NCIC CLINICAL TRIALS GROUP
SPRING MEETING OF PARTICIPANTS

DATA SAFETY MONITORING COMMITTEE
Friday, May 2, 2008

SUMMARY REPORT

Open NCI US-Affiliated Trials

MA.17R

A double blind re-randomization to letrozole or placebo for women completing five years of adjuvant letrozole in the MA.17 study
Activation Date: October 14, 2004

As requested by the DSMC following Fall Meeting, the MA.17R study team supplied a report indicating how it will attempt to increase accrual.

Recommendation: The DSMC reviewed this information and agreed this strategy should increase accrual. Review in the Fall.

Director Response: Recommendation accepted

MA.27

A randomized phase III trial of exemestane versus anastrozole in postmenopausal women with receptor positive primary breast cancer
Activation Date: June 2, 2003

On 1 April 2008, the trial biostatistician provided the DSMC with the first of two planned interim analyses. The Committee did not have any issues with regard to the analysis or the trial.

Recommendation: The DSMC recommended that the trial should continue as planned.

Director Response: Recommendation accepted

MA.27B

The influence of five years of adjuvant anastrozole or exemestane on bone mineral density in postmenopausal women with primary breast cancer - a companion study to MA.27
Activation Date: April 24, 2006

There were no toxicity or accrual issues with this trial.

Recommendation: No concerns. Review at Fall Meeting.

Director Response: Recommendation accepted

PR.11

A Phase III Study of Active Surveillance Therapy Against Radical Treatment in Patients Diagnosed with Favourable Risk Prostate Cancer (START)
Activation Date: June 15, 2007

Accrual is getting off to a relatively slow start. The DSMC will have a better sense of accrual by Fall Meeting. There were no toxicity concerns.

Recommendation: Review at Fall Meeting.

Director Response: Recommendation accepted

Closed NCI US-affiliated Trials

BR.19

A phase III prospective randomized double blind placebo controlled trial of the epidermal growth factor receptor antagonist ZD1839 (IRESSA) in completely resected Stage 1B, II, and IIIA non-small cell lung cancer
Closing Date: April 22, 2005

The final analysis of BR.19 is date-determined, not event-determined. The BR.19 Trial Committee is considering whether the date of the scheduled final analysis could be moved up in order to meet timelines for submitting an abstract to the 2009 meeting of the American Society of Clinical Oncology and requested the advice of the DSMC.

Recommendation: If the Trial Committee is requesting permission to conduct an earlier analysis, the DSMC agrees.

Director Response: Recommendation accepted. The Trial Committee will prepare an analysis for the 2009 meeting of the American Society of Clinical Oncology

HD.6

A phase III study of radiotherapy or ABVD plus radiotherapy versus ABVD alone in the treatment of early stage Hodgkin's disease
Closing Date: April 05, 2002

There were no issues with this trial.

Recommendation: No action required. Review in the Fall.

Director Response: Recommendation accepted

PR.3

Intergroup (NCIC CTG, CUOG, SWOG, MRC-UK) phase III randomized trial comparing total androgen blockade versus total androgen blockade plus pelvic irradiation in clinical adenocarcinoma of the prostate
Closing Date: August 31, 2005

This trial is in follow-up mode. The event rate was reviewed and it is recognized that a protocol-mandated interim analysis will not occur until there have been 281 deaths. The DSMC did not identify reasons to request an earlier analysis. This analysis will focus on the primary outcome.

Recommendation: No action required. Review in the Fall.

Director Response: Recommendation accepted

PR.7

A phase III randomized trial comparing intermittent versus continuous androgen suppression for patients with Prostate-Specific-Antigen progression in the clinical absence of distant metastases following radiotherapy for prostate cancer
Closed to accrual: November 30, 2005

The issues related to this trial were clarified by the Trial Committee in the last couple of months. The Director has indicated in his trial summary report to the DSMC that Central Office has taken steps to ensure that the consent forms related to the risk of hormonal therapies with respect to vascular events are included in a standardized manner across each of these trials.

