

Paroxetine/Tamoxifen: More Breast Ca Deaths

VITALS

Major Finding: Risk of breast cancer death was 24%-91% higher when women took paroxetine while on tamoxifen.

Source of Data: Retrospective, population-based cohort study of 2,430 women.

Disclosures: None reported.

BY BETSY BATES

SAN ANTONIO — Breast cancer patients who took the antidepressant paroxetine during their course of tamoxifen therapy were up to 91% more likely to die of their disease than were those who did not take the two drugs together, according to a retrospective, population-based cohort study conducted in the Canadian province of Ontario.

Investigators used health card identification numbers to track women aged 66 years and older who were treated with tamoxifen for breast cancer between 1993 and 2005. Almost a third of patients were taking an antidepressant during their tamoxifen therapy, including 2,430 who were taking a selective serotonin reuptake inhibitor.

As a class, SSRIs are known to inhibit cytochrome P450 2D6 (CYP 2D6), an enzyme

critical for the conversion of tamoxifen to endoxifen, its active metabolite, in the body. The ability of SSRIs to interfere with the efficacy of tamoxifen—at least in some women—has been theorized, but studies attempting to clarify the issue have reported conflicting results.

In the Canadian study reported at the annual meeting of the San Antonio Breast Cancer Symposium, 1,074 (44.2%) of the women taking an SSRI during tamoxifen

CERVARIX®

[Human Papillomavirus Bivalent (Types 16 and 18) Vaccine, Recombinant]

Suspension for Intramuscular Injection

The following is a brief summary only; see full prescribing information for complete product information.

1 INDICATIONS AND USAGE

1.1 Indications: CERVARIX® is indicated for the prevention of the following diseases caused by oncogenic human papillomavirus (HPV) types 16 and 18 [see *Clinical Studies (14) of full prescribing information*]: cervical cancer, cervical intraepithelial neoplasia (CIN) grade 2 or worse and adenocarcinoma *in situ*, and cervical intraepithelial neoplasia (CIN) grade 1. CERVARIX is approved for use in females 10 through 25 years of age. **1.2 Limitations of Use and Effectiveness:** CERVARIX does not provide protection against disease due to all HPV types [see *Clinical Studies (14.3) of full prescribing information*]. CERVARIX has not been demonstrated to provide protection against disease from vaccine and non-vaccine HPV types to which a woman has previously been exposed through sexual activity [see *Clinical Studies (14.2) of full prescribing information*]. Females should continue to adhere to recommended cervical cancer screening procedures [see *Patient Counseling Information (17)*]. Vaccination with CERVARIX may not result in protection in all vaccine recipients.

2 DOSAGE AND ADMINISTRATION

2.1 Preparation for Administration: Shake vial or syringe well before withdrawal and use. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. CERVARIX also should be inspected visually for cracks in the vial or syringe prior to administration. If any of these conditions exist, the vaccine should not be administered. With thorough agitation, CERVARIX is a homogeneous, turbid, white suspension. Discard if it appears otherwise. **2.2 Dose and Schedule:** Immunization with CERVARIX consists of 3 doses of 0.5-mL each, by intramuscular injection according to the following schedule: 0, 1, and 6 months. The preferred site of administration is the deltoid region of the upper arm. Do not administer this product intravenously, intradermally, or subcutaneously.

4 CONTRAINDICATIONS

Severe allergic reactions (e.g., anaphylaxis) to any component of CERVARIX [see *Description (11) of full prescribing information*].

5 WARNINGS AND PRECAUTIONS

5.1 Syncope: Because vaccinees may develop syncope, sometimes resulting in falling with injury, observation for 15 minutes after administration is recommended. Syncope, sometimes associated with tonic-clonic movements and other seizure-like activity, has been reported following vaccination with CERVARIX. When syncope is associated with tonic-clonic movements, the activity is usually transient and typically responds to restoring cerebral perfusion by maintaining a supine or Trendelenburg position. **5.2 Latex:** The tip cap and the rubber plunger of the needleless prefilled syringes contain dry natural latex rubber that may cause allergic reactions in latex sensitive individuals. The vial stopper does not contain latex. **5.3 Preventing and Managing Allergic Vaccine Reactions:** Prior to administration, the healthcare provider should review the immunization history for possible vaccine hypersensitivity and previous vaccination-related adverse reactions to allow an assessment of benefits and risks. Appropriate medical treatment and supervision should be readily available in case of anaphylactic reactions following administration of CERVARIX.

