KDIGO GN Guideline update – Evidence summary

Infection-related glomerulonephritis

Immunosuppressive therapy of hepatitis B or C related glomerulonephritis

PICO question
In adult patients with hepatitis B or C related glomerulonephritis, what antiviral treatment therapy compared to no treatment/placebo or standard of care improves efficacy (all-cause mortality, end-stage kidney disease, ≥50% loss of GFR, annual loss of GFR, complete remission) outcomes and reduces adverse effects (infection, and malignancy)?

Search strategy and selection
The Cochrane Kidney and Transplant Specialized Register was searched for all randomized control trials (RCTs) examining hepatitis B and C infection-related glomerulonephritis and antiviral therapy, published up to June 2018.

Search results
The June 2018 search identified 33 relevant citations, 32 of these were excluded because they were not RCTs, or did not include participants with hepatitis related glomerulonephritis, or not on antiviral therapy. There were no studies found regarding hepatitis B infection-related glomerulonephritis. There was one RCT with 12 participants found on antiviral therapy in patients with hepatitis C infection-related glomerulonephritis.

Summary of the main findings
Hepatitis B infection-related glomerulonephritis
- No RCT were identified

Hepatitis C infection-related glomerulonephritis
Interferon therapy versus prednisone (1 study, 13 participants)
- Critical and important outcomes (all-cause mortality, end-stage kidney disease, ≥50% loss of GFR, infection malignancy, annual loss of GFR) were not reported in RCTs or there were too few who experienced events to be certain of the effect (complete remission).
- Interferon therapy compared with prednisone probably decreases liver function (ALT (U/I)) after 6 months of therapy. (MD 33 lower, 95%CI 58.5 lower to 7.5 lower) and at 18 months of therapy (MD 25 lower, 95%CI 49.39 lower to 0.61 lower).
- Interferon therapy compared with prednisone may have little or no effect on kidney function (serum creatinine after 6 months of therapy (MD 0.30 lower, 95%CI 0.97 lower to 0.37), and at 18 months of therapy (MD 0.20 higher, 95%CI 1.21 lower to 1.61 higher); daily proteinuria after 6 months of therapy (MD 0.0, 95%CI 1.10 lower to 1.61 higher) and after 18 months (MD 0.0, 95%CI 1.75 lower to 1.75 higher).
Immunosuppressive therapy of HIV associated nephropathy

**PICO question**
In patients with HIV-associated nephropathy, what antiretroviral treatment (HAART alone or combined with antihypertensive agents, corticosteroids and immunosuppressive therapies) compared to no treatment/placebo or standard of care improves efficacy outcomes (all-cause mortality, end-stage kidney disease, ≥50% loss of GFR, annual loss of GFR, complete remission) and reduce adverse effects (infection, and malignancy)?

**Search strategy and selection**
Medline, EMBASE, Central, and AIDSEARCH and the Cochrane renal register were searched in 2009. The Cochrane Kidney and Transplant Specialized Register was searched for all randomized control trials (RCTs) examining anti-viral therapy, published up to May 2018.

**Search results**
The 2009 search of Medline, EMBASE, Central, AIDSEARCH and the Cochrane renal register found 893 studies. A total of 878 studies were excluded due to being the wrong population or intervention or for not being a RCT or Quasi-RCT, and from the remaining 15 studies, four were eligible. Out of these four studies, two were ongoing and two were suspended and therefore excluded. There was updated searched in 2018 found one additional study by Abgrall, 2015, this was also excluded because it was the wrong intervention. The previous two on-going studies (NCT00000819 – completed in 1996; NCT00089518 – completed in 2005) identified in the 2009 search have been completed according to clinical trials.gov but have not been published and therefore have been included as studies awaiting classification.

**Summary of the main findings**
No studies were found.

**Effect modifiers**
The following effect modifiers were considered:

- Kidney function (GFR, proteinuria, presence of albuminuria)
- Gender
- Age (adults vs. pediatrics)
- Presence of cryoglobulinemia in patients with hepatitis C

There was insufficient data to allow for the assessment of effect modifiers.

