

**For Medical Press only**

## **TAXUS™ Stent in diabetes**

Coronary artery disease (CAD) is the most common cause of death among diabetic patients.<sup>1</sup> CAD is characterised by the presence of fatty deposits (plaques) in the coronary arteries. These plaques progressively narrow the coronary arteries and interfere with normal blood flow to the heart, leading to heart attack and death.

Coronary revascularisation procedures tend to be more difficult to perform in diabetic patients than in non-diabetic patients.<sup>2</sup> This is because diabetic patients typically have complex CAD with long diseased vessels containing plaques that can be found in small, difficult to reach coronary vessels. As a result, the vessels can become reblocked leading to further heart attacks. Improving outcomes for diabetic patients is of key importance because they represent approximately 30% of all patients undergoing percutaneous coronary intervention (PCI) procedures.<sup>3</sup>


PCI with a TAXUS paclitaxel-eluting stent system opens the diseased coronary artery allowing blood flow to be resumed. Once in place within the artery, the stent releases paclitaxel, a drug that helps to prevent the vessel from becoming reblocked. TAXUS stent systems have been examined in both clinical trials as well as in real world studies which have shown to provide more benefit to diabetic patients than either bare-metal stents (BMS)<sup>4-6</sup> or sirolimus-eluting stents.<sup>6-8</sup>

**TAXUS™ Liberté™ paclitaxel-eluting coronary stent system has received European CE Mark approval for use in patients with diabetes\*\*.**

**To date, this is the only drug-eluting stent to have a specific indication for diabetes patients.**

### ***What is the clinical evidence for TAXUS stent systems in diabetic patients?***

Combined data from four TAXUS ATLAS trials supported the efficacy and safety of the TAXUS Liberté stent system in diabetic patients.<sup>9</sup> The trials examined 1,529 patients treated with the TAXUS Liberté stent system, 413 of whom had diabetes, and reported similar rates of target lesion revascularization (TLR, or retreatment), cardiac death, myocardial infarction (MI, or heart attack) and stent thrombosis (clotting) between diabetic and non-diabetic stent recipients after adjustment for differences in risk at baseline.



TAXUS paclitaxel-eluting stent systems have been studied in more diabetic patients than any other drug-eluting stent to date\*\*\* A total of 814 diabetic patients were included in the four largest TAXUS trials (TAXUS II, IV, V and VI), which compared TAXUS stents with BMS. The results show that diabetic patients have significantly better early (9 months)<sup>4</sup> and late (4 years) outcomes<sup>5</sup> if they are treated with a TAXUS stent.

Patient outcomes were assessed using target lesion revascularisation (TLR), which is the need for a repeat procedure primarily due to reblocking at the site of the original blockage and MACE rates (a composite of death, heart attack or TLR).

At 9 months, TAXUS™ stent recipients had 59% less TLR ( $p=0.0001$ ) and a 41% reduction in MACE rates ( $p<0.0001$ ) compared with BMS recipients.<sup>4</sup> Significant improvements in TLR were also seen for diabetic patients on insulin therapy. These patients tend to be at higher risk than patients taking oral diabetic medications and often have more complex CAD.

Significant improvements compared with BMS were still clear 4 years after stent placement, with a 49% reduction in TLR rates compared with BMS (13.1% for TAXUS stent recipients vs. 25.5% for BMS;  $p<0.0001$ ).<sup>5</sup> Significant improvements were also maintained for diabetic patients on insulin therapy. Mortality rates and the incidence of heart attacks were similar in the two groups, indicating that TAXUS stents and BMS are equally safe 4 years after placement.

A pooled analysis of patients from TAXUS IV and TAXUS V randomized clinical trials comparing the safety and efficacy of the TAXUS® Express<sup>2</sup>™ Paclitaxel-Eluting Coronary Stent System in diabetic versus non-diabetic patients demonstrated that despite the known increased rates of mortality and restenosis for diabetics versus non-diabetics in patients with cardiovascular disease, the TAXUS Stent had comparable levels of late loss and target lesion revascularization (TLR) across these patient populations. The study also showed no significant differences in target vessel revascularization (TVR), stent thrombosis, or myocardial infarction (MI), after adjustments were made for differences in other baseline characteristics between patients with or without diabetes.

The TAXUS IV/V analysis also compared 338 diabetic patients treated with the TAXUS Stent versus 336 diabetic patients treated with bare-metal stents (BMS). Three-year rates of TVR and TLR were reduced by roughly 50 percent in diabetic patients treated with the TAXUS Stent compared to BMS, consistent with results seen in other high-risk patient groups. The TAXUS Stent showed comparable safety to BMS in diabetics, with no significant differences in death (7.3% vs. 7.1%,  $p=0.91$ ), cardiac death (4.6% vs. 2.7%,  $p=0.23$ ), MI (6.5% vs. 6.6%,  $p=0.83$ ) or ARC Definite/Probable stent thrombosis (1.6% vs. 1.5%,  $p=1.00$ ) in TAXUS and BMS, respectively.



