Managing Advanced Prostate Cancer with Viadur™ (Leuprolide Acetate Implant)

Judd W. Moul
Karen Civitelli

Current advanced prostate cancer therapies are aimed at relieving symptoms and increasing life expectancy. Prostatectomy, external beam radiation therapy, and brachytherapy are generally used to treat localized prostate cancer. Hormone therapy, used primarily to relieve symptoms, is the mainstay for advanced disease because of the hormone-dependent nature of prostate cancer cells (Huggins & Hodges, 1941). The definition of advanced prostate cancer has broadened (Moul, 1998a). Locally advanced prostate cancer is considered advanced and is treated with long-term adjuvant hormonal therapy with radiation (Bolla et al., 1997). The development of prostate-specific antigen (PSA) based screening and increased public awareness precipitated a stage-migration in detecting prostate cancer such that fewer patients present with traditional advanced prostate cancer. At the same time, the definition of advanced prostate cancer has broadened (Moul, 1998a). Locally advanced prostate cancer is considered advanced and is treated with long-term adjuvant hormonal therapy with radiation (Bolla et al., 1997). Men who have a PSA-based relapse after surgery or radiation therapy are now considered advanced and are candidates for hormone therapy.

Viadur™ (leuprolide acetate implant), providing a sustained release of drug over a 12-month duration, decreases serum testosterone in advanced prostate cancer patients, providing long-term, palliative medical hormonal therapy. Clinical experience suggests Viadur implants are safe, effective, and generally well tolerated. The continuous drug delivery provided by Viadur ensures compliance. The Viadur implant was designed to be maintenance-free, thereby allowing nurses and other health professionals to focus on other patient needs, such as followup visits and diagnostic tests. Viadur is one aspect of a comprehensive approach to patient management, which also includes regular followup for prostate-specific antigen testing, digital rectal examination, and other tests throughout the 1-year therapy.

Objectives
This educational activity is designed for nurses and other health care professionals who care for and educate patients regarding advanced prostate cancer. The multiple choice examination that follows is designed to test your achievement of the following educational objectives. After studying this offering, you will be able to:

1. Describe the procedure for a Viadur implant.
2. Create a plan of care for the patient with a Viadur implant.

Definition of advanced prostate cancer has broadened (Moul, 1998a). Locally advanced prostate cancer is considered advanced and is treated with long-term adjuvant hormonal therapy with radiation (Bolla et al., 1997). Men who have a PSA-based relapse after surgery or radiation therapy are now considered advanced and are candidates for hormone therapy.

The male androgen testosterone is a mitogenic factor that contributes to tumor cell proliferation in the prostate (Cook & Sheridan, 2000; Huggins & Hodges, 1941). The testes produce approximately 95% of circulating androgens and the remaining 5% are produced by the adrenal glands. Hormonal therapy significantly reduces serum testosterone levels, resulting in diminished tumor size (Auclerc et al., 2000; Moul, 1998a). At present, hormone therapy is achieved surgically by orchietomy or medically by administration of estrogens, antiandrogens, or luteinizing hormone-releasing hormone (LHRH) agonists. These therapies reduce serum testosterone levels and provide subjective improvement in about 80% of patients with metastatic prostate cancer (Moul, 1998a & b).

LHRH agonists mimic the action of natural LHRH, causing...
an initial increase in luteinizing hormone (LH) secretion from the anterior pituitary, which stimulates testosterone production by the testes (Cook & Sheridan, 2000). However, continuous administration of the drug results in the desensitization of the pituitary LHRH receptors within a few days, resulting in a profound decrease in LH release and consequent suppression of gonadal testosterone (Bhasin & Swerdloff, 1986; Kuret & Murad, 1990; Schally et al., 1989; Schally & Comaru-Schally, 1997). Reduction of serum testosterone to castrate levels is achieved in about 2 to 4 weeks (Hanks, Myers, & Scardino, 1993). In contrast to orchiectomy, testosterone levels can be reversed by discontinuing agonist therapy. Leuprolide acetate and goserelin, two LHRH agonists, are approved for palliative treatment of advanced prostate cancer in the United States. These agents are as effective as orchiectomy in decreasing the level of circulating testosterone (Moul, 1998a).

**Viadur™ (leuprolide acetate implant)**

LHRH agonists were originally formulated for daily subcutaneous administration. To increase patient compliance, depot LHRH agonist formulations were developed (Dijkman et al., 1995; Murphy et al., 1987; Sharifi, Soloway, and the Leuprolide Study Group, 1990; Sharifi et al., 1996; Sharifi, Knoll, Smith, & Kramolowsky, 1998). However, in certain populations, particularly indigent patients, compliance has been a concern with LHRH agonist therapy (Shaheen, Amin, & Harty, 1993). Therefore, research efforts have focused on developing longer-acting formulations to encourage compliance.

