the various therapy options. Kidney biopsy is a mandatory for LN trials, as a gold standard for biomarker studies, and for research on pathophysiology. However, can the initial biopsy really tell us anything about the immunopathogenesis of lupus in spleen and lymph nodes or about which drugs to choose or if the patient will respond to an adequate therapy? Will the recent discovery of EXT1/EXT2 deposits in about 1/3 of patients with Class V LN help to define subgroups of patients with unique phenotypes and prognosis? Isn’t the scientific attention to a biopsy that confirms the diagnosis and grossly defines intensity of treatment a bit irrational?

Too few kidney biopsies? Serum and urine biomarkers are used to guide immunosuppressive treatment of lupus nephritis, although there is compelling evidence that they poorly indicate persistent LN even in patients with a complete clinical response. The same problem in kidney allograft recipients is addressed by protocol biopsies, why is this not so in LN? A repeat biopsy at 12 months may be of utmost value to guide treatment and to predict long-term prognosis, something the first diagnostic biopsy hardly can do. The REBILUP trial will address this question. Other important repeat biopsy indications are the ‘partial responder biopsy’, the ‘smoldering lupus nephritis biopsy’, the ‘chronic kidney disease progression biopsy’ and the ‘drug withdrawal biopsy’.

Too many kidney biopsies? The least useful re-biopsy maybe when the patient flares as flare biopsies in patients with a previous Class III-V hardly ever affect treatment decisions. When patients with LN ‘flare’, drug non-adherence or recent reductions in drug doses are the most common cause, rather than a switch of the underlying disease. Systemic lupus erythematous (SLE) is chronic autoimmune disease with continued disease activity, albeit at different levels in different patients. Therefore, LN does not require ‘induction’ and ‘maintenance’ therapy, but a constant long-term treatment usually with a combination of immunosuppressive drugs. SLE is heterogeneous across individuals but not within an individual. Repeat biopsies are needed to detect inflammation when you are not sure about it, not when it is obvious.

Learning Objectives

- Explain the importance of not overestimating the potential of the first diagnostic biopsy as a source of insights into pathophysiology and predictive power beyond what is known
- Describe the value of treatment response as the main predictor for outcome and the potential use of a protocol biopsy at 1 year in this context because serum and urine markers are unreliable
- Discuss and question the value of a ‘flare repeat biopsy’, because it rarely affects treatment decisions
- Discuss the use of repeat biopsies in non- or partial responders, smoldering lupus nephritis, CKD progression and before drug withdrawal
- Explain the important concept that SLE is a chronic autoimmune disease that requires constant long-term treatment usually with a drug combination (not transient ‘induction and maintenance therapy’ with single drugs), identical to how we control persistent alloimmunity in kidney transplant recipients

### Debate: In with the new, out with old?

**Should all patients with lupus nephritis receive new generation therapies in addition to established standard of care?**

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**ALL LUPUS NEPHRITIS PATIENTS SHOULD BE INITIALLY MANAGED WITH BOTH ESTABLISHED STANDARD THERAPIES AND THE NEW GENERATION DRUGS**

YK Onno Teng. Leiden University Medical Center (LUMC), the Netherlands

The year 2020 has been an extraordinary year in many ways but especially for patients with lupus nephritis (LN), as 2020 saw two novel agents (belimumab and voclosporin) finding FDA-approval for the treatment of LN. These agents will both enrich the therapeutic armamentarium, allowing physicians to better treat their LN patients, as well as broaden treatment strategies that can be employed.

In this pro-con debate, I will highlight the trial data that have led to the FDA approval of belimumab and voclosporin for the treatment of LN. I will also address the unmet needs these new compounds can address in the treatment of LN. Lastly, the potential treatment strategies emerging from the approval of these new agents will be addressed.

**Learning Objectives**

- Describe the evidence for the latest FDA-approved drugs for LN: Belimumab and voclosporin
- Describe the current challenges physicians face when treating patients with LN
- Describe possible new treatment strategies for patients with LN

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**ALL LUPUS NEPHRITIS PATIENTS SHOULD BE INITIALLY MANAGED WITH ESTABLISHED STANDARD THERAPIES ALONE**

Dimitrios Boumpas. National and Kapodistrian University of Athens, Greece

Lupus nephritis (LN) is extremely heterogenous with most patients responding to standard immunosuppressive therapy within 6–12 months. Post hoc analyses suggest that proteinuria at 12 months represents the best single predictor for long-term renal outcome (i.e., risk for end-stage kidney disease (ESKD) or doubling of serum creatine after 10 years). Accordingly, therapy should aim for proteinuria reduction to below 0.7 gm-1/day by 12 months (complete renal response) with patients with nephrotic range proteinuria reaching this milestone for later, by approximately 24 months. Even patients without a complete response at 12–24 months (defined as proteinuria below 1 gm/day and stable creatinine) have an excellent 10-year prognosis.

Based on the above, rushing into using novel therapies from the beginning has the risk of overtreating the vast majority of patients. This is especially true for patients that receive...