P5-11-14

Physician Perceptions of Estrogen Agonist/Antagonists in Menopausal Health: A Survey to Address Osteoporosis, Urogenital Health and Breast Concerns in Menopause and Breast Cancer Survivorship

Shari Goldfarb, MD[1], Michael Krychman, MD[2], Paul Plourde, MD[3], and David Portman, MD[3]

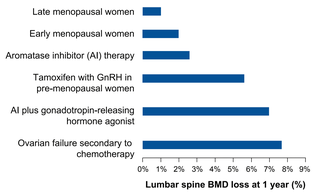
[1] Memorial Sloan Kettering Cancer Center, New York, New York; [2] Southern California Center for Sexual Health and Survivorship Medicine, Inc, Newport Beach, CA; [3] Sermonix Pharmaceuticals, Columbus, OH

Sermonix Pharmaceuticals

Introduction

Postmenopausal women, particularly those with a history of breast cancer, are in great need of effective and safe treatment to maintain bone and genitourinary health. As shown in Figure 1, many common therapies in breast cancer are associated with increased bone loss.

Figure 1. Increased bone loss associated with common treatments in the breast cancer population compared to late and early menopausal controls[1]



- **The enhanced bone loss in women with breast cancer has been associated with a 31% increase in clinical fracture rate.[2,3] Moreover, in postmenopausal women, long-term aromatase inhibitors (AI) are associated with a 36% higher fracture rate[4].**
- **Another common symptom seen in postmenopausal women and women with a history of breast cancer, and especially those who also have a history of AI use, is vulvovaginal atrophy (VVA). These treatments can significantly increase the incidence and severity of VVA symptoms in the survivor population and lead to dyspareunia, vaginal dryness, and recurrent vaginal and urinary tract infections. Non-hormonal lubricants are largely inadequate for symptom relief and fail to restore the underlying tissue damage.[5]**
- **Symptoms of vaginal atrophy have a severe detrimental effect on the quality of life of breast cancer patients and it is estimated that up to 20% of all patients actually discontinue or consider discontinuing adjuvant endocrine therapy for this reason.[6] Only partial recovery of bone mass is seen following cessation of AIs and some vaginal symptoms may persist in this group long after treatment discontinuation.[7]**
- **One of the most effective treatments for osteoporosis and VVA is estrogen administered either systemically or locally; both of these, however, are contraindicated in women with a history of breast cancer.**
- **As a consequence, breast cancer survivors suffer disproportionally from these menopausal conditions and have limited options, and thus may indicate the need for expanded therapeutic options.**

Study Objectives

1. **Profile current treatment practices for prevention/treatment of osteoporosis and VVA in a sample cohort of postmenopausal women**
2. **Identify any trends/changes occurring in treatment**
3. **Identify factors influencing product selection**
4. **Reactions to the product profile of an investigational SERM lasofoxifene**

Methods

A 60 minute self-administered Internet survey was conducted with physicians who were potential prescribers of SERMS. The data were collected between May 11-18, 2015 and analyzed to assess for statistically significant differences between OB/GYN and PCPs at a 95% confidence interval. Selection criteria were:

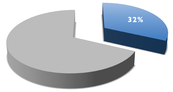
- **Community based OB/GYN and Primary Care Physicians (PCP) [Family Practice, General practice or Internal Medicine]**
- **Treatment of a minimum number of postmenopausal patients per month for osteoporosis/osteopenia and/or VVA.**

Results

Most physicians in this study evaluate and treat between 100-250 postmenopausal patients per month. Although not statistically significant, OB/GYNs reported a higher monthly average volume of postmenopausal patients (186 patients) versus PCPs (140 patients). SERMs currently capture only a relatively small share of HCP prescriptions.

OSTEOPOROSIS PREVENTION: At the current time, only about a third of postmenopausal patients receive prescription medications for the prevention of osteoporosis.

Figure 2. Current % of Postmenopausal Patients Receiving Rx Medications for PREVENTION of Osteoporosis (n=108)



Still, nearly half of the physicians (48%) reported that the number of their postmenopausal patients who are receiving prescription medications for prevention of osteoporosis is increasing.

Raloxifene (Evista®) is currently used for 13% of prevention patients; conjugated equine estrogen/bezadozifene CEE/BZA (Duavee®) is used for 5% of patients for the prevention of osteoporosis; a statistically greater number of PCPs prescribed alendronate (Fosamax®) (p<0.05) for prevention of osteoporosis.

