BIOSENSORS INTERNATIONAL

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Attn Joanne Richardson

Dear Madame,

Further to your letter of 18 th September and our subsequent e-mail exchange and telephone conversations please find enclosed a brief background summary of our drug eluting stent technology relating to our CE marked Axxion stent system. We would be very pleased to meet with you to present this information to you and your colleagues if you feel that that is beneficial. We will also be making a further submission in the near future relating to our BioMatrix DES system that is currently in the CE marking process. Our response is based on the data available at present and the time available for the preparation of our reply

Biosensors International Group through their Occam International BV Division was granted CE Mark by TNO in the Netherlands on July 11, 2005 for a non-polymeric paclitaxel eluting stent system (Axxion). The Axxion DES consists of an open celled 316 L stainless steel stent (Nexus) on Biosensors Senso balloon catheter. The stent surface is modified through a covalent bonding process that adds a synthetic form of a naturally occurring endothelial carbohydrate called glycocalix. Biocompatible and non-inflammatory, synthetic glycocalix coating forms a clean foundation for the drug and because of its passive properties helps to inhibit interference with healing and re-endothelialization. Paclitaxel is spray coated to the abluminal surface (only) of the coated Nexus stent, and not on the interior bloodstream side of the stent.

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As previously stated Cook and Guidant have successfully developed non-polymeric paclitaxel eluting products, were granted CE Mark and subsequently established clinical safety and efficacy results through several publications. The results of Cook and Guidant's trials; ASPECT, ELUTES and DELIVER were published in peer review journals and demonstrated the safety and efficacy of DES without drug elution polymer. These studies, and the equivalency of the elution curves of the Axxion stent system were also considered in the decision for review by MHRA and subsequent approval by TNO.

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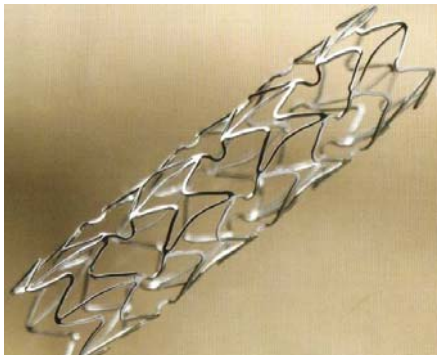
Biosensors began a safety and efficacy study at three German Centers in April of 2005 and have completed intended enrolment. Details of the study are as follows:

E.A.G.L.E.
European study of Axxion and Glycocalix Long term Evaluation



Centers and Investigators at currently enrolling centers:

- Prof. Ischinger (Principle Investigator) at the Heart and Lung Division of Krankenhuas Munich-Bogenhausen in Munich,
- Prof. Sievert at the Cardiology Center of Catherinen Krankenhaus in Frankfurt,
- Prof. Hauptman at Heart Center of the Krankenhaus der Barmherzingen Bruder in Treier.

1 Clinical Study Summary

Title: European study of **A**xxion and **G**lycocalix **L**ong term **E**valuation (**EAGLE**)

Design: This is a prospective, randomized, multi-center study on the treatment of patients with *de novo* lesions in native coronary vessels. The participating patients will be divided into 2/3 Axxion and 1/3 Calix users (total: 125). All patients are to return for a clinical follow-up visit at 6 months following the procedure. Repeat coronary angiography examination is optional and will be performed at 6 months after the procedure if clinically indicated. Thereafter, they will have telephone interviews annually for 5 more years (i.e.1, 2, 3, 4, and 5 years after the procedure).

Objectives: The objective of the study is to determine the safety and efficacy of using Occam's Paclitaxel and Calix coated Nexus II + stents in patients undergoing percutaneous coronary treatment of significant coronary artery narrowing. Clinical and angiographic results of the Axxion (Paclitaxel coated) and Calix (identical stent without Paclitaxel coating) stent system are compared.

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Enrolment: Study intends to enroll approximately 125 patients from participating centers.

Primary Endpoint: Major Adverse Cardiac Event (MACE) at 30 days. MACE consists of the occurrence of one of the following events: death, myocardial infarction (Q-wave and non-Q wave), target vessel and target lesion revascularization rates and vascular/hemorrhagic complications.

