The following protocol information is provided solely to describe how the authors conducted the research underlying the published report associated with the following article:

A phase III randomized, placebo-controlled trial of docetaxel with or without gefitinib in recurrent or metastatic head and neck cancer: an Eastern Cooperative Oncology Group trial

Argiris, et al

DOI: 10.1200/JCO.2012.45.4272

Eastern Cooperative Oncology Group

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TO: ECOG Clinical Research Associates and Investigators with Patients for E1302

FROM: ECOG Coordinating Center

DATE: July 9, 2008

SUBJECT: E1302, Addendum #8

This addendum has been reviewed and approved by the Central IRB.

Enclosed is Addendum #8, for E1302, *A Phase III Randomized, Placebo Controlled, Trial of Docetaxel Versus Docetaxel Plus ZD1839 (Iressa, Gefitinib) In Performance Status 2 Or Previously Treated Patients With Recurrent Or Metastatic Head And Neck Cancer.*

A revised cover sheet, indicating the date of the revisions, and replacement pages, incorporating the changes to the protocol, have been provided. Please remove the outdated pages and replace them with the enclosed cover and current pages. We recommend that each institution maintain a file containing the original protocol and all subsequent revisions. **A revised eligibility worksheet is attached.**

This addendum contains changes to the eligibility section. Full IRB review of this addendum is **recommended**. However, it is your IRB's decision whether full or expedited review is appropriate. This addendum must be submitted and reviewed by your IRB within 90 days of receipt of this notice, unless your local IRB has different written SOPs, which must be available at future ECOG audits.

Please note: The increased use of cetuximab in the initial radiotherapy of head and neck cancers has posed an increasing barrier to accrual to E1302. Eligibility has been amended to permit limited exposure to radiosensitizing doses of cetuximab only, if a suitable period has elapsed.

Addendum #8 includes the following changes:

1. Title Page: Changed the version date.
2. Schema: Added a fourth stratification factor: "Prior cetuximab treatment (yes or no)".
3. Section 3.5, Page 11: Added the following as a "NOTE": "The use of cetuximab given concurrently with radiation or chemoradiotherapy for up to 9 total weekly doses, as part of initial potentially curative therapy is allowed, if completed >6 months prior to registration." As a result of this change, sections 3.9 and 3.10 were pushed onto page 11a.
4. Section 4.4.4, Page 15: Added this subsection regarding the fourth stratification factor.
5. Section 4.7, Page 16: Updated this section regarding unblinding.
6. Section 5.11.2, Page 28: Revised the first bullet point to read as follows: "**Arm C**- the current NCI Agent-Specific Adverse Event List (Arm C was closed to accrual on 8/23/07, however adverse event reporting is required for patients still being treated on Arm C, as outlined below).
7. Section 8.2, Page 45: Updated the section titled "Emergency Unblinding".
8. Section 9.2, Page 50: Added a fourth stratification factor, "prior cetuximab treatment (yes vs no)" and changed the number of possible stratification combinations from 8 to 16.

9. Section 9.3, Page 50: In the first sentence, changed “3 stratification factors” to “4 stratification factors”.
10. Appendix Ia, Page 1: Changed the version date.
11. Appendix Ia, Page 12: In the last sentence of the 3rd paragraph, “…during the first two cycles of your treatment” was changed to “…throughout your treatment”.
12. Appendix Ib, Page 1: Changed the version date.
13. Appendix VII, Page 2: Per NCI’s request, the following wording was added to the “Special Materials or Substudies” section: “All specimens submitted for this study must be entered and tracked using the ECOG Sample Tracking System. Upon registering new patients to these studies, you can expect to receive an automatic email with instructions for logging into the system and shipping samples. You can also access the Tracking System from the CTSU Member Web Site. Go to the protocol number protocol page and click on the link provided under the Case Report Forms header. Questions may be sent to ecog.tst@jimmy.harvard.edu. Please refer to section 10.0 for details on how to use the ECOG Sample Tracking System.”

Enclosure

C: CTSU Ops Office

Eastern Cooperative Oncology Group

Phase III Randomized, Placebo Controlled, Trial Of Docetaxel Versus Docetaxel Plus ZD1839 (Iressa, Gefitinib) In Performance Status 2 or Previously Treated Patients With Recurrent Or Metastatic Head And Neck Cancer

	STUDY CHAIR:	Athanassios Argiris, M.D.
	STUDY CO-CHAIR:	Jill Gilbert, M.D.
Rev. 4/05	DEVELOPMENTAL THERAPEUTICS COMMITTEE CO-CHAIRS:	Manuel Hidalgo, M.D. Jill Kolesar, Pharm.D.
Rev. 3/07	STUDY STATISTICIAN:	Musie Ghebremichael, Ph.D.
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	HEAD AND NECK COMMITTEE CHAIR:	Arlene Forastiere, M.D.
Rev. 4/05	OUTCOMES COMMITTEE CHAIR:	David Cella, Ph.D.

Version Date: April 16, 2008

Update Date: 10/17/07

Rev. 9/07

STUDY PARTICIPANTS	***ACTIVATION DATE***
ECOG Entire Group CTSU	August 6, 2004 Addendums #1& #2 incorporated prior to activation Addendum #3, April 2005
ZD1839 (Iressa, gefitinib) NSC #715055, IND #61187	Addendum #4, June 2005 Addendum #5, March 2006 Update #1, August 2006 Addendum #6, March 2007 Addendum #7, September 2007 Update #2, September 2007 Update #3, October 2007 Addendum #8, July 2008

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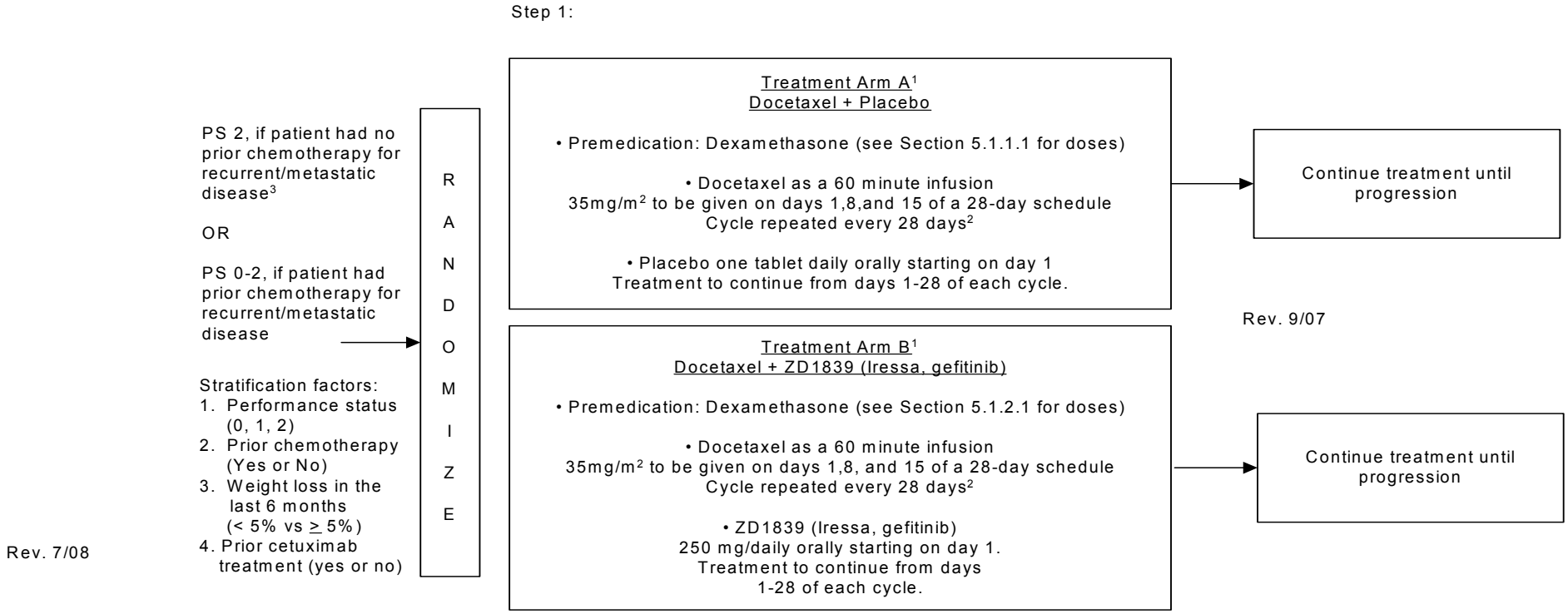
Schema



