33]. Concerning chemotherapy induced radiosensitisation, 10 randomised trials are available as shown in table II [34-43]. Four indicate significantly improved survival, confirmed by two specific meta-analysis [33,44] (Table III).

Recommendation: Radical chest irradiation should not be administered as a single modality treatment in unresectable stage III NSCLC. It should be combined with platinum-based chemotherapy (level of evidence: multiple randomised trials and meta-analysis).

QUESTION 4: DOES THE ADDITION OF RADIOTHERAPY ADD AN ADVANTAGE TO CHEMOTHERAPY?

Data are too limited to adequately address this question. Indeed, almost all randomised trials have been using chest irradiation alone, as a control arm. Only three trials, summarised in table IV, have tested chemotherapy with or without thoracic radiotherapy [45-47]. The trial by Johnson *et al* [45] failed to show significant survival difference between treatment with Vindesine alone, radiotherapy alone or combination of both. This study can be strongly criticised because both chemotherapy regimen and radiotherapy techniques used are obsolete. In the Kubota trial, the addition of radical chest irradiation after two courses of cisplatin-based chemotherapy resulted in significantly improved survival [46]. Comparing, in responders to three courses of MIP chemotherapy, three further courses of the same chemotherapy versus the addition of radical radiotherapy, the ELCWP group demonstrated significant benefit in terms of local control in favour of the combined modality approach [47]. A Scandinavian trial comparing chest irradiation (40 Gy) with chemotherapy (cisplatin + etoposide) found no significant difference in survival but in this study the dose of irradiation administered was palliative, not with a curative intent [48].

Recommendation: Combined radiochemotherapy should be administered instead of chemotherapy alone in unresectable stage III NSCLC (level of evidence: two randomised trials).

QUESTION 5: IS IRRADIATION AS EFFECTIVE AS SURGERY FOR MARGINALLY RESECTABLE STAGE III?

The preferred local treatment of Stage IIIA N2 disease is controversial. Surgery, radical radiotherapy or both have been proposed. The threshold between resectable and unresectable disease differs from surgeon to surgeon and there is a lack of published randomised trials on the topic, excepting a small feasibility study [49]. Very recently, at the ASCO 2005 and at the World Conference of Lung Cancer, two large trials were presented about the role of surgery in stage IIIA N2 NSCLC.

In the North American INT 0139 trial, patients with initially resectable N2 disease were randomised between bimodality (chemotherapy with cisplatin and etoposide + radiotherapy) and trimodality (same + surgery) approaches. A total of 396 eligible patients were enrolled and there was no significant difference in survival between both arms. Surgery was nevertheless associated with improved progression-free survival. In addition, pneumonectomy, especially if complex, e.g. intrapericardial, appeared associated with a particularly high mortality (22% if standard and 29% if complex), while lobectomy had a very low mortality (1%). It is thus possible that surgery is beneficial, when a pneumonectomy is not required. In the EORTC trial 08941, enrolled patients had to have pathologically proven stage IIIA N2 NSCLC considered to be unresectable by the surgeon. Three courses of platinum-based chemotherapy was administered and in case

TABLE I. Randomised trials comparing sequential chemotherapy and radiotherapy with irradiation alone (OR: objective response; MST: median survival time; yr: year; mo: month; pts: patients; CPA: cyclophosphamide; ADR: adriamycine; CDDP: cisplatin; RT: radiotherapy; NA: not available; S: significant; NS: not significant; VBL: vinblastine; MTX: methotrexate; VDS: vindesine; Ifo: ifosfamide; MMC: mitomycin C).

