The safety of pharmacological treatment options for lupus nephritis

Alba Velo-Garcia, Eleana Natskaki & David Hemberg

To cite this article: Alba Velo-Garcia, Eleana Natskaki & David Hemberg (2016) The safety of pharmacological treatment options for lupus nephritis, Expert Opinion on Drug Safety, 17:10, 1182-1195

1. Introduction

Lupus nephritis (LN) is one of the most common and severe manifestations of systemic lupus erythematosus (SLE) occurring in 40-70% of patients (1-2) associated with significant morbidity and mortality (3).

When glucocorticoids (GC) and antimalarials were first introduced for the treatment of SLE in the 1950s, the reported survival rate for SLE was <50% at 4 years (4). This was due to the severe complications associated with these treatments, such as infection, gastrointestinal bleeding, and osteoporosis, as well as the lack of effective treatment options. The introduction of cyclophosphamide and cyclosporine (CyA) in the 1970s and 1980s led to significant improvements in the management of SLE (5-7).

In recent years, new treatment options have emerged, including biologic agents, which have shown promise in improving disease control and remission rates (8-10). However, the use of biologic agents is associated with significant financial and ethical concerns (11).

2. Conventional induction and maintenance treatments

A summary of conventional treatments with their main mechanisms of action and common side effects is presented in Table 3 and is matched to the corresponding medications in Table 1.

2.1. Glucocorticoids

Glucocorticoids are considered the mainstay of treatment for SLE and are used to reduce inflammation in the kidneys. They are effective in reducing disease activity and improving renal function.

2.2. Cyclophosphamide

Cyclophosphamide is a cytotoxic alkylating agent that has been shown to be effective in inducing remission in patients with severe lupus nephritis. It is typically given as a pulse IV infusion every 4-8 weeks.

2.3. Mycophenolate Mofetil

Mycophenolate mofetil (MMF) is a purine analogue that inhibits the production of guanine nucleotides, leading to inhibition of T-cell proliferation. It is commonly used as a maintenance therapy in patients with SLE and is associated with fewer side effects than cyclophosphamide.
by treatment of relapse-288 for maintenance therapy, low to moderate prerenal contribution (up to 10 mg/mg/m) is used.

The use of clinical trials directly comparing the different dosage regimens of GC, in mixed data from the Euro-RA/Nephrology Trial 2017 (15) (16), suggests that a lower GC regimen (1% of 700 mg of methylprednisolone followed by 2 weeks of 0.5 mg/kg/day prednisone) has similar outcomes and less adverse effects when compared to other high dose regimens. Conversely, Groth et al. (23) showed the efficacy of methylprednisolone (400 mg) using two different GC regimens: 1 mg/kg/day or 0.5 mg/kg/day in two randomized groups after 12 weeks of treatment, with similar outcomes in both groups. Both regimens were well tolerated and 10% of patients experienced adverse events.

American College of Rheumatology and the European League Against Rheumatism/European League of Interstitial Nephritis (ALR/G) guidelines, the same dose of GC that was effective in inducing remission, can be used for maintenance therapy. Low to moderate prerenal contribution (up to 10 mg/mg/m) is used.

Table 1: Lupus nephritis classifications.

<table>
<thead>
<tr>
<th>Class</th>
<th>Monoclonal lupus nephritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class II</td>
<td>Monoclonal antibody deposits</td>
</tr>
<tr>
<td>Class III</td>
<td>Lupus nephritis</td>
</tr>
<tr>
<td>Class IV</td>
<td>Lupus nephritis</td>
</tr>
<tr>
<td>Class V</td>
<td>Lupus nephritis</td>
</tr>
<tr>
<td>Class VI</td>
<td>Lupus nephritis</td>
</tr>
</tbody>
</table>

Adapted with permission from(22).

Table 2: LN classification treatment regimens depending on class of LN.

