NCIC Clinical Trials Group

RADIATION ONCOLOGISTS' FORUM

AGENDA

Hilton Montreal Bonaventure
Friday, April 28th, 2005 - 9:00 a.m. – 12:00 p.m.
Room: Cote St. Luc

Chair: John Hay

9:00 am.	Introduction	John Hay
9:05	Update: Accel'd hypofractionated 3D Conformal RT as curative treatment for Stage 1 medically inoperable NSLC - BR 25	Patrick Cheung
9:15	Update: SC-20.	Jackson Wu
9:20	A phase III double-blind study of Dexamethasone vs. Placebo in the Prophylaxis of radiation-induced Pain Flare following palliative radiotherapy for bone metastases.	Jackson Wu
9:40	Hypofractionated radiotherapy in early Prostate Cancer 2 proposals	Carole Lambert Dilip Panjwani
10:10	Ph 2 trial of carboplatin and XRT for patients with bladder cancer	Jonathan Greenland
10:30	*Coffee*	
11.0	Metachronous malignancy surveillance of ENT patients in remission from their initial cancer	Libni Eapen
11:20	Canadian Partial Breast Irradiation Trial.	Tim Whelan
11:30	Radiation Oncology Quality Assurance Committee	Peter Dixon

NATIONAL CANCER INSTITUTE OF CANADA CLINICAL TRIALS GROUP (NCIC CTG)

A PHASE II STUDY OF ACCELERATED HYPOFRACTIONATED 3-DIMENSIONAL CONFORMAL RADIOTHERAPY (3DCRT) FOR INOPERABLE STAGE I/II NON-SMALL CELL LUNG CANCER (NSCLC)

NCIC CTG Protocol Number: BR.25

STUDY CO-CHAIRS:PATRICK CHEUNG, SERGIO FARIA

TRIAL COMMITTEE: ISLAM MOHAMED, DORIANNE RHEAUME, FRANCES SHEPHERD, COLUM SMITH, JIM WRIGHT, YEE UNG

TREATMENT SCHEMA

This is a multi-centre, prospective, single arm, phase II trial measuring local tumour control, toxicity, and survival in medically inoperable patients with stage I/II (peripheral T1-3, N0, M0) non-small cell lung cancer (NSCLC) treated with an accelerated, hypofractionated course of radiotherapy alone.

T1-2 (≤5 cm), T3 (≤ 5 cm, chest wall tumours only), N0, M0
NSCLC
(peripheral tumours only, see section 5.1 and 5.2 for details)

Registration
Radiotherapy must begin within 21 days of registration

3-dimensional conformal radiotherapy, 60 Gy in once daily
4 Gy fractions (Monday to Friday) over 3 weeks

Follow-Up for 5 years

Planned Sample Size: 80

Primary Endpoint:

- Local tumour control rate at two years

Secondary Endpoints:

- Toxicity
- Rates of regional and distant recurrence
- Progression free survival
- Overall survival
- Changes in pulmonary function
- Quality of Life

Concept Proposal: **A phase III double-blind study of Dexamethasone vs. Placebo in the Prophylaxis of radiation-induced Pain Flare following palliative radiotherapy for bone metastases (Pain Flare Prevention Study)**

Investigators: Edward Chow, Graeme Duncan, Andrew Loblaw, Rebecca Wong, Jackson Wu

Objectives:
1. To determine the effectiveness of dexamethasone in preventing radiation induced pain flare
2. To examine the toxicity of a brief course of dexamethasone
3. To correlate the pain flare (or not) with pain relief at 6 weeks after palliative RT.

Primary Endpoints:
Complete control of pain flare during and for 5 days after the completion of palliative RT

> Pain flare is defined as a 2-point increase on the worst pain score (0-10) compared to baseline worst pain level or a 25% increase in daily oral morphine equivalent
> To distinguish pain flare from pain progression (confounding), the worst pain score and analgesic intake must to return baseline levels after the flare.