Among the results of this research has been an implantable leuprolide acetate system, Viadur™, a trademark of ALZA Corporation under license to Bayer Corporation, that provides continuous delivery of leuprolide acetate for 1 year and effective suppression of serum testosterone during this period (see Figure 1). The Viadur implant consists of a small cylindrical titanium drug reservoir that is capped by a semi-permeable membrane at one end and a drug-flow moderator at the other end (see Figure 2). Two osmotic tablets are adjacent to the membrane, and a sliding piston separates the tablets from the drug. After implanting the device subcutaneously, water from the surrounding tissue is drawn through the membrane causing the osmotic tablets to swell and thereby exerting pressure on the piston. The piston is consequently pushed down, forcing drug into the subcutaneous tissue at a rate equal to that of the water entering the other end of the system.

**Figure 1.**
Mean (+ SD) Serum Testosterone Concentrations Measured from Patients Who Received One Viadur Implant (N=107) During the 12-month Treatment Phase. No Increased Levels of Serum Testosterone Were Observed Following Reimplantation at 52 Weeks.

**Figure 2.**
Schematic of a Viadur Implant
Administration. Insertion and removal of the Viadur implant can be performed in an outpatient setting. While the patient is lying on his back, his nondominant arm is flexed at the elbow, and his hand is positioned out to the side. The site of insertion in the upper arm is anesthetized, and, using sterile technique, a small incision is made through the skin approximately 8 to 10 centimeters above the elbow crease in the fossa between the biceps and the triceps. The implant is inserted subcutaneously through the incision using a sterile implanter. The incision site is closed with a sterile wound closure strip and covered with a sterile bandage. To facilitate future removal of the implant, the location of implant placement should be carefully noted with a drawing in the patient’s chart.

At the completion of the 12-month therapy, the device must be removed and a new Viadur implant can be inserted. The implant is located by palpating the upper-arm area. Once found, the tissue must be anesthetized prior to removal. If a new Viadur implant will be inserted, then the tissue along the entire path of the implant should be anesthetized. However, if the procedure is simply to remove the old implant, then only the tissue at the distal end of the implant requires anesthesia. Pressure is applied to one end of the implant to elevate the other end for better visibility, and, using sterile technique, a 4 to 5 millimeter incision is made at the elevated end of the implant. By applying gentle pressure, the end of the implant will emerge from the incision site. If necessary, the scalpel can be used to nick any fibrotic encapsulation to free the implant, and a curved mosquito clamp can be used to facilitate expulsion.

After insertion or removal, the patient must be observed for signs of bleeding from the incision site before discharge. Patients must be instructed to keep the area clean and dry for 24 hours and to avoid strenuous physical activity for 48 hours. The wound closure strip can be removed in about 3 days, after the incision has sealed.

Side effects. Possible complications of inserting the implant include infection, reactions to the dressing, and expulsion of the implant, all of which are relatively rare. Most patients experience some transient bruising and edema, whereas local allergic reactions are rare. Patients should be advised that any application-site reactions that occur are likely to be mild and might require minimal intervention such as an over-the-counter analgesic. The patient should be aware of signs and symptoms of infection and instructed to contact his physician assistant or physician promptly should they occur. It should be noted that Viadur was not studied in women or children and is contraindicated in female and pediatric patients. In addition, Viadur is contraindicated for patients with hypersensitivity to GnRH, GnRH agonist analogues, as analogues to synthetic GnRH or GnRH agonist analogs have been reported (MacLeod, Eisen, & Sussman, 1987).

Potential side effects of androgen deprivation, particularly hot flashes and sexual dysfunction, should be discussed, and patients should be informed about measures that can be employed to alleviate these problems if they become too distressing. Viadur, like other LHRH agonists, causes a transient increase in serum concentrations of testosterone during the first week of treatment. Patients may experience worsening of symptoms or onset of new symptoms, including bone pain, neuropathy, hematuria, or ureteral or bladder outlet obstruction. Cases of ureteral obstruction and spinal cord compression, which may contribute to paralysis with or without fatal complications, have been reported with LHRH agonists. If spinal cord compression or renal impairment develops, standard treatment of these complications should be instituted. Several interventions for side effects related to Viadur implant therapy are presented in Table 1.

Nursing interventions. Thorough patient assessment should be conducted on a regular basis to monitor any change in disease symptoms and drug-related side effects. Most men with advanced prostate cancer are seen every 3 to 6 months in followup. Symptom assessment, physical examination including DRE, and laboratory tests such as PSA are obtained. Testosterone levels should also be assessed for patients demonstrating an increase in PSA levels. In addition, patients who are taking anti-androgens must have periodic measurements of liver enzymes. Complete blood count and renal function are assessed based on history and physical examination, or at least annually. Skin integrity at the insertion site of the Viadur implant should be observed and documented. Rare implant insertion complications include infection and reactions to the dressing. Transient bruising and edema often occur after insertion. Patients should be advised that any local reactions that occur are likely to be mild and transient, and may require minimal treatment such as an over-the-counter analgesic. The patient should also be aware of signs and symptoms of infection and instructed to contact his nurse or physician promptly if they occur.

