

International Conference on

Autoimmunity

October 13-14, 2016 Manchester, UK

Dapirolizumab pegol: A novel treatment of patients with SLE by inhibiting CD40L

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CD40 ligand (CD40L) has been described as one of the key players in regulating T cell, B cell and antigen-presenting cell activity. Pre-clinical evidence and phase 1 and 2 clinical studies with anti-CD40L antibodies, such as ruplizumab (Antova™) and toralizumab suggest that CD40L blockade may be efficacious in the treatment of inflammatory and autoimmune conditions. However, clinical development of these antibodies was discontinued because of significant thromboembolic events, due to Fc-mediated cross linking, resulting in platelet activation. UCB and Biogen have developed Dapirolizumab pegol (DZP) which comprises of Fab fragments with a high affinity for CD40L, conjugated to polyethylene glycol (PEG) scaffolding to deliver desired pharmacokinetic characteristics. Lacking any Fc moiety, DZP has been engineered to minimise the risk of platelet activation through Fc-mediated cross-linking. To date UCB and Biogen have completed two clinical studies with DZP. The first in human study (SL0013) demonstrated a dose-proportional pharmacokinetics of DZP. The second clinical study was a Phase Ib multiple dose study (SL0014) in patients with mild to moderate SLE. Whole blood transcriptomic profiling demonstrated a reduction in B cell transcript levels on active treatment supporting the proposed mode of action for DZP. Lupus response rates were notable: 5/12 SRI4 and 5/11 BICLA responders in the CDP7657 arm, in comparison with 1/7 in the placebo arm. DZP was well tolerated with no changes in coagulation parameters or serious treatment emergent adverse events.

Biography

Farnaz Fallah-Arani is currently a Senior Group Leader in the therapeutic area of immunology at UCB Celltech in Slough and has experience in pre-clinical research and drug discovery of biologics and small molecules. She is an Immunologist by training and has a strong interest in the biology of autoimmune disease and transplantation.

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