Name That Tune!

Pharmaceutical Management Branch
Cancer Therapy Evaluation Program
Division of Cancer Treatment and Diagnosis
National Cancer Institute
6130 Executive Blvd * Suite 7149
Rockville, Maryland 20852
Phone: (301) 496-5725
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Could be Reveille,Could be Taps

PMB rarely closes and makes every attempt to provide reliable service. That said, mother nature sometimes tunes us out, especially in the winter, and the next few months are full of holidays.

Please plan ahead.

Remember five of the US's 11
Federal holidays fall in the next three months (see sidebar)!

No next day shipment on
November 25, or December 24, or December 31!

Allow lots of time for shipping.

Order sufficient quantities.

Send homemade cookies to PMB.

Have enjoyable holidays!

Veteran's Day (11/11), Thanksgiving (11/26), Christmas (12/25), New Year's Day (1/1), MLK's Birthday (1/18)

INSIDE PMB

November 2009

Humming Along at PMB

Humming is a big deal at PMB. We like to hum along and make sure your every need is met. So who's in our chorus of voices?

Our Managers:
- •Skip Hall, Branch Chief
- •Patricia Schettino, Associate Chief

Our Clinical Research Pharmacists:
- •Matthew Boron
- •Michelle Eby
- •Rodney Howells
- •Tali Johnson (after November 9)
- •Ravie Kem
- •Donna Shriner
- •Jeannette Wick

Our Project Managers:
- •Melizza Ford
- •Arie Gray

Our Clinical Trials Support Specialists:
- •Marta Cardenas
- •LaKita Haskins
- •Ajohnie (Johni) Johnston

Our Protocol Registration Specialist:
- •Beverly Bailey

Our Inventory Management Specialist:
- •Frank Scott

Our Technical Receptionist:
- •Jualiana Megyer

Please note that Juliana will always ask what your call concerns, and direct you to the most appropriate help!

Music to Our Ears

It is no longer necessary to dispense open label lenalidomide (CC-5013, NSC 703813) in its original container! You can now dispense the exact quantity needed for any given cycle. Use the same accountability procedure you use for other oral medications on the Drug Accountability Record Form (DARF) :

- If you need to dispense a quantity different than the bottle size that is provided for your study, maintain a running balance of capsules remaining.
- If you are going to dispense full bottles, keep a running total of how many bottles remain in the inventory.

As always, if the patient returns capsules, you should pitch them according to your local destruction policy.

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Sing in Tune with CTEP PIO

We try not to harp on problems, but there are ways you can tune up your CTEP Protocol Information Office (PIO) Experience!

1. Check the CTEP web site first for information: http://ctep.cancer.gov/protocolDevelopment/default.htm
2. Send all PIO correspondence to pio@ctep.nci.nih.gov
3. Status updates must be submitted by the lead site and must be for the entire protocol
4. IRB approvals must be submitted by the lead site for all participating sites
5. LOI submissions must be complete including IDSC check mark and signature dates. Career Development LOIs also need: CV, Mentor Letter, Institutional Support Letter.
6. Include a new version date for all amendments and revisions
7. PIO does not accept concepts for Task Force review, send them straight to the Coordinating Center for Clinical Trials (http://ccct.cancer.gov/)
8. Check the pagination and legibility of each protocol before submitting to prevent being placed on hold
9. Understand that CAEPR requests are confidential, and check with lead site first. Include the approved Protocol or LOI number, and Study PI name!
10. And finale, in complete protocol submissions, kindly include:
    - Completed Current Version of Protocol Submission Worksheet (PSW)
    - A clean (not highlighted or changes tracked) protocol document
    - An informed consent document, in WORD format, that addresses all the elements required by FDA regulations

New Shipment Record Form

If it's not baroque, don't fix it, that's our motto. The old system for creating shipment records was becoming dissonant, so it had to go. By the end of the calendar year, you will begin seeing a new Shipment Record of Clinical Drug Request form in shipments received from PMB. This new form is a prelude to future on-line clinical drug request processing and shipment tracking. As we move forward with these changes, please note (in most cases) only one agent will be included on each shipment record form. Therefore, you'll find multiple forms included in your shipment if you order multiple agents or agents for multiple protocols. It will be especially important to thoroughly unpack and check each shipment to ensure you retain all records for the shipment.

PMBafterhours

Do you have a question and need an answer soon, but not necessarily right this minute?
E-mail pmbafterhours@mail.nih.gov
Any time day or night!

Won't You Come Home Bill Bailey?

