EDITORIAL

PSA: The Little Kallikrein that "COULD" and "SHOULD"

The U.S. Preventative Services Task Force (and later the Canadian Task Force on Preventive Health Care) recommended against using the PSA test to screen for prostate cancer, since it could result in "overdiagnosis" and "overtreatment" because "most prostate cancer is asymptomatic for life."[1] However, prostate cancer remains the number-one diagnosed cancer in men in North America and the second- or third-most-common "killing cancer" in North American men.

Dr. T. Ming Chu and colleagues from Roswell Park Cancer Institute in Buffalo, New York were the first group to really purify and characterize PSA and show that it was virtually "prostate specific," as they described in their 1979 article.[2] In 1991, Catalona published the first results of a study showing that PSA was the most accurate method for detecting prostate cancer and suggested that it should be used as a first-line screening test for prostate cancer.[3] However in 2011, Gomella et al noted that there was conflicting evidence about using PSA tests to screen for prostate cancer and suggested that physicians should discuss this with their patients.[4]

Since the early 90s, after the widespread use of PSA tests to screen for prostate cancer, we have seen a drop in deaths due to prostate cancer. Prostate-cancer screening trials such as the Göteborg trial have demonstrated significant survival benefits with a relatively small "number needed to screen."[5]

However, some researchers have suggested that the incidence of significant morbidity associated with trans-rectal ultrasound (TRUS)-guided biopsies can be as high as 5%.[6] Because of this, we have almost reversed our approach and are looking for an excuse not to biopsy patients, for fear of causing morbidity and/or detecting an "insignificant" cancer.

Today, abnormal values for total PSA, age-related PSA, free-to-total PSA ratio, and PSA density are still the primary drivers of first-time prostate biopsies. If a patient is diagnosed with cancer, we use PSA values as one of the significant factors to insert into Partin tables to predict risk of cancer spread.

After primary prostate-cancer treatment, we again use PSA as the marker to indicate success or failure. With post-secondary therapy with hormonal manipulation, rising PSA levels suggest the development of castrate-resistant prostate cancer. We use the PSA doubling time to determine whether to escalate to the next treatment. We then look to PSA to signal failure of the newer "super hormonal manipulators" such as abiraterone and enzalutamide.

New biomarkers have been promoted in the pre-biopsy space to determine the risk of finding significant cancer. Some clinicians have advocated the use of the 4Kscore test, which uses 4 kallikreins—total PSA, free PSA, intact PSA and human kallikrein 2 (hK2).[7]

Thirty-six years after Chu and colleagues proved the significance of PSA as a marker, it is still the kallikrein marker that could, and now more than ever should, be used to prevent unnecessary biopsies while helping us detect clinically significant prostate cancers.

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4. Gomella LG, Liu XS, Trabulsi EJ et al. Screening for prostate cancer : the current evidence and guidelines controversy. *Can J Urol* 2011;18(5): 5875-5883.
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7. Parekh DJ, Punnen S Sjoberg JJ et al. A multi-institutional prospective trial in the USA confirms that the 4Kscore accurately identifies men with high-grade prostate cancer. *Eur Urol* 2014. Epub ahead of print.

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BONE METASTASES CAN OCCUR IN 90% OF MEN WITH ADVANCED PROSTATE CANCER[2]

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XGEVA reduced the risk of developing first and subsequent on-study SREs vs. zoledronic acid by 18% in castrate-resistant prostate cancer patients with bone metastases (mean number of SREs per patient: 0.52 vs. 0.61, RR: 0.82; 95% CI, 0.71–0.94, superiority p-value adjusted for multiplicity: p=0.008, secondary endpoint).[1,3]

XGEVA® is reimbursed under specific criteria in BC, SK, MB, ON, QC, NB, NS and NL.

XGEVA is not indicated for reducing the risk of developing skeletal-related events in patients with multiple myeloma.

XGEVA is not indicated for reducing the risk of developing skeletal-related events in pediatric patients.

Refer to the page in the bottom right icon for additional safety information and for a web link to the Product Monograph discussing:

- contraindications in patients with pre-existing hypocalcemia, which must be corrected prior to initiation.
- most serious warnings and precautions relating to osteonecrosis of the jaw.
- other relevant warnings and precautions: do not use concurrently with Prolia; do not use concurrently with bisphosphonates; hypocalcemia has been reported (including severe symptomatic hypocalcemia and fatal cases postmarketing). Monitor calcium prior to the initial dose, within two weeks after the initial dose, and if suspected symptoms of hypocalcemia occur. Administer calcium, magnesium and vitamin D as necessary. If hypocalcemia occurs while receiving XGEVA, additional short-term calcium supplementation and additional monitoring may be necessary; caution on risk of hypocalcemia in patients with renal impairment; skin infections; hypersensitivity reactions including anaphylaxis; atypical femoral fractures; not recommended for use in pregnant women. Women should not become pregnant during treatment and for at least 5 months after the last dose of XGEVA.
- conditions of clinical use, adverse reactions, drug interactions, and dosing information that have not been discussed here.

In addition, the page contains the reference list and study parameters relating to this advertisement.

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