M
dical advances in the
field of oncology have
increased life expectancy
and decreased mortality rate for
many patients diagnosed with
cancer. These improvements are
associated with the administration
of chemotherapeutic or antineo-
plastic agents. Unfortunately, these
agents can result in side effects
that impact the musculoskeletal
system.

Such effects are notable in the
female population and include
arthralgia, peripheral neuropathy,
myositis, stiffness, osteopenia, os-
teoporosis, and fragility fractures.
In this article, we review the com-
mon antineoplastic agents used in
women and their associated mus-
culoskeletal side effects.

Antineoplastic agents
Aromatase inhibitors
Aromatase inhibitors are used to
treat postmenopausal women with
breast cancer. The three aromatase
inhibitors currently approved by
the U.S. Food and Drug Admin-
istration are anastrozole, exemes-
tane, and letrozole. This class of
drugs work by interfering with the
enzyme aromatase, which produces
estrogen from androgens in the
body through a process called aro-
matization. Lower estrogen levels
result in slowed growth of cancers
that require estrogen.

Selective estrogen receptor
modulators
Selective estrogen receptor modula-
tor (SERM) drugs, such as tamoxi-
fen, are used to treat breast cancer
in both pre- and postmenopausal
women. Tamoxifen blocks the
gonadotropin-releasing hormone
gonadotropin. SERMs have been
shown to be effective in the control
of tumor cell development.

Vinca alkaloids
Vinca alkaloids work by halting
cell division and mitosis, causing
cell death, and angiogenesis. Vinca
alkaloids are used for the treatment
of many malignancies including
Hodgkin’s disease, non-Hodgkin’s
lymphoma, breast cancer, and
colorectal cancer. The four major
vinca alkaloids in clinical use are
vinblastine, vincoreline, vincristine,
and vindesine. General side effects
of their use include toxicity to
white blood cells, nausea, vomit-
ing, and fatigue.

Taxanes
Taxanes promote cell death by in-
terfering with normal cell division.
Taxanes such as paclitaxel and
docetaxel are commonly used to
treat breast cancer and non–small
lung cancer.

Musculoskeletal effects
Arthralgia can be a common side
effect of antineoplastic agents
such as taxanes and aromatase inhibi-
tors. Most of the studies on cancer
treatment-induced arthralgias have
focused on aromatase inhibitors.
The use of aromatase inhibitors
as adjuvant endocrine therapy has
led to the discovery of a signifi-
cant profile of musculoskeletal symp-
toms, especially arthralgia. It is
estimated that up to 50 percent of
patients treated with aromatase
inhibitors experienced arthralgia.
Aromatase inhibitors are also
associated with bone pain, tendini-
tis, tendinopathy, carpal tunnel
syndrome, trigger finger, and joint
stiffness in the hands, wrist, knees,
and ankle. At this time, the mecha-
nism or cause of symptoms associ-
ated with the aromatase inhibitors
is not understood; current theories
involve inflammatory cytokines
such as IL-1, TNF alpha, and IFN
gamma.

Patients with chemotherapy-
treatment-induced arthralgias will gen-
erally report symmetric joint pain,
including pain in the hands and/or
wrists, decreased grip strength,
morning stiffness, and improve-
ment in joint discomfort with use
or exercise. Symptoms may im-
prove or resolve for most, but not all,
women within 2 weeks of stop-
ping aromatase inhibitor therapy.
Promising symptom management
approaches include exercise and
acupuncture, but more trials are
needed to confirm the benefits.

Osteoporosis and osteopenia
Decreased bone mineral density is
a side effect of chemotherapeutic
regimens, including SERMs and
aromatase inhibitors, that are
used to treat common neoplasms
such as breast cancer. Studies have
shown that the decrease in bone
mineral depletion is faster and
more severe in patients with can-
cer treatment-induced bone loss
compared to menopause bone
loss. The prevention, detection,
and early management of cancer
treatment-induced bone loss are
essential to reduce the risk of frac-
ture in these patients.

Standard recommendations for
bone health in a postmenopausal
woman include calcium, vitamin D
supplementation, smoking cessa-
tion, decreased alcohol consump-
tion, and normalization of body
mass index. In addition, a com-
nutation of resistance and aerobic
exercise has been associated with
improvements in lean mass and
muscle strength and slow decline of
bone mineral density. Other treat-
ments include the use of bisphos-
phonates, estrogen, parathyroid
hormone agonists, and RANKL
inhibitors.

Chemotherapy-induced
peripheral neuropathy
Chemotherapy-induced peripheral
neuropathy (CIPN) is a progres-
sive, enduring, and often irrevers-
bile condition that causes pain,

Putting sex in your
orthopaedic practice
This quarterly column from the
AAOS Women’s Health Issues
Advisory Board and the Ruth
Jackson Orthopaedic Society
provides important information
for your practice about issues
related to sex (determined by our
chromosomes) and gender (how
we present ourselves as male or
female, which can be influenced
by environment, families and
peers, and social institutions).
It is our mission to promote the
philosophy that male and female
patients experience and react
to musculoskeletal conditions
differently; when it comes to
patient care, surgeons should not
have a one-size-fits-all mentality.

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