### ***How does the TAXUS™ stent perform in the real world?***

Since patients in clinical trials are carefully selected, they may differ from patients in normal clinical practice. As a result it is important to confirm clinical trial results in a real world setting. Recent real-world studies have shown a clinical benefit for TAXUS paclitaxel-eluting stent systems compared with Cypher sirolimus-eluting stents or BMS in diabetic patients.

#### *RESEARCH/T-SEARCH registry*

The independent RESEARCH/T-SEARCH registry examined 708 consecutive diabetic patients treated with TAXUS, Cypher Stents and BMS.<sup>6</sup> Importantly, patients who received TAXUS stents had the most complex CAD, with the highest incidence of multivessel treatment, the greatest number of stented vessels and the longest stented length. Patients who received BMS had the least complex CAD. Despite the increased complexity, TAXUS patients had the lowest rate of TLR (5.3% vs. 13.2% for Cypher and 15.6% for BMS) and the lowest incidence of heart attack at 2 years (3.4% vs. 5.1% for Cypher and 7.7% for BMS).

#### *TC-WYRE\* study*

The TC-WYRE study found a highly significant 67% reduction in TVR rates for 289 diabetic patients with complex CAD who received a TAXUS stent compared with 247 patients with a Cypher sirolimus-eluting coronary stent (2.8% vs. 8.5% for Cypher;  $p=0.004$ ).<sup>7</sup>

#### *Kaiser Permanente registry*

Similarly, the independent Kaiser Permanente registry revealed a significant 56% reduction in the MACE rate for 227 TAXUS stent recipients compared with 272 Cypher stent recipients after 1 year (4.0% vs. 9.0% for Cypher;  $p=0.02$ ).<sup>8</sup>

#### *TAXUS ARRIVE 1 and 2 registries*

TAXUS ARRIVE 1 and 2 registries are designed to assess the performance of the TAXUS Stent in real-world practice.

The one-year pooled ARRIVE data on 1530 medication-requiring diabetic patients and 3242 non-diabetic patients confirmed the known higher mortality rate for diabetics versus non-diabetics with cardiovascular disease, but showed that the TAXUS Stent had similarly low rates of stent-related cardiac death, myocardial infarction (MI), stent thrombosis, and major cardiac events (MCE) across those two patient subsets. The study also showed similar rates of target vessel re-intervention (TVR) and TAXUS-related TVR in indicated patients per the European Union (EU) label, whether or not they had diabetes despite the known higher risk for re-intervention in diabetic patients.



***Is there any difference between paclitaxel and sirolimus?***

The medications contained in drug-eluting stents help to prevent arteries from becoming reblocked due to the build-up of plaque. The drug is released from the stent over the period of time when reblockage is most likely to occur.

Both paclitaxel and sirolimus prevent reblockage by stopping cells close to the plaque from multiplying and migrating. Patients with diabetes have difficulties with producing or using insulin. This creates an environment within the blood vessels which is changed due to insulin resistance and poorly regulated glucose levels in the blood. Studies with cultured cells show that in a high glucose environment there is a stimulation of two cellular pathways that promote reblockage of the vessel. Since paclitaxel works to shut down these pathways to prevent reblockage, it may have an advantage over sirolimus, which can only shut down one such pathway.<sup>10</sup>

***How do TAXUS™ stents perform compared with other revascularisation techniques?***

When a patient has more than one diseased vessel which needs to be treated, the physician can provide the option of a surgical intervention called coronary artery bypass grafting (CABG). To date there is no data suggesting that CABG or PCI is better when treating multi vessel disease. TAXUS stents are currently being studied against coronary artery bypass grafting (CABG) in a large clinical trial (SYNTAX Study) that includes over 1500 patients with complex CAD.<sup>11</sup> The study includes patients with CAD in three vessels or left main disease (isolated or in association with 1, 2, or 3 vessel disease), who were recruited on an 'all comers' basis. The primary outcome is 12-month occurrence of MACCE (all cause death, stroke, heart attack and repeat revascularisation).

The trial includes patients from Europe and the United States and should help evaluate the best treatment option. Results of the one-year follow-up from the SYNTAX study will be presented in 2008. The study will continue to follow patients for 5 years.

## References

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\*TC WYRE is a registry sponsored by Boston Scientific

\*\* For patients with concomitant diabetes mellitus

\*\*\* In randomized controlled trials, a total of 814 TAXUS diabetes patients were studied in the TAXUS meta-analysis<sup>5</sup> compared with 428 Cypher patients in the Cypher integrated analysis (Spaulding *et al. NEJM* 2007; 356:989-97) and 204 Endeavor patients in the Endeavor II and III studies (Fajadet J, *et al. Circulation* 2006; 114:798-806, Kandzari *et al. J Am Coll Cardiol* 2006; 48: 2440-7)