From: Ward Byrne
To: Robinson, Dean
CC: larryv@pain.com; joannk@pain.com; Pyfer, Andy; Castagno, Paula; Terifay, Terrence
Sent: 12/8/2004 3:15:57 PM
Subject: Fwd: RE: RE: Invitation to be an Expert Interview on Pain.com
Attachments: Q&A_Webster.doc; Webster Bio-UPDATE1.doc

Hi Dean,

FYI.

As promised, Dr. Webster's Expert Interview is in hand. Next up is Dr. Foley.

Hope you are doing well,

Ward

Subject: RE: RE: Invitation to be an Expert Interview on Pain.com
Date: Tue, 7 Dec 2004 15:32:11 -0700
X-MS-Has-Attach: yes
X-MS-TNEF-Correlator:
Thread-Topic: RE: Invitation to be an Expert Interview on Pain.com
Thread-Index: AcTZVzuYlPSp/OpAQ6Wy3f2/+dyOowDVRlIA
From: "Lynn Webster"
To: "Ward Byrne"
Cc: "Lynn Webster"
X-RCPT-TO:

Ward,

Please see if this is what you need. I can make changes, add or subtract if you want. Initially I had about twice the amount but cut it down to this.

I attached a bio if you need it.

-----Original Message-----

From: Ward Byrne [mailto: wardbyrne@250west49.com]

Sent: Friday, December 03, 2004 9:46 AM

To: Lynn Webster

Cc: joannk@pain.com; larryv@pain.com

Subject: RE: RE: Invitation to be an Expert Interview on Pain.com

Good day Dr. Webster,

How are you progressing with your Expert Interview for Pain.com? Could you let me know when we can expect it?

HAPPY HOLIDAYS !

Ward

===

Ward Byrne, Industry Liaison,

Dannemiller Memorial Educational Foundation

250 West 49th Street, Suite 401, New York, NY 10019

Phone: (212) 957-1797; Fax: (212) 489-2468;

Email: wardbyrne@250west49.com

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At 07:16 AM 10/28/2004 -0700, you wrote:

I am out of town for the next 10 days. I will be working on it while am gone but it should be done within two week from today.
-----Original Message-----
From: Ward Byrne [mailto: wardbyrne@250west49.com]
Sent: Wednesday, October 27, 2004 8:35 AM
To: Lynn Webster
Subject: RE: RE: Invitation to be an Expert Interview on Pain.com

Hi Dr. Webster,

Could you let me know the current status on your Expert Interview for Pain.com?

Thank you and have a great day,

Ward

At 10:43 AM 10/12/2004 -0700, you wrote:

Yes I can get it to you probably by the end of next week or during the week following.
Certianly within 30 days
-----Original Message-----
From: Ward Byrne [mailto: wardbyrne@250west49.com]
Sent: Tuesday, October 12, 2004 6:47 AM
To: Lynn Webster
Subject: Fwd: RE: Invitation to be an Expert Interview on Pain.com

Good day Dr. Webster:
Could you let us know when you can do the Expert Interview? Is it possible to complete your Q&A presentation over the next month?
If I can be of any further help, please let me know. Need: your picture, bio and either Tax ID# or SS# for honorarium.
Thank you and have a great day,
Ward

Date: Thu, 07 Oct 2004 10:02:34 -0400
To: "Lynn Webster"
From: Ward Byrne
Subject: RE: Invitation to be an Expert Interview on Pain.com
Cc: MJBMD58@aol.com
Bcc: vignone@250west49.com
Dear Dr. Webster:
Thank you for your participation in an Expert Interview on Pain.com. We are looking forward to your presentation based on your 2004 APS abstract on "Utilization of OTFC in Chronic NonCancer Pain: A Retrospective Survey of 100 Patients."
For "posting on Pain.com" scheduling, could you let us know when you can develop the Q&A Expert Interview?
Please forward your picture and bio so that we can post them with the Expert Interview.
Again, we use the Q&A format (where you develop both questions and answers) which works well

for delivering your educational points. For a reference, please go to Pain.com, then go to "Professional Information," then scroll down to "Expert Interviews" to see various examples.
Please let us know your tax ID # or your social security number for the honoraria payment.
If you have any questions or fulfillment needs, just let me know.
Have a great day,
Ward
At 04:08 PM 10/2/2004 -0700, you wrote:

Yes I would be willing to be interviewed. I don't recall receiving the invitation but would interested in the invitation.
Thank you.
-----Original Message-----
From: Ward Byrne [mailto: wardbyrne@250west49.com]
Sent: Thursday, September 30, 2004 10:18 AM
To: Lynn Webster
Cc: Kerrie Turner
Subject: Invitation to be an Expert Interview on Pain.com

Dear Dr. Webster,
I am following up on behalf of Dr. Michael Brennan to confirm receipt of an invitation for you to participate as an Expert Interview on Dannemiller's Internet Site, Pain.com. Please see attached file. I will resend a hard copy via mail.
Thank you,
Ward

==
Ward Byrne, President,
Enhanced Medical Communications, Ltd.
250 West 49th Street, Suite 401, New York, NY 10019
Phone: (212) 957-1797; Fax: (212) 489-2468;
Email: wardbyrne@250west49.com
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Dr. Webster recently published an abstract on the treatment of noncancer pain with oral transmucosal fentanyl citrate (OTFC).