<table>
<thead>
<tr>
<th>Class</th>
<th>Treatment Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>Immunosuppressive therapy for 4 weeks/6 months</td>
</tr>
<tr>
<td>Class II</td>
<td>Immunosuppressive therapy combined with pulse therapy, with or without oral prednisone</td>
</tr>
<tr>
<td>Class III</td>
<td>Immunosuppressive therapy combined with pulse therapy, with or without oral prednisone</td>
</tr>
<tr>
<td>Class IV</td>
<td>Immunosuppressive therapy combined with pulse therapy, with or without oral prednisone</td>
</tr>
<tr>
<td>Class V</td>
<td>Immunosuppressive therapy combined with pulse therapy, with or without oral prednisone</td>
</tr>
<tr>
<td>Class VI</td>
<td>Immunosuppressive therapy combined with pulse therapy, with or without oral prednisone</td>
</tr>
</tbody>
</table>

Adapted with permission from(22).

Challenged this assumption. An uncontrolled trial of Rituximab (RTX) (22) combined with GC prednisolone followed by RTX in 50 patients with lupus nephritis (Class III or IV) showed that most subjects achieved complete renal remission without any GC. The ongoing randomized controlled trial (RCT) RTXUSP17 (NCT03777079) is currently enrolling patients to answer this key question and may lead to steroid-avoiding regimens to decrease the burden of long-term GC-related adverse effects.

2.1.2. Glucocorticoid safety concerns

Long-term glucocorticoid exposure induces complications specific to GC. There is a direct linear correlation between increasing dose of GC with adverse effects, the most important of which are the increased infection risk, diabetes, hypertension, fat accumulation, and osteoporosis. Glucocorticoids include prednisone, prednisolone, dexa-methasone, and dexamethasone. An elevated frequency of adverse events beyond a certain threshold value has been observed. This "threshold pattern" has been described as >3 mg/day for glucocorticoids, median weight gain for ADAs and CHCs, and >5 mg/day for prednisone and weight gain. A lower threshold was seen for myelosuppression (1-5 mg/day)(22).

Infections are also a dose-related complication, with clinical vigilance needed especially for opportunistic infections such as pneumococcal pneumonia, tuberculosis reactivation, and overwhelming sepsis. Susceptibility to major infections occurs at the dose of >3 mg/day (23). Cardiovascular risk is another major concern, with an increased risk of cardiovascular and cerebrovascular events. The SLE mortality rate of 40% is comparable to the risk of heart failure. Over 24% of patients with lupus nephritis, including prednisone patients, with a 2-3-fold increased fracture risk, compared with age- and sex-matched controls (24). This increased bone loss effect of GC in LN patients is aggravated by the nephrotic syndrome. The risk of fracture depends on the dosage and duration of GC therapy. Specifically, after 3 months of GC use, the relative risk of vertebral fracture is increased from 1.5 to 1.6 when the dose is increased from 2 mg/day to >3 mg/day (25). Moreover, there is a 1.7-fold increase in hip fractures and a 1.6-fold increase in vertebral fractures with doses >10 mg/day (25).

2.2. Conventional immunosuppressive drugs

2.2.1. Azathioprine

Azathioprine (AZA) is a purine analog drug that acts at the level of DNA replication and can block the nuclear pathway of purine synthesis. It has been used since the 1980s in LN, mainly as maintenance therapy including 233 patients with LN published in 1994 indicated that patients on AZA and CHCs had a better renal outcome when compared with those given GC doses (26).

2.2.2. Mycophenolate mofetil (MMF)

Mycophenolate mofetil (MMF) is a potent immunosuppressant used in LN. It is an oral medication that blocks the production of interferon-α. MMF is commonly used in LN, with a high success rate and lower risk of adverse effects compared to GC. The recommended dose is 1-2 g/day, divided into two or three doses, depending on the individual patient's response and tolerance.
AZA is well tolerated overall. In maintenance therapy trials in patients with LN, no differences were found when comparing AZA with CYP ( ciclosporin A, MMF or tacrolimus (140) in terms of drug tolerability (141,142). The limited toxicity of AZA has been related to a decrease in the sensitive population that reduces the activity of the thymopoietic mechanism. However, adverse events can occur in homunculus patients (<1% of those given the drug).

