

Blacks Just as Likely as Whites to Pursue BRCA Test

BY LINDA LITTLE
Contributing Writer

GRAPEVINE, TEX. — African American women are almost as likely to pursue genetic testing for breast cancer as are white women, North Carolina researchers report.

"There is a perception in the genetic counseling field that African Americans are less likely to pursue genetic testing when it's offered," said Lisa Susswein, ge-

netic counselor, University of North Carolina at Chapel Hill. "It has been thought that there were cultural barriers and, possibly, the inability to pay that kept African Americans from genetic testing."

But when women diagnosed with or at high risk for breast cancer were offered a test to detect *BRCA1* or *BRCA2* gene mutations, both African Americans and whites accepted. The results were presented at a meeting sponsored by the American College of Medical Genetics.

The test was offered to women who exceeded a 5%-10% risk of harboring a *BRCA* mutation as well as to women recently diagnosed with breast cancer. The test was offered to more than 800 women referred to the center.

Of those in the overall high-risk population who were offered the test, 58% of white women and 43% of African American women pursued the test. Among those women recently diagnosed with breast cancer, acceptance was 61% among whites and 50% among African American women, which was not a statistically significant difference.

Many studies have shown African American women are less likely to pursue ge-

netics testing, she said. "This may have been perpetuated by physicians not offering genetics testing, and it's a circle that continues."

Overall, regardless of race, it is important to do testing in breast cancer patients before the primary surgery so they can be given the opportunity to have one surgery with prophylactic double mastectomies, Ms. Susswein said.

"This could save the patient from multiple surgeries down the line," she commented.

"This shows that African American women are interested in *BRCA* testing," Ms. Susswein said. "We ... shouldn't shy away from offering them the test." ■

Men

In two placebo-controlled, double-blind, multicenter studies in men (a two-year study of FOSAMAX 10 mg/day and a one-year study of once weekly FOSAMAX [alendronate sodium] 70 mg) the rates of discontinuation of therapy due to any clinical adverse experience were 2.7% for FOSAMAX 10 mg/day vs. 10.5% for placebo, and 6.4% for once weekly FOSAMAX 70 mg vs. 8.6% for placebo. The adverse experiences considered by the investigators as possibly, probably, or definitely drug related in ≥2% of patients treated with either FOSAMAX or placebo are presented in the following table.

	Osteoporosis Studies in Men Adverse Experiences Considered Possibly, Probably, or Definitely Drug Related by the Investigators and Reported in ≥2% of Patients			
	Two-year Study		One-year Study	
	FOSAMAX 10 mg/day % (n=146)	Placebo % (n=95)	Once Weekly FOSAMAX 70 mg % (n=109)	Placebo % (n=58)
Gastrointestinal				
acid regurgitation	4.1	3.2	0.0	0.0
flatulence	4.1	1.1	0.0	0.0
gastroesophageal reflux disease	0.7	3.2	2.8	0.0
dyspepsia	3.4	0.0	2.8	1.7
diarrhea	1.4	1.1	2.8	0.0
abdominal pain	2.1	1.1	0.9	3.4
nausea	2.1	0.0	0.0	0.0

Prevention of osteoporosis in postmenopausal women

The safety of FOSAMAX 5 mg/day in postmenopausal women 40-60 years of age has been evaluated in three double-blind, placebo-controlled studies involving over 1,400 patients randomized to receive FOSAMAX for either two or three years. In these studies the overall safety profiles of FOSAMAX 5 mg/day and placebo were similar. Discontinuation of therapy due to any clinical adverse experience occurred in 7.5% of 642 patients treated with FOSAMAX 5 mg/day and 5.7% of 648 patients treated with placebo.

In a one-year, double-blind, multicenter study, the overall safety and tolerability profiles of once weekly FOSAMAX 35 mg and FOSAMAX 5 mg daily were similar.

The adverse experiences from these studies considered by the investigators as possibly, probably, or definitely drug related in ≥1% of patients treated with either once weekly FOSAMAX 35 mg, FOSAMAX 5 mg/day or placebo are presented in the following table.