Pain.com: Please explain a little about the study detailed in your abstract and what you were hoping to accomplish.

Dr. Webster: This was a retrospective chart review of 100 patients treated for noncancer pain in five clinics throughout the country. My colleagues and I wanted to know several things: The optimal starting dose of OTFC, its effectiveness, whether the dose should be increased over time and the most frequently reported problems.

Typical of most pain practices, low back pain and headaches were the most common types of chronic pain diagnoses studied. Other common diagnoses were complex regional pain syndrome, neuropathies, abdominal pain and generalized musculoskeletal pain, including fibromyalgia. We also took note of pain intensity scores from first to last visits. Some of the patients we studied had only incident pain. Others had episodic pain unrelated to movement and without persistent pain. Still others had persistent pain with episodes of breakthrough pain (BTP).

We evaluated usage and titration patterns of OTFC and concomitant analgesics. Over 80% of the patients were on long-acting opioids, while 70% also were receiving short-acting opioids. These included around-the-clock (ATC) medications such as sustained-release morphine, oxycodone and methadone. ATC medications remained unchanged throughout the study period. Most of the patients were also on non-opioid analgesics including anticonvulsants and antidepressants. OTFC was a supplemental medication to all of these medications -- 73% of the patients used one to four OTFC doses per day. Most patients (68%) were on the same dose of OTFC at the conclusion of our study as they were at the beginning. It did not appear that the patients developed a tolerance to OTFC.

Pain.com: What type of pain conditions do you treat with OTFC?

Dr. Webster: OTFC is FDA-approved for the treatment of BTP in opioid-tolerant patients with cancer pain. However, I use OTFC predominantly for noncancer BTP or incident pain. Many patients who have moderate persistent pain find that sustained-released opioids relieve most of the pain but still experience one to four episodes of severe BTP each day. Rather than

increase the amount of the ATC sustained-released opioids, I use OTFC to treat these breakthrough events.

Pain.com: Please define BTP.

BTP is a transitory exacerbation of pain that usually occurs on a background of otherwise controlled persistent pain. BTP is characterized by an unpredictable rapid onset of pain -- usually within five minutes -- that is usually very intense and of short duration. A typical example is a lancinating pain that reaches its peak within seconds, lasts for several minutes, then wanes. Unfortunately, most short-acting opioids will not begin to work before most of the BTP experience has passed. The ideal treatment for BTP is a medication with a rapid onset and a relatively short duration that matches the onset of the pain and its duration.

Pain.com: How would you compare the speed of onset of morphine with OTFC?

Dr. Webster: The analgesic onset from oral morphine is 30 to 40 minutes. The analgesic onset for OTFC is 5 to 10 minutes, comparable to that of

intravenous (IV) morphine. OTFC is rapidly absorbed across the mucous membrane because it is highly lipid soluble, unlike morphine, which is water-soluble. Once the fentanyl is in the bloodstream it will cross the blood-brain barrier much more rapidly than morphine because of fentanyl's lipophilicity. In fact, in clinical trials on human volunteers, the onset and peak effect of 200 mcg of OTFC was comparable to 2 mg of IV morphine.

Pain.com: How did you decide on the first dose of OTFC?

Dr. Webster: To those of us who have used fentanyl as an IV anesthetic in the operating room, 200 mcg of fentanyl sounds like a lot. However, when administered as a transmucosal product, only 25% of 200 mcg will be immediately absorbed into the bloodstream. Another 25% will be absorbed from the GI tract at a much slower pace. The total amount of OTFC absorbed is approximately 50%. For significant BTP, 200 mcg is usually inadequate. Therefore, I begin with either a 400 mcg or 800 mcg dose depending on the severity of the pain.

Q. Does age affect your starting dose?

Dr. Webster: Age along with severity and duration of pain, general health and type of pain treated may affect the starting dose. Patients who are elderly, opioid naïve or in general poor health would be started on a lower dose -- perhaps 200 mcg. Then potential adverse effects would be assessed before any change of dose. The nice thing about OTFC is how easy it is to titrate. You can begin with a high strength but advise patients to remove the medication from their mouths when they begin to feel the analgesic effect. This not only prevents toxicity but also helps assess the amount needed to provide relief. Using this method, I have frequently advised elderly patients (>75 years of age) who are opioid naïve and have only incidental pain to start dosing with 400 mcg. At times, I have even recommended 600 mcg or 800 mcg if the incident or BTP is very intense.

Pain.com: Is your starting dose influenced by the amount of sustained-release opioids a patient is receiving?

Dr. Webster: A patient on sustained-release opioids may have acquired some tolerance that lessens the sedative effect of OTFC. However, the amount of persistent pain appears to have very little relationship to the frequency or

intensity of BTP. Therefore, the effective dose of OTFC does not appear related to the amount of sustained-release opioids a patient is receiving.