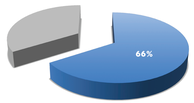
Table 1. Average % of Patients Treated for Prevention of Osteoporosis

	Total (n=108)	OB/GYN (n=53)	PCP (n=55)
Fosamax	26%	21%	**31%***
Systemic estrogen +/- progestin	16%	18%	14%
Evista	13%	15%	12%
Actonel	12%	12%	12%
Boniva	11%	12%	10%
Prolia	6%	4%	7%
Reclast	6%	5%	7%
Duavee	5%	6%	4%
Forteo	3%	2%	4%
Other	2%	4%	-

* p<0.05

OSTEOPOROSIS TREATMENT: PCPs reported having a greater share of postmenopausal patients who have been diagnosed with osteoporosis: 36% of patients versus 25% of patients diagnosed by OB/GYNs. Both specialties reported that the majority of patients diagnosed with osteoporosis are treated with prescription medications.

Figure 3. Current % of Postmenopausal Patients Receiving Rx Medications for TREATMENT of Osteoporosis (n=108)



Raloxifene is currently utilized for 9% of treatment patients; CEE/BZA is utilized for 5% of patients; a statistically greater number of PCPs prescribed alendronate (p<0.05) for treatment versus OB/GYNs.

Table 2. Average % of Patients Treated for Osteoporosis

	Total (n=108)	OB/GYN (n=53)	PCP (n=55)
Fosamax	28%	23%	**34%***
Actonel	13%	14%	12%
Boniva	11%	13%	10%
Systemic estrogen +/- progestin	11%	13%	9%
Prolia	10%	9%	12%
Evista	9%	12%	7%
Reclast	8%	6%	9%
Duavee	5%	6%	4%
Forteo	4%	4%	4%
Other	1%	1%	1%

* p<0.05

VULVOVAGINAL ATROPHY TREATMENT: Overall, nearly half of the postmenopausal patients represented in this survey have been diagnosed with VVA (47%, on average)

Figure 4. Current % of VVA patients (n=108)

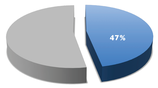


Table 3. % of postmenopausal patients diagnosed with VVA

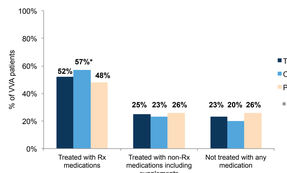
OB/GYN (n=53)	PCP (n=55)
58%*	36%

*OB/GYNs reported a significantly higher share of VVA diagnosed patients than PCPs (*p<0.005).*

Slightly more than half of the postmenopausal VVA patients are currently treated with prescription medications (52%, on average).

OB/GYNs treat significantly more of their VVA patients with prescription medications than PCPs: 57% versus 48%, respectively (p<0.05).

Figure 5. Average % of VVA patients



On average, 10% of VVA patients are reported to be treated with ospemifene and 6% are treated with CEE/BZA. A statistically significantly greater number of OB/GYNs prescribed vaginal estrogen tablets (p<0.05).

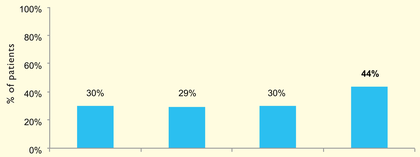
Table 4. Average % of Patients Treated for VVA

	Total (n=108)	OB/GYN (n=53)	PCP (n=55)
Vaginal estrogen cream	43%	42%	45%
Systemic estrogen +/- progestin	19%	16%	22%
Vaginal estrogen tablet	13%	**16%***	10%
Osphena (ospemifene)	10%	10%	11%
Vaginal estrogen ring	8%	9%	6%
Duavee (bazedoxifene/conjugated estrogens)	6%	6%	6%
Other	1%	1%	1%

* p<0.05

PHYSICIAN PERCEPTIONS OF THE INVESTIGATIONAL SERM LASOFOXIFENE

A single agent treating both vaginal symptoms and osteoporosis was viewed favorably by both OB/GYNs and PCPs and would impact their Rx choice:



	VVA	Prevention of osteoporosis	Treatment of osteoporosis	Both VVA and osteoporosis
OB/GYN (n=53)	31%	32%	32%	**46%**
PCP (n=55)	30%	27%	28%	**42%**