Potential side effects of hormone therapy, particularly hot flashes and sexual dysfunction, should be discussed, and patients should be informed about potential interventions to alleviate these problems if they become too distressing (see Table 1). Nurses
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<th>Nursing Diagnosis</th>
<th>Expected Outcome</th>
<th>Nursing Interventions</th>
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| **Knowledge deficit regarding treatment with Viadur implant** | Patient will verbalize understanding of treatment plan and the effects of Viadur implant. | 1. Assess baseline knowledge of disease and treatment strategies.  
2. Explain purpose of drug, potential side effects, and side effect management.  
4. Caution patients against having any procedures done in the implanted arm that could displace the implant.  
5. Stress importance of replacing Viadur implant in 12 months.  
6. Encourage questions.                                                                                                                                 |
| **Anxiety related to cancer diagnosis and treatment**   | Patient will demonstrate effective coping strategies.                            | 1. Assess patient and family member or caretaker for signs and symptoms of anxiety.  
2. Explore specific factors, which may be triggering anxiety.  
3. Encourage coping strategies such as involvement of group support systems, use of previous coping strategies, and alternative coping strategies.  
4. Provide referrals as indicated.                                                                                                                                 |
| **Altered comfort related to hot flashes**              | Patient will verbalize feelings regarding hot flashes and identify coping strategies. | 1. Assess patient for signs and symptoms of flushing.  
2. Discuss effect that hot flashes have on the patient's life. If significant, discuss pharmaceutical options such as megestrol or estrogen with physician. Vitamin E or soy supplement may be helpful.  
3. Suggest that avoiding caffeine, spicy foods, and alcohol may be helpful.  
4. Advise patient to lower room temperature and wear several layers of loose-fitting clothes, which can be removed when a hot flash occurs. |
| **Risk for sexual dysfunction**                        | Patient or his partner is able to verbalize concerns about sexual functioning.    | 1. Give patient or partner permission to express sexual concerns.  
2. Explore current and past sexual patterns and expectations for sexual function.  
3. Provide privacy and confidentiality during all conversations.  
5. Help couple communicate sexual concerns to each other. Assist in identifying options to deal with sexual dysfunction, such as alternative ways to express intimacy. |
should review signs and symp-
toms that may arise as a result of
disease flare, such as new or
increasing bone pain, urinary
obstruction, or parasthesia of the
legs. Patients should be instructed
to promptly notify their nurse or
physician if any of these events
occur; rapid treatment may be
required to prevent or remedy any
serious complications.

Summary
The Viadur implant is an
osmotically driven therapeutic
system for the palliative treat-
ment of advanced prostate can-
cer. It is designed to deliver a sus-
tained, low dose of leuprolide
acetate at levels necessary to
achieve hormone ablation. Clini-
cal experience suggests that
Viadur is safe, effective, and gen-
erally well tolerated. Urology
nurses will be responsible for
assisting in the insertion and
removal of Viadur implants, and
educating patients about hor-
mone therapy and the Viadur
implant system. The once-a-year
placement of the Viadur implant
may allow for fewer office visits
and decreased staff time for
administration. However, moni-

table 1. (continued)
Nursing Care Plan for Patients Treated with Viadur Implant

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<tr>
<th>Nursing Diagnosis</th>
<th>Expected Outcome</th>
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| Risk for sexual dysfunction (continued)|                                                                                   | 6. Discuss therapies available to deal with erectile dysfunction, such as drugs and external devices.  
|                                        | Patient will identify signs and symptoms to report to health care provider.         | 7. Provide professional referrals as indicated.                                          |
| Risk for flare reaction                 | Patient will identify signs and symptoms to report to health care provider.         | 1. Provide ongoing patient assessment.                                                 |
|                                        |                                                                                   | 2. Closely monitor patients with metastatic lesions for signs of spinal cord compression. |
|                                        |                                                                                   | 3. Instruct patient to call health care provider immediately if signs of tumor progression appear:  
|                                        |                                                                                   | • Progressive pain.                                                                   |
|                                        |                                                                                   | • Weakness.                                                                           |
|                                        |                                                                                   | • Motor impairment.                                                                   |
|                                        |                                                                                   | • Autonomic dysfunction.                                                              |
|                                        |                                                                                   | • Sensory changes.                                                                   |
|                                        |                                                                                   | • Impaired urinary flow or retention.                                                 |
| Impaired skin integrity                | Patient will identify signs and symptoms to report to health care provider and describe measures to protect and heal incision site. | 1. Instruct patient on post-discharge care of implant incision site:  
|                                        |                                                                                   | • Temporary or transient bruising, swelling, and pain may occur.                      |
|                                        |                                                                                   | • Keep site clean and dry for 24 hours.                                               |
|                                        |                                                                                   | • Avoid strenuous activity for 48 hours.                                              |
|                                        |                                                                                   | • Remove dressing when the incision has sealed, usually in 3 to 4 days.               |
|                                        |                                                                                   | 2. Teach patient to promptly report signs and symptoms of infection, bleeding, or implant expulsion to the health care provider. |
|                                        |                                                                                   | 3. Assess skin integrity on ongoing basis.                                            |
toring patients for emerging drug side effects and disease symptoms is still necessary. Therefore, careful assessment and coordination of the patient’s overall treatment plan will be key to maximizing the benefits of therapy.

References


Additional Reading