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NOTE: Docetaxel dose based on actual body weight.

1. Treatment ongoing until progression of disease, unacceptable toxicity or patient withdrawal.
2. 28 days = 1 cycle.
3. Patients who receive chemotherapy as part of potentially curative therapy of primary disease within 6 months of randomization will be considered as having prior chemotherapy for recurrent/metastatic disease, whereas patients who received chemotherapy as part of potentially curative therapy of primary disease > 6 months of randomization will be considered as having no prior chemotherapy for recurrent/metastatic disease.

Rev. 9/07 4. [Footnote deleted in Addendum #7]

Rev. 6/05
Rev. 4/05

_____ 3.5 No prior systemic EGFR inhibitors, such as ZD1839 (Iressa, gefitinib)/Iressa (AstraZeneca), ABX-EBX (Abgenix), MDX-447 (Medarex/Merck), OSI-774/Tarceva (OSI pharmaceuticals), C225/Cetuximab (ImClone), PKI166 (Novartis), CI-1033 (Parke-Davis), EKB-569 (Wyeth Ayerst). Treatment with paclitaxel is allowed if the patient did not progress while on paclitaxel.

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NOTE: The use of cetuximab given concurrently with radiation or chemoradiotherapy for up to 9 total weekly doses, as part of initial potentially curative therapy is allowed, if completed > 6 months prior to registration.

_____ 3.6 Patients must not be receiving any other investigational agent while on the study.

3.7 Patients must have either:

_____ Strata A

ECOG performance status 2 (in bed 50% of the time. Ambulatory and capable of all self-care, but unable to carry out any work activities. Up and about more than 50% of waking hours), AND no prior chemotherapy for recurrent metastatic head and neck cancer.

OR

_____ Strata B

PS 0-2 AND prior chemotherapy (i.e. one or more prior chemotherapy regimens (without docetaxel)) for locally recurrent/metastatic disease or exposure to prior chemotherapy (without docetaxel) as part of primary curative therapy ≤ 6 months prior to randomization.

Patients who receive chemotherapy as part of potentially curative therapy of primary disease within 6 months of randomization will be considered as having prior chemotherapy for recurrent/metastatic disease, whereas patients who received chemotherapy as part of potentially curative therapy of disease > 6 months of randomization will be considered as having no prior chemotherapy for recurrent/metastatic disease.

_____ 3.8 Patients must have fully recovered from the effects of any prior surgery, chemotherapy, or radiation therapy.

3.8.1 A minimum time period of 3 weeks must elapse between the completion of radiation therapy and randomization to the study.

3.8.2 A minimum period of 4 weeks must elapse between the last administration of any prior chemotherapy and randomization to the study.

3.8.3 At least 2 weeks must elapse between the last administration of biologic/targeted therapy and randomization to the study.

3.8.4 Patients must be ≥ 3 weeks since major surgery, or significant traumatic injury prior to randomization.

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_____ 3.9 No unstable systemic disease, including active infection, uncontrolled hypertension, unstable angina, congestive heart failure, or serious arrhythmia requiring medication.

3.10 CBC requirements $\leq$ 2 weeks prior to randomization:

_____ 3.10.1 Absolute neutrophil count (ANC) $\geq$ 1500 /mm^3

ANC: _____ Date of test: _____

_____ 3.10.2 Platelets $\geq$ 100,000 /mm^3

Platelet count: _____ Date of test: _____

_____ 3.10.3 Hemoglobin $\geq$ 8.0 g/dl

3.11 Hgb: _____ Date of test: _____

3.12 Chemistry requirements $\leq$ 2 weeks prior to randomization:

_____ 3.12.1 Bilirubin within normal limits

Bilirubin: _____ Date of test: _____

_____ 3.12.2 Alkaline phosphatase, SGOT (AST), and SGPT

SGOT (AST): _____ Date of test: _____

SGPT (ALT): _____ Date of test: _____

_____ 3.12.3 Creatinine < 2.0 or creatinine clearance of > 60 ml/min

Creatinine: _____ Date of test: _____

*AST/ALT level is based upon more abnormal of the two.

	AST or ALT:			
ALK PHOS:	**≤ ULN**	**>1x but ≤1.5x**	**>1.5x but ≤5x**	**>5x ULN**
≤ ULN	Eligible	Eligible	Eligible	Ineligible
>1x but ≤2.5x	Eligible	Eligible	Ineligible	Ineligible
>2.5x but ≤5x	Eligible	Ineligible	Ineligible	Ineligible
>5x ULN	Ineligible	Ineligible	Ineligible	Ineligible

_____ 3.13 No hypercalcemia related to head and neck cancer.

_____ 3.14 No known brain metastasis.

_____ 3.15 Age ≥ 18 years.

_____ 3.16 Females should not be pregnant or breast feeding because chemotherapy may be harmful to the fetus or the nursing infant. Also, the effects of ZD1839 (Iressa, gefitinib) on the developing human fetus are unknown.

_____ 3.17 All females of childbearing potential must have a blood test or urine study within 2 weeks prior to randomization to rule out pregnancy.

Female? _____ (Yes or No) Date of blood test or urine study:_____

_____ 3.18 Women of childbearing potential and sexually active males must use an accepted and effective method of contraception while on treatment and for three months after the completion of treatment.

_____ 3.19 Patients must have measurable or non-measurable disease based on RECIST (see Sec. 6.0). Baseline measurements and evaluations must be obtained ≤ 4 weeks of randomization. All areas of disease should be recorded and mapped out in order to assess response and uniformity of response to therapy. Disease in previously irradiated sites is considered measurable if there has been unequivocal disease progression or biopsy-proven residual carcinoma following radiation therapy. Persistent disease after radiotherapy must be biopsy proven at least 8 weeks after completion of radiation therapy.

