
**Day 1**
**Leonid D. Zamora, MD**

**The Intersection of Art and Science: Gaudí's Creations and Lupus Treatment**

At first glance, Antoni Gaudí's architectural marvels and the treatment of lupus, particularly with drugs like anifrolumab and belimumab, may seem to inhabit different realms. However, they share a common thread of innovation, complexity, and vibrancy.

Gaudí's architectural masterpieces, such as the Sagrada Familia or Park Güell, are renowned for their intricate designs and vibrant mosaics. They stand as a testament to Gaudí's innovative spirit, pushing the boundaries of design and engineering. Each creation is unique, tailored to its environment and purpose. This mirrors the aspiration of personalized treatments for systemic lupus erythematosus (SLE), where each patient's needs are considered individually.

The treatment of lupus is a complex process that requires a deep understanding of the disease and the patient's condition. The introduction of drugs like anifrolumab and belimumab has revolutionized lupus treatment. These drugs, much like Gaudí's vibrant mosaics, add color to the treatment landscape of lupus. They offer new hope to patients by improving their quality of life and potentially altering the course of this chronic disease.

The 12th annual meeting of the Lupus Academy opened with a hybrid session moderated by Professors Ricard Cervera (Spain) and Sandra Navarra (Philippines). Professors Eric Morand (Australia) and Ronald van Vollenhoven (Netherlands) presented compelling data on anifrolumab and belimumab, respectively, during the "New Era of Treatments for SLE" session. They tackled which drug to try first and in which patients, providing important data supporting the efficacy and safety of these two FDA-approved biologic DMARDs for the treatment of moderate to severe active SLE.

**Anifrolumab: A New Hope**

Professor Morand presented compelling data on the efficacy of anifrolumab for non-renal SLE, focusing on long-term extension data. Anifrolumab is an anti-IFNAR1 therapy that might elicit organ-specific effects, consistent with clinical efficacy data. The case for anifrolumab as a first-line biologic in SLE rests on several points: fast onset of action, efficacy in various domains suggesting broad effects in SLE, robust glucocorticoid sparing effects, attainment of remission or LLDAS, good tolerance in long-term trials, and prolonged reduction in disease activity. Importantly, data is lacking for its efficacy in lupus nephritis (LN).

**Belimumab: A Proven Efficacy**

Professor Vollenhoven defended belimumab based on its mechanism. Belimumab is an anti-BAFF therapy that blocks a key element of the adaptive immune system involved in SLE without interfering with innate host defense. He presented large RCTs proving the efficacy and safety of belimumab. Further analysis demonstrated that patients with high anti-dsDNA and low complement had the highest likelihood of benefiting from the treatment. Belimumab has been shown to be effective in various formulations, reducing rates of flares, maintaining responses for many years, allowing glucocorticoid dose reductions, and reducing damage accrual.

Belimumab and anifrolumab have indeed ushered in a new era of promise in the treatment of Systemic Lupus Erythematosus (SLE). These treatments, however, are not without their complexities. Patient stratification and specific precautions are crucial to minimize risks and maximize the beneficial effects of these treatments. The potential for certain patient groups to derive greater benefits from either anifrolumab or belimumab is an exciting prospect, highlighting the need for robust predictors that can guide a more personalized selection of these biological agents.

The question that looms large is, “Why wait for conventional therapies to fail before introducing these drugs?” Answering this requires careful consideration of various geographical, political, and socio-economic factors. In the not-so-distant past, our options for treating SLE were limited to prednisone. Today, we have a range of immunosuppressives, biologics, and more treatments on the horizon being tested for our lupus patients.

The future indeed looks bright for our patients. The hope is that one day we won’t have to wait but instead be able to offer personalized treatment tailored to the unique needs of each lupus patient. This is not just about managing a disease; it’s about transforming lives, one patient at a time.

Both Gaudí's creations and lupus treatments embody a spirit of innovation and vibrancy. They stand as testaments to human ingenuity and the relentless pursuit of improving lives, whether through awe-inspiring architecture or life-changing medical treatments.

