INSIDE PMB
August 2015

Cancer Therapy Evaluation Program
Division of Cancer Treatment & Diagnosis

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A new staff member has joined PMB! Eileen Wu received her Pharm.D degree from Rutgers the State University of New Jersey in 2007, and Eileen joined the Children's Hospital of Philadelphia where she first worked in the central pharmacy then transitioned to the Investigational Drug Service (IDS). In the IDS, Eileen was responsible for reviewing protocols for the IRB, assisting investigators in developing protocols, and training the pharmacy staff and residents in the procedures for conducting and supporting investigational drug protocols. She was also responsible for dispensing all investigational agents for inpatient and outpatient settings, providing patient counseling, and developing randomization schemes and placebo controls for blinded studies. It is with a great deal of pleasure that we welcome Dr. Eileen Wu to the PMB staff.

PMB Investigational Drug Accountability - Next 3 Videos!

New Videos are live at:

http://ctep.cancer.gov/branches/pmb/drug_training_videos.htm

- Agent Dispensing (length 00:09:34)
- Patient-Specific DARFs (length 00:10:14)
- Agent Transfers (length 00:07:37)

These videos build off previously released videos:

- DARF Basics (length 00:05:05)
- DARF Header (length 00:04:33)
- Oral DARF (length 00:06:12)
- Agent Receipt (length 00:06:03)

Upcoming Changes to Shipping Containers

In the next few months, agents that are shipped at room temperature will be sent from the NCI Clinical Repository in new pre-qualified shipping containers. These containers will contain various types of phase-change material to maintain ambient or controlled-room temperature conditions as required for the specific agent. Please always refer to the agent product label for appropriate storage conditions upon receipt.

With this change, the NCI Clinical Repository will only ship agent on Monday through Thursday to domestic sites (unless Saturday delivery is requested). There will be no ability to receive agents on Monday at domestic sites. Plan accordingly.

Requests for Next-Day Receipt of Agent Orders

While our repository does an admirable job of processing approved clinical supply requests for sites as efficiently as possible, there is no guarantee that orders will ship the same business day as they are received. Normal processing time for routine orders is two business days – this has always been our procedure and it is in the Policy and Guideline for Investigational Agent Ordering on the PMB Agent Management website at:

http://ctep.cancer.gov/branches/pmb/agent_management.htm

Any requests for next-day delivery MUST be accompanied by a site-provided courier account number to ensure next-day delivery, regardless of the normal shipment mode for the agent. Please remember that all requests for next-day delivery must be submitted before 2:00 p.m. Eastern Time.

Example:

STUDY DRUG INFORMATION WALLET CARD

You are enrolled on a clinical trial using the experimental study drug_____. This clinical trial is sponsored by the NCI.

_____ may interact with drugs that are [processed by your liver, or use certain transport proteins in your body or affects the electrical activity of your heart]. Because of this, it is very important to:

- Tell your doctors if you stop taking any medicines or if you start taking any new medicines.
- Tell all of your health care providers (doctors, physician assistants, nurse practitioners, or pharmacists) that you are taking part in a clinical trial.
- Check with your doctor or pharmacist whenever you need to use an over-the-counter medicine or herbal supplement.

http://ctep.cancer.gov/protocolDevelopment/templates_applications.htm

Patient Drug Information Handout and Wallet Card

Taking appropriate medications is essential in optimizing drug therapy for patients who are participating in CTEP-sponsored trials. Potential drug-interactions (DDIs) are problematic and may be complex to manage; thus, both prescriber and patient need specific drug information for the proper use of the drug to avoid DDIs .

For this reason, PMB proposes using the Patient Drug Handout and Wallet Card. Patients should keep a copy with them at all times and share it with their regular doctor, nurses, pharmacist, or other healthcare professionals so that the healthcare providers can manage patients' medications appropriately.

The location of drug interaction information in the protocol document has varied in the past. It may be in the body of the protocol or in an appendix. For uniformity, the Pharmaceutical Management Branch (PMB) will provide a Patient Drug Information Handout and Wallet Card as an appendix for CTEP-held IND agents that are not FDA approved.

The Patient Drug Information Handout and Wallet Card is a two to three page document specific to an investigational agent.

The handout discusses potential interactions between the agent and 1) isozymes responsible for the biotransformation of many drugs; and 2) transport proteins. It also comments on an agent's ability to affect the heart's electrical activity (specifically QTc prolongation).

The Patient Drug Information Handout and Wallet Card resources are included as an appendix to the protocol.

As such, IRB approval is required prior to patient distribution. Spaces are available to insert the patient's name and the study contact name and phone number. No other additions are necessary.

The PMB will update the handout and wallet card as appropriate, based on information received from the company collaborator. Please note that once an agent becomes commercially available, the handout and wallet card will no longer be maintained by CTEP.

Drug interaction information is contained within the package insert of commercial agents. Therefore, CTEP will not create or maintain Patient Drug Information Handouts and Wallet cards for commercially marketed agents. The PI may create an agent specific handout and wallet card or maintain the documents if currently in the protocol.

The generic appendix template is available as Appendix C of the Generic Protocol Template found on the CTEP website.

Example:

APPENDIX __: PATIENT DRUG INFORMATION HANDOUT AND WALLET CARD

Information for Patients, Their Caregivers and Non-Study Healthcare Team on Possible Interactions with Other Drugs and Herbal Supplements

[Note to authors: This appendix consists of an "information sheet" to be handed to the patient at the time of enrollment. Use or modify the text as appropriate for the study agent, so that the patient is aware of the risks and can communicate with their regular prescriber(s) and pharmacist. A convenient wallet-sized information card is also included for the patient to clip out and retain at all times. If you choose to use them, please note that the information sheet and wallet card will require IRB approval before distribution to patients.]