Secondary Endpoints:
- Complete control of pain flare from day 6-10 after the completion of RT
- Quality of life
- Toxicity

Study Population:
Include: Cancer patients planned for palliative RT (single 8 Gy) for bone metastases. KPS $\geq$ 40. Patient able to isolate pain intensity score at the treatment (irradiated) site.
Exclusion: any oral steroid at baseline, diabetes, pathologic fracture at irradiated site, spinal cord compression, language barrier

Treatment Arms:

RANDOMIZE		Dexamethasone 4mg po at least one hour before RT and then once a day for 3 days after RT
		Placebo po OD at least one hour before RT and then once a day for 3 days after RT

Study Period:
Day of RT to 6 weeks post treatment

Data Collection:
- Brief Pain Inventory and EORTC QLQC30 (baseline and 6-week F/U)
- 10-day **diary** of worst-pain-score and pain medications, with telephone reminder.

Sample Size:
Total 110 patients. Assume control arm 30% pain flare be reduced to 5% with dexamethasone. Alpha=0.05 (1-tailed) and beta=0.1 (i.e. power=0.9), requires a sample size of 42 patients. Including 30% attrition rate, 55 patients in each arm.

Hypofractionated treatment of patients with prostate cancer.

There are two proposals which may be combined. Dr Lambert's trial is already accruing patients

ÉTUDE DE PHASE I-II D'UN RÉGIME HYPOFRACTIONNÉ DE RADIOTHÉRAPIE DE 45 GY EN 9 FRACTIONS SUR 9 SEMAINES POUR LE TRAITEMENT DU CANCER DE LA PROSTATE DE FAIBLE RISQUE (HYPO-1)

CAROLE LAMBERT

Objectifs de l'étude

Primaires
- -la toxicité aiguë
- -la toxicité tardive

Secondaires
- -le contrôle biochimique à 5 ans

Randomisation

T1c-T2a, Gleason $\leq$ 6 et APS $\leq$ 10ng/ml	45 Gy en 9 fx de 5 Gy, 1 fraction/semaine

Nombre de patients

Nous prévoyons recruter dans l'étude un total de 150 patients, dont environ 60-70 au CHUM, Hôpital Notre-Dame.

Critères d'éligibilité

1-Patients porteurs d'un adénocarcinome de la prostate non traité de stade T1 ou T2a, de grade de Gleason inférieur ou égal à 6 et avec un APS inférieur ou égal à 10. Le grade de Gleason doit être obtenu par la lecture pathologique d'au moins 6 spécimens provenant des deux lobes prostatiques prélevés sous guidage échographique.

2-Bon statut de performance (ECOG/ZUBROD 0-1).
3-Les patients doivent signer un formulaire de consentement avant de débuter l'étude.
4-Aucune évidence de maladie ganglionnaire au CT-SCAN abdomino-pelvien.
5-Le patient doit avoir une espérance de vie estimée de plus de 10 ans.

6-Les patients avec une histoire antérieure de cancer sont éligibles à condition qu'ils soient sans évidence de maladie depuis plus de 5 ans. Les patients porteurs de cancers basocellulaires ou épidermoïdes de la peau sont éligibles.
7-Le patient doit être disponible pour le traitement et les visites de suivi.
8-Aucune évidence de maladie métastatique au questionnaire, à l'examen clinique ou aux épreuves de laboratoire. En cas de doute clinique, l'absence de maladie métastatique devra être confirmée par une scintigraphie osseuse et au besoin des études radiographiques négatives.

7.2 Critères d'inéligibilité

1-Patient porteur de problèmes médicaux sévères ou psychiatriques qui peuvent compromettre la compliance à l'étude.
2-Patient qui, selon son radio-oncologue, nécessite un traitement prophylactique des vésicules séminales.
3-Patient atteint d'une maladie intestinale inflammatoire active.
4-Patient sous hormonothérapie.

7.3 Évaluation initiale

1- Histoire (incluant évaluation des symptômes urinaires, digestifs et de la fonction sexuelle), questionnaire de qualité de vie EPIC, examen clinique et ÉCOG.
2- Histopathologie avec score de Gleason tel que décrit en 6.1.1. en dedans de 6 mois du début du traitement.
3- APS en dedans de quatre semaines avant le début du traitement.
4- CT-SCAN pelvien de stadification.

8- TECHNIQUE DE RADIOTHÉRAPIE

8.1 Horaire

-45 Gy en 9 fx de 5 Gy: un traitement par semaine pour un total de 9 semaines consécutives.

