

**EFFECTS OF LIRAGLUTIDE vs GLICLAZIDE TREATMENT ON CIRCULATING
ENDOTHELIUM-DERIVED MICROVESICLES (EMV) AND ENDOTHELIAL
PROGENITOR CELLS (EPC) IN TYPE 2 DIABETIC PATIENTS:**

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Introduction: EMV and EPC are circulating cellular markers of endothelial function and dysfunction which in turn are indicators of vascular health. It is presently unknown whether a reduction in EMV and/or an increase in EPC levels could be counted among the several potentially protective actions that GLP-1 receptor agonists (GLP-1RA) seem to exert on the vascular wall.

Aim: to investigate whether GLP-1RA (liraglutide) could specifically modulate the EMV/EPC circulating levels as compared to sulphonylurea (gliclazide).

Methods: Twenty-four T2DM subjects treated with metformin, HbA1c >7%, were randomized to either liraglutide or gliclazide therapy (12 per group). The EMP and EPC count was obtained by flow cytometry performed before and after a 12 week-treatment period. The EMV and EPC count was evaluated in freshly drawn whole blood, using a single platform count.

Results: In both treatment groups a significant reduction in circulating EMV (30% decrease, $p < 0.05$) was observed. Liraglutide, however, was significantly more effective than gliclazide in reducing the circulating EMV ($p < 0.05$). Most ancestral EPC increased 60-fold from the baseline in all patients (events/ml; $p < 0.0009$); a more differentiated EPC (2.5 times, events / ml; $p = ns$) showed a trend towards an increase only in the group treated with liraglutide. No relationship between EMV/EPC change and improvement in HbA1c levels was observed.

Conclusions: Liraglutide modulates circulating EMV/EPC levels independently of metabolic control improvement. This must therefore be regarded as a Liraglutide direct effect which might contribute to the cardiovascular protection demonstrated by this molecule in vivo.