2.2.2. Cyclophosphamide
For 17 years the cyclophosphamide standard induction therapy for severe LN consisted of GC with CYC (143,144). The use of intravenous CYC is based on the 1980s (145) and was recommended from the National Institute of Health (NIH) that high-dose CYC induction would be used as a first-line therapy in the treatment of LN (0.5-1 g/m² monthly x 6 followed by capsule for 2 years). The NIH regimen showed fewer side effects when compared with prolonged daily dosing regimes (146). Patients treated with chronic CYC (monthly pulses) CYC only) had a higher probability of remission than those treated with CYC alone or in combination with steroids (147). The toxicity of CYC includes myelosuppression, nausea, vomiting, alopecia, and interstitial lung disease (148). Myelosuppression is most common during the first 3 months of treatment and can be severe in patients with a history of radiation therapy or prior chemotherapy (149). The risk of infertility is also a concern for female patients, who may need to use contraception during treatment (149). Adverse effects include gastrointestinal symptoms, rash, and fever. Treatment is usually started at a lower dose and slowly increased to reach the target dose. The median duration of treatment is 6 months in the induction setting (144,145).

2.2.3. Mycophenolate
Mycophenolate sodium has no significant genetic effects in 0 and 1 phenotypes. It is a reversible inosine monophosphate dehydrogenase (IMPDH) inhibitor that acts by binding with high affinity to the isoform of IMPDH in leukocytes. This drug has a selective action in the lymphocytes with less toxicological toxicity (150). Mycophenolic acid is an active pharmacological form that can be obtained by first pentadecanol metabolism and enteric-coated recycling after the administration of pro-drug MMF or directly from the sodium with 1-α-methylene-guanosine (MPA) (151).

2.2.3. Mycophenolate mofetil. The original pilot study of MMF in LN patients showed MMF 12 mg/day for 6 months and then 1 g/m² for 6 months and oral C reaction 0.2 mg/kg/d. Both groups received GC. Complete remissions occurred, partial remissions, relapse rates and rate of kidney disease were similar between both groups with black, Latin American and mixed patients responded better to MMF on sub-analysis. Although there were more infections in the GC group, but these were not clinically significant (152-154). The largest randomized clinical trial (RCT) comparing MMF with CYC in LN patients is the Japanese Lupus Management Study (JLMS). This 24-weeks study aimed to test both induction and maintenance strategies (155). The induction component included 379 patients with LN, 1/4 of LN unconditioned for receiving MMF (1 g/day) or CYC 6 mg/m² intravenous infusion (0.5-1 g/m²) with GC in both groups. Renal outcomes such as decline in creatinine, proteinuria, renal function decline, and complete or partial remission were similar in both groups and adverse events showed no significant difference (156). MMF versus CYC 6 mg/m² was shown in clinical trials with less myelosuppression, mortality, incidence of malaria-related kidney disease and time to treatment failure (156,157).

The use of MMF with CYC has lower risk of infection failure, leukopenia and anemia when compared with CYC either orally (17) or intravenous (158,159). MMF is not associated with increased risk for infections (160). Major infections occur more often in oral CYC treated patients compared to those treated with MMF (161), but there was no difference between MMF and CYC (162). The only adverse event more prevalent in the MMF group was diarrhea (163). These studies suggest that MMF is as active as CYC as an induction agent for LN with less severe adverse effects. When regards to variation of incidence of side effects in different ethnic groups, the JLMS study showed that although patients from Asia reported adverse events more frequently than those in Europe, these infections were more likely to be severe, resulting in hospitalization or death. Furthermore, patients in the Asian MNP group had a higher withdrawal rate due to adverse events, compared with other racial groups (163). However, MMF patients had less incidence of high dose prednisone and CYC (150). Nevertheless, adverse events in the MMF group were lower (mainly Chinese). However, few conditions can be taken from the present data and further clinical trials are necessary to clarify these issues.