3.19.1 Radiographic findings are acceptable providing that clear-cut measurements can be made.

_____ 3.20 Patients with a prior history of squamous cell or basal carcinoma of the skin or *in situ* cervical cancer must have been curatively treated. Patients with a history of other prior malignancy must have been treated with curative intent and must have remained disease-free for 5 years post diagnosis.

_____ 3.21 No current peripheral neuropathy ≥ grade 2 at time of randomization.

_____ 3.22 Patients must not have any co-existing condition that would preclude full compliance with the study.

_____ 3.23 No known hypersensitivity to ZD1839 (Iressa, gefitinib) or any excipients of this product. No prior history of severe hypersensitivity reaction to Docetaxel or other drugs formulated with polysorbate 80.

_____ 3.24 Drugs that are CYP3A4 inhibitors should be generally avoided and if possible, discontinued, 1 week prior to initiating study drug. However, if medically necessary, they can be taken with caution after consulting with the study chair. See Appendix IV for a complete list of inhibitors.

4.1.3.3 Patient demographics

4.1.3.3.1 Sex

4.1.3.3.2 Birth date (mm/yyyy)

4.1.3.3.3 Race

4.1.3.3.4 Ethnicity

4.1.3.3.5 Nine-digit ZIP code

4.1.3.3.6 Method of payment

4.2 Eligibility Verification

Patients must meet all of the eligibility requirements listed in section 3. An eligibility checklist has been appended to the protocol. A confirmation of registration will be forwarded by the ECOG Coordinating Center.

4.3 Additional Requirements

4.3.1 All patients must provide a signed and dated, written informed consent form.

Rev. 3/06, 3/07

4.3.2 [Section deleted in Addendum #6]

Rev. 3/06, 3/07

4.3.3 Correlative samples are to be submitted from patients participating in the additional laboratory studies as indicated in sections 10 and 11.

Rev. 3/06, 3/07

[Note and bullets deleted in Addendum #6]

4.4 Stratification Factors

Patients must have either:

4.4.1 PS 2, if there was no prior chemotherapy for recurrent/metastatic disease.

4.4.2 PS 0-2, if there was prior chemotherapy for recurrent/metastatic disease.

4.4.2.1 Patients who receive chemotherapy as part of potentially curative therapy of primary disease within 6 months of randomization will be considered as having prior chemotherapy for recurrent/metastatic disease, whereas patients who received chemotherapy as part of potentially curative therapy of disease > 6 months of randomization will be considered as having no prior chemotherapy for recurrent/metastatic disease.

4.4.3 Weight loss < 5% vs. $\geq$ 5% of total body weight in the last 6 months.

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4.4.4 Prior cetuximab treatment vs. no prior cetuximab treatment.

4.5 Instructions for Patients Who Do Not Start Assigned Protocol Treatment

If a patient does not receive any assigned protocol treatment, baseline and follow-up data will still be collected and must be submitted according to the instructions in the E1302 Forms Packet. Document the reason for not starting protocol treatment on one of the baseline forms. Also report the date and type of the first non-protocol treatment that the patient receives.

Rev. 9/07

4.6 [This section deleted in Addendum #7]

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4.7 Emergency Unblinding

NOTE: The information provided below is for the use by a physician, nurse, CRA or pharmacist treating the patient. These contact numbers should not be used by patients. Patients should be instructed to call their doctor's office in the event of an emergency or adverse event that may result in the need to unblind the patient.

In the event of an emergency or severe adverse reaction necessitating identification of the medication for the welfare of the patient, please contact the Study Chair, Dr. Athanassios Argiris, at 412-648-6619, first to ensure the reason for unblinding is valid. Then call a member of the ECOG Coordinating Center drug team at 617-632-3610 Monday through Friday between 9:00AM and 5:00PM Eastern Time. For unblinding outside of these hours, contact AnswerConnect at 1-866-296-8940. This service will request the reason for unblinding and then page the on-call ECOG staff who will return your call and provide the unblinded treatment assignment if applicable. Remember, AnswerConnect should only be contacted outside of normal business hours and only in the event of an emergency. The ECOG Coordinating Center or AnswerConnect will require the protocol number (i.e., "E1302"), the patient ID number (e.g., "99999"), and the patient initials (e.g., "FL") to unblind the patient. Please note that if a patient is emergently unblinded he/she is considered to be off-therapy and must discontinue protocol treatment. However, follow-up according to the protocol schedule is still required.

5.8 Extraordinary Medical Circumstances: If at any time the constraints of this protocol are detrimental to the patient's health, protocol treatment should be discontinued. In this event submit forms according to the instructions in the E1302 Forms Packet.

5.9 Patient withdraws consent.

5.10 Duration of Follow-up

For this protocol, all patients, including those who discontinue protocol therapy early, will be followed for survival for 5 years from the date of registration. All patients must also be followed through completion of all protocol therapy.

Rev. 3/06

5.11 Adverse Event Reporting Requirements

5.11.1 Purpose

Adverse event data collection and reporting, which are required as part of every clinical trial, are done to ensure the safety of patients enrolled in the studies as well as those who will enroll in future studies using similar agents. Adverse events are reported in a routine manner at scheduled times during a trial (please refer to the E1302 Forms Packet for the list of forms with directions for routine adverse event reporting). Additionally, certain adverse events must be reported in an expedited manner for more timely monitoring of patient safety and care. The following sections provide information about expedited reporting.

5.11.2 Determination of reporting requirements

Reporting requirements may include the following considerations: 1) whether the patient has received an investigational or commercial agent; 2) the characteristics of the adverse event including the grade (severity), the relationship to the study therapy (attribution), and the prior experience (expectedness) of the adverse event; 3) the phase (1, 2, or 3) of the trial; and 4) whether or not hospitalization or prolongation of hospitalization was associated with the event.

An investigational agent is a protocol drug administered under an Investigational New Drug Application (IND). In some instances, the investigational agent may be available commercially, but is actually being tested for indications not included in the approved package label.

Commercial agents are those agents not provided under an IND but obtained instead from a commercial source. The NCI, rather than a commercial distributor, may on some occasions distribute commercial agents for a trial.

When a study arm includes both investigational and commercial agents, the following rules apply.

- *Concurrent administration:* When an investigational agent(s) is used in combination with a commercial agent(s), the combination is considered to be investigational and expedited reporting of adverse events would follow the guidelines for investigational agents.

Steps to determine if an adverse event is to be reported in an expedited manner:

Step 1: *Identify the type of event using the NCI Common Terminology Criteria for Adverse Events (CTCAE) Version 3.0*. The CTCAE provides descriptive terminology and a grading scale for each adverse event listed. A copy of the CTCAE can be downloaded from the CTEP home page (http://ctep.cancer.gov). Additionally, if assistance is needed, the NCI has an Index to the CTCAE that provides help for classifying and locating terms. All appropriate treatment locations should have access to a copy of the CTCAE.

Step 2: *Grade the event using the NCI CTCAE*.

Step 3: *Determine whether the adverse event is related to the protocol therapy (investigational or commercial).* Attribution categories are as follows: Unrelated, Unlikely, Possible, Probable, and Definite.