6 ADVERSE REACTIONS

The most common local adverse reactions ($\geq 20\%$ of subjects) were pain, redness, and swelling at the injection site. The most common general adverse events ($\geq 20\%$ of subjects) were fatigue, headache, myalgia, gastrointestinal symptoms, and arthralgia.

6.1 Clinical Studies Experience: Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared with rates in the clinical trials of another vaccine, and may not reflect the rates observed in practice. There is the possibility that broad use of CERVARIX could reveal adverse reactions not observed in clinical trials.

Studies in Females 10 Through 25 Years of Age: The safety of CERVARIX was evaluated by pooling data from controlled and uncontrolled clinical trials involving 23,713 females 10 through 25 years of age in the pre-licensure clinical development program. In these studies, 12,785 females (10 through 25 years of age) received at least one dose of CERVARIX and 10,928 females received at least one dose of a control. Data on solicited local and general adverse events were collected by subjects or parents using standardized diary cards for 7 consecutive days following each vaccine dose (i.e., day of vaccination and the next 6 days). Unsolicited adverse events were recorded with diary cards for 30 days following each vaccination (day of vaccination and 29 subsequent days). Parents and/or subjects were also asked at each study visit about the occurrence of any adverse events and instructed to immediately report serious adverse events throughout the study period. These studies were conducted in North America, Latin America, Europe, Asia, and Australia. Overall, the majority of subjects were white (59%), followed by Asian (26%), Hispanic (9%), black (3%), and other racial/ethnic groups (3%). The reported frequencies of solicited local injection site reactions and general adverse events are presented in Table 1. An analysis of solicited local injection site reactions by dose is presented in Table 2. Local reactions were reported more frequently with CERVARIX when compared with the control groups; in $\geq 84\%$ of recipients of CERVARIX, these local reactions were mild to moderate in intensity. Compared with dose 1, pain was reported less frequently after doses 2 and 3 of CERVARIX, in contrast to redness and swelling where there was a small increased incidence. There was no increase in the frequency of general adverse events with successive doses.

BRIEF SUMMARY

Table 1. Rates of Solicited Local Adverse Reactions and General Adverse Events in Females 10 Through 25 Years of Age Within 7 Days of Vaccination (Total Vaccinated Cohort^a)

Adverse Reaction/Event	CERVARIX (10-25 yrs) %	HAV 720 ^b (15-25 yrs) %	HAV 360 ^c (10-14 yrs) %	AI(OH) ₃ Control ^d (15-25 yrs) %
Local Adverse Reaction	N = 6,431	N = 3,079	N = 1,027	N = 549
Pain	91.8	78.0	64.2	87.2
Redness	48.0	27.6	25.2	24.4
Swelling	44.1	19.8	17.3	21.3
General Adverse Event	N = 6,432	N = 3,079	N = 1,027	N = 549
Fatigue	55.0	53.7	42.3	53.6
Headache	53.4	51.3	45.2	61.4
GI ^e	27.8	27.3	24.6	32.8
Fever ($\geq 99.5^\circ\text{F}$)	12.8	10.9	16.0	13.5
Rash	9.6	8.4	6.7	10.0
	N = 5,881	N = 3,079	N = 1,027	—
Myalgia ^f	49.1	44.9	33.1	—
Arthralgia ^f	20.8	17.9	19.9	—
Urticaria ^f	7.4	7.9	5.4	—

^a Total vaccinated cohort included subjects with at least one documented dose (N).

^b HAV 720 = Hepatitis A Vaccine control group [720 EL.U. of antigen and 500 mcg AI(OH)₃].

