Supporting Evidence Document:
Corticosteroid Protocol for MCD and FSGS

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Objective

The purpose of this protocol is to facilitate the initial treatment of minimal change disease (MCD) or focal segmental glomerulosclerosis (FSGS) with oral corticosteroids. The following document summarizes the scientific evidence supporting the recommendations found in the protocol.

1. Primary MCD and FSGS

Primary MCD and FSGS are often grouped together, even though there is debate as to whether they are variants of the same disease, or represent separate pathogenetic entities. As you will read, corticosteroid resistance is suggestive of FSGS compared to MCD, a condition that is associated with a worse prognosis.[1] Until further research is completed, drug therapy is approached similarly, often with extrapolation of data from MCD studies to FSGS patients.[1,2] In this document, we will highlight where such data is being extrapolated.

2. Evidence for corticosteroids as initial therapy

Both diseases are initially treated with corticosteroids, but the response is much more predictable in patients with MCD. Studies demonstrate that over 80% of adults will experience complete remission (CR) with corticosteroid therapy, compared to 28 to 74% of patients with FSGS.[1,3–13] Even though a significant number of untreated patients with MCD will experience spontaneous remission within 2 years,[3,14] leaving nephrotic syndrome untreated exposes these patients to significant morbidity such as dyslipidemia, infections and thromboembolic events.

3. Duration of corticosteroid therapy

In general, the duration of therapy will vary according to the degree and rapidity of response, whether full or partial remission is achieved, and the degree of steroid toxicity. In patients with MCD, the response to corticosteroids is abrupt, with prompt resolution of proteinuria in over 80% of patients in the first 2 months;[3,14] a longer duration of therapy is required for patients with FSGS, as the average time to achieve complete remission is 3 to 4 months.[12,15–17]

We suggest patients continue on full dose corticosteroid therapy for 2 additional weeks after achieving proteinuric remission before slowly tapering therapy as long as a minimum of 4 weeks of full dose therapy is completed, or a maximum of 16 weeks of full dose is not exceeded.

Very short courses of corticosteroids (< 2 months) are not recommended as they result in much lower remission rates (20 to 30% in patients with FSGS). On the other hand, if there is no response by week 16, the patient is unlikely to respond and should be presumed to be steroid resistant.[11]

4. Corticosteroid tapering regimen and corticosteroid-dependent disease

The optimal corticosteroid-tapering regimen is unknown, but it is commonly tapered by 5 to 10 mg/week or less, after achieving remission for a total exposure period of at least 6 months.[8,10,18] In about 30% of patients, proteinuria will

increase while prednisone is being tapered despite previously achieving complete or partial remission.[9] For these corticosteroid-dependent patients, we recommend stopping the taper, temporarily maintaining the current prednisone dose and adding a calcineurin inhibitor (CNI) or cyclophosphamide.[1]

In patients with corticosteroid-dependent MCD, both cyclophosphamide and CNIs induce remission in about 75% of patients.[4,8–10,18,19] However, patients treated with cyclophosphamide have a higher likelihood of achieving sustained remission;[20,21] of course this comes at the expense of being exposed to a more unfavorable side effect profile.

In patients with steroid-dependent FSGS, a CNI is favored. Data for cyclophosphamide is limited to a few retrospective observational studies in these patients,[12,16,22–30] but it is fairly established that patients with steroid-resistant FSGS don't respond well to cyclophosphamide.[23] More details on the use of cyclophosphamide and CNIs for the treatment of MCD and FSGS can be found in their respective supporting evidence documents.

5. Patients who relapse after a successful initial course of corticosteroids

In patients with MCD, 50 to 75% of responders will have a relapse, usually within the first year after discontinuing the corticosteroid, but occasionally many years later.[6,8,9] In patients with FSGS, the Toronto GN Registry reported a relapse rate of 36% in patients who experienced complete remission and 52% in patients who were partial responders.[31] Unfortunately, treatment of relapses has not been well studied in clinical trials.

Often an abbreviated course of corticosteroids (to avoid toxicity) can be used if the patient did not experience significant toxicity or developed a condition that increases their risk of toxicity (e.g. obesity, psychiatric condition, severe osteoporosis, uncontrolled diabetes); however, dose, duration and subsequent taper should be based the patient's previous clinical response to corticosteroids. If a patient relapses within 2 months of corticosteroid cessation, they are considered steroid-dependent.

6. Patients who are corticosteroid resistant or at high risk of corticosteroid-induced toxicity.

In patients with MCD initially treated with corticosteroids, 5 to 10% of patients will be considered resistant (defined as no response to 16 weeks of corticosteroid therapy).[1] In patients with FSGS, resistance has been reported to be as high as 39%.[31] In these patients, CNIs or mycophenolate mofetil may be appropriate options. In patients at high risk of corticosteroid-induced toxicity, but not corticosteroid resistant (e.g. obese, psychiatric conditions, severe osteoporosis, uncontrolled diabetes), cyclophosphamide may also be an option, please refer to their respective treatment protocols and supporting evidence.

7. Prevention of corticosteroid-induced osteoporosis and gastrointestinal complications

Supporting evidence for prevention of glucocorticoid-induced osteoporosis and gastrointestinal complications has previously been summarized and can be found in the document titled "Supporting Evidence Document for the Prevention of Glucocorticoid-induced Osteoporosis and Gastrointestinal Complications" at BCRenalAgency.ca.

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