Recommendation: No action required. Review in the Fall.

Director Response: Recommendation accepted

Open Non-NCI US-Affiliated Trials

BI.1

Phase III Trial Of Combined Gemcitabine Plus Capecitabine Chemotherapy Versus Gemcitabine Alone In Advanced Biliary Cancer
Activation Date: March 19, 2008

This trial was only recently activated.

Recommendation: No concerns. Review in the Fall.

Director Response: Recommendation accepted

BL.11

A phase III study of Iressa® in combination with intravesical BCG versus intravesical BCG alone in high risk superficial transitional cell carcinoma of the bladder
Activation Date: April 12, 2006

Accrual continues to be an issue.

Recommendation: Request report from trial team at Fall Meeting indicating its plan to increase accrual.

Director Response: Recommendation accepted

CE.5S

Socio-behavioral Study: Work, Marriage/Social Support, Anxiety and Depression
Activation Date: June 11, 2007

Since there is no intervention being studied on this trial, it likely can be removed the from DSMC agenda.

Recommendation: Will clarify review of this trial with the Director. If the DSMC does need to review, then it needs to know in what context and what it should be reviewing.

Director Response: Recommendation accepted; this sub-trial will be withdrawn from routine DSMC oversight.

CE.6

A Randomized Phase III Study of Temozolomide and Short-Course Radiation vs. Short-Course Radiation Alone in the Treatment of Newly Diagnosed Glioblastoma Multiforme in Elderly Patients
Activation Date: May 1, 2007

This trial is just getting off the ground. Accrual appears to be getting off to a slow start.

Recommendation: Review accrual at the Fall Meeting. Request information regarding the planned accrual period.

Director Response: Recommendation accepted. The Trial Committee will update planned vs actual accrual at the Fall 2009 meeting.

CO.20

A Phase III Randomized Study of Brivanib Alaninate (BMS-582664) in Combination with Cetuximab (Erbitux) Versus Placebo in Combination with Cetuximab (Erbitux) in Patients Previously Treated With Combination Chemotherapy for Metastatic Colorectal Carcinoma
Activation Date: February 5, 2008

This trial was just activated.

Recommendation: No action required. Review at Fall Meeting.

Director Response: Recommendation accepted

HN.4

A phase II study of cisplatin and gemcitabine in patients with locally advanced/ recurrent or metastatic malignant salivary gland tumours
Activation Date: October 23, 2003

As per the DSMC recommendation of the Fall 2007 meeting, this trial is scheduled to close to accrual on May 5 short of reaching its targeted accrual. In the last 6 months, no patients have been put on study.

Recommendation: Request follow-up information from the Trial Committee explaining why accrual was slow.

Director Response: Recommendation accepted; a summary of analysis of trial results and interpretation for its conduct details will be provided by the Trial Committee to the DSMC.

LY.12

A phase III study of gemcitabine, dexamethasone, and cisplatin compared to dexamethasone, cytarabine, and cisplatin plus/minus rituximab as salvage chemotherapy for patients with relapsed or refractory aggressive histology non-hodgkin's lymphoma prior to autologous stem cell transplant and followed by maintenance rituximab versus observation
Activation Date: August 7, 2003

On 21 April 2008, the DSMC received the interim analysis. The trial was to accrue 630 patients over 3 years. To date, 392 patients have been accrued with recent accrual being in the range of 6-7 patients per month.

Recommendation: Trial should continue. The trial team should make every effort to improve accrual. Review at Fall Meeting.

Director Response: Recommendation accepted

LY.13

A multi-centre phase II trial investigating the efficacy and tolerability of bortezomib added to cyclophosphamide, vincristine, prednisone and rituximab (BCVP-R) for patients with advanced stage follicular non-hodgkin's lymphoma requiring systemic first-line treatment
Activation Date: December 14, 2006

There has been accrual of 26 of the planned 90 patients. There was no unexpected or severe neurotoxicity. There are not yet enough patients to evaluate response.

