

The Australian Lupus Registry and Biobank: a timely initiative

A collaborative effort to provide real world evidence for therapies for patients with lupus

Systemic lupus erythematosus (SLE) is a complex autoimmune disease with diverse clinical manifestations, which places an unacceptable level of burden on affected patients. Australian data on lupus are scarce, with figures suggesting a prevalence of SLE that ranges from 19 per 100 000 in people of European ancestry to 92 per 100 000 in Indigenous Australians,¹ similar to other chronic diseases such as hepatitis C.² Survival rates for SLE patients in the 1950s were as low as 50% at 5 years. With improvements in the treatment of renal disease and infection, survival rates in most studies improved to around 90% at 10 years by the 1990s. However, it is still a sobering thought that SLE, which typically presents in women in their second or third decade of life, confers a 1 in 10 chance of dying before the age of 40.³ Damage accumulation, long term medication side effects (particularly steroids side effects), fatigue and uncertainty profoundly affect quality of life.⁴ Fundamental data regarding age, geographic and ethnic distribution; natural history of the disease; currently used treatments; and unmet needs of patients in Australia have not been well defined.

Since it is a relatively rare and heterogeneous disease, longitudinal registry studies play an essential role in improving our understanding of SLE. Registry studies are ideally suited to capturing real world data on a large number of subjects, giving insights into disease course and treatment practices. Moreover, they may serve as a platform to inform planning of randomised controlled trials (RCTs) and subcohort studies. In contrast to RCTs, they typically have broader inclusion criteria and allow for long term follow-up. Registry findings can complement RCT results, as demonstrated by the increased risk of tuberculosis associated with the use of tumour necrosis factor inhibitors in patients with rheumatoid arthritis, which was not identified in clinical trials, but rather revealed and quantified through registry studies.⁵ Despite the inherent limitations, a great deal can be learnt from single-centre SLE registries, such as the seminal 1974 observation in the Toronto lupus cohort of a bimodal mortality pattern, with early deaths due to active disease and infection, and later deaths due to premature cardiovascular disease.⁶ However, much progress has been made in past 40 years, with large multicentre cohorts from predominantly Europe and North America contributing to our understanding of the disease, particularly with reference to real world epidemiology, clinical features, natural history and long term outcomes.⁷

A national registry based in Australia may be a late starter, but it has the potential to be a world leader, with carefully collected data that provide assessment of visit-to-visit disease activity and of medication exposure. It also enables the conduct of studies specific to the Australian health care settings and the demographics of a



multicultural Australian population. The Australian Lupus Registry and Biobank (ALRB) was created in 2012, with seed funding from MOVE Muscle, Bone and Joint Health (formerly Arthritis and Osteoporosis Victoria) and contributions from the industry in the form of unrestricted grants.

The ALRB is an online platform that enables the longitudinal collection of systematic and comprehensive data. One of the first studies using the registry aimed at understanding the disease characteristics and treatment patterns in Australia. Using the framework provided by the registry, we have also undertaken a study to validate a consensus-based treatment target to determine whether this can be a data-driven treatment endpoint associated with better patient outcomes.⁸ The effects of long term use of immunosuppressive medication in SLE patients are not well understood, and data from the registry may give us a better understanding of the incidence of adverse effects and benefits, such as reduction in flares and accumulated damage over time. In addition, biomarker studies examining the interferon- α gene signature and disease manifestations, response to treatment, vitamin D status and disease manifestations, and patient-reported quality of life are in the planning stages.⁹⁻¹²

The registry also collects patient-reported outcomes, such as Short Form 36 and multidimensional health assessment questionnaires. Patients' self-reported data complement physician-reported data in the ALRB to capture the breadth of experiences of patients with SLE in Australia and provide a meaningful assessment of the disease burden and treatment shortfalls.

There are now ten institutions recruiting patients with SLE to the ALRB across Victoria, New South Wales, South Australia and Western Australia, with the common goal of improving treatment and outcomes for people with

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SLE. The expansion of the ALRB to involve more practices across Australia may be easier if the platform imports from existing electronic medical records or health systems (administrative, laboratory or radiological) to avoid duplicated data entry — provided data fields are matched according to a stringent data dictionary. Periodic auditing, involving cross-checking data with source records, will be done by principal investigators at each site and will be reported to the ALRB Management Committee to ensure data completeness and accuracy. This committee may also request the de-identified source documentation for quality assurance purposes.

One of the key strengths of the ALRB rests in its ability to examine a variety of health care outputs over time. At present, in the complex Australian health care system, it is difficult to examine the different components of health care use; therefore, the true economic costs for a disease such as SLE are often grossly underestimated. The ALRB will allow the tracking of health care uses related to the care of SLE in Australia and will provide data for benchmarking. With the rising costs of health care and a limited health budget, it is paramount that data are available to study the cost effectiveness of various management strategies. Health care use, based on annual patient self-reporting of hospitalisations, investigations and other health complications, may form the basis to derive cost. The ALRB information may help measure the health consequences of different health care interventions.

The overarching principle of the ALRB is to foster collaborative research and, with the same purpose, the simultaneous development of the Asia–Pacific Lupus Collaboration (www.asiapacificlupus.com) brings together researchers from Australia, China, Dubai, Hong Kong, Indonesia, Japan, Malaysia, Philippines, Singapore, Taiwan and Thailand. More than 2000 patients with lupus

across the Asia–Pacific region have been recruited in the Lupus Low Disease Activity State study to validate a treatment target.⁸ This type of research is consistent with the Australian Research Council strategy to encourage international collaboration — especially where it has been led by the Australian site (www.arc.gov.au/international-collaboration).

Finally, the parallel development of a biobanking system to complement clinical data from the ALRB means that more questions into aetiology and novel biomarkers can be answered. The fostering of closer links between basic science researchers and clinicians is the foundation of good translational research. Linking clinical phenotype to genetic polymorphisms and novel laboratory parameters has been valuable in understanding pathogenesis and prognosis, and in predicting SLE manifestations and response to treatment in such a heterogeneous disease.¹³

The ALRB is still in its infancy and will require significant inputs from various funding sources to continue its growth. We expect that, as the registry grows, it will serve as a valuable resource for clinicians, scientists, epidemiologists, patient advocacy groups, industry and government to provide real world evidence of clinical effectiveness of existing or new therapies and management strategies in patients with SLE in Australia.

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