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Efficacy of AGB-100, TGF-β type I receptor (ALK5) inhibitor, using renal fibrosis on a chip model

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Objectives: Renal fibrosis is a central mechanism in the progression of chronic kidney disease, ultimately leading to end-stage kidney disease. Although many approaches have combated renal fibrosis, the experimental model to evaluate currently available drugs could be better. We previously developed a fibrosis-mimicking system using three-dimensional culture devices designed with three separate layers of renal tubular epithelial, endothelial, and fibroblastic cell layers. We evaluated the efficacy of novel AGB-100 (TGF-beta type 1 receptor (ALK5) inhibitor) as a highly potent, selective, bioavailable, and safe drug by applying renal fibrosis on a chip.

Methods: We evaluated tubular epithelial-mesenchymal transition (EMT), secretion protein, vascular and mRNA alteration in a renal fibrosis-on-a-chip model using three different dosages of AGB-100(2, 10, and 50μM) to overcome challenges associated with renal disease modeling.

Results: As Fibrosis and EMT markers, alpha-SMA expression specifically decreased, and KRT-8 levels increased compared with TGF-β induced fibrosis group in an AGB-100 dose-dependent manner. AGB-100 dramatically declined the mRNA expression of TGF-β and simultaneously increased the level of VEGFR2 and IL-10, an anti-inflammatory cytokine. The total length of thin vessels was decreased by AGB-100 significantly. AGB-100 meaningfully diminished the TGF–β1 and TGF-β3 protein secretion and the renal inflammatory cytokine. However, AGB-100 reduced the release of IL-1β and made no difference in TNF-α production.

Conclusions: The efficacy evaluation of AGB-100 will increase their reliability and the understanding of the use of novel TGF-β inhibitors as therapeutic agents. We found that AGB-100 may be a drug candidate that can help treat renal fibrosis.
*AGB-100 was provided by Biophammer Inc. (Korea)