In the search of concepts at the last decade of the 19th century, the use of CYC as an induction agent has become more common. In several studies it was shown that both MMF and CYC were more effective in LN and less toxic than CYC, and equally effective with oral CYC. When comparing AZA with MMF for maintenance therapy in proliferative LN, there are two meta-analyses which found no differences in terms of safety and efficacy (164,165). In the MMF-ONAN trial and its follow-up study (166), 105 patients were randomized to MMF or AZA, 24.48 months follow-up there were no differences in terms of efficacy (number of relapses, time to relapse, and side effects). Therefore, in the second phase of the AURAS (167) and other studies including Hispanic and African-American patients (168) and the other studies indicated: Hispanic and African-American patients (168) and others such as the other studies included in this trial.
safety profile of Aza versus MMF was a higher risk of leuko-

aemia in Aza treated patients.[20/20]
Importantly, MMF, unlike Aza, is contraindicated in preg-
nancy and not recommended during breastfeeding, although
there are no data on excretion into breast milk. MMF is com-
patible with paternal exposure, but this recommendation is
based on limited evidence and further studies are neces-
sary.[20]
2.3.3.2. Sodium mycophenolate. The evidence for the effectiveness and safety of MMF in pregnant and non-pregnant patients is very com-
promising. A meta-analysis of 5 studies, patients with LN treated over 13 years comparing MMF with other immunosup-
pressant regimens showed higher efficacy and survival rate in
the MMF group. The rate of progression to stage 3 chronic
kidney disease was similar and there were no significant dif-
ferences in adverse events. However, the heterogeneity in the
timing of treatment, duration of follow-up and diversity of the
treatment groups are important limitations of the studies.[20] MMF has also been compared with CYC in studies with recalcitrant lupus nephritis with less adverse events than the latter.[20] Other studies reported similar outcomes; nevertheless larger prospective trials are still needed in order to make substantive recommendations.

2.4. Calcineurin inhibitors

Cyc and Tac are widely used in immunosupression pote-
tugential transplantation and they are also effective in LN.
Calcineurin inhibitors have two potential beneficial effects in
active LN. The immunosuppressive effects of calcineurin inhibitors are associated with their ability to inhibit the tran-
scription of the early activation genes of interleukin-2 (IL-2) and
Tac. Tac-induced activation of tumor necrosis factor (TNF)-α, IL-1 and IL-6. Thus these signals for cell activation, clas-
switching and immunomodulation are significantly allevi-
ated.[21] The anti-proliferative effect of Cyc has been noted to
be able to inhibit the B cells proliferation in kidney biopsy.[21]

2.4.1. Calcineurin-inhibitors Cyc and Tac have been shown to be as effective as CYC in induction and maintenance treatments in LN patients with proteinaceous renal failure.[22] Cyc is more effective in metabolic LN than induction regimens using GC alone.[23/24]
Mehran et al. [25] performed a comparison between mainte-
nance regimens: cyclophosphamide versus Aza in a cohort of 62 and 18 LN patients. No differences were observed in reducing proteinuria, renal biopsy record or improving creatinine. Cyc improved proteinuria and kidney biopsy in patients with nephrotic disorders who did not respond to maintenance treatments with CYC or Aza[25,26]. It is an option in this pathology, however, Cyc is associated to transplant renal function impairment hypothyroidism, gingival hyperplasia and arthralgia, so often Tac is preferred.[27]

2.4.2.3. Tacrolimus. Tac is effective in treating nephro-

10

genic LN and refractory disease. Cyc and Tac have similar efficacy but Tac has more side-effects.[22] Multi-drug thera-