Reference	treatment	n pts	OR (%)	MST (mo)	2 yr survival	p
Mattson,	1. CPA-ADR-CDDP (2x) then RT (55Gy)	76	49	NA	NA	S
1988 [18]	2. RT (55Gy)	78	44	NA	NA	
Dillman,	1. CDDP-VBL (2x) then RT (60Gy)	78	46	13.8	26%	S
1990 [19;20]	2. RT (60Gy)	77	35	9.7	13%	
Morton,	1. MTX-ADR-CPA-CCNU (2x) then (60 Gy)	56	55	10.	21%	NS
1991 [21]	2. RT (60 Gy)	58	64	10.	16%	
Le Chevalier,	1. VDS-CPA-CDDP-CCNU (3x) then (65 Gy)	176	31	12	21%	S
1991 [22;23]	2. RT (65 Gy)	177	35	10	14%	
Gregor,	1. CDDP-VDS (2x) then RT (50 Gy)	39	62	12.1	NA	NS
1993 [24]	2. RT (50 Gy)	39	42	12.4	NA	
Crino,	1. CDDP-VP16 (3x) then RT (56 Gy)	29	53	12.1	28%	NS
1993 [25]	2. RT (56 Gy)	32	32	8.4	14%	
Wolf,	1. Ifo-VDS (2x) then RT (50 Gy)	37	57	13.7	24 %	S
1997 [26]	2. RT (50 Gy)	41	41	9	12%	
Sause,	1. CDDP-VBL (2x) then RT (60 Gy)	164		13.8	NA	S
1995 [27,28]	2. RT (60 Gy)	163		11.4	NA	
	3. bifractionated RT (69.6 Gy)	163		12.3	NA	
Planting,	1. CDDP-VDS (2x) then RT (55Gy)	37	41	12.0		NS
1996 [29]	2. RT (55 Gy)	33	55	12.0		
Brodin,	1. CDDP-VP16 (2x) then RT (56 Gy)	163	26	11	21%	NS
1996 [30]	2. RT (56 Gy)	164	25	10.5	17%	
Cullen,	I. MMC-Ifo-CDDP	223	54	12		NS
1999 [31]	II. RT	223		10		
Mattson,	I. Docetaxel (x3) then RT	134	28	14.8		NS
2003 [32]	II. RT	140		12.6		

of response, patients were randomised between surgery (plus optional postoperative radiotherapy) or chest irradiation. On 572 registered patients, 333 were randomised. No significant difference in survival was observed, with median survival time and 5 year survival rates of 16.4 months and 15.7% for surgery and 17.5 months and 14% for radiotherapy, respectively. Postoperative mortality was 4%.

Recommendation: Treatment of marginally resectable stage IIIA N2 NSCLC should be multimodal and contains in any case chemotherapy. The choice between surgery and radical radiotherapy as local treatment should be based on the resectability of the disease after chemotherapy, on the possibility to include the disease in a single irradiation field and on the local capacities of the centre. Inclusion of those patients in clinical trials is highly recommended (level of evidence: unpublished randomised trials and expert opinion).

QUESTION 6: HOW TO BEST COMBINE CHEMOTHERAPY AND RADIOTHERAPY: SEQUENTIALLY, CONCOMITANTLY, AS CONSOLIDATION, AS INDUCTION, AS RADIOSENSITISER?

In their guidelines, the FNLCC recommends the sequential approach (induction chemotherapy followed by chest irradiation) and the ACCP concurrent chemoradiotherapy in stage IIIB.

Evidence from randomised clinical trials is limited.

TABLE II. Randomised trials comparing irradiation with or without radiosensisation by chemotherapy (OR: objective response; MST: median survival time; yr: year; mo: month; wk: week; d: day; pts: patients; CDDP: cisplatin; RT: radiotherapy; CBDCA: carboplatin; NS: not significant; VBL: vinblastine).

reference	Thoracic RT	chemotherapy	n	MST	2 yr survival	p
Schaake-Koning, 1992 [34]	30 Gy/10 x + 25 Gy/10x (split)	I. -	108		13%	
		II. CDDP (30 mg/m^2/wk)	98		19%	0.04
		III. CDDP (6 mg/m^2/d)	102		26%	
Trovo, 1992 [35]	45 Gy/15x	I. -	88	10.3 mo		NS
		II. CDDP (6 mg/m^2/d)	85	10.0 mo		
Blanke, 1993 [36]	60-65 Gy	I. -	111	46 wk	13%	NS
		II. CDDP (70 mg/m^2/3 wk)	104	43 wk	18%	
Jeremic, 1995 [37]	64,8 Gy (bifractionated)	I. -	61	8 mo	25%	
		II. 1x/wk CBDCA (100 mg d1,2) + VP 16 (100 mg d1,2,3)	52	18 mo	35%	0,002
		III. 1x/2wk CBDCA (20 mg d1,2) + VP16 (100 mg d1-5)	56	13 mo	27%	NS
Jeremic, 1996 [38]	69,6 Gy (bifractionated)	I. -	65	14 mo	26%	
		II. CBDCA (50 mg/d) + VP16 (50 mg/d)	65	21 mo	43%	0,02
Bonner, 1998 [39]	60 Gy	I. -	33			NS
		II. CDDP(30x3) - VP16 (100x3) x 2	32			
Ball, 1999 [43]	60 Gy 1x/d	I. -	53			NS
		II. CBDCA (70 d1-5)	54			
	60 Gy 2x/d	III -	46			
		IV. CBDCA (70 d1-5)	51			
Clamon, 1999 [40]	60 Gy d50 after 2 induction courses by CDDP-VBL	I. –	120	13 mo		NS
		II. CBDCA 100 mg/m^2/wk	130	13 mo		
Groen, 2004 [41]	60 Gy (2 Gy/d 5x/wk)	I. -	78	11.7 mo	28%	NS
		II. CBDCA 20 mg/m^2/d	82	11.8 mo	20%	
Cakir, 2004 [42]	64 Gy (2 Gy/d 5x/wk)	I. -	88		2% (3 yrs)	0.0002
		II. CDDP (20 d1-5)	88		10% (3 yrs)	

