

Postexposure HIV Regimens in Kids Reviewed

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FROM AN ANNUAL CONFERENCE ON
PEDIATRIC INFECTIOUS DISEASES

VAIL, COLO. — A 5-year-old boy finds a used condom in the park. He decides that it would be a really cool balloon, so he puts it in his mouth and tries to blow it up.

Should he receive HIV postexposure prophylaxis or not?

How about prophylaxis for a 3-year-old girl with an accidental fingerstick from a needle she found while playing in a park? Or for an 18-month-old girl in a homeless shelter who reached under a

In a recent study of 274 pediatric patients with community-acquired needlestick injuries, 82 received postexposure prophylaxis, but no seroconversions occurred in any of the 274 patients.

sofa cushion and discovered treasure in the form of an old tampon with dried blood on it, which she promptly put in her mouth? Or a 3-year-old boy who cut himself on the cheek while pretending to shave with a used razor belonging to his HIV-positive uncle?

The pediatric infectious diseases staff at the Children's Hospital, Denver, has encountered all of these situations. Those clinicians recommended HIV postexposure prophylaxis in only one of these four situations: the boy who sustained a large laceration while he was playing with his HIV-positive uncle's razor, Heather R. Heizer said at the conference, which was sponsored by the hospital.

That is consistent with a generally conservative approach to postexposure prophylaxis that prevails among the hospital's infectious diseases staff. That stance is based upon the intervention's substantial financial cost, significant toxicities, and a complete absence of pediatric clinical trials data that might help guide clinical decision making, explained Ms. Heizer, who is a physician assistant and instructor in pediatrics at

the hospital and the University of Colorado, Denver.

When the Denver pediatric infectious diseases staff does offer HIV postexposure prophylaxis following nonsexual, nonoccupational exposures, the favored approach—based largely upon studies done in animals—is a triple-drug antiviral regimen that is prescribed for 28 days, but only if it can be started within 72 hours of the exposure, she continued.

In children younger than age 13 years who may have difficulty swallowing pills, the staff generally uses 28 days of zidovudine (Retrovir), lamivudine (Epivir), and Kaletra (a combination of lopinavir plus ritonavir), because all are available in liquid formulations.

Older children receive Combivir (zidovudine plus lamivudine) and Truvada (tenofovir plus emtricitabine), or Combivir plus Kaletra.

HIV transmission requires exposure to an infectious body fluid (defined as blood, breast milk, semen, or vaginal secretions) through broken skin or mucous membranes. Saliva, tears, and urine are considered noninfectious unless blood is visibly present.

The half-life of HIV in serum is about 1.2 days; the virus can survive only for about 6 hours extracellularly.

Returning to her specific case exam-

Now Approved



Image of trabecular bone insert reproduced with permission from David W. Dempster, PhD.

INDICATION

Prolia™ is indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy. In postmenopausal women with osteoporosis, Prolia™ reduces the incidence of vertebral, nonvertebral, and hip fractures.

IMPORTANT SAFETY INFORMATION

- ❖ **Hypocalcemia:** Prolia™ is contraindicated in patients with hypocalcemia. Pre-existing hypocalcemia must be corrected prior to initiating Prolia™. Hypocalcemia may worsen, especially in patients with severe renal impairment. In patients predisposed to hypocalcemia and disturbances of mineral metabolism, clinical monitoring of calcium and mineral levels is highly recommended. Adequately supplement all patients with calcium and vitamin D.
- ❖ **Serious Infections:** In a clinical trial (N = 7808), serious infections leading to hospitalization were reported more frequently in the Prolia™ group than in the placebo group. Serious skin infections, as well as infections of

the abdomen, urinary tract and ear, were more frequent in patients treated with Prolia™. Endocarditis was also reported more frequently in Prolia™-treated subjects. The incidence of opportunistic infections was balanced and the overall incidence of infections was similar between the treatment groups. Advise patients to seek prompt medical attention if they develop signs or symptoms of severe infection, including cellulitis.

Patients on concomitant immunosuppressant agents or with impaired immune systems may be at increased risk for serious infections. In patients who develop serious infections while on Prolia™, prescribers should assess the need for continued Prolia™ therapy.

- ❖ **Dermatologic Adverse Reactions:** Epidermal and dermal adverse events such as dermatitis, eczema and rashes occurred at a significantly higher rate in the Prolia™ group compared to the placebo group. Most of these events were not specific to the injection site. Consider discontinuing Prolia™ if severe symptoms develop.

- ❖ **Osteonecrosis of the Jaw (ONJ):** ONJ, which can occur spontaneously, is generally associated with tooth extraction and/or local infection with delayed healing, and has been reported in patients receiving Prolia™. An oral exam should

Spanish-Language Shingles Fact Sheet

The National Institute on Aging's newest Spanish-language fact sheet, "Vivir Mejor la Tercera Edad: La culebrilla," describes shingles, risk factors for the disease, prevention tips, and treatment to relieve symptoms. It also offers a list of resources. For information call 800-222-2225 or visit www.nia.nih.gov/healthinformation/publications/spanish/shingles-sp.htm, which offers an option for English. ■

ples of potential HIV exposure, Ms. Heizer said that the pediatric infectious diseases staff declined to offer prophylaxis to the young girl in the homeless shelter with the bloody tampon. The tampon was old and the blood was dried, she explained, making for an extremely low HIV transmission risk.

