BACKGROUND: B cell targeted therapies (BCTTs) are effective for the management of a large number of rheumatic conditions. Although, effective the use of BCTT is associated with risk of hypo-gammaglobulinemia and its attendant risk i.e serious infections. The incidence of hypo-gammaglobulinemia in various rheumatic diseases following BCTT ranges from 14-22%. Secondary immunodeficiency, including secondary hypogammaglobulinemia is of rising concern ; however, there is scant data available on the natural history of hypogammaglobulinemia and the indications for immunoglobulin replacement therapy (IGRT) in BCTT-associated hypo-gammaglobulinemia. The recommendations and points to consider are intended for use by health-care professionals to aid diagnostic and therapeutic clinical decision making for patients with hypo-gammaglobulinemia.

METHODS:
The multi-speciality taskforce committee carried out a modified Delphi exercise to identify topics required for the recommendations. Further, the evidence was discussed by the committee at a face-to- face meeting to agree on the wording of the statements, and to divide them into overarching principles (OPs), and recommendations.

ACADEMIC P.E.A.R.L.S

Pediatric Evidence And Research Learning Snippet

Recommendations for the Management of Secondary Hypogammaglobulinaemia due to B Cell Targeted Therapies in Autoimmune Rheumatic Diseases.

Wijetilleka S, Jayne DR, Mukhtyar C, et al. Rheumatology (Oxford, England). 2019 May;58(5):889-896. DOI: 10.1093/rheumatology/key394.

Results

Overarching principles	
OP1	Patients and their parents/carers should be specifically informed about the possibility and implications of developing hypogammaglobulinaemia secondary to BCTT. There should be a locally agreed pathway for patients to report infections.
OP2	Health-care professionals using BCTT should be aware of local referral pathways for hypogammaglobulinaemia and its complications.
OP3	The commencement of IGRT, and its route of administration, should follow a shared decision-making process between the patient, the clinician supervising the care of the underlying autoimmune disease, and a clinical immunology service.
Recommendations	
Recommendation 1	The decision to start IGRT should be informed by degree of hypogammaglobulinaemia, SPUR infections, demonstration of impaired antibody responses to polysaccharide antigens and poor response to antibiotic prophylaxis.
Recommendation 2	The predisposing factors for the development of clinically significant hypogammaglobulinaemia during or after BCTT include a pre-existing low IgG level and previous and/or concomitant immunosuppressive therapies
Recommendation 3	Patients with AIRD who have hypogammaglobulinaemia and SPUR infections should be referred to a Clinical Immunology service for assessment.
Recommendation 4	Immunoglobulin levels should be measured prior to commencement of BCTT and repeated every 6–12 months for the duration of BCTT and a minimum of one year after stopping treatment. In selected patients, it may be appropriate to monitor for longer.
Recommendation 5	In hypogammaglobulinaemia related to BCTT, initial dosing of IGRT should be 0.4 g/kg/month. The route of administration should take into account patient preference, comorbidities and local availability.
Recommendation 6	A low IgG level is not an absolute contra-indication to commencing or continuing BCTT. The decision should be based on an individualised benefit-risk analysis.
Recommendation 7	The decision to continue IGRT should be reviewed annually and based upon clinical and laboratory parameters.
Recommendation 8	There is no available evidence comparing the use of antibiotic prophylaxis with IGRT in symptomatic hypogammaglobulinaemia caused by BCTT; however, an initial trial of antibiotic prophylaxis may be appropriate.

AIRD: autoimmune rheumatic disease; BCTT: B cell targeted therapy, IGRT: immunoglobulin replacement therapy, SPUR: serious, persistent, unusual or recurrent; OPs: overarching principles.

Conclusion: These are the first recommendations specifically formulated for BCTT related hypogamma- globulinemia in AIRD. The benefit of B cell targeted therapies should be balanced against the risk of inducing sustained secondary antibody deficiency. A shared decision making involving the patient and the clinician is warranted for institution of Immunoglobulin replacement therapy.

EXPERT COMMENT

Immunoglobulin levels should be done at baseline and then 6-12 monthly during and one year after BCTT . Low baseline values of IgG increases the risk of subsequent BCTT related hypogammaglobulinemia. However, a low IgG levels are not a contra-indication for BCTT; and the same may be initiated weighing risk-benefit ratio. Immunoglobulin replacement therapy (0.4g/kg/mo) may be considered for those with hypogammaglobulinemia and SPUR (serious, persistent, unusual and recurrent) infections.

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Reference

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