

INSIDE PMB FALL FASHION ISSUE NOV 2006

Look for INSIDE PMB QUARTERLY.
NEXT ISSUE: FEBRUARY 2007

HOT COLORS: RED & WHITE & BLACK & GRAY

INSIDE PMB is similar to this autumn's popular colors: it's black and white, read all over, and attempts to elucidate those all too common gray areas. (Old joke, but I couldn't help myself!) In this issue, we'll try to cover what's in, what's out, and whether or not you can accessorize. Look for these fashion do's and don't's in this issue:

- The scoop on Investigator Brochure distribution (this page)
- An update on glucarpidase (page 2; note that glucarpidase is to carboxypeptidase as leggings is to tights)
- The classically popular QUIZ (page 2)
- A designer's inside look at starter supplies (page 2)
- A hairy exposé on page 3!



WHY FASHION?

Our themes come from any number of sources, but this one just seemed right. In addition to the fact that PMB employees are slaves (to fashion, that is; note the splash of animal print in the header), fashion, like drug discovery, tends to occur in three phases. First, the trend emerges (called the "distinctiveness" part of the fashion cycle, when everyone wants it). These fashions appear on the runway, red carpet or music video. The emulation phase follows, where everyone who can fabricate the style or something similar does. Eventually, the market saturation phase hits, and the item becomes widely available as a knock-off.

ICONOCLASTIC CUSTOMER SERVICE

A technician checking DARFs saw disbursed
An agent that expired and cursed,
She was rather ruffled,
Her expletive muffled,
And she put a reminder in her purse.



Don't depend on remembering a note later when you need guidance! Reach us day or night at pmbafterhours@mail.nih.gov. Expect an answer on the next business day.

TAILORED TO YOUR EVERYDAY NEEDS

- Need an Investigator Brochure for an agent for which NCI holds the IND? 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? Send 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
- Questions about a foreign shipment? We have a coordinator for those, too! Send E-mail to PMBafterhours@mail.nih.gov and use the subject, ATTN: Foreign Shipment Coordinator.

IN VOGUE: E-TRANSMISSION

PMB has been distributing Investigator Brochures (IB) by E-mail for a number of months. Our back-up procedure (sending a paper copy by snail mail) was SO yesterday--our new approach is edgier. Big and bulky is out, sleek and small is in. Effective immediately, E-mail attachment is our preferred method for IB distribution, and the back-up method will be sending IBs on CD-ROM when E-mail is impossible. The CD-ROM has the IB in "pdf" format, readable with free Adobe Acrobat software. Detailed instructions will be sent with each CD.

To request an IB, E-mail our IB Coordinator mailbox at ibcoordinator@mail.nih.gov; this ensures we have an accurate electronic address for you, and promotes efficiency.

THE SKINNY ON SHIPPING

Like fashion, our ability to deliver is predicated on two influences: weather and holidays. Whether you need a designer drug or an off-the-rack antineoplastic, keep this in mind:

- Next day delivery is almost impossible from December 23rd through January 4th.
- If possible, consider ordering the bulk of your needs before December 15th.

BELT OUT THE BRAVOS!

Most of you apparently thought you couldn't pull off that last issue's contest, but a few brave souls had a vested interest. Our sincere congratulations to

Susan L. Finley
Baton Rouge, Louisiana

Linda Schultz, R.Ph.
Marshfield, Wisconsin

Oscar Martin, PharmD
Duarte, CA

MEETING WITH APPROVAL

PMB cannot process Clinical Drug Requests without IRB approval. E-mail non-group IRB approvals to our Protocol and Information office (PIO@ctep.nci.nih.gov). For group studies, notify the group office. PIO receipt of your IRB approval activates your site in our database, allowing agent ordering.

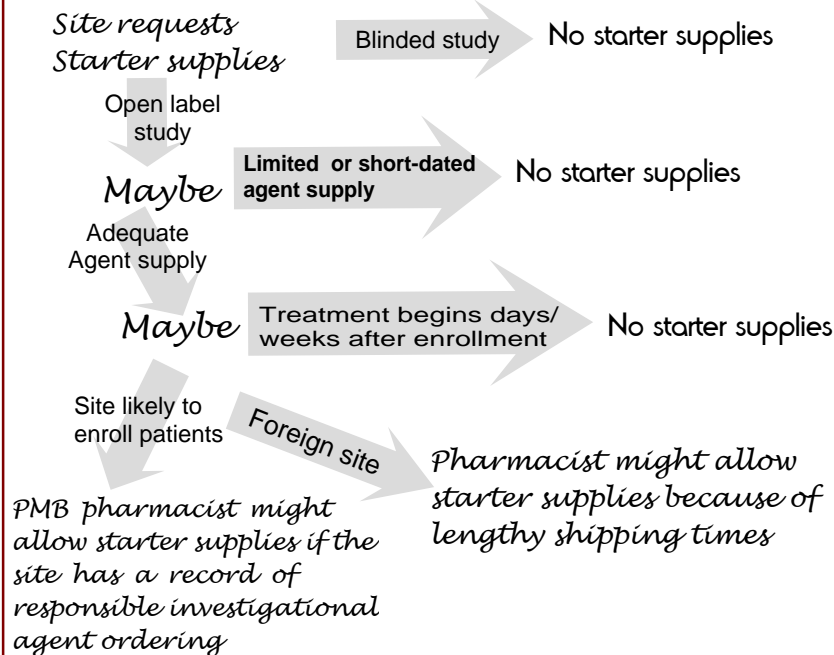


BRIEFS OR BOXERS?