^c HAV 360 = Hepatitis A Vaccine control group [360 EL.U. of antigen and 250 mcg AI(OH)₃].

^d AI(OH)₃ Control = control containing 500 mcg AI(OH)₃.

^e GI = Gastrointestinal symptoms, including nausea, vomiting, diarrhea, and/or abdominal pain.

^f Adverse events solicited in a subset of subjects.

Table 2. Rates of Solicited Local Adverse Reactions in Females 10 Through 25 Years of Age by Dose Within 7 Days of Vaccination (Total Vaccinated Cohort^a)

Adverse Reaction	CERVARIX (10-25 yrs) %			HAV 720 ^b (15-25 yrs) %			HAV 360 ^c (10-14 yrs) %			AI(OH) ₃ Control ^d (15-25 yrs) %		
	Post-Dose			Post-Dose			Post-Dose			Post-Dose		
	1	2	3	1	2	3	1	2	3	1	2	3
N	6,415	6,197	5,936	3,070	2,919	2,758	1,027	1,021	1,011	546	521	500
Pain	86.9	76.2	78.7	65.6	54.4	56.1	48.5	38.5	36.9	79.1	66.8	72.4
Pain, Grade 3 ^e	7.5	5.7	7.7	2.0	1.4	2.0	0.8	0.2	1.6	9.0	6.0	8.6
Redness	27.8	29.6	35.6	16.6	15.2	16.1	15.6	13.3	12.1	11.5	11.5	15.6
Redness, >50 mm	0.2	0.5	1.0	0.1	0.1	0.0	0.1	0.2	0.1	0.2	0.0	0.0
Swelling	22.7	25.2	32.7	10.5	9.4	10.5	9.4	8.6	7.6	10.3	10.4	12.0
Swelling, >50 mm	1.2	1.0	1.3	0.2	0.2	0.2	0.4	0.3	0.0	0.0	0.0	0.0

^a Total vaccinated cohort included subjects with at least one documented dose (N).

^b HAV 720 = Hepatitis A Vaccine control group [720 EL.U. of antigen and 500 mcg AI(OH)₃].

^c HAV 360 = Hepatitis A Vaccine control group [360 EL.U. of antigen and 250 mcg AI(OH)₃].

^d AI(OH)₃ Control = control containing 500 mcg AI(OH)₃.

^e Defined as spontaneously painful or pain that prevented normal daily activities.

The pattern of solicited local adverse reactions and general adverse events following administration of CERVARIX was similar between the age cohorts (10 through 14 years and 15 through 25 years).

Table 3. Rates of Unsolicited Adverse Events in Females 10 Through 25 Years of Age Within 30 Days of Vaccination ($\geq 1\%$ For CERVARIX and Greater Than HAV 720, HAV 360, or AI(OH)₃ Control) (Total Vaccinated Cohort^a)

Adverse Event	CERVARIX % (N = 6,654)	HAV 720 ^b % (N = 3,186)	HAV 360 ^c % (N = 1,032)	AI(OH) ₃ Control ^d % (N = 581)
Headache	5.3	7.6	3.3	9.3
Nasopharyngitis	3.6	3.4	5.9	3.3
Influenza	3.2	5.6	1.3	1.9
Pharyngolaryngeal pain	2.9	2.7	2.2	2.2
Dizziness	2.2	2.6	1.5	3.1
Upper respiratory infection	2.0	1.3	6.7	1.5
Chlamydia infection	2.0	4.4	0.0	0.0
Dysmenorrhea	2.0	2.3	1.9	4.0
Pharyngitis	1.5	1.8	2.2	0.5
Injection site bruising	1.4	1.8	0.7	1.5
Vaginal infection	1.4	2.2	0.1	0.9
Injection site pruritus	1.3	0.5	0.6	0.2
Back pain	1.1	1.3	0.7	3.1
Urinary tract infection	1.0	1.4	0.3	1.2

^a Total vaccinated cohort included subjects with at least one dose administered (N).