Pain.com: Are there any patients with whom you would not use OTFC?

Dr. Webster: The same pharmacokinetic properties of OTFC that make it effective also make it a treatment to avoid for some patients. I would be cautious in prescribing OTFC to patients who are known addicts or patients with mental diseases who use opioids, not primarily to relieve pain, but to chemically cope with their anxiety or depression.

Pain.com: Does this mean you believe OTFC is more addictive than other opioids?

Dr. Webster: All opioids have the potential of contributing to abuse and addiction. Addiction is a brain disease that is influenced by an individual's genetics and environment. The pharmacokinetic properties of a medication may contribute to the vulnerability of addiction, but that is not the primary factor. If no environmental or genetic risk factors exist, the potential for OTFC contributing to abuse or addiction is extremely low.

Pain.com: What adverse events have you observed with OTFC?

Dr. Webster: The most common adverse event is dental decay. Many of the medications that are used concomitant with OTFC will produce a dry mouth. OTFC has a sugar base. The combination of a dry mouth and a sugar base can lead to dental decay. This can usually be avoided with good oral hygiene. It's important for clinicians to advise patients to rinse their mouths following use. I have not noticed any other significant adverse events. Obviously, there are risks of excessive sedation, nausea and mental confusion as with all opioids.

Pain.com: What advantage do you see in using OTFC rather than increasing ATC opioids?

Dr. Webster: Some patients with mild persistent pain don't need ATC opioids. Treating chronic pain with fewer ATC opioids could reduce costs. It could also reduce the side effects and potential complications associated with ATC opioids. For instance, we now know that ATC opioid therapy produces panhypothalamic suppression in a subset of patients. Testosterone,

estrogen and possibly ADH are decreased with chronic opioid therapy (COT) in some patients. Additionally, it appears some patients are at risk of producing obstructive sleep apnea and central sleep apnea with moderate-to-high doses of ATC opioids . Therefore, I try to minimize the amount of ATC opioids and will treat BTP with OTFC or short-acting opioids.

Pain.com: Any advice for a doctor using OTFC for the first time?

Dr. W.: I believe that OTFC is a safe and effective medication. However, I can appreciate the concerns of some clinicians who have not been exposed to it. For those who are apprehensive, I would suggest they think of OTFC`s strength in comparison to oxycodone: 200 mcg of OTFC is comparable to 5 mg of oxycodone. For clinicians who are still concerned, I would suggest they ask their patients to fill the prescription and return to their clinic for the first administration. This will allow clinicians to observe patients using the drug for the first time. Clinicians will gain enormous insight as to onset of effect and potential side effects. More importantly, clinicians will gain comfort in knowing how the medication affects patients as the patients leave the clinic.

Q. Are there any other conditions in which OTFC may be used?

Dr. Webster: OTFC can be used in a variety of situations. I use OTFC to help patients avoid emergency-room (ER) visits. For instance, patients with severe migraine headaches unresponsive to normal treatments may use OTFC as an effective abortive treatment. An ER is a terrible place to send migraine patients, because it is loud there and has bright lights, both of which exacerbate most migraine headaches. Many migraine patients are treated in an ER as if they are drug seekers and are required to wait extended periods before being treated. I have found that OTFC helps my patients to avoid these unpleasant experiences.

Realizing that OTFC has a rapid onset and relatively short duration, it can be used for debridement of wounds, office procedures like endoscopies, colonoscopies, sigmoidoscopies, minor surgery like biopsies and vasectomies. Anytime a clinician expects a patient to experience a rapid-onset though transient experience of pain, OTFC may be a useful prophylactic analgesic.

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Bio:

Lynn R. Webster, MD, FACPM, FASAM
Medical Director, Lifetree Pain Clinic
Medical Director and CEO, Lifetree Clinical Research
President, Utah Academy of Pain Medicine
Chief of Anesthesiology, Health South Salt Lake Surgical Center
Associate Clinical Professor, University of Utah Medical Center

Dr. Webster is board certified in anesthesiology and pain management and is also certified in addiction medicine. In his private practice, he treats chronic-pain patients, many of whom have complex diagnoses. He also detoxes opioid-addicted patients. This dual role lends Dr. Webster a valuable perspective. He is dedicated to treating patients in pain while simultaneously working to minimize the potential for abuse and addiction.

His clinical research interests are diverse. They include pain and pain mechanisms, substance abuse and addiction, and cultural and political attitudes toward pain management. Dr. Webster earned his doctorate of medicine from the University of Nebraska Medical Center and completed his residency in the University of Utah Medical Center's department of anesthesiology. He has authored numerous scientific abstracts and journal articles and lectures extensively.

Earlier this year, Dr. Webster was instrumental in launching the Utah chapter of the American Academy of Pain Medicine of which he is president. This organization seeks to achieve high medical standards, improve access to pain care and educate all interested parties about the many pain-related scientific and social issues.