8.2 Matériel

-Accélérateur linéaire $\geq$ 10 MV, DSA 100 cm.
-Équipement nécessaire pour effectuer thérapie conforme 3-D.

8.3 Positionnement

-Patient traité en décubitus dorsal.
-Système d'immobilisation pieds-jambes (coussin personnalisé).

8.4 Planification
-Urétrographie pour définir la partie inférieure de la prostate.

-Une tomodensitométrie, avec contraste IV de préférence, est requise pour la planification. Acquérir les coupes CT dans les mêmes conditions qui prévaudront en cours de traitement (voir item 8.6). Obtenir des coupes CT $\leq$ 5mm au niveau du volume cible et $\leq$10 mm au delà de celui-ci .
-Délimiter le CTV, PTV, le volume du rectum, de la vessie ainsi que des 2 têtes fémorales.

8.5 Champs et volumes

8.5.1 Champs
-Une technique isocentrique à 5, 6, 7 ou 9 champs selon le centre participant.

8.5.2 Volumes
-GTV = la prostate dans sa totalité (limite inférieure à 9-10 mm au-dessus du pic de l'urétrogramme).
-Dans ce protocole, le GTV (Gross Tumor Volume) = CTV (Clinical Tumor Volume).
-Le PTV (Planning Target Volume) est déterminé par l'ajout d'une marge de 1.0-1.5 cm dans toutes les directions sauf en postérieur où elle sera de 0.5-1 cm. Après 35 Gy, les marges pourraient être réduites à 0.5-1.0 cm dans toutes les directions. Les marges seront déterminées par chaque établissement selon la technique de localisation de la prostate utilisée.
-Les vésicules séminales et les ganglions pelviens ne seront pas volontairement inclus dans les volumes de traitement.
-Les organes à risque suivants devront être délinéés : le rectum (de l'angle recto-sigmoïdien au sphincter anal), la vessie et les 2 têtes fémorales (jusqu'au niveau de la partie inférieure des tubérosités ischiales).

8.6 Dose et dosimétrie

-L'irradiation est délivrée au rythme de 5 Gy/fraction, une fraction par semaine pour un total de 45 Gy, selon l'horaire décrit en 8.1.
-La dose sera prescrite à l'isocentre, en autant que l'inhomogénéité respecte les recommandations de l'ICRU (-5%, +7%).
-Le calcul de la dose sera effectué sans correction de l'hétérogénéité tissulaire.
-Les limites de dose aux organes à risque suivants devraient être respectées:

	Pas plus de 15% du volume reçoit une dose qui excède	Pas plus de 30% du volume reçoit une dose qui excède	Pas plus de 50% du volume reçoit une dose qui excède
Vessie	49 Gy	45 Gy	40 Gy
Rectum	46 Gy	43 Gy	37 Gy

'Pure Hypofractionation' in early Prostate Cancer Dilip Panjwani

We are currently conducting a Phase I/II study on 'Pure Hypofractionation' in early Prostate Cancer, and the preliminary results show a very low acute GI toxicity and low GU toxicity, even without IMRT. The RT schedule is 6000cGy in 20 fractions over **8 weeks** for intermediate risk patients, and 5000cGy in 15 fractions over **7 weeks** for low risk patients. The radiobiological rationale is as follows:

- Given the very long potential doubling time for prostate cancer, the biochemical control rate should not be different from 'accelerated' hypofractionation (e.g. 6000/20 over 4 weeks).
- Given the rapid potential doubling time for epithelium, the acute toxicities should be less.
- Given that the major component of late rectal (and probably other hollow organ) toxicity is 'consequential' toxicity, the late rectal toxicity (and probably also late GU toxicity) should be less.

We are proposing a randomized trial to test Pure Hypofractionation vs. Accelerated Fractionation vs. Conventional Fractionation. Such a study would be uniquely able to answer quite definitively lingering questions about the alpha/beta ratio of prostate caner, potential doubling time of prostate cancer, and the importance of consequential toxicity's contribution to the total late toxicity for rectum and bladder.