^b HAV 720 = Hepatitis A Vaccine control group [720 EL.U. of antigen and 500 mcg AI(OH)₃].

^c HAV 360 = Hepatitis A Vaccine control group [360 EL.U. of antigen and 250 mcg AI(OH)₃].

^d AI(OH)₃ Control = control containing 500 mcg AI(OH)₃.

therapy had died as of Dec. 31, 2007, when primary data analysis began. After statistical adjustment for age, socioeconomic status, comorbidity, use of other CYP 2D6 drugs, and timing and duration of tamoxifen therapy, investigators found that the breast cancer mortality risk was increased 24% among women who were coprescribed paroxetine during 25% of their tamoxifen treatment.

If patients took paroxetine longer (that is, for more than half of their tamoxifen course) their breast cancer mortality risk rose to 54%. Patients who took both drugs for 75% of the time they received

tamoxifen had a 91% risk of breast cancer mortality ($P = .0028$).

Mortality from any cause was also sharply elevated among women who took paroxetine for 75% or more of their tamoxifen course ($P = .0027$).

The striking results were significant only for paroxetine, and not for other SSRIs—including fluoxetine, sertraline, fluvoxamine, or citalopram—that were taken concurrently with tamoxifen, reported Dr. Catherine M. Kelly at the meeting.

Dr. Kelly hypothesized that the explanation lies in the degree to which various SSRIs inhibit CYP 2D6. “Paroxetine

is the only SSRI that is an irreversible—or ‘suicide’—inhibitor of CYP 2D6,” she said in an interview.

The dose-response curve of the study, with escalating mortality risk paralleling time on paroxetine, adds significant weight to the findings with regard to paroxetine, marketed as Paxil by GlaxoSmithKline. (The company did not respond to a request for a comment.)

Fluoxetine is also a potent inhibitor of CYP 2D6, but was not shown to increase breast cancer mortality in the study. “I would like to see further data on that and would use caution in using any

of the drugs that inhibit CYP 2D6 in women who are taking tamoxifen, said Dr. Kelly, who was with the University of Toronto Sunnybrook Health Sciences Centre while conducting the study and is currently a breast medical oncology fellow at the University of Texas M.D. Anderson Cancer Center in Houston.

“There are other options,” she noted, including non-SSRI antidepressants that do not inhibit CYP 2D6.

Women need to discuss their choices with a medical oncologist, psychiatrist, or family physician before undergoing tamoxifen therapy, she suggested. ■

New Onset Autoimmune Diseases (NOADs): The pooled safety database, which included controlled and uncontrolled trials which enrolled females 10 through 25 years of age, was searched for new medical conditions indicative of potential new onset autoimmune diseases. Overall, the incidence of potential NOADs, as well as NOADs, in the group receiving CERVARIX was 0.8% (95/12,533) and comparable to the pooled control group (0.8%, 87/10,730) during the 4.3 years of follow-up (mean 3.0 years) (Table 4). In the largest randomized, controlled trial (Study 2) which enrolled females 15 through 25 years of age and which included active surveillance for potential NOADs, the incidence of potential NOADs and NOADs was 0.8% among subjects who received CERVARIX (78/9,319) and 0.8% among subjects who received Hepatitis A Vaccine [720 EL.U. of antigen and 500 mcg Al(OH)₃] control (77/9,325).

Table 4. Incidence of New Medical Conditions Indicative of Potential New Onset Autoimmune Disease and New Onset Autoimmune Disease Throughout the Follow-up Period Regardless of Causality in Females 10 Through 25 Years of Age (Total Vaccinated Cohort)^a