Figure 2. This figure illustrates the pathogenesis of LN and potential targets with the reported biological drugs. When the monoclonal rheumatic drugs bind to immune complexes in the kidney, they weaken the complex by affecting the C3 convertase and C5 convertase, causing complement activation. The complement C3 convertase is composed of C5, C5b, C6, C7, C8, and C9, while the C5 convertase is composed of C5, C5b, C6, C7, and C8. The binding of monoclonal antibodies to the C5b, C6, C7, C8, and C9 components can lead to the complement activation, which results in the formation of a membrane attack complex (MAC) that can lyse the cells. On the other hand, the binding of biologics such as rituximab to CD20 or belimumab to BAFF-R can block the interaction of B cells with BAFF or APRIL, respectively, leading to the inhibition of B cell proliferation and differentiation. The binding of biologics to IL-6R can block the interaction of IL-6 with IL-6R, leading to the suppression of the proliferation and differentiation of B cells.

Table 2. Table 2: Biological drugs for LN (compared to Cyc).

<table>
<thead>
<tr>
<th>Drug name</th>
<th>Type of drug</th>
<th>Main effects</th>
<th>Treatment groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biologics</td>
<td>Anti-CD20 (Rituximab)</td>
<td>B-cell depletion in B cells and plasma cells</td>
<td>Rituximab 375 mg/m²; 2 infusions at 1 month and at 12 weeks post first infusion.</td>
</tr>
<tr>
<td>Biologics</td>
<td>Anti-BAFF (Belimumab)</td>
<td>B-cell depletion in B cells and plasma cells</td>
<td>Belimumab 10 mg/kg; two infusions at 1 month and at 12 weeks post first infusion.</td>
</tr>
<tr>
<td>Biologics</td>
<td>Anti-IL-6R (Tocilizumab)</td>
<td>B-cell depletion in B cells and plasma cells</td>
<td>Tocilizumab 8 mg/kg; two infusions at 1 month and at 12 weeks post first infusion.</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>Calcineurin inhibitor</td>
<td>Inhibition of immune responses</td>
<td>Tacrolimus 1 mg/kg; one infusion at 1 month and at 12 weeks post first infusion.</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>Immunosuppressant</td>
<td>Inhibition of B-cell proliferation</td>
<td>Cyclophosphamide 1 mg/kg; one infusion at 1 month and at 12 weeks post first infusion.</td>
</tr>
</tbody>
</table>

Lupus nephritis is a type of autoimmune disease that affects the kidneys. Lupus nephritis is characterized by the deposition of immune complexes in the kidney, which can lead to inflammation and damage to the renal tubules and blood vessels. The pathogenesis of lupus nephritis is complex and involves interactions between the immune system and the kidney. The typical presentation of lupus nephritis is nephrotic syndrome, which is characterized by the presence of proteinuria, edema, and hyperlipidemia. The treatment of lupus nephritis is typically a combination of immunosuppressive and anti-inflammatory drugs. The use of biologics in lupus nephritis has shown promise in improving renal outcomes and reducing disease activity. 

Biologics, a new class of immunosuppressive agents that are targeted to specific immune pathways, have been shown to improve renal outcomes and reduce disease activity in lupus nephritis. The most commonly used biologics in lupus nephritis are rituximab and belimumab. Rituximab is a monoclonal antibody that targets the CD20 antigen on B cells, leading to the depletion of B cells in the blood and the spleen. Belimumab is a monoclonal antibody that targets the B lymphocyte stimulator (BLyS) protein, which is involved in the proliferation and differentiation of B cells.

In lupus nephritis, the presence of immune complexes in the kidneys leads to inflammation and damage to the renal tubules and blood vessels. Rituximab and belimumab have been shown to reduce the proliferation and differentiation of B cells, leading to a decrease in the formation of immune complexes and the inflammatory response in the kidneys.

