

CANCER AND LEUKEMIA GROUP B

MEMORANDUM

To: Principal Investigators, CCOP Responsible Investigators, Statistical Center, Data Operations

From: Linda Bressler, Pharm.D., Director of Regulatory Affairs

Subject: CALGB 80405 and 80702 Revised Guidelines Related to Leucovorin Shortage

Date: 11 March 2011

There continues to be a nationwide shortage of injectable racemic leucovorin that is having variable effects on oncology practices in North America. There remains uncertainty when the supply of leucovorin will fully meet demand. In addition, certain practices are having difficulty securing adequate levoleucovorin supplies.

In December 2008, CALGB issued a memorandum instructing institutions to not register new patients on trials that include treatment with leucovorin unless a 4-week supply of IV racemic leucovorin or levoleucovorin was available for each new patient.

Given the continued shortage problem for over 2 years, CALGB is revising its instructions regarding leucovorin and levoleucovorin supplies for institutions enrolling in CALGB 80405 (metastatic colorectal cancer) or CALGB 80702 (adjuvant stage III colon cancer).

Oncologists should realize that data supporting the use of FOLFIRI or FOLFOX (in metastatic colorectal cancer) and FOLFOX (in stage III colon cancer) are derived from trials that utilized IV racemic leucovorin at standard doses. There are no data supporting lower doses of leucovorin, substitution of levoleucovorin, or omission of leucovorin in the regimens utilized in CALGB 80405 and 80702. We encourage treating physicians to review the ASCO clinical alert on this issue:

<http://www.asco.org/ASCOv2/Department%20Content/Cancer%20Policy%20and%20Clinical%20Affairs/Downloads/Cancer%20Policy%20News/Cancer%20Policy%20Alert/Leucovorin%20Alert%208-5-2010.pdf>

For practices experiencing shortage of IV racemic leucovorin who wish to enroll new patients to either CALGB 80405 or CALGB 80702, we recommend (in order of preference):

- (1) Substitute IV levoleucovorin (at a dose of 200 mg/m² or 50% of the protocol-specified dose IV racemic leucovorin) for IV racemic leucovorin. Change to protocol-specified racemic leucovorin when supplies become available.

OR

- (2) Substitute a lower dose of IV racemic leucovorin (20 mg/m²) for the standard dose of 400 mg/m². Change to the protocol-specified dose when supplies become available.

OR

- (3) If neither racemic leucovorin or levoleucovorin are available at any dosage, treatment without leucovorin would be acceptable but should be re-addressed with each treatment.

For institutions with patients already receiving treatment on either study, consider (in order of preference) option 2 or 3 above, or omission of leucovorin, for each dose for which leucovorin is not available.

If you have any question or concerns, please contact the CALGB Protocol Coordinator and the respective study chair

| | | |
|----------------------|--------------------|--|
| Protocol Coordinator | Shivani Shah | sshah11@uchicago.edu |
| CALGB 80405 | Bert O'Neil | bert_oneil@med.unc.edu |
| | Alan Venook | venook@cc.ucsf.edu |
| CALGB 80702 | Jeffrey Meyerhardt | jeffrey_meyerhardt@dfci.harvard.edu |