Step 4: *Determine the prior experience of the adverse event*. *Expected* events are those that have been previously identified as resulting from administration of the agent. An adverse event is considered *unexpected*, for expedited reporting purposes only, when either the type of event or the severity of the event is **NOT** listed in:

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- **Arm C** – the current NCI Agent-Specific Adverse Event List (Arm C was closed to accrual on 8/23/07, however adverse event reporting is required for patients still being treated on Arm C, as outlined below)
- **Arm X (Arm A or B)** – the current NCI Agent-Specific Adverse Event List for the investigational agent or package insert/protocol for the commercial agents

NOTE: The NCI Agent-Specific Adverse Event List (ASAEL) is included in section 5.12 of the protocol. The ASAEL is a list of events that should be considered 'expected' for adverse reporting purposes. The ASAEL is located in the third column of the Comprehensive Adverse Event and Potential Risks (CAEPR) List in the third column and identified with ***bold*** and ***italicized*** text.

Step 5: *Review the "Additional instructions, requirements, and exceptions for protocol E1302" table in section 5.11.6 for protocol and/or ECOG specific requirements for expedited reporting of specific adverse events that require special monitoring.*

NOTE: For general questions regarding expedited reporting requirements, please contact the NCI Medical Help Desk: 301-897-7497.

5.11.3 Reporting methods

- **Arm X (Arm A or B) and Arm C**– This study requires that expedited adverse event reporting use the NCI's Adverse Expedited Reporting System (AdEERS). The NCI's guidelines for AdEERS can be found at http://ctep.cancer.gov. For questions regarding the use of the AdEERS application, please contact the NCI Technical Help Desk: 301-840-8202.

An AdEERS report must be submitted to ECOG and the appropriate regulatory agencies by one of the following methods:

- Electronically submit the report via the AdEERS Web-based application located at http://ctep.cancer.gov

  or

- Fax the completed NCI Adverse Event Expedited Report – Single Agent or Multiple Agents paper template located at http://ctep.cancer.gov to ECOG (617-632-2990), Attention: AE and the NCI (301-230-0159).

NOTE: Paper copies of AdEERS reports will only be accepted if the AdEERS system is down. Once the system is restored, a report submitted on a paper template must be entered into the AdEERS system by the original submitter of the report at the site.

Any supporting or follow up documentation must be faxed to ECOG (617-632-2990), Attention: AE. In addition, supporting or follow up documentation must be faxed to the NCI (301) 230-0159.

5.11.4 When to report an event in an expedited manner

Some adverse events require 24-hour notification (refer to Section 5.11.6). Please complete a 24-Hour Notification Report via the NCI AdEERS website (http://ctep.cancer.gov/reporting/adeers.html) within 24 hours of learning of the event. The full AdEERS report must be completed and submitted via AdEERS within 5 calendar days.

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Drug Transfers: Bottles **MAY NOT** be transferred from one patient to another patient or from one protocol to another protocol. All other transfers (e.g., a patient moves from one participating clinical site to another participating clinical site, the principal investigator at a given clinical site changes) must be approved **in advance** by the PMB. To obtain an approval for transfer, investigators should complete and submit to the PMB (fax number 301-480-4612) a Transfer Investigational Agent Form available on the NCI home page (http://ctep.cancer.gov) or by calling the PMB at 301-496-5725. The patient ID number (e.g., "44444"') and the patient initials (e.g., "FL") should be entered in the "Received on NCI Protocol No." and the "Transferred to NCI Protocol No." fields in addition to the protocol number (i.e., "**E1302**").

Drug Returns: **Only undispensed drug supplies should be returned to the PMB.** When it is necessary to return study drug (e.g., sealed bottles remaining when a patient permanently discontinues protocol treatment, expired bottles recalled by the PMB), investigators should return the study drug to the PMB using the NCI Return Agent Form available on the CTEP home page (http://ctep.cancer.gov) or by calling the PMB at 301-496-5725. The patient ID number (e.g., "44444") and the patient initials (e.g., "FL") should be entered in the "Lot Number" field. Opened bottles with remaining tablets should be documented in the patient-specific NCI Investigational Agent Accountability Record (i.e., logged in as "returned by patient" and logged out as "destroyed on site") and destroyed on-site in accordance with institutional policy.

Drug Accountability: The investigator, or a responsible party designated by the investigator, must maintain a careful record of the receipt, disposition, and return of all drugs received from the PMB using the NCI Investigational Agent Accountability Record available on the NCI home page (http://ctep.cancer.gov) or by calling the PMB at 301-496-5725. A separate NCI Investigational Agent Accountability Record must be maintained for each patient ID number (e.g., "44444") on this protocol.

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Emergency Unblinding:

NOTE: The information provided below is for the use by a physician, nurse, CRA or pharmacist treating the patient. These contact numbers should not be used by patients. Patients should be instructed to call their doctor's office in the event of an emergency or adverse event that may result in the need to unblind the patient.

In the event of an emergency or severe adverse reaction necessitating identification of the medication for the welfare of the patient, please contact the Study Chair, Dr. Athanassios Argiris, at 412-648-6619, first to ensure the reason for unblinding is valid. Then call a member of the ECOG Coordinating Center drug team at 617-632-3610 Monday through Friday between 9:00AM and 5:00PM Eastern Time. For unblinding outside of these hours, contact AnswerConnect at 1-866-296-8940. This service will request the reason for unblinding and then page the on-call ECOG staff who will return your call and provide the unblinded treatment assignment if applicable. Remember, AnswerConnect should only be contacted outside of normal business hours and only in the event of an emergency. The ECOG Coordinating Center or AnswerConnect will require the protocol number (i.e., "E1302"), the patient ID number (e.g., "99999"), and the patient initials (e.g., "FL") to unblind the patient. Please note that if a patient is emergently unblinded he/she is considered to be off-therapy and must discontinue protocol treatment. However, follow-up according to the protocol schedule is still required.

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8.2.1 Other names

Iressa, NSC #715055, ZD1839 (Iressa, gefitinib), IND # 61,187

8.2.2 Classification

Signal Transduction Inhibitor

8.2.3 Mode of action

Selective, reversible, inhibitor or EGFR tyrosine kinase.

8.2.4 How supplied

ZD1839 (Iressa, gefitinib) and matching placebo are supplied as round, biconvex, brown film-coated tablets containing either 250 mg of ZD1839 (Iressa, gefitinib) or 0 mg of ZD1839 (Iressa, gefitinib) (Placebo). Excipients in both tablets include lactose monhydrate, microcrystalline cellulose, croscarmellose sodium, povidone, sodium lauryl sulphate, and magnesium stearate. The tablet coating for both tablets includes hypromellose (methylhydroxypropylcellulose), macrogol 300 (polyethylene glycol 300), red iron oxide, yellow iron oxide, and titanium dioxide.

8.2.5 Storage and stability

ZD1839 (Iressa, gefitinib) tablets should be stored at room temperature 20° - 25° C (68° - 77° F) and protected from light. Shelf life stability testing of the intact bottles is ongoing.

8.2.6 Dose Specifics

Arm A

Placebo will be given at a dose of one (1) tablet orally each day starting on day 1 and continuing for days 1 to 28 of each cycle until progression.

Arm B

ZD1839 (Iressa, gefitinib) will be given at a dose of 250mg (1 tablet) orally each day starting on day 1 and continuing for days 1 to 28 of each cycle until progression.