In conclusion, biologics have shown promise in improving renal outcomes and reducing disease activity in lupus nephritis. The use of biologics in combination with standard immunosuppressive and anti-inflammatory drugs has led to significant improvements in renal function and quality of life in patients with lupus nephritis. Further research is needed to determine the optimal use of biologics in lupus nephritis and to identify subgroups of patients who may benefit the most from these agents.
In terms of safety, most of these bisphosphonates have an established side-effect profile when used in SLE and other rheumatic conditions. Long-term toxicity data in patients with renal disease are scarce. However, the burden of disease in the US population and the complexity of the clearance of medications through an affected liver mechanism is an additional cause for caution (i.e., additional vigilance with close-level monitoring and dose adjusting for renal function).

3.1. Teriparatide

Teriparatide is a humanized recombinant analog of the 200 amino acid-long PTH and was the first PTH-like peptide to be used in the treatment of SLE. Initial investigations consider PTH to be effective in treating inflammatory SLE, although two large trials, LUPARF (study of rapid repair) (LP) and EXPLORE (study of replaced patients) (ER) did not meet their primary end points. However, both the ASC and SLAM guidelines for the treatment of SLE and LN mention ETX as a possible therapy [10-12].

In the LUPARF study, 72 patients with LN class III or IV were randomized to receive 20 mg or placebo. In addition to standard care (SOC) treatment of MPA and GC, although there was a significant difference in proteinuria patients having a greater improvement in anti-DNA titer and C3 levels, there were no differences in CR or partial remission between the two groups (p = 0.05). The trial concluded that in patients with refractory, advanced chronic kidney disease, the addition of rituximab to induction therapy with MPA did not provide better clinical outcomes [12].

The LUPARF trial has been criticized because of its poor design relating to its statistical power defined on an extremely optimistic superiority effect in favor of RTX. If the LUPARF trial data were analyzed according to the BLISS trial design (MNH), which was successful trials for both MPA and GC included some patients with mild to moderate renal involvement, then the beneficial effect of RTX would have reached statistical significance.

RTX is also being clinically studied as an SC-agent trial, the BLazine trial is based on published pilot data suggesting that the addition of RTX to MPA alone is ineffective. The BLazine trial included patients with LN class III or IV with at least an effect on inducing a minimal response as the primary end point. The BLazine trial is an open-label, dose-escalating, multicenter, double-blind trial designed to demonstrate whether the addition of RTX to MPA therapy is useful in treating a new flare of LN and whether it has a long-lasting non-renal, beneficial effect with equal efficacy and safety than a conventional regimen of MPA and oral prednisone.

In a recent study, RTX has been directly compared to rituximab in patients with SLE patients who had a non-renal flare of LN. RTX was given in addition to MPA and oral prednisone. The results showed that RTX was more effective in reducing the number of LN flares and improving renal function compared to rituximab. The findings suggest that RTX may be a safer and more effective option for treating LN flares in SLE patients.

3.2. Safety

Side effects include infusion reactions, diarrhea, and suspected infections. Although there is no evidence on the use of RTX in patients who have had previous infections or who are immunocompromised, it is important to monitor patients for any signs of infection and to ensure that the patient is not at risk for severe infections. The most common side effects of RTX are infusion reactions, which can range from mild to severe. These reactions usually occur within the first few hours after the infusion and can include fever, chills, and nausea. In patients with a history of severe infusion reactions, it is recommended to use prophylactic medications such as prednisone and antihistamines.

In conclusion, RTX is a promising therapeutic option for the treatment of LN in SLE patients. However, further research is needed to determine the optimal dosing regimen and to assess the long-term safety and efficacy of RTX in this population.
more BHF patients had received ≥1 g/m²/m² methotrexate compared with patients on the SLT background arm, suggesting that it may well have been the increased IV GC use that caused the higher infection rate observed in patients treated with the combination of DAK and BHF.

3.7. Antibiotics

Antibiotics are recommended for all patients with influenza-like illness and improve the prognosis of infected patients. Amantadine or rimantadine should be given as soon as possible after the onset of symptoms.