Similarly, the boy with the "balloon" was deemed at very low risk because the condom was old and dried out, with no visible blood or semen.

The girl who stuck herself with a needle that she found in a park was not offered postexposure prophylaxis, Ms.

Heizer explained, because there was no visible blood in the needle, the park wasn't thought to be a hangout for injection drug use, and exposure to discarded needles is generally thought to carry a low risk of transmission for HIV.

That last point was demonstrated in a classic study of 308 children who were exposed to discarded needles and were subsequently tested for HIV: Not one case of transmission occurred (Pediatrics 1999;104:318-24).

More recently, pediatricians in Montreal reported on 274 patients with com-

munity-acquired needlestick injuries. In all, 82 received postexposure prophylaxis, of whom 69 completed the 4-week treatment course.

No seroconversions occurred in any of the 274 patients, confirming that the transmission risk is quite low, Ms. Heizer noted.

She found that study particularly useful because it paints a picture of situations in which accidental pediatric needlesticks are most likely to occur, and to whom.

About 29% of the needlesticks happened in a street or alley, and another

24% occurred in a park. The patients' mean age was 7.9 years. Nearly two-thirds of the injuries occurred in boys. In 65% of the injuries, the child purposely picked up the needle.

A particularly gratifying study finding was that three-quarters of the children with community-acquired needlestick injuries were brought to medical attention on the day of the injury (Pediatrics 2008;122:e487-92). ■

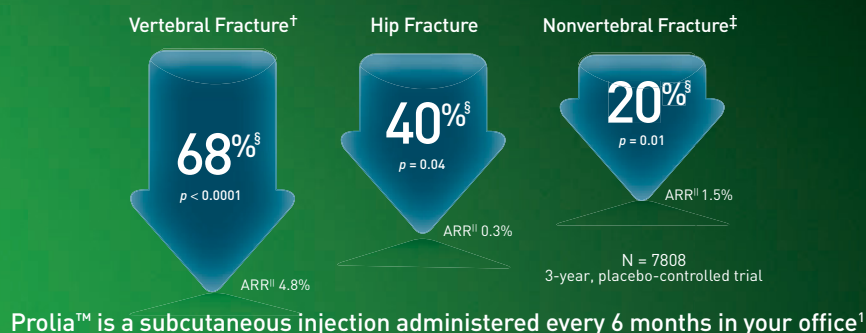
Disclosures: Ms. Heizer reported having no financial conflicts regarding her presentation.

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Prolia™ significantly reduced fracture risk at key sites in a phase 3 trial*^{1,2}



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Please see Brief Summary of Prescribing Information on the following page.

be performed by the prescriber prior to initiation of Prolia™. A dental examination with appropriate preventive dentistry should be considered prior to treatment in patients with risk factors for ONJ. Good oral hygiene practices should be maintained during treatment with Prolia™.

For patients requiring invasive dental procedures, clinical judgment should guide the management plan of each patient. Patients who are suspected of having or who develop ONJ should receive care by a dentist or an oral surgeon. Extensive dental surgery to treat ONJ may exacerbate the condition. Discontinuation of Prolia™ should be considered based on individual benefit-risk assessment.

Suppression of Bone Turnover: Prolia™ resulted in significant suppression of bone remodeling as evidenced by markers of bone turnover and bone histomorphometry. The significance of these findings and the effect of long-term treatment are unknown. Monitor patients for consequences, including ONJ, atypical fractures, and delayed fracture healing.

Adverse Reactions: The most common adverse reactions (> 5% and more common than placebo) are back pain, pain in extremity, musculoskeletal pain, hypercholesterolemia, and cystitis. Pancreatitis has been reported with Prolia™.

The overall incidence of new malignancies was 4.3% in the placebo and 4.8% in the Prolia™ groups. A causal relationship to drug exposure has not been established. Denosumab is a human monoclonal antibody. As with all therapeutic proteins, there is potential for immunogenicity.

Prolia™ Postmarketing Active Safety Surveillance Program:

The Prolia™ Postmarketing Active Safety Surveillance Program is available to collect information from prescribers on specific adverse events. Please go to www.proliasafety.com or call 1-800-772-6436 for more information about this program.

* Key sites: vertebral, hip, and nonvertebral.^{1,2}
 † Includes 7393 patients with a baseline and at least one post-baseline radiograph.^{1,2}
 ‡ Composite measurement excluding pathological fractures and those associated with severe trauma, fractures of the vertebrae, skull, face, mandible, metacarpals, fingers, and toes.^{1,2}
 § RRR = relative risk reduction.
 ¶ ARR = absolute risk reduction.

References: 1. Prolia™ (denosumab) prescribing information, Amgen. 2. Cummings SR, San Martin J, McClung MR, et al. Denosumab for prevention of fractures in postmenopausal women with osteoporosis. *N Engl J Med.* 2009;361:756-765.

For more information, visit www.ProliaHCP.com/FPI