Ph 2 trial of carboplatin and XRT for patients with bladder cancer. Jonathan Greenland

Category: Palliation

Trial design: phase 2

Inclusion: Locally advanced TCC urinary tract (bladder, ureter, renal pelvis, urethra) not eligible for radical therapy because of disease extent or co-morbidities at clinician's discretion. May be recurrent post cystectomy, but may not have had prior chemo/RT to abdomen/pelvis. Must have symptoms requiring treatment. Need to have been assessed by urologist, medical oncologist and radiation oncologist. Fairly broad inclusion criteria.

Radiotherapy: 40Gy/15 fractions to gross tumor + 1-1.5 cm to PTV (no attempt at treating clinically negative nodes on CT). 3D planning required

Chemotherapy: concurrent weekly carboplatin AUC 2 (3 cycles)

Endpoints: local control (primary); DFS, quality of life, OS (secondary)

Background: Many patients with locally advanced TCC urinary tract are elderly, have significant co-morbidities or have disease bulk, which precludes radical therapy. Palliative radiotherapy has generally been considered standard of care, although more recently chemotherapy alone using gemcytabine/cis or carboplatin has been shown to have significant benefit.
The combination of cisplatin/radical radiotherapy and maximal TURBT has been shown in phase 2 studies to have a significant rate of long-term disease control without cystectomy in younger, fit patients. Phase 3 data has established the superiority of radical chemo/RT over RT alone. There is limited retrospective data on the use of palliative RT alone, although from published data benefits are modest.

Because of the latter, some have been using low dose carboplatin combined with palliative radiotherapy for loco regional symptom control, including our institution. This combination remains relatively unproven; a larger prospective multicentre phase 2 investigation of this approach may be reasonable.

A PHASE 3 STUDY PROPOSAL FOR METACHRONOUS MALIGNANCY SURVEILLANCE OF ENT PATIENTS IN REMISSION FROM THEIR INITIAL CANCER

LIBNI EAPEN MD

HYPOTHESIS:

Regular PET scan surveillance of patients in remission from their first ENT squamous cell carcinoma will result in the diagnosis of twice the number of stage one and two metachronous cancers compared to current routine management.

RATIONALE:

Approximately 15-35% of patients who have a diagnosis of ENT mucosal squamous cell carcinoma develop other primary malignancies both within the aerodigestive tract as well as at other sites. Whilst these can occur synchronously with the initial index tumor the majority develop metachronously with a 10 year actuarial risk approximating 40%. Large European and North American trials have unfortunately demonstrated the inutility of currently available chemoprevention strategies in reducing this risk.The bleak outlook following the discovery of these subsequent new primaries partly reflects the advanced stage at which the diagnosis is made.In the absence of effective chemoprevention an alternate strategy is to pursue screening in an effort to diagnose these cancers at earlier, more curable stages.PET scanning in ENT cancer is being investigated as an aid to optimizing locoregional management. The sparse literature to date does demonstrate that these PET scans have a significant yield in the identification of both synchronous and metachronous primaries. This study will evaluate wether or not routine PET scan surveillance results in the diagnosis of a higher number of stages 1 and 2 metachronous malignancies compared to current routine care.Should this study demonstrate that PET scanning increases the diagnosis of these cancers at lower stages the potential survival impact of such an increase would require further research.

STUDY DESIGN:

Prospective randomized phase 3 trial.Patients who have no signs of recurrence two years following any curative cancer treatment for primary squamous cell carcinoma of the oral cavity,oropharynx,hypopharynx or larynx will be randomized between the experimental arm of q6monthly whole body PET scans(till the diagnosis of an incurable malignancy) or the standard arm of routine patient care. When the PET scan arm or routine non PET based surveillance arm yields the diagnosis of a second malignancy the diagnosed cancers will be fully staged as per the UICC TNM classification system.

ENDPOINTS: Primary endpoint will be the number of stage one and two cancers diagnosed in each arm.

Secondary endpoints will include the overall number and stage distribution of metachronous cancers,compliance of patients with the PET surveillance arm, false positive and false negative PET scan findings, economic analysis of dollar cost associated with diagnosis versus non diagnosis of early stage cancers.

PATIENT NUMBERS: Using the expected numbers of metachronous primaries available from the RTOG and EORTC data bases, we will accrue the required number of patients calculated to reject the null hypothesis that routine PET surveillance will not result in a doubling of the number of stage one and two cancers diagnosed compared to routine care.This is estimated to be approximately one hundred and fifty patients per arm.