**Day 2**
**Melissa Aquino-Villamin, MD**

As the city of Barcelona continues to unravel its architectural wonders and delectable dishes, the second day of the 12th Lupus Academy offered more engaging topics starting with Meet the Editor workshop with Professor Vollenhoven, followed by interactive case study workshops on the management of (1) Pediatric lupus moderated by Professor Murray Urowitz, (2) Cardiovascular involvement in SLE moderated by Professor Thomas Dorner, (3) Lupus nephritis moderated by Professor David Isenberg, (4) Musculoskeletal involvement in SLE by Professor Zahir Amoura, and (5) Skin involvement in SLE moderated by Professor Vollenhoven. The important issues raised during the workshop will be discussed in the last part of this write up.

The session on Thieves Market followed where discussion of three interesting cases were given: (1) juvenile lupus who had a stormy course and suffered from hemophagocytic lymphohistiocytosis, (2) antiphospholipid syndrome complicated by hypoprothrombinemia, and lastly (3) an initial lupus case who turned out to have lymphoma. The afternoon sessions were on the "Patient being at the center stage," and the last panel discussion closed with topics on Treatment Optimization and Disease Modification in Lupus.

**Patient at the Center Stage**

From the patient's voice by Jeanette Andersen and the nurse's perspective by Ada Ferenkeh-Koroma, both emphasized that lupus is a systemic disease with varying manifestations and organ involvement, requiring multi-specialties. Though treated by different doctors, the patients should continue to be in the core when making management decisions. Inadvertently, communication gaps may arise that can hinder optimal lupus management. About 48% of SLE patients have difficulty describing their symptoms to their doctor, 52% minimize their symptoms to their physicians, and 72% of doctors are not aware of patients minimizing their symptoms. Many of these issues could be solved through better communication with clear expectations on both sides. The role of the rheumatologist is emphasized, being the over-all coordinator to other specialties like hematology, pulmonology, cardiology, and others.


Lupus recognition and diagnosis also poses a challenge. The delay in referral from the healthcare professional to the rheumatologist is a significant factor. In European countries as shared by Professor Marta Mosca, the creation of ERN-ReCONNET, a European Reference Network on rare and complex connective tissue diseases, aims at connecting healthcare providers by providing a framework for the delivery of care and practice to European patients. Its initial scientific activity focused on reviewing existing clinical practice guidelines and publications and appraising articles that will help in the diagnosis and management of these rare diseases, specifically SLE.

**Treatment optimization and disease modification in lupus**

Optimizing steroid sparing drugs for SLE is recommended as discussed by Professor Guillermo Ruiz-Irastorza, because of the adverse effects of glucocorticoid use. Some of these adverse effects are development of osteoporosis, cataracts, hyperglycemia, coronary heart disease and cognitive impairment. Hence, the lowest possible steroid dose is ideal. Optimizing the use of steroid sparing therapies like hydroxychloroquine, immunosuppressive agents like mycophenolate mofetil, azathioprine, and use of calcineurin inhibitors like voclosporin for LN, use of biologics like belimumab or anifrolumab, and lastly the "extra-friend" of lupus which is the use of the "pulse" doses of steroids can be used for severe lupus activity. Disease modification in SLE requires minimizing disease activity with the fewest treatment-associated toxicities AND slowing or preventing organ damage progression (or, in the case of LN, progression to ESRD). Disease modification in LN, as discussed by Professor Manuel Praga, from the KDIGO 2021 guideline, the management of LN now includes the use of calcineurin inhibitors specifically voclosporin and biologics like belimumab. The use of voclosporin, a novel calcineurin inhibitor was seen in the AURORA 1 trial for its efficacy and safety. On the other hand, the addition of belimumab to mycophenolate mofetil, resulted to a lower rate of decline in estimated GFR from week 24 to 104 with lower risk of renal flare. Goal of treatment on proteinuria reduction should be at least 25% in 3 months, 50% in 6 months and reduction to <0.5-0.7mg/mg in 12 months. Addition of sodium-glucose co-transporter (SGLT2i) seem to be beneficial with a change of proteinuria of 35% at 3 months, 41% at 6 months, 45% at 9 months and 48% at 12 months. Questions on weaning from mycophenolate or azathioprine showed that those who were weaned off had a higher relapse rate at 27.3% compared to those who continued at 12.5% rate. Predictors of relapse are low complement levels, proteinuria and high levels of anti-dsDNA. In relapsing patients, the following measures can be considered: 1) extending the mycophenolate beyond 3-5 years after relapse, 2) for repeated relapses consider indefinite treatment with low dose mycophenolate, 3) consider adding belimumab and lastly 4) consider a new kidney biopsy to evaluate active lesions and chronicity scores.

