1028

Clinical evaluation of patients with pulmonary arterial hypertension transitioned from the combination of bosentan and sildenafil to alternative therapy

Verlinden NJ, Stanton BE, Raina A, Benza RL
Allegheny General Hospital, Pittsburgh, PA

Background: Current clinical practice guidelines endorse the use of combination therapy with an endothelin receptor antagonist (ERA) and a phosphodiesterase type 5 inhibitor (PDE-5i) in treating PAH. Although bosentan and sildenafil have often been used in combination, there is evidence of a mutual, negative pharmacokinetic drug interaction with this particular combination. Recent clinical trial evidence has failed to show significant clinical benefit with this specific combination. Data are limited on the clinical effects of transitioning patients on this combination to alternative medications.

Methods: A retrospective chart review was performed on patients with PAH who were treated with the combination of bosentan and sildenafil and transitioned to alternative treatment from January 2010 to February 2019 at our center. Data collected included patient demographics, WHO functional class (FC), 6-minute walk distance (6MWD), invasive hemodynamics, tricuspid annular plane systolic excursion (TAPSE), and N-terminal pro-B-type natriuretic peptide (NT-proBNP) values. Patient parameters were evaluated at baseline and after transition. A stable 6MWD was defined as a post-transition change less than 15% compared to the baseline value, whereas a clinically meaningful change was defined as an increase or decrease in 6MWD by more than 15% after transition.

Results: A total of 16 patients with PAH (10 idiopathic, 2 connective tissue disease, 2 heritable, 2 other) were treated with the combination of bosentan and sildenafil for a median of 7 years (range 1-13 years) and transitioned to alternative therapy. The mean age of patients was 57.4 (± 14.8) years and a majority (87.5%) were female. Eleven patients (68.7%) were taking a concomitant prostacyclin medication at baseline. The reason for transition was concern due to drug interaction (7 patients), to reduce laboratory monitoring (5 patients), to improve adherence (2 patients), and clinical worsening (2 patients). Therapy was transitioned from bosentan to macitentan in 8 patients, bosentan to ambrisentan in 2 patients, dual therapy changes in 3 patients, sildenafil to tadalafil in 2 patients, and sildenafil to riociguat in 1 patient. Fifteen patients (93.7%) tolerated the transition. One patient resumed sildenafil and bosentan therapy due to intolerable adverse events after transition. An additional 3 patients had minor adverse events during transition. One patient was excluded from further clinical evaluation due to initiation of intravenous treprostinil after transition. In the remaining 14 patients who were successfully transitioned, WHO FC remained stable in 12 patients and improved in 2 patients. 6MWD was stable or improved in 82% of patients and declined in the other 18% of patients. The median change in 6MWD was +8 m (range -50 to +70 m; p = 0.46). There were no significant differences after transition in mean pulmonary artery pressure (mPAP), pulmonary vascular resistance (PVR), cardiac index (CI), TAPSE, and NT-proBNP.

Conclusions: Transitioning patients from the combination of bosentan and sildenafil to alternative therapy resulted in clinical stability and was generally well tolerated. Additional prospective data with a larger sample size is needed to better characterize the efficacy and safety of this transition.

Presented at the 2019 Pulmonary Hypertension Association (PHA) Pulmonary Hypertension Professional Network (PHPN) Symposium.