

No Difference in High-Def Endoscopy Comparison

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A new high-definition, wide-angle videoendoscope did not detect significantly more colorectal adenomas or polyps, compared with a conventional colonoscope in a randomized study.

The study's researchers noted that although it seemed logical that a higher resolution endoscope would yield better results, the nonacademic, real-world setting for the study could explain the nonsuperiority of the high-definition scope.

Dr. Maria Pellise said she and her colleagues chose to increase the clinical relevance of their results by enrolling nonselected, consecutive adult patients referred to Hospital Clinic de Barcelona, a community hospital in Spain.

After exclusions, 310 patients were randomly assigned to colonoscopy with a wide-angle (170-degree), high-definition videoendoscope (Olympus prototype XCF H160AY2L, Olympus Europe, Hamburg, Germany). This prototype is now available commercially. Another 310 patients were randomized to a standard-angle (140-degree), standard-resolution videocolonoscopy (Olympus Q160).

A team of seven full-time, board-certified gastroenterologists who spend at least 50% of their time doing endoscopy evaluated both groups.

The participants did not constitute a selected or high-risk population for colorectal cancer, unlike those in other studies. Only 25% were referred for screening or surveillance reasons, only 15% had a personal history of colorectal cancer (including adenoma), and mean age was less than 60 years.

Both devices detected a similar number and type of lesions. In fact, there were no significant differences between the two scopes in several different measures of efficacy, including overall number of adenomas and polyps, the ratio of flat or small adenomas, or the number of patients with high-risk lesions.

A total of 418 of the 518 lesions (81%) detected in the entire study population yielded pathology results. Findings included 272 adenomas (65%), 109 hyperplastic polyps (26%), and 37 inflammatory lesions (9%).

There were no differences between groups in degree of dysplasia or the morphology of adenomas, although there was a trend toward increased detection of small adenomas with the high-definition device. Overall, the majority of adenomas, 235 (86%), were low-grade dysplasia. The remaining 14% were high-grade dysplasia or carcinoma. Just more than half of adenomas were smaller than 5 mm, and 68% were sessile or pedunculated (doi:10.1053/j.gastro.2008.06.090).

A total of 82 patients in the high-definition group and 79 in the standard group had at least one adenoma detected. Also, 42 patients in the high-definition group and 39 in the standard group had at least one hyperplastic polyp detected.

The number of high-risk patients in each group did not differ significantly. The number of patients with three or more adenomas was 10 in the high-definition group versus 16 in the standard group.

Also, a high-grade adenoma was found in 14 patients in the high-definition group and in 13 in the standard group.

Dr. Pellise and her colleagues also recorded the time to reach the cecum. The standard scope was slightly faster than the high-definition scope (mean 8.2 minutes versus 8.9 minutes), but the difference was not statistically significant.

The findings support those of two previous studies that found no difference in adenoma miss rates with a wide-angle

prototype endoscope similar to the one used in the current study, the authors noted (*Am. J. Gastroenterol.* 2004;99:2138-42; *Am. J. Gastroenterol.* 2003;98:2000-5).

The study was underpowered to find differences between groups in adenoma detection less than 30%, a potential limitation. In addition, the researchers only employed chromoendoscopy to increase detection after a suspicious lesion was identified.

Nevertheless, there still may be advantages to the high-definition device. "The

wide-angle facility has [been] demonstrated to shorten endoscopic time without decreasing the diagnostic efficiency ... and the high-definition screen provides a high-quality and clear image that is restful for the endoscopist's eyes."

One of the study coauthors is a research nurse supported by Olympus Medical Systems, Europe. The company also supplied the prototype high-definition system for the study. There were no other disclosures. ■

IMPORTANT CORRECTION OF DRUG INFORMATION ABOUT EFFEXOR XR® (VENLAFAXINE HCl) EXTENDED-RELEASE CAPSULES

An advertisement in professional journal publications for EFFEXOR XR® (venlafaxine HCl) Extended-Release Capsules for the treatment of major depressive disorder was the subject of a Warning Letter issued by the U.S. Food and Drug Administration (FDA) in December 2007. The FDA stated that the journal ad was misleading because it overstated the efficacy of EFFEXOR XR, made unsubstantiated superiority claims, and contained other unsubstantiated claims regarding EFFEXOR XR.

Wyeth would like to take this opportunity to clarify the content of the advertisement.

Claims that Reference the Baldomero et al Study and Other Related Claims

The FDA objected to the claim, "In an open-label study of patients who failed previous antidepressant treatment, nearly 60% achieved remission when changed to EFFEXOR XR." The FDA determined that the Baldomero study (the cited reference for this claim) could not be relied upon as substantial evidence to support the claim due to the following reasons: (1) the study was an open-label study, which is not an appropriate study design to measure subjective end points because it fails to minimize potential bias; (2) the study did not include a placebo group, so there was no way to determine the actual effect size of the drug; and (3) the study did not provide information about whether EFFEXOR XR was superior to failed therapy because study subjects were not randomized to their previously failed therapy. Therefore, the FDA stated that the study failed to support the 60% remission rate claim as well as any conclusion that EFFEXOR XR is superior to other antidepressant treatments. In addition to the above claim, the FDA stated that other claims added to the misleading impression that patients who have failed previous antidepressant therapy can expect improvement when switching to EFFEXOR XR.

Claims from the PREVENT Study

The FDA objected to the claim, "In the PREVENT study, the probability of preventing a new episode of depression was 92% with EFFEXOR XR in maintenance year 2 vs. 55% with placebo." The FDA stated that the cited claim overstated the efficacy of EFFEXOR XR by implying that the general patient population suffering from major depressive disorder can expect a 92% probability of preventing a recurrent depressive episode after two years of treatment when this is not supported by substantial evidence.

The cited study for this claim was a randomized, multicenter, double-blind study (n=1096) comparing EFFEXOR XR with placebo. The study was designed to provide efficacy data regarding recurrence prevention with EFFEXOR XR after two years of maintenance

treatment. It followed patients through 4 different time periods: a 10-week acute period, a 6-month continuation period, an initial 12-month maintenance period (maintenance year 1), and a second 12-month maintenance period (maintenance year 2). At the end of each period, patients were only considered eligible for inclusion in the next period if they were still responding to the drug. Patients dropped out of the study during each of the periods for different reasons (eg, lack of efficacy, adverse events). At the start of each maintenance period, the remaining patients who still showed a response to EFFEXOR XR were re-randomized to EFFEXOR XR or placebo. Because a high percentage of EFFEXOR XR patients were either re-randomized to placebo or were discontinued from the study before entering maintenance year 2 and because only patients who responded to EFFEXOR XR were selected to continue to the next phase of treatment, the FDA determined that the results of the study could not be extrapolated to the general patient population suffering from major depressive disorder.

Claim Regarding Clinical Experience and Number of Patients

The FDA objected to the claim, "More than 12 years of clinical experience and over 20 million patients treated with EFFEXOR/EFFEXOR XR." The claim of 20 million EFFEXOR/EFFEXOR XR patients was estimated from the number of U.S. prescriptions, average daily consumption, and average length of therapy. The FDA determined that this claim was misleading based on the referenced data because the calculations used did not reflect the number of "unique" patients. Because there are no unique patient-level data available for the entire 14-year period during which EFFEXOR/EFFEXOR XR has been on the U.S. market, the claim is no longer used in EFFEXOR XR promotional materials.

Please see brief summary of Prescribing Information on adjacent page.

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