The PMB Barbershop Quartet, Three Pills and a Tablet, are serenading you:

•The lead sings the melody:
There's a new Agent Return Form on CTEP's web site!
•The tenor harmonizes above the melody:
It's-a-new-one! {pause} A-new-one! {pause} A-real-beauty!
•The bass sings the lowest harmonizing notes:
Check the web site, check the web site, check the web site.
•The baritone completes the chord, usually below the lead:
There's a new Agent Return Form on CTEP's web site!

PMB posted a revised Agent Return Form on the CTEP web site earlier this year. Please look sharp and discard older versions of the form (hard or electronic) if you have any. Please complete all information requested on the return forms completely and accurately to receive credit for the return–just reed the directions and fill in every box! All agent-related forms are available on the CTEP web site at http://tinyurl.com/yhx23bm.

Avoid Sour Notes!
It's your responsibility to ensure the information provided is complete and accurate and that you return ONLY CTEP-supplied agents to the NCI Clinical Repository. The repository will destroy all agent returns received, but PMB will not provide documentation of return for agents that we didn't supply!

Other than including the Investigational Agent Return Form, don't return any other documentation. We don't need copies of Drug Accountability Record Forms or copies of the PMB-issued stock recovery letter. For sites returning patient-specific supplies of NCI-supplied agents—please make sure to remove personal identifying information on the agent label (i.e., please "black-out" patient names).

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Row Row Row Your Dose*

The controversy surrounding using BSA to calculate dose is an ongoing debate; however, it is still the most common method employed to determine antineoplastic doses. Most antineoplastic agent doses are calculated using the body surface area (BSA) calculation and rounding to the nearest whole number, although some institutions calculate doses to two decimal places!

What's the controversy? Data shows inter- and intrapatient variability in pharmacokinetics; thus, using an exact calculated dose might be unnecessary. And, when the fractional dose means you need to open another vial and waste 90% of it, it begs the question, "Is this necessary?" With the introduction of new treatment options, treatment costs have increased exponentially.

M.J. Dooley et al. conducted a clinical trial in Australia looking at the effect of dose rounding to the nearest whole vial strength for marketed antineoplatics including docetaxel, liposomal doxorubicin, gemcitabine, oxaliplatin and vinorelbine. About 2840 patients participated in the study. The results show no significant difference between administering the mean calculated dose and administering the rounded dose. For most patients, the dose rounded to the nearest vial size was within ± 5% of the calculated dose. And the savings were between 4% and 14.2%.

Dose rounding to the nearest vial size is a judgment call, and it depends on the availability of the agent's dosage forms and strengths. For example, rounding a dose of 78 mg of oxaliplatin would mean using a 100mg dose (the larger vial size) is not a good idea. Thus, the oxaliplatin should not be rounded to the nearest vial size because the difference in dose is substantial. It is simpler to round the dose to the nearest vial size for drugs available in multiple vial sizes.

The author suggests that if institutions consider rounding doses to the nearest vial size, the difference in dose delivery should not exceed more than 5%.

A Row of Doses

*Sung in the Round

FAQ: Injectable agents in vials (sharing and overfill)

Question: Two patients receive the same agent on the same open label NCI study at the same institution. Can we share vials?

If the patients are being treated on the same day, this is acceptable. Document this on the DARF by noting patient initials/number used 1 vial and patient initials/number used 0 vials. Tie the lines together with a "]". Document each of the patients' actual doses on the DARF.

Note: This is not how you document trastuzumab, our only multi dose vial. Trastuzumab is documented by mg (often with confusing results).

Question: Our patient's dose of godzillaplatin is 104 mg, and the NCI supplied vials contain 100 mg in 5 mL, but they have ample overfill. If we can draw 5.2 mL from the vial, can we use it instead of opening another vial?

You bet, especially if the vial was filled by the manufacturer. If the product is lyophylized, however, please make sure that you reconstituted it exactly as directed, and the overfill isn't the result of an error. (Please note that you might suggest to your physicians that the difference between 104 mg and 100 mg is very small, and they can round to 100 mg without a problem in most cases. See "Row, Row, Row Your Dose!)

Phonaesthetics: Euphony (Inherent Pleasantness) or Cacophony (Unpleasantness)

What's our phone service like? Although most of our calls with customers are euphonic, we have those occasional cacophonic calls—you know the type—the calls where it seems like everyone is talking, but not about the same things, or you have needs, but they are not being met. If you experience a less-than-satisfactory telephone conversation, please.....

(1) Try to start over, and explain your problem using different words. It may be that our staff member doesn't understand what you mean and using different words will clarify the issue.

(2) Ask, "How can I explain this differently?" Our staff member may be able to tell you where the gaps in your explanation are.

(3) Ask to speak to a manager or the subject expert. We all know here that sometimes, misunderstandings can't be resolved until a third party intervenes, and we take no offense if you ask to speak with someone else.