The patient _____ is enrolled on a clinical trial using the experimental study drug, [insert study drug name]. This clinical trial is sponsored by the National Cancer Institute. This form is addressed to the patient, but includes important information for others who care for this patient.

These are the things that you as a healthcare provider need to know:

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NCI-MATCH Study to Open with Ten Arms

EAY131, otherwise known as NCI-MATCH (NCI-**M**olecular **A**nalysis for **T**herapy **Ch**oice), is a multi-arm clinical trial that will analyze patients' tumors to determine whether they contain actionable mutations of interest. Treatment is assigned based on the actionable mutation with the overall objective of determining whether treating cancers according to their molecular abnormalities is effective. ECOG-ACRIN Cancer Research Group is coordinating the trial through the National Clinical Trials Network (NCTN). Agents can only be ordered from the PMB when a patient is assigned to a specific arm. Starter supplies are not provided for this study.
Some quick facts about NCI-MATCH.

- Up to 2,400 clinical sites in NCTN can enroll
- Central IRB review is required
- Patient enrollment involves two steps: screening and treatment
- Screening will involve 3,000 tumor biopsy specimens
- Treatment will involve about 1,000 patients
- Each arm will enroll 30 evaluable patients

Because it is difficult to perform molecularly targeted clinical trials except in the most prevalent types of cancer, NCI-MATCH is designed to detect responses in various tumor types, especially rarer histologies. Such findings can be followed up with additional clinical trials to learn more about the effect of the drug on patients whose tumors have the targeted mutation. The study will drop completed arms and add new arms over time, with upwards of 25 agents being tested in different arms. Study activation is expected this summer. The first 10 NCI-MATCH arms are listed in the Table 1.

Target Agent/s	Molecular Target/s	Estimated Mutation Prevalence
Arm A: Afatinib	EGFR activating mutations	1-4%
Arm B: Afatinib	HER2 activating mutations	2-5%
Arm E: AZD9291	EGFR T790M mutations and rare EGFR activating mutations	1-2%
Arm F: Crizotinib	ALK rearrangement	4%
Arm G: Crizotinib	ROS1 translocations	5%
Arm H: Dabrafenib/Trametinib	BRAF V600E or V600K mutations	7%
Arm Q: Ado-trastuzumab emtansine	HER2 amplifications	5%
Arm R: Trametinib	BRAF fusions/non-V600E/non-V600K BRAF mutations	2.8%
Arm U: VS6063 (defactinib)	NF2 loss	2%
Arm V: Sunitinib	cKIT mutations	4%

Table 1

For more information, visit:
http://www.cancer.gov/about-cancer/treatment/clinical-trials/nci-supported/nci-match

- Labor Day: Monday, Sept 7
- Columbus Day: Monday, Oct 12
- Veterans Day: Wednesday, Nov 11

Up-coming federal holidays

Please note the NCI Clinical Repository will be closed on these federal holidays.

Please plan accordingly.

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New and Ongoing CTEP-Agents Portfolio

Tables 2 & 3 highlight some of the relatively newer agents in the CTEP portfolio. Some may already be used in active protocols. The complete list of all agents in the CTEP portfolio can be found on the CTEP website.

Please always refer to the most current version of the protocol for up to date storage, shipping, dosage form, and drug interaction information.

http://ctep.cancer.gov/protocoldevelopment/docs/ctep_active_agreements.xlsx

Table 2

Agent Name	NSC Number	Mechanism of Action / Class	Route of admin	Dosage Form	Storage
Onalespib (AT13387)	749712	Inhibitor of heat shock protein 90 (HSP90)	IV	265 mg vial	Room Temp
SGI-110	780463	A dinucleotide antimetabolite of decitabine linked via phosphodiester bond to deoxyguanosine. Inhibitor of DNMT enzymes.	Subcutaneous	100 mg vial, 3mL diluent vial	Refrigerated
CDX-1401	772468	A fusion protein consisting of a fully human monoclonal antibody directed against DEC-205, linked to tumor-associated antigen NY-ESO-1	Intracutaneous (combination of intradermal and subcutaneous)	1 mg/mL, 1 ml vials	Frozen

Table 3

Agent Name	NSC Number	Mechanism of Action / Class	Route of admin	Dosage Form	Storage
INCB024360	766086	Potent and selective orally available inhibitor of IDO-1	Oral	300 mg tablets	Room Temp
MLN0128 (INK128)	768435	Potent and selective ATP-competitive inhibitor of TORC1/TORC2	Oral	1 and 3 mg capsules	Room Temp
AZD9291	781254	3rd generation EGFR inhibitor; mEGFR	Oral	40 and 80 mg tablets	Room Temp

Listserv - A New PMB Communication Process

PMB will be implementing a listserv called NCI DCTD-CTEP-PMB in the next couple of months. The purpose of this listserv is to provide a method of communicating PMB news and announcements to our customers in real time. This will include new issues of the Inside PMB Newsletter, new Investigational Drug Accountability Training Videos, issues related to weather, holiday closure reminders, and other news. It is important to note that the listserv does not replace our current system of notifying relevant parties about critical information such as stock recovery, protocol/IND status updates, and amendment requests.

All current subscribers to the Inside PMB Newsletter will be automatically added to the listserv. Anyone interested in subscribing to the listserv can find the link to subscribe on our website when activated.

This listserv is for announcement only so please continue sending specific questions to pmbafterhours@mail.nih.gov. We will make an announcement to the listserv once the listserv and website links are live.