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8.2.7 Preparation

If a patient forgets to take a dose, the last missed dose should be taken as soon as the patient remembers, as long as it is at least 12 hours before the next dose is due to be taken.

ZD1839 (Iressa, gefitinib) tablets cannot be crushed. Experimentation has shown that ZD1839 (Iressa, gefitinib) tablets will break up into a fine dispersion within 5 to 7 minutes when they are dropped whole into lukewarm water. There are no known risks to the chemical stability of ZD1839 (Iressa, gefitinib), providing this process occurs immediately before administration to the patient. There may be a risk to ensuring delivery of the whole dose because a certain

Rev. 3/06

8.2.10.2 Also reported on ZD1839 (Iressa, gefitinib) trials but with the relationship to Iressa still undetermined:

Allergy/immunology: allergic reactions including angioedema and urticaria (rare)

Bone/Bone Marrow: anemia, leukopenia, thrombocytopenia, neutropenia

Cardiovascular (Arrhythmia): tachycardia,

Cardiovascular (General): edema

Constitutional Symptoms: chills, weight loss, fatigue (asthenia, lethargy, malaise)

Dermatology/skin: alopecia, toxic epidermal necrolysis (rare), erythema multiforme (rare), rash, acneiform rash, dry skin, nail changes, pruritis/itching

Gastrointestinal: taste perversion, pancreatitis (rare), diarrhea, nausea, vomiting, anorexia, dehydration, dry mouth (xerostomia), mucositis/stomatitis

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Hemorrhage: tumor related hematuria, epistaxis, CNS hemorrhage

Hepatobiliary/pancreas: liver dysfunction

Hepatic: hyperbilirubinemia

Lymphatics: limb edema

Metabolic/Laboratory: hypokalemia, increased lactic dehydrogenase, hypofibrinogenemia, elevated ALT, AST, bilirubin, creatinine

Musculoskeletal: weakness

Neurology: depression, paraesthesia, motor neuropathy

Ocular/Visual: photophobia, ambylopia, dry eyes, eyelid infection, corneal infection, inflammation/corneal ulceration, aberrant eyelash growth

Pain: headache, back pain, abdominal pain, eye, muscle

Pulmonary/upper respiratory: pneumonitis/pulmonary infiltrates

Renal/Genitourinary: albuminuria, urinary frequency, proteinuria

Other: sudden death (2 cases)

Rev. 3/06

Also reported on ZD1839 trials but with the relationship to ZD1839 still undetermined:
allergic reaction; allergic rhinitis; decreased hemoglobin, leukocytes, and platelets; conduction abnormality; ventricular tachycardia; fibrinogen; elevated INR in patients taking Warfarin; rigors/chills; weight loss; sudden death; alopecia; erythema multiforme; seborrhea; urticaria; taste alteration; CNS hemorrhage; GI hemorrhage; lung hemorrhage; nose hemorrhage; urinary hemorrhage; pancreatitis; pneumonia with neutropenia; albuminuria; hypokalemia has been seen with diarrhea related to ZD1839; hypoproteinemia; proteinuria; muscle weakness; depression; motor neuropathy; sensory neuropathy; somnolence/depressed level of consciousness; blurred vision has been seen in patients with corneal abrasions related to ZD1839; corneal membrane sloughing; ocular ischemia/hemorrhage; photophobia has been seen in patients with corneal abrasions related to ZD1839; back pain; ARDS; cough, dyspnea and hypoxia have been seen with pneumonitis related to ZD1839; renal failure has been seen with diarrhea related to ZD1839; urinary frequency; acute vascular leak syndrome; thrombosis/thrombus/embolism

9. Statistical Considerations

9.1 Introduction

The major endpoint of this phase III randomized trial is the comparison of overall survival in poor prognosis SCCHN patients treated with docetaxel with or without ZD1839 (Iressa, gefitinib). Secondary endpoints include time to progression, response rate, and quality of life in these patients. Correlative studies of the expression and activation of the EGFR and signaling pathways and of the prevalence of common polymorphisms of CYP3a, EGFR, and pgp with clinical outcome will be conducted.

9.2 Randomization

Patients will be equally randomized to the two arms, docetaxel plus placebo arm (Arm A) and docetaxel plus ZD1839 (Iressa, gefitinib) arm (Arm B). Randomization will be stratified by prior chemotherapy status (pretreated/untreated), performance status (0, 1, 2), weight loss in the last 6 months (< 5% vs > 5%), and prior cetuximab treatment (yes vs no). Patients with performance status of 0 or 1 are eligible only if they had prior chemotherapy for recurrent/metastatic disease. Therefore, there are 16 possible stratification combinations. The sample size will be calculated based on the primary endpoint, overall survival.

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9.3 Accrual

The primary analysis of overall survival will be performed using a one-sided log-rank test stratified on the 4 stratification factors listed above, using an overall type I error of 2.5%. This will be an intention to treat analysis (defining groups by assigned treatment) on the subset of eligible patients. The study hypothesis is that patients on the docetaxel plus placebo arm will have a median survival of 6 months and that the addition of ZD1839 (Iressa, gefitinib) will increase the median survival by 40%, which corresponds to a difference in median survival of 6 versus 8.4 months, or a 28.6% reduction in the failure hazard rate assuming an exponential distribution. Allowing for the interim analysis plan discussed below, a total accrual of 314 eligible patients and a total information of 286 failures is needed to attain 80% power with 2.5% type I error. To allow for up to 5% of the patients to be ineligible, a total of 330 patients will be accrued. Assuming an accrual rate of 10 eligible patients per month, we expect to finish the accrual within 31.5 months, with an additional 13 months of follow-up.

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9.4 Data Monitoring and Early Stopping Rules

Interim analyses comparing overall survival between the two arms using the stratified log-rank test will be performed for all semi-annual DMC meetings beginning when approximately 25% of the planned full information has occurred, about 14.5 months after the study opens, continuing until either criteria for early stopping are met or full information is reached. 25% of the full information under the alternative hypothesis is equal to 72 failures. To preserve the overall type I error rate, critical values at the interim analyses will be determined using a truncated version of the Lan-DeMets error spending rate function corresponding to the O'Brien-Fleming boundary. Boundary values at a nominal significance less than 0.0005 will be truncated at 0.0005, with the boundary also adjusted to preserve the overall type I error rate of 2.5%.

Under the accrual and failure rate assumptions above, the following table gives the interim analysis times, information times, and the corresponding O'Brien Fleming boundary values. Because of delays in initiation of accrual and delays in data submission and processing, it is likely that the actual analysis times will be 6-12 months later.

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Appendix Ia

Suggested Patient Consent Form

Version Date: 4/16/08

You are being asked to take part in this study because you have a head and neck cancer that has spread to other parts of your body.

The standard treatment for your type of tumor is chemotherapy (anti-cancer medications). Several chemotherapy medications have been found to shrink tumors of the head and neck. Unfortunately, these agents can shrink or control the spread of tumor in only a few patients. Therefore, more effective treatments are needed.

This is a clinical trial (a type of research study). Clinical trials include only patients who choose to take part. Please take your time to make your decision and discuss it with your friends and family.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to compare the effects (good and bad) of chemotherapy (docetaxel) plus ZD1839 (Iressa, gefitinib) with docetaxel and placebo on the head and neck cancer to see which is better.