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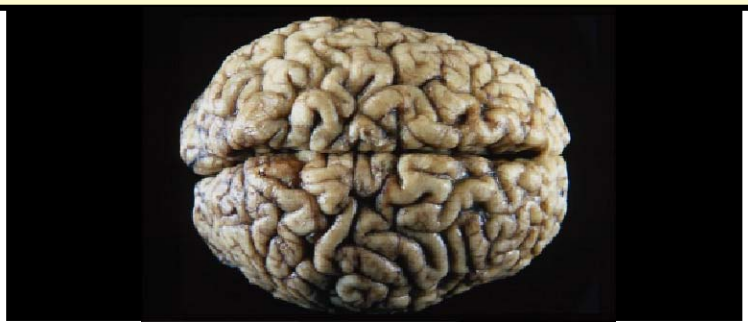

Current Management: Brain Metastases

Historically, brain metastases developed in the setting of multi-organ metastatic disease in end-stage cancer patients. Now, they often develop in patients with well-controlled systemic disease and are caught more often due to improved detection of subclinical disease and better systemic cancer control. Around 200,000 cancer patients are stricken annually in the United States. Brain mets devastate patients. "Your brain controls your independence, your quality of life, your entire existence. Brain mets can bring on a loss of hope and a fear of loss of self," one woman wrote. (Mayer M. *Clin Cancer Res* 2007;13: 1623-4.)

Although many approaches have been tried, no standard therapy for brain metastases has been established and the outcome remains poor. Nonetheless, aggressive management with whole-brain radiation therapy (WBRT), surgery, and/or stereotactic radiosurgery (SRS)have been shown to improve symptoms and prolong survival.

WBRT is used most frequently—think of it as a canon. Its early side effects include fatigue, drowsiness, headache, hair loss, skin erythema, and hyperpigmentation. Long-term neurocognitive effects include dementia, ataxia, and urinary incontinence; these toxicities may be more problematic in today's longer lived patients.
Surgery or craniotomy is usually performed *a capella* on large single lesions that are readily accessible. It may result in rapid symptom control in patients with cerebral edema. Surgery is often followed by WBRT.

On the other hand, SRS is instrumental in delivering a large single dose of three-dimensional radiation to small intracranial targets that can be deep in the brain. Unlike WBRT, SRS minimizes exposure to normal surrounding tissues. It is less invasive than surgical resection. Can these modalities work in harmony? Addition of WBRT to SRS may improve local and central nervous system control rates. Although there was no difference in survival, one study reports SRS plus WBRT resulted in improved Karnofsky performance status. Controversy remains as to whether WBRT should be postponed in patients treated with SRS to minimize complications from WBRT. In the absence of WBRT, frequent monitoring of patients for disease recurrence is necessary.

Chemotherapy has not yet demonstrated a survival advantage in management of intracranial metastasis. Most chemotherapeutic agents do not cross the blood brain barrier. Many patients have been heavily pretreated with therapy aimed at their systemic cancer. The development of cranial metastasis could represent drug resistant clones.

We still need to identify a standard therapy for brain metastases. Until then, a multimodality approach (a concerted effort, if you will) may prolong survival, enhance quality of life, and decrease neurologic deterioration in some patients.

Progressive Rock: Fast, Easy, Bass-ic Information

•Need an Investigator Brochure for an agent for which NCI holds the IN-D (LOL! Pronounced Indie, get it?)? E-mail to ibcoordinator@mail.nih.gov or call 301-496-5725 and ask for the IB Coordinator.

•Have investigator registration questions? E-mail PMBRegPend@ctep.nci.nih.gov or call 301-496-5725 and ask for the Registration Coordinator.

•Want to request agent for non-human use? Synthesize an E-mail to PMBafterhours@mail.nih.gov and use the subject ATTN: NHU Coordinator. Or call the NHU Coordinator here at PMB.

•Have issues with investigator-held INDs? Send an E-mail to PMBafterhours@mail.nih.gov and use the subject, ATTN: Investigator-Held IND Coordinator

Singing the Blues?

If you consider preparation of any NCI-supplied agent difficult, confusing, or unreasonably costly, don't dance around the issue! Let us know. Your concerns might include
• You need a doctorate to read the directions
• Stability times are short
• The glass ampule is impossible to crack
• It seems like the vials crack easily
• When the agent is infused, it always occludes the line
• It requires a brand of IV bag or equipment that you don't stock.

Let us know—we're very interested in saving time or money for you! Even if we can't help, there's no harm done by asking.

LOOK FOR INSIDE PMB QUARTERLY
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