	Osteoporosis Prevention Studies in Postmenopausal Women Adverse Experiences Considered Possibly, Probably, or Definitely Drug Related by the Investigators and Reported in ≥1% of Patients			
	Two/Three-Year Studies		One-Year Study	
	FOSAMAX 5 mg/day % (n=642)	Placebo % (n=648)	FOSAMAX 5 mg/day % (n=381)	Once Weekly FOSAMAX 35 mg % (n=382)
Gastrointestinal				
dyspepsia	1.9	1.4	2.2	1.7
abdominal pain	1.7	3.4	4.2	2.2
acid regurgitation	1.4	2.5	4.2	4.7
nausea	1.4	1.4	2.5	1.4
diarrhea	1.1	1.7	1.1	0.6
constipation	0.9	0.5	1.7	0.3
abdominal distention	0.2	0.3	1.4	1.1
Musculoskeletal				
musculoskeletal (bone, muscle or joint) pain	0.8	0.9	1.9	2.2

Concomitant use with estrogen/hormone replacement therapy

In two studies (of one and two years' duration) of postmenopausal osteoporotic women (total: n=853), the safety and tolerability profile of combined treatment with FOSAMAX 10 mg once daily and estrogen ± progestin (n=354) was consistent with those of the individual treatments.

Treatment of glucocorticoid-induced osteoporosis

In two, one-year, placebo-controlled, double-blind, multicenter studies in patients receiving glucocorticoid treatment, the overall safety and tolerability profiles of FOSAMAX 5 and 10 mg/day were generally similar to that of placebo. The adverse experiences considered by the investigators as possibly, probably, or definitely drug related in ≥1% of patients treated with either FOSAMAX 10 mg/day (n=157), FOSAMAX 5 mg/day (n=161), or placebo (n=159), respectively, were: *Gastrointestinal*: abdominal pain (3.2%; 1.9%; 0.0%), acid regurgitation (2.5%; 1.9%; 1.3%), constipation (1.3%; 0.6%; 0.0%), melena (1.3%; 0.0%; 0.0%), nausea (0.6%; 1.2%; 0.6%), diarrhea (0.0%; 0.0%; 1.3%); *Nervous System/Psychiatric*: headache (0.6%; 0.0%; 0.0%; 1.3%).

The overall safety and tolerability profile in the glucocorticoid-induced osteoporosis population that continued therapy for the second year of the studies (FOSAMAX: n=147) was consistent with that observed in the first year.

Paget's disease of bone

In clinical studies (osteoporosis and Paget's disease), adverse experiences reported in 175 patients taking FOSAMAX 40 mg/day for 3-12 months were similar to those in postmenopausal women treated with FOSAMAX 10 mg/day. However, there was an apparent increased incidence of upper gastrointestinal adverse experiences in patients taking FOSAMAX 40 mg/day (17.7% FOSAMAX vs. 10.2% placebo). One case of esophagitis and two cases of gastritis resulted in discontinuation of treatment.

Additionally, musculoskeletal (bone, muscle or joint) pain, which has been described in patients with Paget's disease treated with other bisphosphonates, was considered by the investigators as possibly, probably, or definitely drug related in approximately 6% of patients treated with FOSAMAX 40 mg/day versus approximately 1% of patients treated with placebo, but rarely resulted in discontinuation of therapy. Discontinuation of therapy due to any clinical adverse experience occurred in 6.4% of patients with Paget's disease treated with FOSAMAX 40 mg/day and 2.4% of patients treated with placebo.

Laboratory Test Findings

In double-blind, multicenter, controlled studies, asymptomatic, mild, and transient decreases in serum calcium and phosphate were observed in approximately 18% and 10%, respectively, of patients taking FOSAMAX versus approximately 12% and 3% of those taking placebo. However, the incidences of decreases in serum calcium to <8.0 mg/dL (2.0 mM) and serum phosphate to <2.0 mg/dL (0.65 mM) were similar in both treatment groups.

