US FDA clears risk of ovarian malignancy algorithm as a test for ovarian cancer

The US FDA has recently granted approval for the marketing and use of a new biomarker test for ovarian cancer. The combination of tests examining levels of HE4 and CA125 with the Risk of Ovarian Malignancy Algorithm (ROMA™), developed at the Women & Infants Hospital of Rhode Island (RI, USA), promises high accuracy and specificity when determining the risk of ovarian cancer in both pre- and post-menopausal women. The new tool may help overcome issues such as distinguishing between benign and malignant pelvic mass, and identifying individuals with a high likelihood of malignancy who would benefit from surgery.

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Presently, testing serum CA125 levels is favored when monitoring patients with ovarian cancer; however, the test is unable to detect all types of ovarian cancer and has limited sensitivity and specificity. Currently, three-quarters of patients are not diagnosed until they are at an advanced stage of the disease.

Speaking to Future Science Group, Richard G Moore, lead author of the study from Brown University (RI, USA), commented that, "Less than 50% of women diagnosed with ovarian cancer are initially operated on by a gynecologic oncologist, despite several studies showing improved outcomes and survival for women who have their surgeries carried out by gynecologic oncologists and at centers familiar with this disease. Combining ROMA with the biomarkers HE4 and CA125 is an excellent triage tool to identify women at high risk for ovarian cancer, allowing for accurate triage of these patients to the most qualified physicians and centers for their care. Hopefully with better triage tools such as ROMA we can increase the number of women receiving their care with specialists trained to manage this disease, resulting in better outcomes and improved survival."

The FDA clearance was based upon prospective, double-blind, multicenter trials that found that the combined HE4 and CA125 algorithm resulted in 95% of epithelial ovarian cancers being correctly classified as high risk. Moore stated that, “We have performed two national validation trials, one in a high-risk population and the second in a low-risk population, with very similar results. The later trial led the FDA, 2 weeks ago, to clear ROMA and HE4 for clinical use in the USA.” In total, 472 patients were tested, and serum HE4 and CA125 levels were measured preoperatively, allowing the ROMA score to be calculated. In the postmenopausal group a sensitivity and specificity of 92.3 and 76.0% were attained, respectively, while in the premenopausal group the sensitivity was 100%, with a specificity of 74.2%.

“ROMA™ is an excellent tool for physicians … to use for the risk assessment of a woman who presents with an ovarian cyst or pelvic mass.”

Further commenting to Future Science Group, Moore added “ROMA is an excellent tool for physicians (i.e., general obstetricians and gynecologists, family practitioners, and internists and surgeons) to use for the risk assessment of a woman who presents with an ovarian cyst or pelvic mass. Women determined to be at high risk for a malignancy can be appropriately referred to a gynecologic oncologist and women found to be at low risk can safely stay in their communities with the physician that knows them best and where they have the support of their family.”

“With this increased ability to improve referral patterns … the healthcare costs involved with cancer diagnosis and treatment should decrease significantly.”

Paul Tohey, president and chief executive officer of Fujirebio Diagnostics (PA, USA), who manufactured the algorithm, believes that, “With this increased ability to improve referral patterns, as well as a price that is comparable to CA125 testing, the healthcare costs involved with cancer diagnosis and treatment should decrease significantly.”

Source: Moore RG, Miller MC, Disilvestro P et al. Evaluation of the diagnostic accuracy of the risk of ovarian malignancy algorithm in women with a pelvic mass. Obstet. Gynecol. 118(2 Pt 1), 280–288 (2011).

About the News in Brief

The News in Brief highlights some of the most important events and launches in the anticancer therapy field. The editorial team welcomes suggestions for timely, relevant items. If you have newsworthy information, please contact: Sophia Maprayil, Assistant Commissioning Editor, Expert Review of Anticancer Therapy, Expert Reviews Ltd, Unitec House, 2 Albert Place, London, N3 1QB, UK Tel.: +44 (0)20 8371 6090 Fax: +44 (0)20 8343 2313 s.maprayil@expert-reviews.com
Intrauterine device use could halve risk of cervical cancer

A research team from the Virus and Cancer research group at Instituto de Investigación Biomédica de Bellvitge (IDIBELL; Barcelona, Spain) have recently published results that contradict the popular belief that intrauterine devices (IUDs) may increase the risk of cervical cancer. The group analyzed ten case–control studies and 16 human papillomavirus (HPV) prevalence surveys, and discovered that IUD use appears to be associated with a significantly decreased risk of squamous-cell carcinoma, and adenocarcinoma and adenosquamous carcinoma.

The researchers analyzed international data from two studies performed by the International Agency for Research on Cancer (Lyon, France) and the Institut Català d’Oncologia (Barcelona, Spain). IUD use, while not affecting the risk of HPV infection, appeared to result in a 44% reduction in the likelihood of squamous-cell carcinoma, and a 54% reduction in the likelihood of adenocarcinoma and adenosquamous carcinoma. The length of IUD use did not appear to significantly alter the risk of cervical cancer, with the protective effect remaining after 10 years of use. The findings were adjusted for relevant covariates, including number of Papanicolau smears and number of sexual partners.

