Methods: The medical records of NHS patients who have received security and effectiveness in a real-world clinical setting.

Results:

Secukinumab is the first IL-17 inhibitor licensed for use in PsA. Background: There is debate about the strength of association, and this study aims to investigate the relationship of periodontitis on systemic inflammation.

Methods:

An established EndoMT in vitro experimental model was used. Human pulmonary artery endothelial cells (HPAECs) were treated with a cocktail of TGF-β (5 ng/mL), TNF-α (5 ng/mL), and IL-1β (0.1 ng/mL) for 5 days. HPAECs were used between passages 4 to 10. Immunohistochemistry and immunofluorescence were used to detect NKX2-5 within endothelial cells undergoing EndoMT. Western blotting and qPCR were performed to evaluate, respectively, protein and mRNA levels of NKX2-5 and of endothelial and mesenchymal markers. ALK5, ERK5, PI3K and casein kinase II (CKII) inhibition was performed to determine the pathways that lead to upregulation of NKX2-5 expression during EndoMT. Tissue-specific deletion of NKX2-5 in a chronic hypoxia mouse model of PAH was used to assess pulmonary vascular remodelling.

Results:

Western blot analysis demonstrated a 2-fold downregulation of CD31 (p < 0.05) and increased production of NKO2-5 (5.5-fold change, p < 0.001) and Procollagen I (12-fold change, p = 0.0009) after 5 days of inflammatory cocktail stimulation on HPAECs. Relative mRNA expression has shown a 3-fold gene downregulation of CD31 (p = 0.0002) and a 2.3-fold reduction of VE-Cadherin (p = 0.0008) in EndoMT, whereas gene expression of COL1α2 (8.5-fold change, p = 0.0001), and NKO2-5 (1.5-fold change, p = 0.003) were upregulated. Immunohistochemistry of SSc-PAH human lungs established a strong expression of NKO2-5 by endothelial cells. Immunofluorescence has also revealed a decreased VE-Cadherin expression concomitant with upregulation of NKO2-5 in HPAECs undergoing EndoMT. Inhibition of PI3K, ERK5, ALK5 and CKII decreased NKO2-5 protein expression. Deletion of NKO2-5 in the mouse model of PAH reduced neo-intima formation and vascular remodelling.

Conclusion:

Activated HPAECs undergoing EndoMT express NKO2-5 in vitro and in vivo, via mediation of CKII, TGF-β, ERK5 and PI3K.
signalings, and upregulate mesenchymal genes and ECM proteins, whereas endothelial markers are downregulated, suggesting that NKX2-5 has a major role in this process. This study highlights a new pathway associated with EndoMT and potentially a novel therapeutic target for vascular remodeling and SSc-PAH. 

Disclosures: The authors have declared no conflicts of interest.