	CERVARIX (N = 12,533) n (%) ^c	Pooled Control Group ^b (N = 10,730) n (%) ^c
Total Number of Subjects With at Least One Medical Condition	95 (0.8)	87 (0.8)
Arthritis ^d	9 (0.0)	4 (0.0)
Celiac disease	2 (0.0)	5 (0.0)
Dermatomyositis	0 (0.0)	1 (0.0)
Diabetes mellitus insulin-dependent (Type 1 or unspecified)	5 (0.0)	5 (0.0)
Erythema nodosum	3 (0.0)	0 (0.0)
Hyperthyroidism ^e	14 (0.1)	15 (0.1)
Hypothyroidism ^f	30 (0.2)	28 (0.3)
Inflammatory bowel disease ^g	8 (0.1)	4 (0.0)
Multiple sclerosis	4 (0.0)	1 (0.0)
Myelitis transverse	1 (0.0)	0 (0.0)
Optic neuritis/Optic neuritis retrobulbar	3 (0.0)	1 (0.0)
Psoriasis ^h	8 (0.1)	11 (0.1)
Raynaud's phenomenon	0 (0.0)	1 (0.0)
Rheumatoid arthritis	4 (0.0)	3 (0.0)
Systemic lupus erythematosus ⁱ	2 (0.0)	3 (0.0)
Thrombocytopenia ^j	1 (0.0)	1 (0.0)
Vasculitis ^k	1 (0.0)	3 (0.0)
Vitiligo	2 (0.0)	2 (0.0)

^a Total vaccinated cohort included subjects with at least one documented dose (N).

^b Pooled Control Group = Hepatitis A Vaccine control group [720 EL.U. of antigen and 500 mcg Al(OH)₃], Hepatitis A Vaccine control group [360 EL.U. of antigen and 250 mcg of Al(OH)₃], and a control containing 500 mcg Al(OH)₃.

^c n (%): number and percentage of subjects with medical condition.

^d Term includes reactive arthritis and arthritis.

^e Term includes Basedow's disease, goiter, and hyperthyroidism.

^f Term includes thyroiditis, autoimmune thyroiditis, and hypothyroidism.

^g Term includes colitis ulcerative, Crohn's disease, proctitis ulcerative, and inflammatory bowel disease.

^h Term includes psoriatic arthropathy, nail psoriasis, guttate psoriasis, and psoriasis.

ⁱ Term includes systemic lupus erythematosus and cutaneous lupus erythematosus.

^j Term includes idiopathic thrombocytopenic purpura and thrombocytopenia.

^k Term includes leukocytoclastic vasculitis and vasculitis.

Serious Adverse Events: In the pooled safety database, inclusive of controlled and uncontrolled studies, which enrolled females 10 through 72 years of age, 5.3% (862/16,142) of subjects who received CERVARIX and 5.9% (814/13,811) of subjects who received control reported at least one serious adverse event, without regard to causality, during the entire follow-up period (up to 7.4 years). Among females 10 through 25 years of age enrolled in these clinical studies, 6.4% of subjects who received CERVARIX and 7.2% of subjects who received the control reported at least one serious adverse event during the entire follow-up period (up to 7.4 years).

Deaths: In completed and ongoing studies which enrolled 57,323 females 9 through 72 years of age, 37 deaths were reported during the 7.4 years of follow-up: 20 in subjects who received CERVARIX (0.06%, 20/33,623) and 17 in subjects who received control (0.07%, 17/23,700). Causes of death among subjects were consistent with those reported in adolescent and adult female populations. The most common causes of death in the vaccine and control groups were motor vehicle accident and suicide, followed by neoplasm, autoimmune disease, infectious disease, homicide, cardiovascular disorders, and death of unknown cause. Among females 10 through 25 years of age, 31 deaths were reported (0.05%, 16/29,467) of subjects who received CERVARIX and 0.07%, 15/20,192 of subjects who received control.

6.2 Postmarketing Experience: In addition to reports in clinical trials, worldwide voluntary reports of adverse events received for CERVARIX since market introduction (2007) are listed below. This list includes serious events or events which have suspected causal association to CERVARIX. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccination. **Immune System Disorders:** Allergic reactions (including anaphylactic and anaphylactoid reactions), angioedema, erythema multiforme. **Nervous System Disorders:** Syncope or vasovagal responses to injection (sometimes accompanied by tonic-clonic movements).