One phase II [50] and two phase III [51,52] randomised trials (table V) have been published comparing concomitant versus sequential approach. In all three, statistically significant improvement in survival was observed in favour of the concomitant treatment. Chemotherapy used consisted of cisplatin-based regimens. There are only two randomised trials comparing various platinum-based regimens in that indication (table VI). The first was a phase II design and the second a phase III [54], both failing to show better results with higher dosage of chemotherapy [53].

Recommendation: When radiochemotherapy has to be administered, the concomitant approach should be preferred to the sequential one. Chemotherapy should be cisplatin-based (level of evidence: two randomised controlled phase III trials). There are no data in favour of radiochemotherapy as induction treatment rather than as consolidation treatment or in favour of radiosensitisation by platinum derivatives instead of administering full radiochemotherapy.

QUESTION 7: IN CASE OF TOO ADVANCED LOCOREGIONAL DISEASE, IS THERE A ROLE FOR CONSOLIDATION (SALVAGE) LOCAL TREATMENT (SURGERY OR RADIOTHERAPY) AFTER INDUCTION CHEMOTHERAPY?

There are no sufficient data on the topic, despite the fact

TABLE III. Meta-analyses of randomised trials performed in unresectable NSCLC (S: significant; NS: non significant; IMA: isolated meta-analysis; MAID: meta-analysis based on individual data of the trials; MASRL: meta-analysis performed in a systematic review of the literature)

Reference	Methodology	Outcome	Number of trials	Number of patients	Results
Chemotherapy added to radical radiotherapy					
Collaborative Group, 1995 [12]	MADI	Overall survival	22	3033	S
Marino, 1995 [58]	MASRL	Survival at 1 and 2 years	14	1887	S (cisplatin)
Pritchard, 1996 [59]	IMA	Survival at 1, 2, 3 years	14	2589	S
Induction chemotherapy before radical radiotherapy					
Sculier, 2001 [33]	MASRL	Overall survival	12	2274	S
Chemotherapy radiosensitising radical radiotherapy					
Sculier, 2001 [33]	MASRL	Overall survival	8	1360	S
Rakovitch, 2004 [44]	IMA	Survival at 1, 2, 3 years	10	1802	S

TABLE IV. Randomised trials comparing chemotherapy with radiotherapy (OR: objective response; NC: no change; MST: median survival time; yr: year; mo: month; wk: week; d: day; pts: patients; CDDP: cisplatin; RT: radiotherapy; NA: not available; S: significant; NS: not significant; VDS: vindesine; Ifo: ifosfamide; MMC: mitomycin C).

reference	treatment	stage	n	% OR	MST	3 yrs survival (%)	p
Johnson, 1990 [45]	I. VDS	Unresectable	106	10	10.1 mo	7	
	II. RT (60 Gy)		106	30	8.6 mo	5	NS
	III. RT + VDS		107	34	9.4 mo	7	
Kubota, 1994 [46]	OR or NC after 2 courses CDDP-VDS (± MMC ± VP16)	III					
	I. -		32	50	447 d	3	S
	II. RT (50-60 Gy)		31	52	461d	29	
Sculier, 1999 [47]	RO after 3 courses of MMC-Ifo-CDDP	III				(2 yrs)	
	I. 3 further courses of chemotherapy		60		42 wk	18	NS
	II. RT (60 Gy)		55		54 wk	22	

that administration of local treatment after good response sounds logical.

Recommendation: This question merits clinical investigations.

QUESTION 8: IN 2005, WHAT ARE THE TECHNICAL CHARACTERISTICS OF AN ADEQUATE RADIOTHERAPY?