Secondary endpoints:

1) Angina status and MACE (MI, vascular complications, death, TVR, TLR) at 6 months
2) Change in neo-intimal lumen diameter: assessed by angiography at 6 month follow-up visit, if this is performed.
3) Binary restenosis rate: the proportion of patients with ≥50% diameter stenosis at the target lesion site (Stent + 5 mm at both stent ends) determined by quantitative coronary angiographic analysis (QCA)
4) Sub study. At 6 months: QCA parameters. Late loss in MLD, binary restenosis and loss index.

Treatment Strategy:

1) Patient is eligible for Percutaneous Coronary Intervention
2) Maximum one discrete target lesion per main vessel (LAD, RCA or LCx)
3) Lesion pre-dilation is required
4) Maximum of two study stents per target lesion
5) Antiplatelet therapy following implant(s) as desired by the investigator
6) Target vessel reference diameter is ≥ 2.5 mm and ≤ 4.0mm (by visual estimate or on-line quantitative coronary analysis)
7) Target lesion length ≤ 25 mm (by visual estimate or on-line quantitative coronary analysis)

2 Study Rationale

2.1 Rationale

In an effort to assess and understand the long-term clinical patient outcomes Biosensors International is sponsoring the EAGLE Study to facilitate a collaborative relationship between the medical professionals and the company. The EAGLE study will allow Biosensors International to observe and evaluate actual clinical experience in a wider subpopulation of patients treated with this promising technology.

3 Description of the Axxion Drug Eluting Stent System

3.1 Stent Platform

The Nexus II is laser cut from a 316L LVM stainless steel tube. The stent is a multi-cellular stent available in large and small models. Stent rings are connected by U shaped links that are positioned between successive rings.

3. 2 Glycocalix Coating

The Nexus II stent is coated with a thin, uniform film of semi-synthetic Glycocalix coating. This patented coating is derived from a commercially approved biocompatible substance commonly used for intravenous injections.

3.3 Anti-proliferative Drug: Paclitaxel

Paclitaxel is an anti-proliferative agent used in treatment of cancer as a broad spectrum chemotherapeutic agent. Paclitaxel-eluting stents have obtained marketing approval in the European Union, Canada, and the US for the treatment of in-stent coronary neointimal hyperplasia. Highly lipophilic and hydrophobic, rapidly absorbed in tissues and able to reversibly bind to immunophillins (growth regulating proteins) found inside most cell types, Paclitaxel inhibits, in a reversible manner, growth factor-stimulated cell proliferation. Paclitaxel binds to microtubules and stabilizes their structure by shifting the dynamic equilibrium between soluble and insoluble tubulin, thereby enhancing microtubule assembly, resulting in inhibition of cellular replication. While cells remain viable, paclitaxel inhibits cell processes that are dependent on microtubule turnover, such as mitosis, migration, endocytosis and secretion. Typical, side effects following oral administration above these blood levels include thrombocytopenia, increased platelet aggregation, dyslipidemia and intestinal dysfunction, but these side effects disappear quickly and reversibly at lower blood concentrations. Since the drug coating on the Axxion drug eluting stent is located only on the abluminal (i.e. outside) surface of the stent, upon implantation, a single 15mm long Axxion stent delivers its 60 µg dose of Paclitaxel only into the vessel wall tissue surrounding the stent. Tissue-based transport of the drug results in a small amount of the drug being released into the blood stream, with a << 1ng/ml, transient 24-hour presence of the drug in the systemic circulation. Blood drug concentrations of paclitaxel used in cancer patients are at least 1000X higher than the transient Paclitaxel concentrations seen in blood following implant of a single Paclitaxel eluting stent, so the change of any systemic side effects are considered to be close to zero.

3.4 AXXION Delivery system

The drug-coated stent is mounted on the Biosensors International Senso Delivery Systems. The Senso (CE Marked) has a nylon copolymer semicompliant balloon. The delivery systems are rapid exchange, high-pressure semi-compliant balloon expandable stent delivery catheters. The catheter has an integrated shaft and a distal balloon and a second lumen with a guidewire entrance port located approximately 25 cm proximal from the balloon for guidewire advancement. Two radio-opaque balloon markers are located in

each end of the balloon to facilitate catheter positioning. The balloon is designed to have a consistent diameter increase at each increment of pressure. A female lr hub, located at the proximal end of the dilation catheter, is used for device inflation.