A NARRATIVE OF STARTER SUPPLIES

A loyal but frustrated reader asked us to explain all there is to know about “starter supplies.” Starter supplies, if you are unfamiliar with the term, are supplies sent when the protocol is open at your site, but no patients have enrolled yet. The PMB pharmacist responsible for the agent you wish to stockpile want in anticipation of enrollment makes the decision about starter supplies. It goes a little like this:



So the decision to send or not to send starter supplies is based on numerous factors invisible to sites. The answer is the same one given by the elderly politician when the reporter asked if he wore briefs or boxers. “Depends.”

WORKIN’ WITH A BUNCH OF HEELS QUIZ

A lot of what PMB does simply involves listening. Two things we hear often combine for this month’s contest. You told us (1) about the crazy clinicians you work with, and (2) you want easy quizzes that don’t necessarily involve drugs. You know the rules: send your answers to pmbafterhours@mail.nih.gov, and you’ll enter our drawing to win cookies or homemade dog biscuits. Match the person in column A to the shoe he or she should wear in column B.

- | | |
|---|--|
| <ol style="list-style-type: none"> 1. The back-stabbing pharmacist who writes up a technician for every error, no matter how teensy and whether or not the tech was responsible. 2. The study coordinator who amends protocols like it’s going out of style, and sends gigantic attachments by E-mail, filling your mailbox. 3. The ordering designee who once again has to order investigational agent STAT because the investigator forgot to tell him that a new patient was enrolled, who has to listen to that same investigator’s empty promises, “It won’t happen again,” and is expected to believe it. 4. The principle investigator who cannot decide whether or not to enroll a patient, report an AE, expand a cohort, etc., etc., etc... 5. The IV nurse who simply vanishes unseen and unheard as soon as the clinic starts to get busy. | <ol style="list-style-type: none"> A. Clogs B. Hush Puppies C. Stilettos D. Flip-flops E. Hip boots |
|---|--|



UPDATING VINTAGE IN THREE IMPORTANT WAYS

Vintage fashion is cool, unless it’s one of those dresses with the really teensy waist and the darned zipper in a gusset under your arm, and you’ve gained a few. That’s why clothing made when flappers did the Charleston is in museums. Retro is one thing; ridiculous is another.

Carboxypeptidase (NSC 732443) is a protein that was actively vintage for a very long time. Our original lot sat on your shelves for about ten years. The subsequent lot, 20903021, expires on November 30, 2006. Sites with protocol T92-0021 open should order replacement drug supply, but do it before returning the old stock.

VINTAGE: The vintage agent was always shipped as sets of six vials; came in a kit accessorized with with pK tubes; and was labeled as carboxypeptidase.

UPDATED LOOK: The new lot ships with four vials--enough to cover an intrathecal or SPEX patient--and no pK or sampling tubes. The new vials are labeled with the generic name, glucarpidase, and proposed brand name, Voraxaze.

Its manufacturer, Protherics, Inc., has stepped onto the runway by submitting a Biologics License Application to the FDA, starting the FDA’s review process. Hopefully, Voraxaze’s availability will be a little more no-fuss in 2007.

YOU CAN DRESS IT UP

(BUT DON’T TAKE IT OUT YET)!

Please remember to ask for and receive PMB’s permission before transferring carboxypeptidase from protocol T92-0021. Even emergency transfers require advance approval from an NCI staff-member. You simply must submit a completed transfer form after receiving said verbal approval. Fax transfer forms to PMB at 301-402-0429. Please include your fax number so that PMB can fax back your official approval for your records. Transfer forms may be found on the CTEP website: <http://ctep.cancer.gov/> forms. So make a note of this:

- (1) Ask
- (2) Fax
- (3) OK to transfer carboxypeptidase, but
- (4) Look for fax-back approval, and maintain it with your DARF!

HABERDASHER'S LAST HOPE: ALOPECIA

Humans have always covered their heads. Initially headwear protected them from the elements, injury, falling rocks, whatever... Later hats came to symbolize status, authority, rank or affiliation. Until the 1920s, they were an art form as well as an essential piece of apparel. Decorative hats fell out of fashion during the world wars when they simply became impractical. Today, people generally wear only practical hats, like ball caps in the sun or hoods in the cold. Cancer patients often wear hats, scarves, and turbans, and we don't have to tell you why.

Many patients find chemotherapy-induced alopecia (CIA) psychologically devastating. Patients have even refused palliative or life-saving treatments because they could not accept temporary or prolonged baldness. Clinicians are prone to dismiss or pooh-poo these concerns--after all, it's only hair!--but thinking like that went out with fedoras! Hair is closely tied to body image, gender identification, self-esteem and sexuality. Some religions have beliefs about hair. Cancer patients' whole-body hairlessness marks them, robbing them of their ability to keep the diagnosis private. Endless "bad hair days" may influence biology; depression dampens immune function. Consequently, more research is being directed at CIA. (And certain bald men may benefit serendipitously.)

