Dutch National Study to the palliative effect of irradiation comparing two different treatment schemes in Non-Small-Cell-Lung-Cancer (NSCLC).

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON25269

Source
NTR

Brief title
0G98/009 LUNGTRIAL

Sponsors and support

Source(s) of monetary or material Support: This study was financially supported by the Dutch Health Care Insurance Board (College voor Zorgverzekeringen) as CVKO study OG98/009

Intervention

Outcome measures

Primary outcome

Palliation of thoracic symptoms measured over 52 weeks after randomization.
The data collection schedule for follow-up is presented in table 2.

A maximum of 33 questionnaires per patient would be sent in case follow-up could be

completed. The first questionnaire was given before randomization, the last questionnaire in the 52nd week after randomization.

Data about effectiveness of the treatment and QOL were based on the Rotterdam Symptom Checklist (10). Seven symptoms could be scored each on a four point validated scale from 1 (no complaints) to 4 (severe complaints) (10). The baseline total symptom score had to be 8 indicating that the patient had at least one tumor related complaint.
The maximum total symptom score could be 28 indicating the patient had all seven complaints in the worst degree.
After response the lowest total symptom score could be 7, having no complaints at all.
Palliation was defined as a average total score below the baseline score.

Secondary outcome

Toxicity, Quality of Life (QOL), and survival.

Quality of life was measured using the EuroQol classification system (EQ-5D), consisting of five questions on mobility, self-care, usual activities, pain/discomfort, and anxiety/depression (11).

In addition, information about acute toxicity as nausea, vomiting, and radiation esophagitis induced dysphagia was collected, based on the NCIC CTG Expanded Common Toxicity Criteria (12).
Patients were also asked to provide information about costs. Together with quality of life data, these data will be published separately in a cost-utility analysis.

Follow up after 52 weeks was continued by the datamanager, who made 3-monthly inquiries after survival of the patient.

Study description

Background summary

Introduction:

The treatment of Non-Small-Cell-Lung-Cancer (NSCLC) is still a challenge for the oncologist. In the last decade combined modality treatment in stage III and chemotherapy in stage IV improved the survival and quality of life (QOL) in NSCLC patients (1). Unfortunately a vast majority of patients will not be fit enough to undergo these intensive treatments (2). And those who underwent chemotherapy as palliative treatment may eventually still suffer from loco-regional complaints.
In general, hemoptysis, chest pain, dysphagia, and dyspnea can all be effectively palliated with acceptable toxicity with all kinds of different radiation treatment schemes (3). The effectiveness of these different treatment schemes however varies for each different

symptom and is most effective for hemoptysis and chest pain in patients with ECOG 2-3 (4). Which dose should be given is still controversial (5). In the first MRC-trial reported in 1991 no differences in palliative effect and in survival were seen between 13 x 3 Gy and 2 x 8.5 Gy (6). In a second MRC study in 1992 (7) for poor prognostic patients only, no differences in palliation or survival were seen between 10 Gy single dose and 2 x 8.5 Gy. However in a study by Bezjak et al. (8) a difference in survival between 20 Gy in 5 fractions and a 10 Gy single dose was demonstrated in favor of the multi-fractionation treatment. In a group-analysis, however, this survival advantage was not seen in patients with an ECOG score of 2 or more. Later data suggested a survival advantage of 13 x 3 Gy over 2 x 8.5 Gy in patients with good performance status (9). For patients in a bad general condition it still has to be proven whether 2 x 8.5 Gy is equally effective as 10 x 3 Gy.

Based on these findings radiation oncologists in the Netherlands could not reach consensus on the appropriate fractionation schedule for palliative irradiation of bad prognosis NSCLC patients.

The presented study therefore was focused on patients with bad general condition and/or significant weight loss with stage III NSCLC or stage IV patients, not suitable for chemotherapy, comparing 10 x 3 Gy with 2 x 8 Gy.

Purpose:

This multicenter randomized National Study compared the efficacy of 2x8 Gy versus our standard 10x3 Gy in patients with inoperable stage IIIA/B (with ECOG score 2-4 and/or substantial weight loss) and stage IV Non-Small-Cell Lung Cancer (NSCLC).