Guidelines for lung cancer management do not provide clear recommendations for the technical aspects of radiotherapy. For ASCO, the dosage should be no less than the biologic equivalent of 60 Gy, in 1.8 to 2.0 Gy fractions. For ACCP, there are no convincing data that hyperfractionated radiotherapy is superior to standard, once-daily treatment. For FNCLCC, a minimal dose of 60 Gy with a conventional fractionation and a weekly dose of 10 Gy should be administered, split course should not be used. Treatment should consist of photons given by a high energy linear accelerator. The technical aspects should conform to the guidelines of the International Commission on Radiation Units (ICRU reports 29, 50 and 62) and to the recommendations of quality assurance programmes (such as those of the French Society of Oncological Radiotherapy). For Cancer Care Ontario Practice, chest irradiation should also be given at a dose of 60 Gy in 30

TABLE V. Randomised trials comparing concomitant with sequential chemoradiotherapy (OR: objective response; NC: no change; MST: median survival time; yr: year; mo: month; wk: week; d: day; pts: patients; CDDP: cisplatin; RT: radiotherapy; VDS: vindesine; MMC: mitomycin C; VBL: vinblastine; VNR: vinorelbine)

Reference	Treatment	Stage	N pts	RO %	MST	5 yr survival	p
Furuse, 1999 [51]	I. Concomitant: CDDP-MMC-VDS x 2 + RT (56Gy d2)	IIIA/B	156	89	16.5 mo	15.8%	0.04
	II. Sequential: CDDP-MMC-VDS x2 then RT (56Gy)		158	66	13.3 mo	8.9%	
Komaki, 2002 [50]	I. Concomitant: CDDP-VP16 + RT (69,6 Gy d1 bid)		81	71	15.5 mo	15.5%	
	II. Sequential: 2 x CDDP-VBL then RT (63 Gy d50) sensitised by CDDP		81	73	16.4 mo	13%	
Zatloukal, 2004 [52]	I. Concomitant: CDDP-VNR (4 cycles) + RT (60 Gy J4 cycle 2)	IIIA/B	52	80	16.6 mo		0.023
	II. Sequential: CDDP-VNR x 4 then RT (60 Gy)		50	47	12.9 mo		

TABLE VI. Randomised trials comparing various induction chemotherapy regimens (OR: objective response; MST: median survival time; yr: year; mo: month; pts: patients; CDDP: cisplatin; RT: radiotherapy; NS: not significant; gemci: gemcitabine; Ifo: ifosfamide; MMC: mitomycin C).

Reference	modality	regimen	N pts	OR	MST	2 yr survival	p
Vokes, 2002 [55]	induction chemotherapy followed by consolidation radiochemotherapy	I. CDDP-gemci then RT-CDDP-gemci	62	40%	18.3 m	37%	
		II. CDDP- paclitaxel then RT-CDDP-paclitaxel	58	33%	14.8 m	29%	
		III. CDDP-vinorelbine then RT-CDDP-vinorelbine	55	45%	17.7 m	40%	
Sculier, 2004 [56]	induction chemotherapy followed by consolidation radiotherapy (60 Gy)	I. MIP: MMC (6 mg/m^2) + Ifo (3 g/m^2) + CDDP (50 mg/m^2)	176	35%	12.5 m		NS
		II. SuperMIP: MMC (6 mg/m^2) + Ifo (4.5 g/m^2) + CDDP (60 mg/m^2) + carboplatin (200 mg/m^2)	175	46%	11.2 m		

fractions over a 6-week period. Hyperfractionated accelerated radiotherapy should be performed only in the context of trials. Hypofractionation or split course should be used only for palliative purposes.

Evidence is mainly based on experts opinion. There are no published randomised trials having tested technical aspects (such as hyperfactionation or FDG-PET for volume delineation) in the context of a combined modality approach with chemotherapy for stage III NSCLC. The EORTC Radiotherapy Group has published, in 2004, literature-based recommendations for treatment planning and administration of radical radiotherapy for lung cancer [55]. Those recommendations concern patient's positioning, planning CT scan (with the use of spiral CT scan), accounting for tumour mobility, generating target volumes, treatment planning (has to be three-dimensional), treatment delivery and evaluation of response and toxicity. Target volume should use the ICRU 50 definitions [56] for the gross tumour volume (GTV), the clinical target volume (CTV) and planning target volume (PTV). There are insufficient data to support the use of elective modal irradiation for any patient. FDG-PET scans are superior to CT scan for staging mediastinal nodes and incorporation of the FDG-PET findings into CT-based planning scan results in changes to radiotherapy plans in a significant proportion

of patients [57].

Recommendation: Standard dosage with daily treatment and a minimal dose of at least 60 Gy over 6 weeks is recommended for routine practice. EORTC Radiotherapy Group recommendations should be respected for treatment planning and administration of radiotherapy.

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