Hair loss (effluvium) is classified according to the stage of the hairs shed. Normal human hairs grow in three phases. *Anagen* (growing) hairs undergo vigorous mitosis at the hair follicle matrix for two to six years. As the anagen phase ends, the amount of pigment at the base of the follicle decreases. The hair enters the *catagen* phase for just a few days, during which mitotic activity decreases. The follicle separates from the dermal papilla and the capillary plexus and moves upward toward the epidermis. (Yikes!) The resulting *telogen* hairs rest for 100 days or so. They lack root sheaths and lose their color, but their short, club-shaped roots anchor them in the follicle. When the anagen stage begins again, new hair growth pushes telogen hairs out. Of the 100,000 hairs on the average scalp, 10-15% are in the catagen or telogen phase at any time, and the same is true for other body hair. Most hair follicles are in the anagen stage.

Anagen effluvium occurs after an insult impairs actively growing hair follicle's mitotic or metabolic activity. Antineoplastics, and combination therapy more so than single agent therapy, can inhibit or arrest matrix cell division creating narrow, weak hair shafts that break easily. These agents can also prevent hair formation, damage the hair bulb, or cause the hair to separate at the bulb and fall out. Since most hair follicles are in the anagen stage, hair loss is widespread. Some antineoplastics can also induce telogen effluvium, causing complete baldness. Alopecia becomes most noticeable when 50% of anagen hairs are lost.

Alopecia's severity is generally dose dependent. The most severe hair loss occurs after topoisomerase inhibitors (e.g. doxorubicin), microtubule agents (e.g. paclitaxel), antimetabolites (e.g. fluorouracil plus leucovorin), or alkylators (e.g. cyclophosphamide). It usually begins 7-14 days after the first dose, peaking within eight weeks. Bleomycin, dactinomycin, daunorubicin, and methotrexate also cause alopecia. Among "regular" drugs, bismuth, levodopa, colchicine, and cyclosporine can also cause anagen effluvium. Among chemicals, thallium, boron, and arsenic exposure can cause alopecia.

Clinicians have tried a few methods of saving hair, but not without controversy. The application of a pressure cuff around the scalp and local hypothermia (cold caps) slow, but do not prevent anagen arrest, if implemented during medication infusion. Both appear to decrease blood flow in and hinder delivery of medication to the scalp. The controversy: the scalp may act as a sanctuary for circulating malignant cells. For this reason, experts indicate patients with leukemia, lymphoma, and other hematologic malignancies are generally not suitable candidates for cold caps or cuffs.

Upon cessation of drug therapy, the follicle resumes its normal activity within a few weeks. On occasion, the patient's hair color and texture after chemotherapy-induced alopecia is different from those of the original hair. Although topical minoxidil will not prevent chemotherapy-induced alopecia, it shortens the period of baldness by about 50 days. Research is underway to find agents that will prevent alopecia without interfering with treatment.

References available upon request.

THE LBD of CONTEMPORARY RESEARCH ONCOLOGY

Believing function follows form, Coco Chanel popularized the little black dress (LBD) in the 1920s. For anyone whose been in Antarctica for nine decades, the LBD is a short, functional evening or cocktail dress. Chanel designed the LBD to hide stains, fit every woman, and dress up or down depending on the occasion. Its prevailing characteristic: ubiquity.

With another approval--this time in combination with chemotherapy for first line treatment of lung cancer--and trials (more than 50 of them) in every cancer imaginable, we hereby dub bevacizumab "the LBD of contemporary oncology research."



Please note that NCI-sponsored trials have been amended to simplify preparation. You can now add the appropriate dose of bevacizumab to a commercially prepared bag of 0.9% normal saline.

DON'T HESITATE

If you consider preparation of any NCI-supplied agent difficult, confusing, or unreasonably costly, please let us know. Your concerns might include

- You must have Cole Hahns to prepare it
- It takes a Wrangler to get the seal off of the bottle
- The glass ampule is impossible to Cocks
- If anyone opens the Dior when you are preparing it--Uggs--you have to start over!
- When the agent is infused Via Spiga, it always occludes the line
- It requires a Lucky Brand of IV bag or equipment that you don't always stock.

Let us know--we're Burberry interested in saving time or money for you! And even if we can't help, there's no Hermes done by asking.

Does she or doesn't she?

French doctors who treated 133 cancer patients with imatinib found that nine grey haired patients lost reverted to their natural hair color! More patients may have accrued this benefit, but many had dyed their hair. Color restoration usually took about five months, but occurred as late as 14 months.

PUT ON YOUR SEQUINS & CELEBRATE!

The FDA approved Vorinostat (Zolinza™) on October 10, 2006 for treatment of cutaneous manifestations in patients with cutaneous T cell lymphoma who have progressive, persistent or recurrent disease on or following two systemic therapies.

