

North Central Cancer Treatment Group

N078D: Phase I/II Trial of Rituximab, Cladribine, and Temsirolimus (RCT) Therapy in Newly Diagnosed Mantle Cell Lymphoma (MCL).

Addendum 10 – May 13, 2011

Summary

- Due to the frequent occurrence of grade 4 hematologic toxicity in patients with lymphoma, these toxicities will be excluded from expedited reporting.
- In order to clarify the study design used, Sections 13.0 and 16.0 have been revised.
- Study Statistician update.
- Research Protocol Specialist update.
- Administrative/editorial changes.

Replacement pages are included. Please incorporate into the protocol and keep this addendum with your protocol.

Title page Addendum 10 has been added and the NCI version date has been revised.

Betsy R. LaPlant, MS has replaced Hui Tang, PhD as the Statistician for this study.

Protocol Resources

Page 2: **Tamra L. Chomjak** replaces ~~Sara M. Braun~~ as the NCCTG *Research Base* Research Protocol Specialist.

Section 10.0 **Adverse Event (AE) Reporting and Monitoring**

Page 28: A new bullet has been added under the “Additional Instructions...” in Section 10.21 as follows:

See Section 10.23 for a list of exceptions to the Expedited Reporting Requirements.

Page 29: Section 10.23 is newly added as follows:

10.23 Protocol-Specific Expedited Adverse Event Reporting Exclusions

For this protocol only, certain AEs/grades are exceptions to the Expedited Reporting Guidelines and do not require expedited reporting (i.e., AdEERS). The following AEs must be reported through the routine reporting mechanism (reported on the nadir/adverse event form):

System Organ Class (SOC)	Adverse Event	Grade	Attribution	Comments
Investigations	White blood cell decreased	4	Possible, probable, definite	This frequent event in patients with MCL will be reported through the routine reporting mechanism
Investigations	Lymphocyte count decreased	4	Possible, probable, definite	This frequent event in patients with MCL will be reported through the routine reporting mechanism
Investigations	Neutrophil count decreased	4	Possible, probable, definite	This frequent event in patients with MCL will be reported through the routine reporting mechanism
Investigations	Platelet count decreased	4	Possible, probable, definite	This frequent event in patients with MCL will be reported through the routine reporting mechanism
Blood and lymphatic system disorders	Anemia	4	Possible, probable, definite	This frequent event in patients with MCL will be reported through the routine reporting mechanism

Page 30: Reference to Section 15.255 has been corrected to read 15.27 in Footnote 1 under the Section 10.3 table.

Section 13.0 **Treatment/Follow-up Decision as Evaluation of Patient**

Page 37: In order to clarify the study design used, Section 13.9d is newly added as follows:

A patient is deemed a cancel if he/she is removed from the study for any reason before any study treatment is given. On-study material and the End of Active Treatment/Cancel Notification Form must be submitted. The patient will go directly to the event-monitoring phase of the study, and event monitoring will be required per Section 18.0 of the protocol.

Section 16.0 **Statistical Considerations and Methodology**

Page 56: The last sentence in Section 16.33 has been revised for clarification as follows:

The following one-stage design with an interim analysis **based on a Fleming design** uses a minimum of 22 and a maximum of 46 evaluable patients to test the null hypothesis that the true success proportion in a given patient population is at most 40%.

Page 56: Section 16.331 has been revised for clarification as follows:
 Interim analysis: An interim analysis will be conducted after the first 22 evaluable patients are accrued to the trial. If 9 or fewer successes are observed in the first 22 evaluable patients, we will consider this sufficient early evidence that the regimen is ineffective in this patient population and we will terminate accrual to this study. **If 15 or more successes are observed in the first 22 evaluable patients, we may recommend further testing of this regimen while continuing to complete the planned accrual specified by the design. Otherwise, if the number of successes is at least 10, we will continue accrual.**

Page 56: The last sentence in Section 16.34 has been corrected as follows:
 The probability of declaring that this regimen warrants further studies (i.e. statistical power) under various success proportions and the probability of stopping accrual after the ~~first stage~~ **interim analysis** can be tabulated as a function of the true success proportion as shown in the following table.

The second row in the table in Section 16.34 has been corrected as follows:

Then the probability of declaring that the regimen warrants further study is...	.10	.267	.51	.75	.91
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Section 18.0 Records and Data Collection Procedures

Page 65: “**Quantitative Flow Cytometry Form**” has been added to the submission timetable as this was inadvertently omitted and will be collected ≤14 days after registration.

Section 20.0 References

Page 68: Due to the revision in Section 16.33, the following reference has been added:
Fleming TR: One sample multiple testing procedures for phase II clinical trials. Biometrics 38:143-151, 1982.