Recommendation: Study should continue. Review at Fall Meeting.

Director Response: Recommendation accepted

MA.22

A phase I/II study of increasing doses of epirubicin and docetaxel plus pegfilgrastim for locally advanced or inflammatory breast cancer
Activation Date: February 25, 2003

Accrual continues to be slow, but it does appear that the trial committee is taking steps to improve accrual.

Recommendation: Review at Fall Meeting.

Director Response: Recommendation accepted

MA.29

A Feasibility Study of Pre-Operative Sunitinib (SU11248) With Multiple Pharmacodynamic Endpoints in Patients with T1c-T3 Operable Carcinoma of the Breast
Activation Date: 12 March 2007

No centres have yet been locally activated although the trial was centrally activated in 2007.

Recommendation: Review at Fall Meeting.

Director Response: Recommendation accepted

MAP.3

A phase III randomized study of exemestane versus placebo in postmenopausal women at increased risk of developing breast cancer
Activation Date: February 11, 2004

This trial has suffered from slow accrual from the beginning. However, accrual has picked up since efforts have been made to bring in cooperative groups from Brazil and France. As a result, it appears that the trial will finish.

Recommendation: The DSMC encourages the collaborations with groups in France and Brazil. Review at Fall Meeting.

Director Response: Recommendation accepted

MAP.3B

The Influence of Five Years of Exemestane on Bone Mineral Density in Postmenopausal Women at Increased Risk of Developing Breast Cancer - A Companion Study to MAP.3
Activation Date: January 23, 2008

This trial was recently activated.

Recommendation: Review at Fall Meeting.

Director Response: Recommendation accepted

MY.10

A randomized phase III study of thalidomide and prednisone as maintenance therapy following autologous stem cell transplant in patients with multiple myeloma
Activation Date: September 16, 2002

On 14 April 2008, the DSMC received the second interim analysis. The trial is currently accruing about 5-6 patients per month.

Recommendation: The trial should continue with primary outcome to remain overall survival.

Director Response: Recommendation accepted

PR.12

Phase III Study of Neoadjuvant Docetaxel And Androgen Suppression Plus Radiation Therapy Versus Androgen Suppression Alone Plus Radiation Therapy For High-Risk Localized Adenocarcinoma Of The Prostate (DART)
Activation Date: March 3, 2008

This trial was recently activated.

Recommendation: Review at Fall Meeting.

Director Response: Recommendation accepted

SC.20 / SC.20U

A phase III international randomized trial of single versus multiple fractions for re-irradiation of painful bone metastases Activation Date: January 7, 2004 **AND** *A phase III study of the effect of re-irradiation for bone pain on urinary markers of osteoclast activity (Companion study of SC.20. Not an intervention study.)*

Accrual continues to be slow. An interim analysis is planned and the DSMC should receive it by Fall Meeting.

Recommendation: Review at Fall Meeting.

Director Response: Recommendation accepted

Closed Non-NCI US-Affiliated Trials

BR.24

A phase II/III double blind randomized trial of AZD2171 versus placebo in patients receiving paclitaxel/carboplatin chemotherapy for the treatment of advanced or metastatic non-small cell lung cancer
Activation Date: September 07, 2005
Closed: 25 February 2008 – as recommended by DSMC

The study has been closed.

Recommendation: No further action.

Director Response: Recommendation accepted

BR.25

A phase II study of hypofractionated 3-dimensional conformal radiotherapy (3DCRT) for inoperable stage I/II non-small cell lung cancer (NSCLC)
Activation Date: April 26, 2006
Closed: 18 April 2008 – Accrual met

This trial was recently closed.

Recommendation: No concerns.