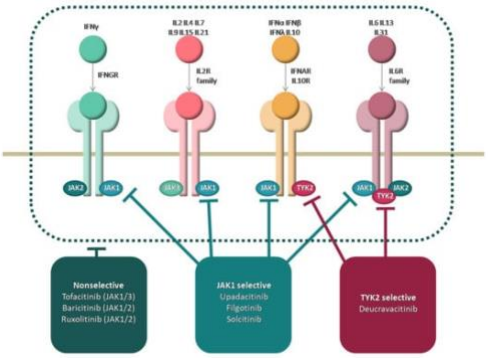

Management of lupus again emphasizes that steroids are not the mainstay of treatment. Use of hydroxychloroquine at a dose of 5mg/kg/day reduces lupus flares and also can significantly reduce glucocorticoid doses. Options for lupus management continue to expand over the years, whether use of immunosuppressive agents and biologics, which reflect the different pathologic mechanisms of SLE. And as we clinicians decide on which of these medications to use, we are reminded to put the patient at the center: individualizing therapies and looking out for possible complications and adverse effects, since these may result to further damage to our patients later on.

This second day of the 12th Lupus Academy serves as an eye opener to continue learning and exploring for new options for the improvement of lupus care and management.

**Day 3**
**Ma. Theresa M. Collante, MD**

The third day of the conference dealt with lupus drugs on the pipeline and other possible therapies. The sessions discussed (1) medications targeting interferons, (2) the potential of cancer immunotherapy, (3) the importance of drug trial designs, and (4) treatment options for autoimmune encephalitis, interstitial lung disease, and capillary leak syndrome.

**Medications targeting interferons and interferon pathway**

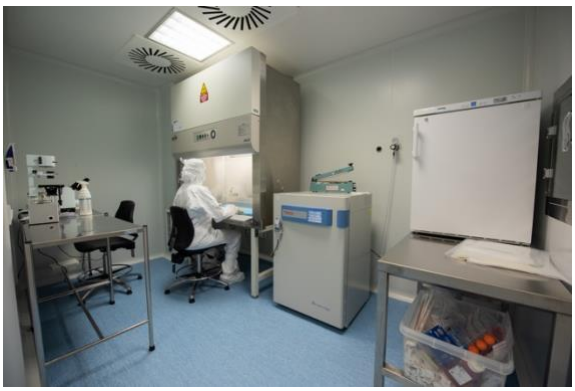



Dr. Antonis Fanouriakis focused the rationale of using **Janus kinase (JAK) inhibitors** in cutaneous lupus and LN. He emphasized that JAK inhibitors can halt or modify signal transduction initiated by interferons which are important players in SLE pathophysiology. At present, there are two drugs on clinical trial-baracitinib and tofacitinib. In the study SLE-BRAVE, **baricitinib** initially had good results (preclinical to phase 2), but was discontinued after two identical phase 3 trials showed conflicting results. Post-hoc analyses are now being done. For **tofacitinib**, the phase 1 trials results are reassuring. **Upadacitinib** has been identified to be a potential treatment for skin and joint involvement in lupus but there are no studies being conducted yet.

**Plasmacytoid dendritic cells** (pDC) as treatment target in lupus was discussed by Dr. Richard Furie. PDC are cells that produce high levels of type I and III interferons, which are abundant in the skin as well as other organs in patients with SLE. This led to studies on **litifilimab**, a monoclonal antibody that binds blood cell dendritic antigen 2 (BDCA2) which is a protein selectively expressed on pDCs. BDCA2 ligation results in the suppression of type I and III interferon production as well as other proinflammatory cytokines and chemokines. Litifilimab is in phase III for SLE and cutaneous lupus. Another antibody of interest is **daxdilimab.** It targets immunoglobulin-like transcript 7 (ILT7) and is also in development for the treatment of SLE.

**Chimeric antigen receptor (CAR) T-cell therapy**

Cellular immunotherapy (particularly CAR T-cell therapy) is now being seen a promising option for autoimmune disease management. At Dr. Manel Juan's division at the Hospital Clinic of Barcelona, a second-generation CAR-T (with 4-1BB as a co-stimulatory motif) targeting CD19 (ARI0001 or varnimcabtagene autoleucel) was developed for the treatment of leukemia and multiple myeloma. It is currently undergoing evaluation under the Priority Medicines (PRIME) designation by the European Medicines Agency (EMA) to obtain centralized marketing authorization. In terms of immune-mediated disorders, T-cell targeting in CAR-T immunotherapies will possibly play a positive role in SLE.



