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# Limited Abciximab in PCI May Facilitate Same-Day Release

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DALLAS — A single bolus of the antiplatelet agent abciximab was as safe and effective as the bolus plus a 12-hour infusion of the drug for patients undergoing transradial coronary artery stenting in a study with about 1,000 patients at one institution.

The results also showed that single-bolus treatment with abciximab (ReoPro) in patients who had an uncomplicated percutaneous coronary intervention (PCI) using the transradial approach made possible a same-day hospital discharge, Dr. Olivier F. Bertrand said at the annual scientific sessions of the American Heart Association.

“The combination of a transradial PCI and single-bolus abciximab is safe and facilitates outpatient PCI in a wide spectrum of patients,” said Dr. Bertrand, a cardiologist at Laval University in Quebec City. “Use of simple risk criteria permits a change of PCI practice offering significant advantages in terms of bed occupancy and cost.”

The study included 1,348 patients who underwent transradial PCI at Laval Hospital during October 2003-April 2005. All patients received a standard bolus treatment with abciximab.

A total of 1,005 patients had no complications during their PCIs and were randomized to receive no additional abciximab (504 patients) or to receive an additional 12-hour infusion of abciximab during overnight hospitalization (501 patients). In those randomized to receive no additional abciximab, 443 (88%) were discharged on the day they had their PCIs.

The other 343 patients who entered the study had complications after PCI that precluded participation in the randomized phase. Complications included a residual dissection that was grade B or worse, a suboccluded side branch at least 1 mm in diameter, impaired blood flow in the treated artery, or development of thrombus after PCI.

The primary end point was the combined rate of death, myocardial infarction, urgent revascularization, repeat hospitalization, major bleeding, access site complication, or severe thrombocytopenia during the first 30 days after treatment. The study was designed to determine whether a single bolus of abciximab without an added 12-hour infusion was or was not inferior to treatment with both the bolus and infusion.

The incidence of the primary end point was 13.5% in patients who received the bolus treatment only, compared with a rate of 10.2% in those treated with the bolus and a 12-hour infusion. The result showed that the bolus alone was not inferior to the other regimen.

Three additional secondary analyses also showed the bolus-only regimen was not inferior. These analyses looked at the combined rate of death, myocardial infarction, and target vessel revascularization at 30 days, during the period from 30 days to 6 months after treatment, and throughout the entire first 6 months after treatment.

“The next step is to repeat this study as a large, multicenter trial,” Dr. Bertrand said.

The study was sponsored by Eli Lilly and Co., Bristol-Myers Squibb Co., and Sanofi-Aventis. Dr. Bertrand reported no financial relationships with these or other companies.

levels are at least partly associated with impaired ET<sub>B</sub> receptor-mediated clearance.<sup>13</sup> Furthermore, the long-term administration of a selective ET<sub>B</sub> receptor antagonist was found to have unfavorable effects on vascular remodeling.<sup>4</sup> This is in sharp contrast to the benefits of selective ET<sub>A</sub> antagonism.<sup>14</sup>

### THE DIFFERENCE LIES IN ET<sub>A</sub> SELECTIVITY

Vasoconstriction, cellular proliferation, and vascular remodeling are the hallmarks of PAH.<sup>12</sup> Studies have demonstrated that selective ET<sub>A</sub> antagonists play a pivotal role in the regulation of ET-1 levels in PAH and have been beneficial for vascular remodeling.<sup>4,7,13</sup>

### ET-1 AND RECEPTOR-MEDIATED ACTIVITIES

Highly selective ET<sub>A</sub> blockade maintains ET-1 clearance, NO and PGI<sub>2</sub> levels, and reduces or maintains circulating ET-1 levels, resulting in vasodilation, increased blood flow, and repair of remodeled vasculature compared to less selective agents.<sup>5-7,14</sup> (See Figures 1,2)

### HOW SELECTIVE TO ET<sub>A</sub> SHOULD TREATMENT BE?

The more selective, the better. One should always be aware of the varying degrees of selectivity, as they equate to differences in blockade of the ET<sub>A</sub> and ET<sub>B</sub> receptors and resulting levels of ET-1.<sup>8,15,16</sup> Figure 3 illustrates the difference between a less selective agent and highly selective agents. These in vitro selectivity ratios demonstrate the stark differences in ET<sub>A</sub> selectivity. Figure 4 depicts how agents with low selectivity of the ET<sub>A</sub> receptor (<2400) increase ET-1 levels whereas highly selective ET<sub>A</sub> receptor (>2400) antagonists have been shown to

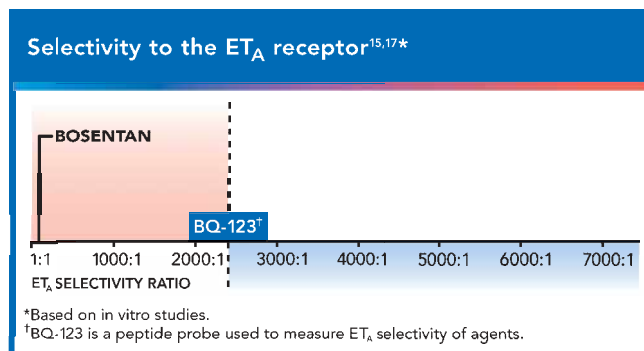


Figure 3

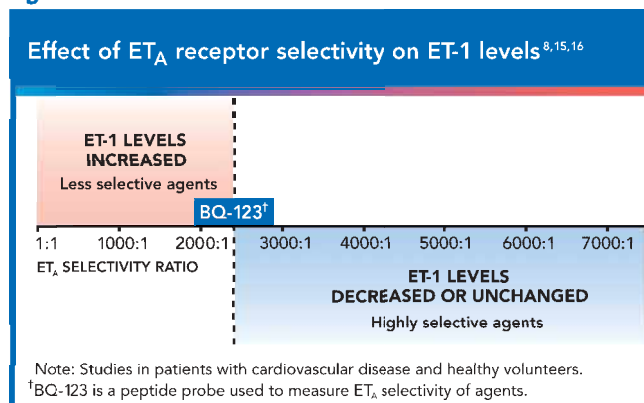


Figure 4

decrease ET-1 levels or leave them unchanged.<sup>6,8,15</sup> The benefits of ET<sub>A</sub> selectivity are being recognized.

### TOWARD BETTER OUTCOMES IN PAH

Currently, there are no highly selective ET<sub>A</sub> antagonists available for the treatment of PAH. In vivo studies have shown that highly selective ET<sub>A</sub> antagonism may lead to better overall outcomes.<sup>7,8,12</sup>

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