Director Response: Recommendation accepted

HN.5

A phase I study of adjuvant OSI-774 (Tarceva) in patients following combined chemo-radiotherapy for locally advanced squamous cell carcinoma of the head and neck
Activation Date: November 5, 2003
Closed: 31 March 2008 – Accrual almost met (19 of 20 patients)

This trial was recently closed. No toxicity concerns.

Recommendation: No concerns.

Director Response: Recommendation accepted

MA.14

A randomized trial of antiestrogen therapy versus combined antiestrogen and octreotide LAR therapy in the adjuvant treatment of breast cancer in postmenopausal women
Closing Date: July 21, 2000

No need to review this trial since final analysis has been conducted and it is being presented at ASCO 2008.

Recommendation: No action required.

Director Response: Recommendation accepted

MA.20

A phase III study of regional radiation therapy in early breast cancer
Closing Date: February 2, 2007

There were no issues with this trial.
Recommendation: No concerns.

Director Response: Recommendation accepted

MA.21

A phase III adjuvant trial of sequenced EC + filgrastim + epoetin alfa followed by paclitaxel versus sequenced AC followed by paclitaxel versus CEF as therapy for premenopausal women and early postmenopausal women who have had potentially curative surgery for node positive or high risk node negative breast cancer
Closing Date: April 29, 2005

The DSMC is unsure as to when the next analyses are to be conducted. No concerns re toxicities.

Recommendation: Ask Trial Committee for a report of the timing of the next analysis.

Director Response: Recommendation accepted. The next protocol-defined analysis is to assess overall survival and is event rate-dependent. The event rate is updated with each report related to survival. The Trial Committee will update its projection for the analysis of oveall survival for the Fall 2008 DSMC meeting.

MY.11

A randomized phase II dose finding study of lenalidomide and melphalan in patients with previously untreated multiple myeloma
Activation Date: December 13, 2005
Closed: 27 March 2008

This trial was recently closed.

Recommendation: No concerns.

Director Response: Recommendation accepted; the trial will be withdrawn from DSMC review as it is now in preparation for its final analysis.

OV.16

A phase III study of cisplatin plus topotecan followed by paciltaxel plus carboplatin versus paclitaxel plus carboplatin as first line chemotherapy in women with newly diagnosed advanced epithelial ovarian cancer
Closing Date: June 29, 2005

No need to review this trial since final analysis has been conducted and it is being presented at ASCO 2008.

Recommendation: No action required.

Director Response: Recommendation accepted; as the primary analysis has been completed, the trial will be withdrawn from DSMC oversight.

PRP.1

A double-blind, placebo-controlled, randomized study of combination vitamin E, selenium and soy protein product in subjects with high grade prostatic intraepithelial neoplasia
Closing Date: July 23, 2004

The DSMC would like confirmation there were no follow-up issues regarding selenium and diabetes.

Recommendation: Request information from the Director regarding whether there were any further issues/follow-up (e.g., possibly screening patients who might be at higher risk).

Director Response: Recommendation accepted. All protocol therapy and follow-up was completed at the time of the selenium publication re diabetes. A notice to all investigators and REBs about the need to inform and assess patients was disseminated. The Trial Committee concluded that amending the protocol to continue follow-up and to re-evaluate all patients, including those who had completed all protocol-mandated interventions (including follow-up) was not feasible. There has been compliance with safety and regulatory accountabilities with the notifications described above.

This trial is undergoing its final analysis and can be withdrawn from DSMC oversight

PRP.1B

An investigation of molecular and genetic risk factors associated with development of prostate cancer in subjects with high grade prostatic intraepithelial neoplasia treated with placebo or combination vitamin E, selenium and soy protein product
Activation Date: July 29, 2005

Not an intervention study.

Recommendation: Request confirmation from the Director that this trial can be removed from the DSMC agenda.

Director Response: Recommendation accepted; this trial can be withdrawn from DSMC oversight.