The authors comment that, “The associations found in our study strongly suggest that IUD use does not modify the likelihood of prevalent HPV infection, but might affect the likelihood of HPV progression to cervical cancer.” They note a possible explanation for the protective effect of IUDs may be that the device may trigger cellular immunity via processes such as induction of chronic mucosal inflammation. It has also been suggested that insertion or removal of the device may destroy precancerous lesions.

Source: Castellsagué X, Díaz M, Vaccarella S et al. Intrauterine device use, cervical infection with human papillomavirus, and risk of cervical cancer: a pooled analysis of 26 epidemiological studies. Lancet Oncol. DOI: 10.1016/S1470-2045(11)70223-6 (2011) (Epub ahead of print).
Merkel cell carcinoma is a rare and aggressive skin cancer caused in most cases by Merkel cell polyomavirus (MCV). A team led by Patrick Moore at the University of Pittsburgh Cancer Institute (PA, USA) have been investigating how the virus operates with the hope that a chemotherapeutic target could be developed in the near future.

Moore commented that, “Unfortunately, Merkel cell carcinoma is difficult to treat and clinical trials of chemotherapeutics have been disappointing in affecting clinical course and survival,” and that the “discovery of the molecular cause for this cancer provides opportunities to directly target the cellular pathways that are perturbed by the virus.”

“MCV is the first polyomavirus to be consistently associated with human cancer, and is believed to cause 80% of Merkel cell carcinoma,” Moore said. According to Moore, MCV is found naturally in the skin and is usually harmless; however, if someone becomes immunodeficient and specific mutations take place in the virus, it can cause Merkel cell carcinoma.

Since their initial discovery of MCV 3 years ago, Moore and colleagues have begun looking at specific characteristics of the virus. Their most recent studies have conveyed that MCV small antigen protein is a new oncogene that can contribute to abnormal cell growth in both rodent and human cells. In addition, unlike other polyomaviruses that have acted as classic models of cancer, which depend on viral interaction with the enzyme PP2A and heat-shock proteins, the group found that MCV differed from them in that they did not depend on PP2A and heat-shock proteins – they just interacted with them. When Moore and colleagues abolished the binding sites of PP2A and heat-shock proteins, MCV could still cause the abnormal cell growth. Based on this research the group hopes to develop treatments that can directly target the cellular pathways affected by MCV. Moore commented, “We are making headway on this approach now and have tested more than 1350 drugs to identify better methods to treat this virus-caused cancer.”

New research shows inner workings of Merkel cell polyomavirus in a rare skin cancer

New research investigating how Merkel cell polyomavirus operates holds hope for a future chemotherapeutic target for Merkel cell carcinoma.

A team of scientists from the University of Maryland Marlene and Stewart Greenbaum Cancer Center (MD, USA) have demonstrated that the choice between breast-conservation therapy and mastectomy does not alter survival rates in young women with early-stage breast cancer. Recently, a rise in the number of mastectomies undertaken due to concerns regarding cancer recurrence has been observed.

Steven J Feigenberg from the University of Maryland Medical System (MD, USA), and senior author of the study believes that “these findings are very significant for young women with early-stage breast cancer who might choose to have a mastectomy in the hope of improving their outcome. This study confirms that breast-conservation therapy is a safe, effective treatment option and will not have a detrimental effect on survival.”

Women under the age of 40 years are often at higher risk of cancer recurrence, and previous studies have implied that women choosing breast-conservation therapy have a higher chance of recurrence. However, previous studies did not analyze the effect of treatment choice on survival rates. The current study involved a retrospective analysis on data from almost 15,000 women from the Surveillance, Epidemiology and End Results (SEER) registry. Of the women, who were aged between 20 and 39 years, 45% chose breast-conservation surgery while 55% opted for mastectomy. The median follow-up was 6 years; the 5-year survival rate was 92.5% for those who selected breast-conservation therapy and 91.9% for those who selected mastectomy. The results were confirmed by performing a matched pair analysis on a smaller group of patients.

E Albert Reece, Dean of the Maryland School of Medicine (MD, USA), commented that, “This large analysis breaks new ground in advancing what we know about how to treat young women with early-stage breast cancer. It will most certainly help young women and their doctors to better understand the most appropriate treatment options and make decisions based on what’s best for each patient.”

Study suggests survival rate is no different for young women undergoing breast-conservation therapy or mastectomy

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Sources: Mahmood U, Morris CG, Neuner GA et al. Comparing survival with breast-conservation therapy or mastectomy in the management of young women with early-stage breast cancer. Presented at: 2011 Breast Cancer Symposium. San Francisco, CA, USA, 9–11 September 2011; University of Maryland Medical Center: www.umm.edu/news/releases/breast-conservation-therapy.htm