Robert L. Barbieri, MD
Editor-in-Chief

The pipeline runneth over

HPV vaccine is next in a long line of new drugs that will change women's health care more than anything since the Pap test.

As soon as this year, the human papillomavirus (HPV) vaccine could transform clinical practice more than anything since the Pap smear was introduced. It won't be the first time that a single breakthrough drug forever changed the practice of medicine. The history of modern medicine for the past 60 years has been dominated by the transformational effect of "blockbuster" medications. Examples include penicillin and other antibiotics, polio and other vaccines, cancer chemotherapeutic agents, blood pressure medicines, contraceptives, and lipid-regulating agents.

The future of medicine is likely to be dominated by powerful new medicines that continually reshape our clinical practice.

The pharmaceutical pipeline is robust. (A full report on medications in phase I, II and III clinical trials is available at http://www.phrma.org/publications/publications/admin/2005-10-20.1301.pdf).

In this editorial, I review new medications with potential applications in women's health, which are in registered phase III clinical trials, the final step before the FDA considers approval. We can expect that many of these medicines will be available within the next few years. The HPV vaccine is expected to be among the first.

***FAST** TRACK*

Not ObGyns, but other primary care physicians will probably administer most HPV vaccinations

2 HPV vaccines and 29 cancer drugs

In clinical trials, 2 vaccines have shown extraordinary efficacy in preventing cervical intraepithelial neoplasia:

- ***Cervarix*** (*GlaxoSmithKline, Philadelphia, Pa*). Recombinant bivalent HPV vaccine with a modified lipopolysaccharide adjuvant prevents infection with HPV types 16 and 18. The modified lipopolysaccharide adjuvant may reduce side effects while maintaining immune stimulation.
- ***Gardasil*** (*Merck, Whitehouse Station NJ*). Recombinant tetravalent HPV vaccine prevents infection with HPV types 6, 11, 16, and 18. Gardasil may simultaneously target the 2 most common HPV types that cause cervical neoplasia (types 16 and 18) and 2 HPV types that cause genital warts (types 6 and 11).

Who will prescribe—internists, oncologists, or ObGyns?

In clinical trials, both Cervarix and Gardasil were demonstrated to be highly effective in preventing cervical intraepithelial neoplasia. FDA approval of these 2 vaccines will likely significantly alter the practice of gynecology. Initial estimates suggest that approximately one-third of the doses of these agents will be prescribed by gynecologists, with the remainder prescribed by internists, family practitioners, and pediatricians.

Of note, 29 additional cancer drugs are in phase III clinical trials for treatment of cancer of the breast and female reproductive tract, including cervical, uterine and ovarian cancers.

Space limitations prevent a detailed discussion of these cancer agents in this editorial. It is likely that use of most of these 29 agents will be largely limited to oncology practice.

CONTINUED

FAST TRACK

Menopause drugs in late-phase trials include 5 agents for hot flashes and 2 topical products for low libido

Long-term drug for fibroids

Asoprisnil *(TAP Pharmaceuticals, Lake Forrest, Ill)* will be a major new alternative to surgery for fibroids. It is a selective progesterone receptor modulator that treats menorrhagia and pelvic bulk symptoms in women with fibroids. In a significant percentage of affected women, asoprisnil produces amenorrhea and decreases uterine fibroid volume. Asoprisnil does not suppress estradiol to the menopausal range. Currently, no medications are approved for long-term treatment of fibroids.

5 menopause medicines

Des-venlafaxine *(Pristiq; Wyeth Pharmaceuticals, Collegeville, Pa)* is a serotonin-norepinephrine reuptake inhibitor (not estrogenic) that is an active metabolite of the parent compound, venlafaxine. It is proposed for treatment of vasomotor symptoms. Venlafaxine has already demonstrated efficacy for reducing vasomotor symptoms, but it is not FDA approved for this indication. An active metabolite of venlafaxine is highly likely to be effective for vasomotor symptoms. Des-venlafaxine is likely to benefit women who want to avoid estrogen treatment or in whom estrogen therapy may be contraindicated (ie, women with invasive estrogen receptor–positive breast cancer).