No study has yet compared ZD1839 (Iressa, gefitinib) and docetaxel in head and neck cancer. It is possible that the addition of ZD1839 (Iressa, gefitinib) to docetaxel will be more effective than docetaxel alone.

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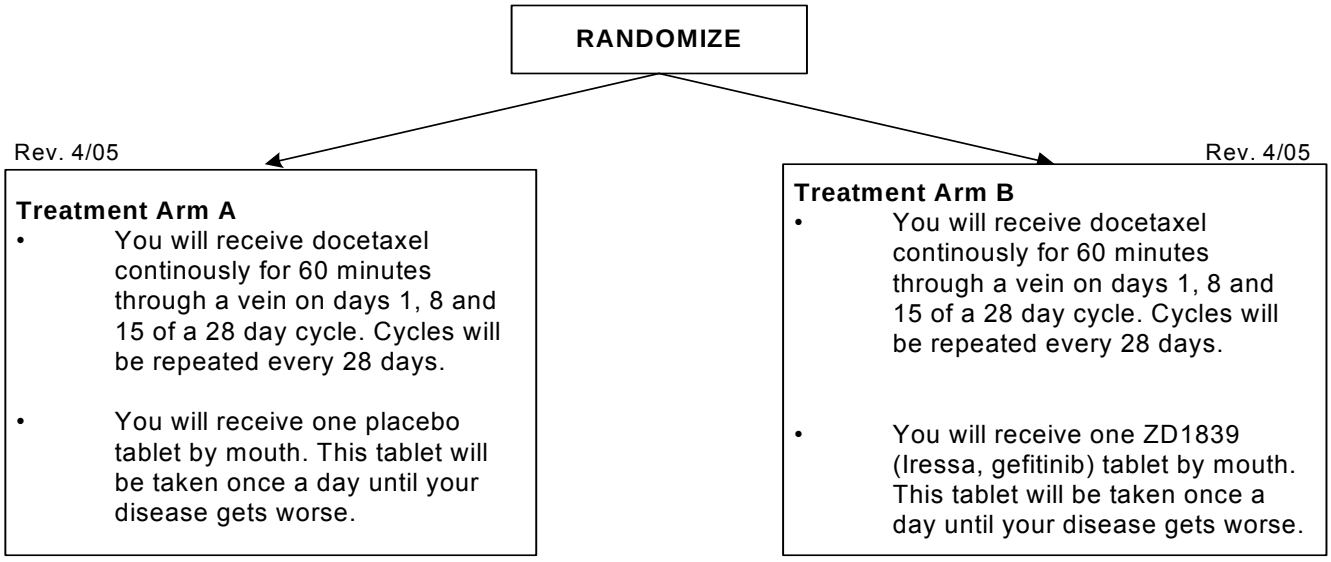
HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

About 330 people will take part in this study.

WHAT IS INVOLVED IN THIS STUDY?

STUDY PLAN



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WHAT ARE MY RIGHTS AS A PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part, or you may leave the study at any time. Leaving the study or choosing not to take part will not result in any penalty or loss of benefits to which you are entitled.

We will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

A Data Safety and Monitoring Board, which is an independent group of experts, will be reviewing the data from this research throughout the study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or a research-related injury, contact your study doctor,

_____ at _____ .

For questions about your rights as a research participant, contact the *[NAME OF CENTER]* Institutional Review Board, which is a group of people who review the research to protect your rights) at _____.

You may also call the Project Office of the NCI Central Institutional Review Board (CIRB) at 888-657-3711 (from the continental US only)

WHERE CAN I GET MORE INFORMATION?

You may call the **National Cancer Institute's (NCI's) Cancer Information Service**.
Voice: **1-800-4-CANCER (1-800-422-6237)**
TTY: **1-800-332-8615**

Visit the NCI Websites:

For clinical trials information go to http://cancer.gov/clinicaltrials
For cancer information go to http://cancer.gov/cancerinformation

You will get a copy of this form.

Upon request, you will also receive a copy of the protocol (full study plan.)

SIGNATURE

I agree to take part in this study.

Participant: _____ Date: _____

RELATED STUDIES

This study includes one or more optional laboratory tests that will analyze small samples of tissue and blood. If you participate in these optional studies, samples of your original biopsy and samples of blood collected throughout your course of treatment will be sent to designated laboratories for analysis.

Rev. 4/05 The tissue samples will be from your original diagnostic biopsy and will not require any further procedure. Blood samples will be taken before you start the treatment for your cancer and 4 weeks after you begin therapy. These samples will be tested to learn more about how your cancer works and how your cells may respond to the therapy.

Rev. 3/06, 4/05, 3/07 On day 1 and day 15 of the first two cycles of your treatment, additional blood samples will be obtained to study levels of docetaxel and ZD1839 in your blood. On these days, blood samples (3-4 teaspoons) will be taken before your treatment (even before you take your ZD1839/placebo) and 1-4 hours after the docetaxel infusion is done. Again, it is important that you take your ZD1839/placebo pill in hospital or clinic on these four days so the first blood draw is before you have had any treatment that day. An additional blood sample, about 2 teaspoons, may be collected at times of your routine blood draws throughout your treatment.

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Researchers will perform these tests in order to understand differences in types of head and neck cancer treatments. They hope this will help them better understand your type of cancer. The results from these tests will not be sent to you or your doctor, and they will not be used in planning your care. You or your insurance company will not be charged for these tests. These tests are only for research purposes.

Making Your Choice

Rev. 4/05 Please read the sentence below and think about your choice. After reading the sentence, circle "Yes" or "No." No matter what you decide to do, it will not affect your care. You can participate in the therapeutic part of the study without participating in the research studies. If you have any questions, please talk to your doctor or nurse, or call our research review board at [ADD TELEPHONE NUMBER].

1. I agree to participate in the scientific laboratory tests that are being done as part of this study.

Yes No

Rev. 3/06 2. I agree to participate in the scientific laboratory tests monitoring drug levels which are being done as a part of this study.

Yes No

Please print and sign your name here after you circle your answer.

Your Name:

Your Signature: Date:

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Appendix Ib

Suggested Patient Consent Form for Patients Opting to Continue Receiving Treatment with ZD1839 (Iressa, gefitinib)

Version Date: 4/16/08

You are being asked to take part in this study because you have a head and neck cancer that has spread to other parts of your body.

The standard treatment for your type of tumor is chemotherapy (anti-cancer medications). Several chemotherapy medications have been found to shrink tumors of the head and neck. Unfortunately, these agents can shrink or control the spread of tumor in only a few patients. Therefore, more effective treatments are needed.

This is a clinical trial (a type of research study). Clinical trials include only patients who choose to take part. Please take your time to make your decision and discuss it with your friends and family.

WHY IS THIS STUDY BEING DONE?

You have participated in a study that compared the effects (good and bad) of chemotherapy (docetaxel) plus ZD1839 (Iressa, gefitinib) with docetaxel and placebo on the head and neck cancer to see which is better. Due to the fact that your cancer progressed and you were in the docetaxel plus placebo arm, you and your doctor decided to continue to receive treatment with ZD1839 (Iressa, gefitinib) alone.

