Effects on re-endothelialisation with Bydureon treatment add on to insulin versus insulin alone, both in combination with metformin in type 2 diabetic subjects: Rebuild study

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Funding Acknowledgements: Type of funding sources: Public Institution(s). Main funding source(s): Hjärt-Lungfonden

Background: Patients with type 2 diabetes (T2D) have a higher risk of in-stent restenosis and stent thrombosis following a percutaneous coronary intervention 1. The key mechanism for preventing these events after stenting is a restored and well-functioning neo-endothelium 2. Several large, randomized trials have shown cardioprotective effect of Glucagon Like Peptide-1 receptor (GLP-1R) agonists therapy lowering the risk of major adverse cardiovascular events. In addition, activation of GLP-1R has been suggested to induce several effects on the vasculature3 that may reduce not only the risk of atherosclerosis progression, but even the risk of stent failure following an angioplasty.

Purpose: To evaluate the potential beneficial effect of the GLP-1R agonist Bydureon in the endothelialisation of modern drug-eluting stents (DES) in patients with T2D.

Methods: 38 subjects with T2D and coronary artery disease who were eligible for revascularisation with implantation of DES were included and randomized to either treatment with Bydureon (once weekly) over the standard treatment, or to standard treatment alone. After 12 weeks, a new coronary angiography was performed to evaluate the coverage of the DES and the presence of neo-atherosclerosis by optical coherence tomography. The main outcome was the percentage of stent coverage at 12 weeks. Descriptive data is shown as median (percentile 25th-75th).

Results: The two groups were well balanced regarding baseline clinical characteristics (Table). Neo-intimal coverage could be assessed in all 33 subjects that completed follow-up. DES coverage was 95% (88.7-98.5%) in the Bydureon group and 91.4% (88.8-98.5%) in the Control group (p=0.692). There were no significant differences between groups neither in the thickness of neo-intima (0.2 mm in both groups, p=0.471), nor the maximal in-stent obstruction by neo-intima (15.5% in Bydureon group vs 14.7% in Control group, p=0.801). Weight decrease was greater in Bydureon group compared to Control group (-7.8 kg vs +0.14 kg, p=0.014), and so was also HbA1c reduction (-11.4 mmol/mol vs -4.7 mmol/mol, p=0.001). No significant differences were detected on the rate of target lesion revascularisation between groups (p=0.224).

Conclusion: Twelve weeks treatment with Bydureon did not lead to a significantly better stent coverage in patients with T2D. No significant differences in the occurrence of neo-atherosclerosis were detected between groups.

Table: Baseline clinical characteristics
Diagram: Rebuild study methods and main results. Parts A to D displays the study's methods. A: a coronary stenosis suitable for angioplasty is identified in a patient with type 2 diabetes. B: a drug eluting stent is implanted. An optical coherence tomography is performed to ensure optimal stent implantation and obtain baseline measurements. C: randomization to either Bydureon over standard treatment or standard treatment alone during 12 weeks. D: new coronary angiography including optical coherence tomography is performed. Part E shows the main results of the intracoronary imaging. Abbreviations: MLA, Minimum Lumen Area.