Abstracts


Opening session (live-streamed with external Q&A)

Keynote

07 B CELLS AS A THERAPEUTIC TARGET IN SLE: WHERE WE ARE TODAY AND WHERE WE MAY BE TOMORROW

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Systemic lupus erythematosus (SLE) is a heterogeneous disease characterised by abnormalities in cellular and humoral immunity with clear hints that abnormalities of B lineage cells (B and plasma cells) are key drivers.

Clinical experiences with belimumab as a first approved targeted SLE treatment provide robust evidence that blocking BLyS/BAFF selectively interfering with B cell survival can change the course of the disease, including prevention of damage accrual. Recent failures of first generation anti-CD20 (rituximab, ocrelizumab) and BTK inhibitors (fenebrutinib/GDC-0853 and evobrutinib) together with the occurrence of anergic B cells in SLE provide the rational for various innovative strategies. These include more profound targeting by second generation anti-CD20 modalities (obinutuzumab and plasma cells) are key drivers.

In addition, enhancing regulatory B-cell functions may hold attractive opportunities. Such strategies have potential to reinstall the balance of pathogenic and protective B cells with the potential of more specific therapies. Moreover, these treatment targets should have the potential to overcome the status of anergic B cells holding promise to escape the detrimental chronic autoimmune process. In this context, targeting checkpoint molecules that downmodulate intracellular phosphatases, such as CD40 or other targets of this family on B cells, and enhancing Treg cells, may provide increased control of B-cell activation. Another potential innovative treatment modality could be the use of non-depleting bispecific antibodies may open more selective B cell subset targeting of enhancing the potency of depletion in the future. 3

Learning Objectives

• Discuss the translational concept of anergic (APA, immunosenescent) B cells in SLE
• Explain the impact of indirect targeting of B cells by anti-BLyS/BAFF treatment
• Discuss depleting versus non-depleting strategies of B cells in SLE
• Explain the concept of overcoming APA (immunosenescent) B cells and the rational of anti-CD40 treatment as a checkpoint modulatory concept

Plenary I: controversial issues in the management of SLE

A5 ARE DOACS DEAD? OR DO THEY STILL HAVE A ROLE IN SLE/APS?

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Since its development in the 1950s, the vitamin K (VKA) antagonist warfarin has been a standard anticoagulant, which for 40 years has utilised the International Normalisation Ratio (INR) to regulate the required dose. Although effective in the treatment of blood clots and reducing the risk of stroke in atrial fibrillation, its use necessitates significant food restrictions and the avoidance of many types of drugs. In contrast, direct oral anticoagulants (DOACs) are fixed-dose, more predictable, require no routine monitoring, have no interactions with food or alcohol and many fewer drug interactions than warfarin.

The RAPS study demonstrated that rivaroxaban is not inferior to warfarin in the treatment of patients with venous thromboembolism with a target INR of 2–3.1 Quality of life consideration favoured rivaroxaban in that study. Notably, 27% of the patients in this trial were triple positive for anti-phospholipid antibodies (APAbs).

In contrast, in the TRAPS trial, patients with high risk triple-positive antiphospholipid syndrome (APS) on rivaroxaban were shown to be at increased risk of developing thromboembolic events2 – a concern mirrored by a report from Ord-Ross et al, although the numbers of arterial events comparing rivaroxaban and warfarin was not in fact statistically significantly different.3 In addition, there are several early studies reporting approximately 3% of patients per year develop recurrent thrombosis while on warfarin.4

Currently, the Medicine and Healthcare Products Regulatory Agencies (MHRA) in the UK advise that DOACs are not recommended for patients with a history of thrombosis who are diagnosed with APS and particularly for those who are triple positive. DOACs may, however, be considered in patients

REFERENCES