Bazedoxifene plus conjugated equine estrogen *(Ligand Pharmaceuticals, San Diego, Calif, and Wyeth Pharmaceuticals, Collegeville, Pa)* is a selective estrogen receptor modulator formulated in combination with conjugated equine estrogen to treat vasomotor symptoms.

Bazedoxifene has mixed estrogen antagonist (endometrium) and agonist (bone) activity. Bazedoxifene may prevent endometrial proliferation caused by conjugated equine estrogen and allow the treatment of vasomotor symptoms without the need for concomitant progestin treatment in women with a uterus. Bazedoxifene as a single agent will likely be effective for treatment of osteoporosis.

Org50081 *(Organon, Roseland, NJ)* is a serotonin 2 blocker that is being studied to treat vasomotor symptoms.

Ospemifene *(QuatRx Pharmaceuticals, Ann Arbor, Mich)* is a selective estrogen receptor modulator being studied to treat vasomotor symptoms. Ospemifene has estrogen agonist effects in urogenital and bone tissues, and is an estrogen antagonist in the breast and endometrium.

Transdermal estradiol gel *(Bio-E-Gel; BioSante Pharmaceuticals, Lincolnshire, Ill)* is intended to treat vasomotor symptoms. Transdermal estradiol has demonstrated efficacy for treatment for vasomotor symptoms when applied in various formulations, including patches and gels.

2 sexual dysfunction drugs

Alprostadil *(Alista; Vivus, Mountain View, Calif)* is a synthetic PGE1 formulation intended to be applied to the genital tissues to increase genital blood flow and sensitivity and sexual arousal.

Testosterone gel *(Tostrelle; Cellegy Pharmaceuticals, Brisbane, Calif)* is intended to treat hypoactive sexual desire disorder in menopausal women by increasing androgen levels toward the normal premenopausal range.

Fibrocystic breast pain

Molecular iodine *(IoGen; Symbollon, Framingham, Mass)* is intended for treatment of severe periodic breast pain associated with fibrocystic breast disease. Molecular iodine treatment increases the concentration of iodolactones that may be antiproliferative and apoptotic in breast tissue.

Contraceptives fight STDs

1% C31G vaginal gel *(Savvy; Cellegy Pharmaceuticals, Brisbane, Calif, and Biosyn Philadelphia, Pa)* is a vaginal spermicide and microbicide intended to reduce

the risk of both pregnancy and transmission of sexually transmitted diseases, including HIV disease. C31G contains 2 surface-active agents, cetyl betaine and myristamine oxide, in an equimolar mixture in a hydroxyethyl cellulose gel.

Ushercell *(Polydex Pharmaceuticals, Toronto, Ontario, Canada)*, a high-molecular-weight cellulose sulfate compound, is a topical contraceptive and microbicide. Ushercell is intended for intravaginal use to protect against transmission of HIV, gonorrhea, chlamydia, and herpes simplex virus 1 and 2.

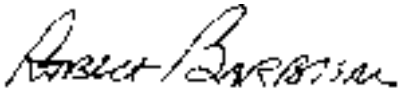
Obstetrics pipeline: Not even a trickle

Once these new medications are approved for use by the FDA, a complex process will begin as clinicians and patients work together to try to understand the best approaches to balance benefits and adverse effects of these medicines in practice.

An interesting side note is that none of these new medications has any obstetrical indication; all are focused on gynecological and women's health clinical problems. The paucity of pharmaceutical innovation focused on obstetrical diseases continues to plague our field.

What is your top concern?

We would like to know what specific clinical problems you face in your daily practice. What problems deserve additional focus and resources from the pharmaceutical discovery industry?



obg@dowdenhealth.com

We want to hear from you!

Have a comment on an article, editorial, illustration, or department? Drop us a line and let us know what you think.

E-mail: obg@dowdenhealth.com

Fax: 201-391-2778

Mail: Editor, OBG MANAGEMENT
110 Summit Ave
Montvale, NJ 07645

Please take a moment to share your opinion!

OBG MANAGEMENT

FAST *TRACK*

What clinical problem should be the pharmaceutical discovery industry's top priority?

Email your thoughts!
obg@dowdenhealth.com