Other targets in SLE treatment as discussed by Dr. Thomas Dörner are drugs that target gain-of-function mutations in toll-like TLR7 signaling. He also mentioned medications that might modify B cell survival can also change the clinical course of SLE. This includes targeting by second generation anti-CD20 modalities (**obinutuzumab**), anti-CD38 (**daratumumab**), anti-B-cell activating factor (BAFF-R) (**ianalumab**), and the use of immune proteasome inhibition (**zetomipzomib**). Moreover, the use of bispecific antibodies can also potentially be used to improve selective immune therapy with at least similar or even better efficacy and safety profile as compared to current approaches.

**Lupus drug trial designs**

Dr. Eric Morand deliver a virtual lecture on how to optimize clinical trials for lupus. He enumerated the reasons for high failure rate in lupus drug trials--issues with the product being tested, biological heterogeneity, and how trials are designed. While the first two problems are usually difficult or beyond our control, faults in trial designs can be avoided. A major challenge in the conduct of these studies is how outcomes are measured, particularly with SLE responder index (SRI) and BILAG-based composite lupus assessment (BICLA) endpoints. SRI and BILAG are old tools and were not created for use in clinical trials. Therefore, more accurate measures should be designed for clinical trials. A global academia-industry-patient collaboration presently heads a project to reinvent clinical outcome assessment for use as a treatment response measure in SLE clinical trials: **treatment response measure for SLE (TRM-SLE)**. It is a five-stage scientific protocol developed using Delphi and nominal consensus methods, and will be eventually validated in the future.

**Challenges in the treatment of autoimmune encephalitis, interstitial lung disease, and capillary leak syndrome**

For autoimmune encephalitis, Dr. Eugenia Martinez-Hernandez highlighted that characterization of neural autoantibodies has now improved immensely, making diagnosis easier, especially that its clinical progression is acute, in contrast to neurodegenerative disorders. Cerebrospinal fluid studies, magnetic resonance imaging should be done along with neural antibody detection for more efficient identification of specific clinical syndromes, different comorbidities, and differential responses to immunotherapy and prognosis.

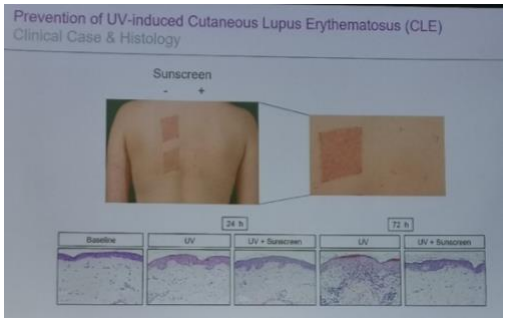
Interstitial lung disease (ILD), as discussed by Dr. Vanessa Smith, is a group of more than 200 parenchymal pulmonary disorders. Connective tissue disease-related ILD comprise almost 20% of all ILD. Several challenges related to CTD-ILD involve multidisciplinary screening and monitoring strategies.

Lastly, an interesting syndrome was discussed by Dr. Zahir Amoura--systemic capillary leak syndrome (CLS), a rare, life-threatening disorder characterized by recurrent episodes of edema, hypotension, hemoconcentration, and hypoalbuminemia. The challenge that he mainly emphasized was on diagnosis because it is made through exclusion, in the presence of serum monoclonal immunoglobulin. Prophylactic treatment is administration of intravenous immunoglobulin which may reduce the frequency and severity of attacks and may improve survival.

**Workshops**
**Peter Paolo T. Daleon, MD**

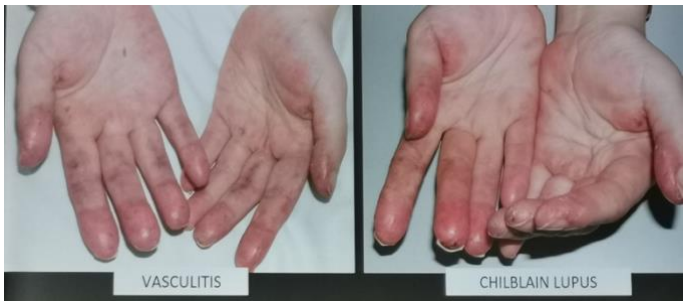
Interesting interactive case study workshops on cardiovascular, nephritis, cutaneous, and musculoskeletal manifestations of SLE as well as management of pediatric SLE were offered to in-person attendees on the 2nd and 3rd days of the meeting. With esteemed speakers from different fields, participants are offered truly interesting cases that allow critical thinking and looking at the cases from a different point of view.