WHAT IS INVOLVED IN THIS STUDY?

You will be receiving ZD1839 (Iressa, gefitinib) until your cancer progresses.

ZD1839 (Iressa, gefitinib) is a new investigational drug treatment that has been shown to slow or stop growth in tumors. In clinical trials, ZD1839 (Iressa, gefitinib) has been able to shrink head and neck cancer tumors but in a small percentage of patients. A clinical trial that compared ZD1839 (Iressa, gefitinib) with methotrexate, a standard chemotherapy in head and neck cancer, showed that ZD1839 (Iressa, gefitinib) was not better than methotrexate. ZD1839 (Iressa, gefitinib) works differently from the way chemotherapy drugs work. Chemotherapy usually targets the cell's DNA and may affect both normal and cancer cells. ZD1839 (Iressa, gefitinib) targets a protein that is on the outside of cancer cells. The protein helps cancer cells to spread and grow. ZD1839 (Iressa, gefitinib) attaches to this protein and "switches it off" so that the cancer cells stop growing.

It will be up to you and your doctor to decide whether continuing ZD1839 (Iressa, gefitinib) is of benefit to you. Alternative options are available to you and it should be discussed with your physician.

During treatment with ZD1839 (Iressa, gefitinib) you will be having tests that would be done even if you do not take part in the research study.

Before the study begins, you will have the following:

Tests

- Blood tests (blood draws for this study should equal approximately 2 ½ tablespoons)
- Pregnancy test if you are a woman of childbearing potential

Procedures:

- A physical examination with medical history, vital signs (blood pressure, pulse, temperature, weight and height)
- CT scans or MRI scans to confirm your type of head and neck cancer
- Electrocardiogram (EKG: a rhythm tracing of your heart)
- Chest x-ray

Every 4 weeks prior to each cycle:

Tests:

- Blood tests. This is considered routine for any patient receiving cancer treatment and will be used to monitor side effects.

Procedures:

- Physical examination with medical history, vital signs (blood pressure, pulse, temperature, weight and height)

Every 8 weeks:

Procedures:

- Tumor measurements (using CT scan or MRI scan) will be done to determine your response to treatment.

Before receiving treatment, at day 15 and 28 of cycle one, and day 28 of every cycle beginning with cycle 2:

- You will be asked to complete a questionnaire with 11 questions. Also, you will be asked to complete a final questionnaire 2-4 weeks after going off study treatment. You can complete the questionnaire at home. Each time, you will be asked 11 questions regarding your symptoms from head and neck, including pain, lack of energy, shortness of breath, ability to eat, and side effects of treatment.

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Appendix VII

Cancer Trials Support Unit (CTSU) Participation Procedures

REGISTRATION/RANDOMIZATION

Prior to the recruitment of a patient for this study, investigators must be registered members of the CTSU. Each investigator must have an NCI investigator number and must maintain an "active" investigator registration status through the annual submission of a complete investigator registration packet (FDA Form 1572 with original signature, current CV, Supplemental Investigator Data Form with signature, and Financial Disclosure Form with original signature) to the Pharmaceutical Management Branch, CTEP, DCTD, NCI. These forms are available on the CTSU registered member Web site or by calling the PMB at 301-496-5725 Monday through Friday between 8:30 a.m. and 4:30 p.m. Eastern time.

Each CTSU investigator or group of investigators at a clinical site must obtain IRB approval for this protocol and submit IRB approval and supporting documentation to the CTSU Regulatory Office before they can enroll patients. Study centers can check the status of their registration packets by querying the Regulatory Support System (RSS) site registration status page of the CTSU member web site at http://members.ctsu.org

All forms and documents associated with this study can be downloaded from the E1302 Web page on the CTSU registered member Web site (https://members.ctsu.org). Patients can be registered only after pre-treatment evaluation is complete, all eligibility criteria have been met, and the study site is listed as 'approved' in the CTSU RSS.

Requirements for E1302 site registration:

- CTSU IRB Certification
- CTSU IRB/Regulatory Approval Transmittal Sheet

Prestudy requirements for patient enrollment on E1302:

- Patient must meet all inclusion criteria, and no exclusion criteria should apply.
- Patient has signed and dated all applicable consents and authorization forms.
- All baseline laboratory tests and prestudy evaluations performed within the time period specified in the protocol.
- Patient completed baseline QOL forms.

CTSU Procedures for Patient Enrollment

Step 1 Registration to Arm A or B:

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1. Contact the CTSU Patient Registration Office by calling 1-888-462-3009 between 9:00 AM and 5:30 PM Eastern Time, Monday – Friday. Leave a voicemail to alert the CTSU Patient Registrar that an enrollment is forthcoming. For immediate registration needs, e.g. within one hour, call the registrar cell phone at 1-301-704-2376.
2. Complete the following forms:
   - CTSU Patient Enrollment Transmittal Form
   - E1302 Step 1 Eligibility Checklist

3. Fax these forms to the CTSU Patient Registrar at 1-888-691-8039 between the hours of 9:00 AM and 5:30 PM, Mon-Fri, Eastern Time (excluding holidays); however, please be aware that registrations received after 5:00 PM will be processed the next day. The CTSU registrar will check the investigator and site information to ensure that all regulatory requirements have been met. The registrar will also check that forms are complete and follow-up with the site to resolve any discrepancies.

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4. Once investigator eligibility is confirmed and enrollment documents are reviewed for compliance, the CTSU registrar will contact the ECOG. The CTSU registrar will access the ECOG's on-line registration system, to obtain and assignment of a unique patient ID (to be used on all future forms and correspondence). Since this is a blinded study, a specific treatment arm will now be assigned. The CTSU registrar will confirm registration by fax.
    - Peripheral blood is to be collected and submitted at baseline after registration and prior to starting therapy, for patients who have given consent. A sample collection and shipping kit is available. Please order kits from Dr. Kolesar's laboratory 2 days prior to the collection of the sample. Since the samples are drawn prior to starting therapy, shipping kits must be requested a minimum of 48 hours (2 business days) prior to initiating therapy. See section 11.0 of the protocol for details.
    - Treatment should start within ten working days after randomization. Allow one week after patient registration for arrival of patient-specific clinical supplies.

DATA SUBMISSION AND RECONCILIATION

1. All case report forms (CRFs) and transmittals associated with this study must be downloaded from the E1302 Web page located on the CTSU registered member Web site (https://members.ctsu.org). Sites must use the current form versions and adhere to the instructions and submission schedule outlined in the protocol.
2. Submit all completed CRFs (with the exception of patient enrollment forms), clinical reports, and transmittals directly to the ECOG [refer to contacts table] unless an alternate location is specified in the protocol. Do not send study data to the CTSU. A completed CTSU-ECOG coversheet should accompany all data submissions.
3. The ECOG Coordinating Center will mail query notices and delinquency reports directly to the site for reconciliation. Please send query responses and delinquent data to the ECOG Coordinating Center and do not copy the CTSU Data Operations. Each site should have a designated CTSU Administrator and Data Administrator and must keep their CTEP AMS account contact information current. This will ensure timely communication between the clinical site and the ECOG Coordinating Center.