3.8. Safety

In the APLS-2233 randomized trial, the 15 mg amoxicillin arm was terminated early due to two fatal infections. APT was started 3 weeks before the onset of symptoms, in the APLS-2233 trial, there was no significant difference in the rate of serious infections between the placebo and amoxicillin arms. The most common infections included meningitis, urinary tract infections, and abscesses. The infection rate in the placebo arm was 15.5%, compared with 2.6% in the amoxicillin arm.

A Phase II study of ceftriaxone was terminated after the enrollment of only 24 patients due to lack of efficacy in the treatment of bacterial meningitis. In the Phase III study, the infection rate in the ceftriaxone arm was 31.4%, compared with 21.2% in the placebo arm.

3.9. Abnormalities

Abnormalities in the laboratory tests of patients with influenza include leukocytosis, elevated liver enzymes, and increased creatinine. The most common infectious complications include pneumonia, urinary tract infections, and abscesses. In the placebo arm, the infection rate in patients with influenza-like illness was 15.5%, compared with 3.1% in the ceftriaxone arm.

3.10. Other infections

3.10.1. Anti-dl-glu activity

In some cases, anti-dl-glu activity may be associated with the development of acute renal failure. However, the incidence of acute renal failure was not significantly different between the placebo and ceftriaxone arms.

3.11. Interstitial pneumonia

Interstitial pneumonia is a complication of bacterial pneumonia. The incidence of interstitial pneumonia was 3.1% in the placebo arm, compared with 0.5% in the ceftriaxone arm.

3.12. Lassitude

Lassitude is an illness that results in decreases in physical activity and resistance of patients infected with influenza. The incidence of lassitude was 3.1% in the placebo arm, compared with 0.5% in the ceftriaxone arm.

3.13. Future targets

There are many other potential target molecules such as other IL-11 receptor antagonists (OPG, EPOC, and IL-10). These molecules include IL-6, IL-10, and IL-1 receptor antagonists. The potential of these molecules in the treatment of influenza is being explored.

4. Conclusion

The main aim of treatment in LIR is to prevent renal impairment and end-stage renal failure leading to renal replacement therapy. In addition to this, induction of immune suppression and prevention of disease recurrence are needed while minimizing side effects and any pharmacological therapy.

Depending on the class of LIR, amphotericin B, and cyclosporine A are used. The incidence of interstitial pneumonia was 3.1% in the placebo arm, compared with 0.5% in the ceftriaxone arm.

5. Expert opinions

The treatment of patients with LIR may significantly improve the outcome of patients with severe infections. The use of ceftriaxone in the treatment of severe infections is recommended due to its efficacy and safety profile.

6. Safety

The safety profile of ceftriaxone is comparable to other antibiotics with minor side effects including rashes such as hives and gastrointestinal symptoms.

7. Others

7.1. Anti-dl-glu activity

Anti-dl-glu activity may be associated with the development of acute renal failure. However, the incidence of acute renal failure was not significantly different between the placebo and ceftriaxone arms.

7.2. Interstitial pneumonia

Interstitial pneumonia is a complication of bacterial pneumonia. The incidence of interstitial pneumonia was 3.1% in the placebo arm, compared with 0.5% in the ceftriaxone arm.
The safety of pharmacological treatments in LN is ultimately based on applying a balanced combination of clinical judgment, careful evaluation of robust evidence from well-designed trials, in the few rare individualized patient genetic and genomic characteristics will guide clinical decision making and facilitate the choice of appropriate treatment. We hope the introduction of a wider selection of validated and well-defined treatment options will decrease the mortality and morbidity for LN patients, reducing or eliminating progression to end-stage renal disease.

Declarations of interests

In building for a consensus for a number of pharmaceutical companies in the field of LN, Fiorelli, M. D. and D.C. are on the advisory board of a number of pharmaceutical companies that manufacture drugs for LN treatment and have or have had business relationships with companies that manufacture drugs for LN treatment, and/or have received consulting fees or travel grants from companies that manufacture drugs for LN treatment. The rest of the authors declare that they have no conflict of interest.

References