**Management of Skin Involvement in SLE**



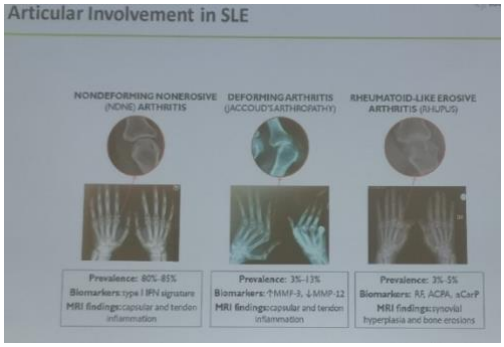

The workshop on cutaneous SLE was given by Professors Annegret Kuhn and Antonio Guilabert, both dermatologists. Prof. Kuhn started by briefly reviewing the participants on the step-wise approach in the management of cutaneous lupus, emphasizing the importance of photoprotection with broad-spectrum sunscreens and smoking cessation. In addition to the established second- and third-line treatment options, they introduced anifrolumab as another option, adding to the treatment armamentarium of difficult-to-treat cutaneous lupus. Lastly, they encouraged the use of the revised CLASI to measure the activity and damage of different skin manifestations of lupus.

Prof. Guilabert shared two interesting cases of unusual skin manifestations of lupus: bullous systemic lupus erythematosus and chilblain lupus. Both of these are rare cutaneous manifestations of lupus and have several potential differential diagnoses, making early treatment difficult. Through the interactive discussion, participants are able to give their opinions and personal experiences with certain medications that can be given to these patients. These cases also reiterated that such manifestations can occur in SLE patients.




**Management of Musculoskeletal Involvement in SLE**

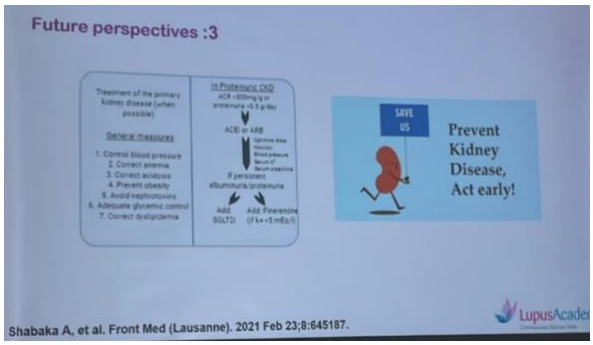
Musculoskeletal involvement is one of the most common manifestations of SLE, though not life-threatening by itself, it greatly affects the quality of life of patients. The cases shared by Professors Andrea Doria and José Goméz-Puerta allowed the participants to freely share their opinions on the cases presented. With no right or wrong answers, the professors moderated the discussion towards a learning process for everyone.



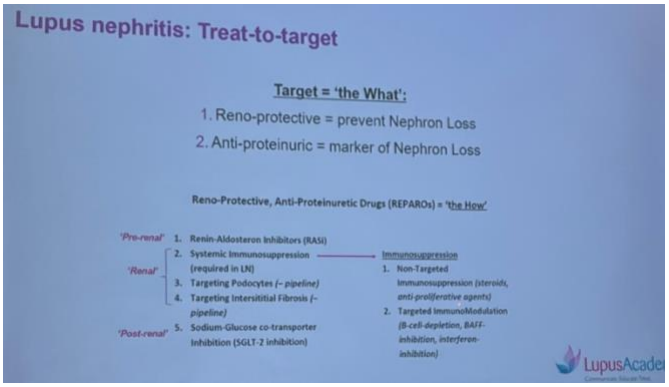
One of the highlights of this workshop is the use of imaging modalities to detect the presence of erosions, synovitis, bone edema, and tenosynovitis, especially for patients who are refractory to usual medications. They highlighted the advantages of radiographs, ultrasound, and MRI in detecting these changes, particularly in cases of Jaccoud's arthropathy and rheumatoid-like erosive arthritis (rhupus). In addition, they emphasized the use of belimumab in decreasing disease activity, improving serologies, and as steroid-sparer, even in those who are not concomitantly treated with immunosuppressives. Lastly, emphasis was placed on achieving an alternative target, that is to achieve low disease activity, should complete remission is difficult.