7 DRUG INTERACTIONS

7.1 Concomitant Vaccine Administration: There are no data to assess the concomitant use of CERVARIX with other vaccines. Do not mix CERVARIX with any other vaccine in the same syringe or vial. **7.2 Hormonal Contraceptives:** Among 7,693 subjects 15 through 25 years of age in Study 2 (CERVARIX, N = 3,821 or Hepatitis A Vaccine 720 EL.U., N = 3,872) who used hormonal contraceptives for a mean of 2.8 years, the observed efficacy of CERVARIX was similar to that observed among subjects who did not report use of hormonal contraceptives.

7.3 Immunosuppressive Therapies: Immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs, and corticosteroids (used in greater than physiologic doses), may reduce the immune response to CERVARIX [see *Use in Specific Populations* (8.6)].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy: Pregnancy Category B. There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed. **Clinical Studies:** Overall Outcomes: In clinical studies, pregnancy testing was performed prior to each vaccine administration and vaccination was discontinued if a subject had a positive pregnancy test. In all clinical trials, subjects were instructed to take precautions to avoid pregnancy until 2 months after the last vaccination. During pre-licensure clinical development, a total of 7,276 pregnancies were reported among 3,696 females receiving CERVARIX and 3,580 females receiving a control (Hepatitis A Vaccine 360 EL.U., Hepatitis A Vaccine 720 EL.U., or 500 mcg Al(OH)₃). The overall proportions of pregnancy outcomes were similar between treatment groups. The majority of women gave birth to normal infants (62.2% and 62.6% of recipients of CERVARIX and control, respectively). Other outcomes included spontaneous abortion (11.0% and 10.8% of recipients of CERVARIX and control, respectively), elective termination (5.8% and 6.1% of recipients of CERVARIX and control, respectively), abnormal infant other than congenital anomaly (2.8% and 3.2% of recipients of CERVARIX and control, respectively), and premature birth (2.0% and 1.7% of recipients of CERVARIX and control, respectively). Other outcomes (congenital anomaly, stillbirth, ectopic pregnancy, and therapeutic abortion) were reported less frequently in 0.1% to 0.8% of pregnancies in both groups. **Outcomes Around Time of Vaccination:** Sub-analyses were conducted to describe pregnancy outcomes in 761 women [N = 396 for CERVARIX and N = 365 pooled control, HAV 360 EL.U., HAV 720 EL.U., and 500 mcg Al(OH)₃] who had their last menstrual period within 30 days prior to, or 45 days after a vaccine dose and for whom pregnancy outcome was known. The majority of women gave birth to normal infants (65.2% and 69.3% of recipients of CERVARIX and control, respectively). Spontaneous abortion was reported in a total of 11.7% of subjects (13.6% of recipients of CERVARIX and 9.6% of control recipients) and elective termination was reported in a total of 9.7% of subjects (9.9% of recipients of CERVARIX and 9.6% of control recipients). Abnormal infant other than congenital anomaly was reported in a total of 4.9% of subjects (5.1% of recipients of CERVARIX and 4.7% of control recipients) and premature birth was reported in a total of 2.5% of subjects (2.5% of both groups). Other outcomes (congenital anomaly, stillbirth, ectopic pregnancy, and therapeutic abortion) were reported in 0.3% to 1.8% of pregnancies among recipients of CERVARIX and in 0.3% to 1.4% of pregnancies among control recipients. It is not known whether the observed numerical imbalance in spontaneous abortions in pregnancies which occurred around the time of vaccination is due to a vaccine-related effect. **Pregnancy Registry:** Healthcare providers are encouraged to register pregnant women who inadvertently receive CERVARIX in the GlaxoSmithKline vaccination pregnancy registry by calling 1-888-452-9622. **8.3 Nursing Mothers:** In non-clinical studies in rats, serological data suggest a transfer of anti-HPV-16 and anti-HPV-18 antibodies via milk during lactation in rats. Excretion of vaccine-induced antibodies in human milk has not been studied for CERVARIX. Because many drugs are excreted in human milk, caution should be exercised when CERVARIX is administered to a nursing woman. **8.4 Pediatric Use:** Safety and effectiveness in pediatric patients younger than 10 years of age have not been established. The safety and effectiveness of CERVARIX have been evaluated in 1,193 subjects 10 through 14 years of age and 6,316 subjects 15 through 17 years of age. [See *Adverse Reactions* (6.1) and *Clinical Studies* (14.5) of full prescribing information.] **8.5 Geriatric Use:** Clinical studies of CERVARIX did not include sufficient numbers of subjects 65 years of age and older to determine whether they respond differently from younger subjects. CERVARIX is not approved for use in subjects 65 years of age and older. **8.6 Immunocompromised Individuals:** The immune response to CERVARIX may be diminished in immunocompromised individuals [see *Drug Interactions* (7.3)].