Patients and Methods:

Primary endpoint was the palliative effect in seven symptoms. Treatments would be different if the average score differed more than 1 point over the initial 39 weeks. Also the course of the symptom score of both treatments was evaluated.

Secondary endpoints were toxicity and survival.

Between January 1999 and June 2002, 297 patients of the 303 included in the study were eligible and randomized to receive either 10 x 3 Gy or 2 x 8 Gy by external beam irradiation.

Results:

Both treatment arms were equally effective, as the average total symptom score over the initial 39 weeks did not differ. However, the pattern in time of these scores differed significantly ($p<0.001$) in time. The duration of the palliative effect in the 10 x 3 Gy arm continued longer till week 22 and was less progressive in intensity than in the 2 x 8 Gy arm.

Survival in the 10 x 3 Gy arm was with a 1-year survival of 19.6% significantly ($p=0.0299$) better than the 10.9% in the 2 x 8 Gy arm.

Conclusion:

The 10 x 3 Gy radiotherapy schedule is preferred over the 2 x 8 Gy schedule as palliative treatment, because of the substantial gain in survival and the longer duration of the palliative response.

Study objective

We expected both treatment arms to have an equal outcome for palliation as for prognosis, because of the above-mentioned results of the MRC studies (6).

Study design

N/A

Intervention

Patients were randomized, without stratification, either to the multiple fractionation scheme of 10 x 3 Gy, 4 - 5 times a week, or the hypofractionation scheme of 2 x 8 Gy, given at day 1 and day 8.

Irradiation was given with two opposing anterior-posterior fields with 6 - 18 MV photon beams.

The treatment portals encompassed the tumor with a margin of 1 ½ - 2 cm including adjacent pathological lymph nodes. No limitations were set for the Target Volume. Dose calculation was not corrected for tissue inhomogeneities.

Co-medication, including corticosteroids and analgetics, and extra oxygen supply were allowed and registered.

Contacts

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Eligibility criteria

Inclusion criteria

1. The diagnosis NSCLC had to be cytologically or histologically confirmed;

2. Tumor stage was IIIA or IIIB in combination with performance status 3 – 4 and/or a weight loss of more than 5% in 3 months or >10% in 6 months prior to diagnosis;

3. Also patients with stage IV NSCLC, not suitable for chemotherapeutic treatment, were included;

4. Patients had to have a minimum total symptom score of 8, indicating a score >1 for at least one of the following complaints caused by the tumor itself: loss of appetite, dyspnea, chest pain, coughing, hemoptysis, hoarseness and/or dysphagia;

5. Furthermore, the patient should be physically and mentally fit enough to participate in this study.

Exclusion criteria

Patients having a Superior Vena Cava Syndrome (SVCS) at presentation, prior radiotherapy to

the chest and/or other malignant diseases in the past, or concurrent chemotherapy were excluded.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-01-1999
Enrollment:	303
Type:	Actual

Ethics review

Positive opinion

Date:	09-09-2005
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL222
NTR-old	NTR260
Other	: N/A
ISRCTN	ISRCTN04886579

Study results

Summary results
J Clin Oncol. 2005 May 1;23(13):2962-70.

Results presented:
1. orally
at 10th World Conference on Lung Cancer 10-14 August 2003, Vancouver, Canada

G.W.P.M. Kramer, S.L. Wanders, E.M. Noordijk, E.J.A. Vonk, A.L.J. Uitterhoeve, J. Bussink, A.H.D. van de Leest, J.C. van Houwelingen, W.B. van den Hout, R.B. Geskus, J.-W.H. Leer
Randomized Dutch National study of the effect of irradiation with different treatment schemes in the palliation of Non-Small-Cell Lung-Cancer (NSCLC);

2. Abstract
of 10th World Conference on Lung Cancer 10-14 August 2003, Vancouver, Canada
G.W.P.M. Kramer, S.L. Wanders, E.M. Noordijk et al.
Randomized Dutch National study of the effect of irradiation with different treatment schemes in the palliation of Non-Small-Cell Lung-Cancer (NSCLC) Lung Cancer: Vol 41; S2: pag.S38.