Post-Marketing Experience

The following adverse reactions have been reported in post-marketing use:

Body as a Whole: hypersensitivity reactions including urticaria and rarely angioedema. Transient symptoms of myalgia, malaise and rarely, fever have been reported with FOSAMAX, typically in association with initiation of treatment. Rarely, symptomatic hypocalcemia has occurred, generally in association with predisposing conditions.

Gastrointestinal: esophagitis, esophageal erosions, esophageal ulcers, rarely esophageal stricture or perforation, and oropharyngeal ulceration. Gastric or duodenal ulcers, some severe and with complications have also been reported (see WARNINGS, PRECAUTIONS, Information for Patients, and DOSAGE AND ADMINISTRATION).

Musculoskeletal: bone, joint, and/or muscle pain, occasionally severe, and rarely incapacitating (see PRECAUTIONS, Musculoskeletal Pain).

Skin: rash (occasionally with photosensitivity), pruritus, rarely severe skin reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis.

Special Senses: rarely uveitis, scleritis or episcleritis.

For more detailed information, please read the Prescribing Information.

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Possible Genetic Basis for Racial Disparities in Endometrial Ca

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Differences in gene expression may be at least partially responsible for the differences in endometrial cancer survival rates and tumor aggression seen between black and white women, results of two studies suggest.

Many previous studies have ascribed racial disparities in endometrial cancer outcome to less aggressive treatment. The

two new studies, which were presented at the annual meeting of the Society of Gynecologic Oncologists, identified a racial disparity in endometrial cancer even in a health care setting where patients receive sim-

The studies showed a racial disparity in cancer in a setting where patients receive similar care, suggesting a genetic role for differences in outcome.

ilar care and suggested a genetic role for differences in outcome, according to Lt. Col. C.G. Larry Maxwell, MC, USA, the studies' lead investigator.

In the first study, the investigators compared tumor aggression and survival rates between 168 blacks and 997 whites with stage III, IV, or recurrent endometrial cancer. The data were drawn from four randomized controlled treatment trials performed by the Gynecologic Oncology Group of Roswell Park Cancer Institute, Buffalo, N.Y.

All patients received chemotherapy with doxorubicin alone or in combination with paclitaxel and/or cisplatin.

Blacks were more likely to have advanced stage disease and poorly differentiated and nonendometrioid tumors—all of which are associated with increased mortality. After adjusting for clinical and treatment factors using multivariate regression, blacks had a 25% increased relative risk of death, compared with whites. The overall survival rate was 10.6 months for blacks and 12.2 months for whites.

"This study clearly shows a survival disadvantage for blacks, even when they are treated as aggressively as whites," Dr.

Maxwell, director of the Gynecologic Disease Center at Walter Reed Army Medical Center, Washington, said in an interview.

"This is extremely important because many prior investigators primarily have attributed the poor survival in African Americans to unequal treatment," he added.

The second study examined gene expression in 45 fresh frozen endometrial tumors. No differences in expression were found between the races in the first analysis, which included early-stage tumors. But

when the researchers analyzed only the 28 advanced tumors (stage II, III, or IV; 10 black, 14 white), clustering emerged. There were 325 genetic transcripts that were differently expressed between the groups, and 66 were differentially expressed by at least twofold.

Among these genes were *phosphoserine phosphatase (PSPH)*, which was most unregulated; *Ras-related associated with diabetes (RRAD)*; and two genes associated with insulin-like growth factor, *insulin-like growth factor 1 receptor (IGF1R)* and a variant, *IMP-2*.

The *IGF1R* is a very important finding, as IGF can support the growth of cancer cells, especially endometrial cancer cells. There also may be a link between some of these differentially expressed genes and obesity, diabetes, and hormonal milieu, he said.

PSPH is an enzyme that catalyzes the last step in the biosynthesis of serine from carbohydrates, he noted. "One paper has linked it to gastric carcinoma metastasis."

The studies' conclusions do not mean that blacks and whites are genetically different, Dr. Maxwell stressed—only that the genes are differently expressed. "The genes may be structurally similar, but there may be environmental influences between the two races that result in epigenetic modulation of gene upregulation or downregulation," he said. "Genes have promoters that can be affected by environmental exposures, such as diet or hormones." ■