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility: CERVARIX has not been evaluated for its carcinogenic or mutagenic potential.

17 PATIENT COUNSELING INFORMATION

Provide the Vaccine Information Statements prior to immunization. This is required by the National Childhood Vaccine Injury Act of 1986 and are available free of charge at the Centers for Disease Control and Prevention (CDC) website (www.cdc.gov/vaccines). Inform the patient, parent, or guardian: Vaccination does not substitute for routine cervical cancer screening. Women who receive CERVARIX should continue to undergo cervical cancer screening per standard of care. CERVARIX does not protect against disease from HPV types to which a woman has previously been exposed through sexual activity. Since syncope has been reported following vaccination in young females, sometimes resulting in falling with injury, observation for 15 minutes after administration is recommended. Information regarding potential benefits and risks associated with vaccination. Report any adverse events to their healthcare provider. Safety has not been established in pregnant women. CERVARIX is not recommended for use in pregnant women or women planning to become pregnant during the vaccination course. Register women who receive CERVARIX while pregnant in the pregnancy registry by calling 1-888-452-9622.

CERVARIX is a registered trademark of GlaxoSmithKline.

Manufactured by **GlaxoSmithKline Biologicals**

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Distributed by **GlaxoSmithKline**

Research Triangle Park, NC 27709

Full prescribing information for CERVARIX is available at www.cervarix.com.

CRX:1BRS



GlaxoSmithKline
Vaccines

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Survival: Breast Conservation vs. Mastectomy

SAN ANTONIO — Breast conservation therapy resulted in significantly better 5-year overall survival, compared with mastectomy, investigators found in a study of 202 patients with triple receptor-negative breast cancer.

Triple receptor-negative breast tumors lack estrogen-, progesterone-, and Her-2/neu-receptor expression. These aggressive cancers account for 15%-20% of the more than 1 million breast cancers diagnosed each year worldwide.

“Despite the aggressive nature [of these tumors], our hypothesis was that breast conservation therapy [might be a] viable option for some patients,” Dr. Catherine C. Parker said at the annual Academic Surgical Congress.

She and her colleagues at Louisiana State University, Shreveport, studied outcomes of 63 patients (31% who had breast conservation therapy and 139 who received mastectomy. Cancer recurrence rates and survival were the primary outcomes. Mean tumor size at baseline was significantly greater in the mastectomy group, 3.1 cm, versus 2.5 cm in the breast conservation group. A total of 26% of the mastectomy patients had T3 or T4 tumors, compared with 5% of the breast conservation group, a statistically significant difference.

All patients were offered standard of care treatment and surveillance. The mean follow-up was 53 months. Disease-free survival at 5 years was 56% for the mastectomy group and 69% for the breast conservation therapy group. The difference was not statistically significant, Dr. Parker said.

“Five-year overall survival was significantly better for breast conservation therapy [89% vs. 69%],” said Dr. Parker of the department of surgery at LSU.

Reasons for disparity in overall survival include the larger mean tumor size and more advanced stage of disease in the mastectomy group, Dr. Parker said.

Recurrence rates were 30% for the breast conservation group and 43% for the mastectomy group.

A multivariate analysis indicated that the surgical approach had no effect on disease-free or overall survival.

Dr. Parker had no relevant disclosures.

—Damian McNamara