Investigations into the Morphology of the XIENCE V® Drug Eluting Stent Coating

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The XIENCE V® everolimus eluting coronary stent system consists of the L-605 cobalt chromium VISION stent platform coated with a poly(n-butyl methacrylate) (PBMA) primer and a drug reservoir layer consisting of poly(vinylidene fluoride-co-hexafluoropropylene) (PVDF-HFP) polymer and the drug Everolimus. This drug-polymer matrix provides manufacturing flexibility, good mechanical integrity, and consistent drug release properties.

Using the XIENCE V® drug coating process as a starting point, the effect of varying the drug/polymer ratio on the in-vitro drug release rate and coating thermal properties was evaluated. To understand the effects of drug release on the coating morphology, XIENCE V® stents were eluted to near complete drug release in albumin solution at 37°C. Coating thickness measurements, SEM micrographs, and thermal analysis were performed pre- and post drug elution.

The polymer melting point with drug is identical to that of the coating without drug. This indicates that the drug does not interfere with the crystallization process and is largely located in the amorphous phase. The glass transition of pure Everolimus at 87°C was not seen in the coating thermogram, indicating that the drug is not extensively phase separated. What may be a weak glass transition at 76°C suggests a phase of everolimus blended with the lower Tg PVDF-HFP (Tg = -29°C)

The change in drug release rate with change in drug/polymer ratio of the coating can be used to infer whether the coating is percolated from drug phase separation. In the XIENCE V® drug reservoir layer, the drug comprises approximately 25% of the coating by volume. With complete drug elution, two limiting cases of morphological change are possible, if collapse of any porosity formed can be prevented. These are formation of 25% void volume, if the drug is phase separated, or a similar degree of coating shrinkage if the drug is dissolved in the amorphous phase of the polymer. SEM examination of the XIENCE V® coating as made reveals a smooth surface with a very fine texture. Post drug elution, some surface pores are evident ranging in size from 22-40 nm. Coating thickness measurements of XIENCE V® stents before and after drug elution revealed an approximately 20% decrease in the overall coating thickness. This decrease in the stent coating thickness, combined with the thermal analysis and SEM observations, describes a system where the drug is neither completely phase separated nor 100% dissolved in the coating.

It is proposed that in the XIENCE V® coating, the majority of the drug is not phase separated. With the drug largely dissolved in the polymer matrix, the drug release rate is less affected by changes in drug domain size and distribution, which become important factors with a phase separated system. This leads to a coating which has robust manufacturing properties and a more reproducible drug release profile.