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5 Study design

5.1 Study Design

The Eagle Stent Clinical Study is a prospective, randomized, multi-centre, web-based Study. This Study will enroll approximately 125 patients from participating centers. Collected data will include stent procedural data and patient follow-up outcomes including MACE clinical events. Follow-up data will be collected at 6 months after the procedure. Telephone interview data will be collected after approximately 1,2,3,4 and 5 years after the procedure. Electronic data capture will de done by using a web-based system. Study participants will be responsible for patient contact, obtaining follow-up data and data submission. Sponsor designated clinical research associated will be responsible for respective site management.

6 Patient Population

Clinical Inclusion Criteria:

1) Age ≥ 21 years old (legal age for consent).
2) Documented angina status or functional testing positive for ischemia including acute coronary syndromes without ST elevation
3) Agreeable for percutaneous coronary intervention
4) Acceptable candidate for bypass surgery
5) Provision of informed consent
6) Agreeable to comply with study specified follow-up procedures

Clinical Exclusion Critérium:

1) Known sensitivity to drugs used before during or after procedure, device, aspirin or clopidogrel.
2) Previous (≤12 months) implantation of any drug-coated or drug-eluting stent device in target vessel.
3) ≤48 hours of a myocardial infarction with ST elevation
4) Previous (≤12 months) cerebrovascular accident
5) Left ventricular ejection fraction ≤30%
6) Blood dyscrasia: leucopenia (leucocytes <3.5 X 10^9/L) or thrombocytopenia (platelets <100 X10^9/L)
7) Currently enrolled in another investigational drug stent study and has not completed the required follow-up period, or has completed all other drug-study required follow-up <30 days to enrolment in this study in the target vessel.
8) Currently enrolled in another drug coated stent study.

Angiographic Inclusion Criteria:

1) Target lesion is located in a native coronary vessel
2) Target is a de novo lesion
3) Target lesion diameter stenosis is between 60% to 99% stenosis (by visual estimate or on-line quantitative coronary analysis)
4) Target lesion length ≤25 mm
5) Target lesion reference diameter is between 2.5 to 4.0 mm (by visual estimate or on-line quantitative coronary analysis)

Angiographic Exclusion Critérium:

1) Unprotected left main stenosis (≥50%) when treating target lesions at the left anterior descending or circumflex arteries

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2) Target lesion was treated with atherectomy devices or laser prior to stent placement
3) Target lesion is ≤2 mm from an origin
4) Stent placement has side branches in segment of >2.5 mm in diameter
5) Target lesion is severely calcified, angulated (>60^{o}) or with severe tortuosity

7 Post-procedure

The following post-procedure testing is recommended:

- ECG should be repeated immediately after the procedure as well as after 90 and 180 minutes. Finally, a discharge ECG should be collected.
- Blood sampling for CK-MB; sample analysis will be performed at investigational site laboratory no central clinical laboratory will be used in this registry.
- Before hospital discharge the patient's clinical status will be assessed including an evaluation of ischemia and angina status, adverse events, and MACE (Major Adverse Cardiac Events).

8 Study Medication

The following medications are recommended for all patients enrolled in this Study:

Medication prior to index procedure

- Aspirin per standard of care

Medication during index procedure

- Heparin after insertion of arterial sheath repeated as needed to maintain an elevated activated clotting time (ACT) in accordance with the sites standard of care.
- Intra-coronary nitroglycerin (NTG) 50 to 200 µg immediately prior to baseline angiography and at the end of the index procedure.
- Clopidogrel 300 mg loading dose (per physician's discretion; ticlopidine 500 mg may be used instead of clopidogrel).

Medication post-procedure

- Aspirin indefinitely per standard of care
- Clopidogrel 75 mg once daily (per physician's standard of care ticlopidine 250 mg twice daily may be used instead of clopidogrel) for minimal 6 – 8 weeks is suggested.

The enrolment will be completed in third quarter of calendar 2005, with follow-up completed during spring 2006

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Current Enrolment (%) by Center

Heart and Lung – Munich	**56%**
Catherinen Krankenhaus – Frankfurt	**22%**
Heart Center of Krankenhous – Treier	**22%**

Biosensors are also finalizing the protocol and CRF for a multi center European and Middle Eastern E-Registry in relation to the Axxion product.

Summary Comments:
Biosensors Europe SA is interested in participating in future reviews. Current data would indicate the product is comparable both clinically and economically.

We look forward to hearing from you in the near future and working with your organization on an ongoing basis. Should you have questions please do not hesitate to contact either myself or Bill Konopisos our Axxion DES Launch Manager as below.

Yours sincerely,
Regional Director

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