For Laxofoxifene, a novel SERM under investigation, the drug features perceived as most favorable by doctors included:

	Perceived as favorable by:
Statistically significant reduction of vertebral fracture by 42% and non-vertebral fracture by 24%	⇦ **76%** *of surveyed doctors*
80% reduction in incidence of ER+ breast cancers at 5 years	⇦ **74%** *of surveyed doctors*
VVA symptom improvement seen within 4 weeks	⇦ **70%** *of surveyed doctors*
5 years of efficacy and safety data from placebo-controlled fracture study	⇦ **70%** *of surveyed doctors*

Summary

1. **For the prevention of osteoporosis, there was no difference between the OB/GYN and PCP specialties prescription profile: bisphosphonates were most frequently used, while only 20% prescribed a SERM.**
2. **For the treatment of osteoporosis, PCPs reported a significantly higher share of patients diagnosed with osteoporosis than OB/GYNs (36% vs, 25%).**
3. **For the treatment of osteoporosis, both specialties prescribed bisphosphonate over other treatments, although PCP prescribed more alendronate (was statistically significant, p < 0.05). For both specialties, SERM share of prescribing was low.**
4. **Nearly half (47%) of the patients were diagnosed with VVA, with OB/GYNs reporting a significantly higher share of VVA diagnosed patients than PCP (58% vs. 36%, p<0.05).**
5. **OB/GYNs treat significantly more of their VVA patients with prescription medications than PCPs: 57% vs 48%, respectively (p<0.05).**
6. **On average, 16% of VVA are reported to be treated with SERM (10% ospemifene and 6% CEE/BZA).**
7. **Lasofoxifene, a novel investigational SERM, if approved for treating VVA and prevention and treatment of osteoporosis, could strongly impact prescription choice.**

Conclusion

Although this survey study was not targeted to clinicians treating breast cancer patients specifically, the results are still highly relevant. Decreased prescribing and poor compliance with bisphosphonates in recent years and the need to avoid exogeneous estrogens in the breast cancer population have significantly limited treatment options for osteoporosis and urogenital atrophy in this population.[8,9]

SERMS were less likely to be prescribed for menopausal conditions in this survey for reasons not fully appreciated. SERMs that specifically target the estrogen receptor selectively with favorable VVA effects, vertebral and non-vertebral fracture prevention, and breast safety might meet the goals of many clinicians treating at-risk patients and breast cancer survivors, and could positively impact health outcomes and quality of life.

REFERENCES

1. Milat F,Vincent AJ. Climacteric 2015;18 Supplement 2:47-55.
2. Body JJ. Increased fracture rate in women with breast cancer: a review of the hidden risk, Cancer 2011;111:384.
3. Chen Z, Maricic M, Bassford TL, et al. Fracture risk among breast cancer survivors: results from the Women's Health Initiative Observational Study Arch Intern Med 2005;165:552–8.
4. Goss PE, Ingle JN, Ki Pritchard. Extending Aromatase-Inhibitor Adjuvant Therapy to 10 Years, N Engl J Med 2016 Jul 21;375(3):209–19.
5. Portman D, Gass M. Genitourinary Syndrome of Menopause: new terminology for vulvovaginal atrophy from the International Society for the Study of Women's Sexual Health and the North American Menopause Society, Oct 2014, 21(10):1062-8.
6. Cella D, Fallowfield LJ. Recognition and management of treatment-related side effects for breast cancer patients receiving adjuvant endocrine therapy. Breast Cancer Res Treat. 2008;107:167–180.
7. Panjari M, Bell RJ, David SR Sexual Function after Breast Cancer J Sex Med 2011;8:294-303.
8. Jha, S, Wang, Z, Laucis, N, Bhattacharyya, T. Trends in Media Reports, Oral Bisphosphonate Perscriptions, and Hip Fractures 1996-2012: An Ecological Analysis. J of Bone and Mineral Research, 2015 30(12).
9. Hadji, P, Ziller, V., Kyvernitakis, J, et al, Persistence with bisphosphonates in patients with metastatic breast cancer: a retrospective database analysis, JCancer Res Clin Oncol, 2013.

Presented at the San Antonio Breast Cancer Symposium, December 6-10, 2016, San Antonio, TX.