SPECIAL MATERIALS OR SUBSTUDIES

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All specimens submitted for this study must be entered and tracked using the ECOG Sample Tracking System. Upon registering new patients to these studies, you can expect to receive an automatic email with instructions for logging into the system and shipping samples. You can also access the Tracking System from the CTSU Member Web Site. Go to the protocol number protocol page and click on the link provided under the Case Report Form header. Questions may be sent to **ecog.tst@jimmy.harvard.edu.** Please refer to section 10.0 for details on how to use the ECOG Sample Tracking System.

1. Pathology Submission (Protocol section 10.0)

    - Submission of pathologic material for diagnostic review is mandatory.
    - Collect, prepare, and submit specimens as outlined in the protocol
    - Do not send specimens, supporting clinical reports, or transmittals to the CTSU

2. Specimen collection for correlatives (Protocol section 11.0)

    - Participation in the correlatives is optional and requires patient consent.
    - Please order kits from Dr. Kolesar's laboratory 2 days prior to the collection of the sample. Since the samples are drawn prior to starting therapy, shipping kits must be requested a minimum of 48 hours (2 business days) prior to initiating therapy.
    - Collect, prepare, and submit specimens as outlined in the protocol.
    - Do not send specimens, supporting clinical reports, or transmittals to the CTSU.

3. Quality of Life Substudies (Protocol section 5.1.3 and 9.5)

874. NOTE: Plasma samples for PK analysis should be collected and shipped as outlined in Section 11.1.2 of the protocol. Kit information for PK sampling is outlined in Section 11.1.2.3.

876. Have you contacted Dr. Kolesar's laboratory to request the PK kit to collect and ship the samples for the PK studies?

1. No, kit will not be requested [next question]
2. Not yet [next question]
3. Yes [next question]
4. Unknown [next question]

882. Have you contacted Zemotak-Chicago to request RNA and DNA PaxGene kits to collect and ship the samples for the applicable correlative studies?

1. No, kit will not be requested [question 900]
2. Not yet [next question]
3. Yes [next question]
4. Unknown [next question]

884. Enter the name of the institutional contact person who coordinates the kit requests.

enter response:

886. Enter the phone number of the institutional contact person who coordinates the kit requests.

enter response:

900. Note: Patients who receive chemotherapy as part of potentially curative therapy of primary disease within 6 months of randomization will be considered as having prior chemotherapy for recurrent/metastatic disease, whereas patients who received chemotherapy as part of potentially curative therapy of disease > 6 months of randomization will be considered as having no prior chemotherapy for recurrent/metastatic disease.

910. Was there prior chemotherapy for recurrent/metastatic disease?

1. No [next question]
2. Yes [question 930]
3. Unknown [INELIGIBLE]

920. What is patient's performance status?
enter value: _____

-less than 2, INELIGIBLE
-equal to 2, question 940.
-greater than 2, INELIGIBLE
-unknown , INELIGIBLE

930. What is patient's performance status?
enter value: _____

-less than 0, INELIGIBLE
-less than or equal to 2, next question.
-greater than 2, INELIGIBLE
-unknown , INELIGIBLE

940. What is patient's weight loss of total body weight in last 6 months?

1. Less than five percent [next question]
2. Five percent or more [next question]
3. Unknown [INELIGIBLE]

945. Does the patient currently have a G-tube?

1. No [next question]
2. Yes [next question]
3. Unknown [INELIGIBLE]

946. Has the patient had prior cetuximab treatment?

1. No [next question]
2. Yes [next question]
3. Unknown [INELIGIBLE]

947. What is the patient's current ECOG performance status value?

0: Patient fully active, able to carry on all pre-disease performance without restriction.
1: Patient restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature.
2: Patient ambulatory and capable of all self care, but unable to carry any work activities, up and about more than 50% of waking hours.
3: Patient capable of only limited self care, confined to bed or chair more than 50% of waking hours.
4: Patient completely disabled, unable to carry on any self care, totally confined to bed or chair.
enter value: _____

-equal to 0, next question.
-equal to 1, next question.
-equal to 2, next question.
-equal to 3, INELIGIBLE
-equal to 4, INELIGIBLE
-unknown , INELIGIBLE

948. The following information is requested for drug ordering.

950. Enter NCI investigator's number.
enter value: _____

-less than or equal to 0, INELIGIBLE
-greater than 0, next question.
-unknown , INELIGIBLE

960. Enter investigator's first name.

enter response:

970. Enter investigator's last name.

enter response:

975. Do you wish to use an express carrier to ship the drugs (at your expense)?

1. No [question 992]
2. Yes [next question]
3. Unknown [INELIGIBLE]

980. Please select name of express carrier.

1. Federal Express [next question]
2. Airborne Express [next question]
3. DHL [next question]
4. Purolater [next question]
5. UPS [next question]
6. Other [INELIGIBLE]
7. Unknown [INELIGIBLE]

990. Enter Express account number.

enter response:

992. Enter the name of the contact person for drug ordering.

enter response:

994. Enter the phone number of the contact person for drug ordering.

enter response:

996. Enter the email address of the contact person for drug ordering.

enter response:

1000. Does patient agree to participate in scientific laboratory tests that are being done as part of this study?

1. No [next question]
2. Yes [next question]
3. Unknown [next question]

1010. Have you obtained patient's consent for their blood, and tissue to be kept for use in research to learn about, prevent, treat, or cure cancer?

1. No [next question]
2. Yes [next question]
3. Unknown [next question]

1020. Have you obtained patient's consent for their blood, and tissue to be kept for research about other health problems (for example: causes of diabetes, Alzheimer's disease, and heart disease)?

1. No [next question]
2. Yes [next question]
3. Unknown [next question]

1030. Have you obtained patient's consent for their doctor (or someone from Eastern Cooperative Oncology Group) to contact them in future to ask them to take part in more research?

1. No [next question]
2. Yes [next question]
3. Unknown [next question]

1040. NOTE: The following 3 questions are mandatory for the Quality of Life portion of the study. Please be sure to complete all 3 questions.

1050. Enter the name of the contact person who will be responsible for overseeing the administration of the quality of life portion of the study.

enter response:

1060. Enter the phone number of the QOL contact person.

enter response:

1070. Enter the e-mail address of the QOL contact person.

enter response:

1080. Enter the name of the contact person responsible for sample submission.

enter response:

1090. Enter the phone number of the contact person responsible for sample submission.

enter response:

1100. Enter the fax number of the contact person responsible for sample submission.

enter response:

1110. Enter the e-mail address of the contact person responsible for sample submission. enter response:

ELIGIBLE...

Demographic Data Required For Patient Registration:

Patient's Sex (m/f) _____ Birthdate (mm/yy) _____

Patient's Race _____ Zip Code _____

Patient's Ethnicity _____

Patient's Hospital No. _____

Patient's Social Security Number _____

Method of Payment _____

Attending Physician _____

Institution Contact _____

Registrar _____

Country of Residence _____

Comments _____

_____

_____

I have reviewed the above data and agree the data are accurate and correct.

_____ _____

signature of treating physician date

Note: Date must be on or before date of registration

OPTIONAL: This signature line is provided for use by institutions wishing to use the eligibility checklist as source documentation.