

## JOURNAL WATCH

Our panel of experts highlight the most important research articles across the spectrum of topics relevant to the field of Clinical Practice

**Expert panel:** Alba A Brandes, Department of Medical Oncology, Bellaria-Maggiore Hospital, Bologna, Italy; Marco Bartolotti, Department of Medical Oncology, Bellaria-Maggiore Hospital, Bologna, Italy; Robert S Dieter, Vascular & Endovascular Medicine, Loyola University Medical Center, IL, USA; Aravinda Nanjundappa, Department of Surgery, Charleston Area Medical Center, WV, USA; Joseph H Friedman, Butler Hospital/Alpert Medical School of Brown University, Providence, RI, USA

Verma S, Miles D, Gianni L *et al*.  
Trastuzumab emtansine for HER2-positive advanced breast cancer. *N. Engl. J. Med.* 367(19), 1783–1791 (2012).

This randomized (randomization ratio 1:1) Phase III trial compared trastuzumab emtansine (T-DM1; 3.6 mg/kg every 21 days) with capecitabine (2000 mg/m<sup>2</sup>/day from days 1 to 14) plus lapatinib (1250 mg/m<sup>2</sup>/day) in 991 patients with HER-2-positive advanced breast cancer. All patients had been previously treated with trastuzumab and a taxane. The primary end points were progression-free survival assessed by independent review, overall survival and safety. The study met its primary end points, demonstrating a significant superiority of T-DM1 over a capecitabine–lapatinib schedule. In fact, progression-free survival was 9.6 months with T-DM1 versus 6.4 months with capecitabine–lapatinib (hazard ratio: 0.65; 95% CI: 0.55–0.77;  $p < 0.001$ ); median overall survival was 30.9 versus 25.1 months (HR: 0.68; 95% CI: 0.55–0.85;  $p < 0.001$ ) favoring T-DM1, and objective response rates were 43.6% with T-DM1 and 30.8% with capecitabine–lapatinib ( $p < 0.0001$ ). In addition, the median duration of response was longer in the T-DM1 arm

(12.6 vs 6.5 months). The benefit gained from T-DM1 was maintained regardless of the number of lines of chemotherapy previously received (382 patients who enrolled underwent more than one line of chemotherapy before the study). Rates of grade 3–4 adverse events were higher with capecitabine–lapatinib compared with T-DM1 (57 vs 41% for adverse events and 18 vs 15.5% for serious adverse events, respectively).

Given the results of this trial, T-DM1 could become another effective therapeutic option for the treatment of advanced, HER2-positive breast cancer.

– Written by Alba A Brandes and Marco Bartolotti

Dvir D, Webb J, Pasic M *et al*.  
Transcatheter aortic valve replacement for degenerative bioprosthetic surgical valves: results from the Global Valve-in-Valve registry. *Circulation* 126(19), 2335–2344 (2012).

At the 2012 TransCatheter Therapeutics conference, a number of very insightful and thought-provoking research was presented. Extending the horizons for transcatheter aortic valve replacement, Dvir and colleagues present what is



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### Journal Watch

likely to become a standard alternative to the treatment of patients who have degenerated bioprosthetic aortic valves. Bioprosthetic aortic valves degrade over time and they usually require replacement by 15–20 years after implantation. In the current study, 416 patients with degenerated aortic bioprosthetic valves (40% stenotic, 30% insufficient and 30% combined stenosis/insufficiency) underwent transcatheter aortic valve replacement. The procedure was associated with a 30-day mortality rate of 7.8%, and 87.5% of patients were classified as New York Heart Association functional class I or II. At 1 year, survival was 82.6%. These outstanding results and future refinements in the technology, as well as in the procedure will allow less invasive treatment of this complex patient population.

– Written by Robert S Dieter and Aravinda Nanjundappa

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Devanand DP, Mintzer J, Schultz SK *et al.* Relapse risk after discontinuation of risperidone in Alzheimer's disease. *N. Engl. J. Med.* 367(16), 1497–1507 (2012).

This article is of interest to neurologists, psychiatrists and primary care providers who treat the elderly. There are no US FDA-approved medications for treating the behavioral problems associated with Alzheimer's or other dementing disorders, but data suggest that antipsychotics may provide limited benefit for some with psychotic symptoms, agitation or

aggression. On the other hand, these drugs carry 'black-box' warnings due to a 1.6-fold increase in mortality. This clever study enrolled patients with Alzheimer's disease who presented with these symptoms and were treated with open-label risperidone. They followed only those who benefited from the drug. After 16 weeks, subjects were treated in a double-blind manner with either risperidone or placebo for 16 weeks, and then underwent another treatment change. Stopping risperidone caused a higher rate of relapse in behavior, but the difference was not great. A large number of patients who had responded to risperidone at 16 weeks were no longer responding by 32 or 48 weeks. Thus, although continuing risperidone was more helpful than stopping it, "risperidone was not highly effective in achieving and maintaining a reduction in symptoms of psychosis and agitation."

– Written by Joseph H Friedman

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