**Management of Lupus Nephritis**

Professors Y. K. Onno Teng and Luis Quintana facilitated the workshop on nephritis. They discussed the patient, histologic, and serologic high risk factors that are associated with poor outcomes in patients with LN, with the risk increasing with each risk factor present. The general measures for nephritis were still emphasized. In patients with persistent proteinuria, the addition of an SGLT2i or finerenone is advised. Just like in the other organ systems, the use of belimumab was highlighted as well, which can also help prevent further deterioration of renal function. In the end, a treat-to-target approach for LN is still recommended, with medications for renal protection and proteinuria available.

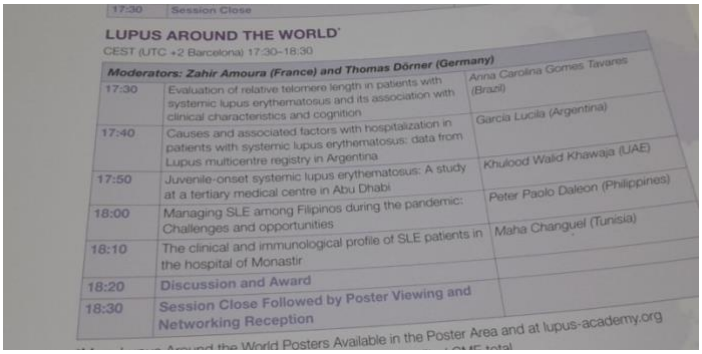



Managing SLE is challenging especially in patients with different organ system involvement, often concomitantly occurring. Some are refractory, requiring second or even third-line treatment options. The future of SLE management has a positive outlook. With newer biologics now approved and with other investigational agents currently being studied, timely diagnosis, proper assessment, and shared decision-making with the patients, there is better hope for our patients.




**Pediatric lupus**

Six cases of pediatric lupus was discussed by Dr. Elizabeth Ang and Dr. Joan Calzada-Hernandez. They presented unique and challenging presentations of juvenile arthritis, pediatric lupus nephritis, and lupus enteritis, as well as their corresponding management based on current recommendations.



17:30 Session Close

**LUPUS AROUND THE WORLD**

CEST (UTC +2 Barcelona) 17:30–18:30

***Moderators: Zahir Amoura (France) and Thomas Dörner (Germany)***

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| 17:30 | Evaluation of relative telomere length in patients with systemic lupus erythematosus and its association with clinical characteristics and cognition | Anna Carolina Gomes Tavares (Brazil) |
| 17:40 | Causes and associated factors with hospitalization in patients with systemic lupus erythematosus: data from Lupus multicentre registry in Argentina | Garcia Lucila (Argentina) |
| 17:50 | Juvenile-onset systemic lupus erythematosus: A study at a tertiary medical centre in Abu Dhabi | Khulood Walid Khawaja (UAE) |
| 18:00 | Managing SLE among Filipinos during the pandemic: Challenges and opportunities | Peter Paolo Daleon (Philippines) |
| 18:10 | The clinical and immunological profile of SLE patients in the hospital of Monastir | Maha Changuel (Tunisia) |
| 18:20 | Discussion and Award | |
| 18:30 | Session Close Followed by Poster Viewing and Networking Reception | |

Posters Available in the Poster Area and at lupus-academy.org


**Lupus Around the World** is a segment in the meeting wherein five innovative and thought-provoking studies chosen from numerous submissions were showcased. Dr. Peter Paulo T. Daleon presented his study entitled "Managing SLE among Filipinos during the pandemic: challenges and opportunities." In his discussion, he described the experience of the University of Santo Tomas (UST) Section of Rheumatology in caring for patients at the height of the COVID-19 pandemic. He depicted the status of the rheumatology workforce in the country and in UST Rheumatology and elaborated on the challenges faced by the patients and the staff, which mainly involved difficulty in accessing health care. He then discussed the actions taken by the section to circumvent the issues and focused on how telemedicine was utilized to care for patients. Dr Daleon then addressed questions from the audience on how the lack of trainees impacted the workload in the hospital and how the staff coped with this concern.