**Studies from the 2012 KDIGO GN guideline evidence tables not included in 2018 evidence review.**
No studies were identified for the infection-related glomerulonephritis chapter for the 2012 KDIGO GN guideline.
**PICO (17.1)**
Population: Patients with hepatitis C associated glomerulonephritis
Intervention: Interferon therapy
Comparator: Prednisone

<table>
<thead>
<tr>
<th>Outcome Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Prednisone</td>
<td>Interferon therapy</td>
<td></td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>(CI 95% - )</td>
<td>Difference: fewer</td>
<td></td>
<td>No studies were found that looked at all-cause mortality</td>
</tr>
<tr>
<td>End-stage kidney disease</td>
<td>(CI 95% - )</td>
<td>Difference: fewer</td>
<td></td>
<td>No studies were found that looked at end-stage kidney disease</td>
</tr>
<tr>
<td>≥50% GFR loss</td>
<td>(CI 95% - )</td>
<td>Difference: fewer</td>
<td></td>
<td>No studies were found that looked at ≥50% GFR loss</td>
</tr>
<tr>
<td>Infection</td>
<td>(CI 95% - )</td>
<td>Difference: fewer</td>
<td></td>
<td>No studies were found that looked at infection</td>
</tr>
<tr>
<td>Malignancy</td>
<td>(CI 95% - )</td>
<td>Difference: fewer</td>
<td></td>
<td>No studies were found that looked at malignancy</td>
</tr>
<tr>
<td>Complete remission</td>
<td>Relative risk (CI 95% - )</td>
<td>0 per 1000 per 1000</td>
<td>Very Low</td>
<td>There were too few who experienced the complete remission, to determine whether IFN compared with prednisone made a difference</td>
</tr>
<tr>
<td>Annual GFR loss 3 years</td>
<td>Measured by: Scale: - Lower better</td>
<td>Difference: null lower</td>
<td></td>
<td>No studies were found that looked at annual GFR loss</td>
</tr>
<tr>
<td>Serum creatinine End of therapy (6 months)</td>
<td>Measured by: mg/dL Scale: - Lower better</td>
<td>Mean</td>
<td>Mean</td>
<td>Low</td>
</tr>
<tr>
<td>Serum creatinine End of follow-up</td>
<td>Measured by: mg/dL Scale: - Lower better</td>
<td>Mean</td>
<td>Mean</td>
<td>Low</td>
</tr>
</tbody>
</table>


Based on data from 13 patients in 1 studies
Follow up 18 months

| (18 months) | Based on data from 13 patients in 1 studies Follow up 18 months | Difference: MD 0.20 higher (CI 95% 1.21 lower - 1.61 higher) | serious imprecision
| Daily proteinuria (g/day) | Mean | Mean | Low | little or no difference on serum creatinine after 18 months
| End of therapy (6 months) | Mean | Mean | Due to serious risk of bias, Due to serious imprecision

| Measured by: Scale: - Lower better Based on data from 13 patients in 1 studies Follow up 18 months | Difference: MD 0 lower (CI 95% 1.10 lower - 1.10 higher) | Due to serious risk of bias, Due to serious imprecision
| Daily proteinuria (g/day) | Mean | Mean | Low | IFN compared with prednisone may have little or no difference on daily proteinuria after 6 months of therapy
| End of follow-up (18 months) | Mean | Mean | Due to serious risk of bias, Due to serious imprecision

| Measured by: Scale: - Lower better Based on data from 13 patients in 1 studies Follow up 18 months | Difference: MD 33 lower (CI 95% 58.5 lower - 7.5 lower) | Moderate | IFN compared with prednisone probably decreases ALT after 6 months of therapy
| Liver function (ALT) (U/I) | Mean | Mean | Due to serious risk of bias, Due to large magnitude of effect
| End of therapy (6 months) | Mean | Mean | Moderate | IFN compared with prednisone probably decreases ALT after 18 months
| Measured by: Scale: - Lower better Based on data from 13 patients in 1 studies Follow up 18 months | Difference: MD 25 lower (CI 95% 49.39 lower - 0.61 lower) | Due to serious imprecision, Due to large magnitude of effect
| Liver function (ALT) (U/I) | Mean | Mean | Due to serious risk of bias, Due to large magnitude of effect
| End of follow-up (18 months) | Mean | Mean | IFN compared with prednisone probably decreases ALT after 6 months of therapy

| Measured by: Scale: - Lower better Based on data from 13 patients in 1 studies Follow up 18 months | Difference: MD 25 lower (CI 95% 49.39 lower - 0.61 lower) | Moderate | IFN compared with prednisone probably decreases ALT after 18 months


1. Primary study Mazzaro 2000 Baseline/comparator: Control arm of reference used for intervention .
2. Risk of bias: Serious. Inadequate/lack of binding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up; Selective outcome reporting; Imprecision: Very Serious. Only data from one study, Low number of patients, due to no events;
4. Risk of bias: Serious. Inadequate/lack of binding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up; Imprecision: Serious. Only data from one study, Low number of patients;
5. Primary study Baseline/comparator: Control arm of reference used for intervention .
6. Risk of bias: Serious. Inadequate/lack of binding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up; Imprecision: Serious. Only data from one study, Low number of patients;
8. Risk of bias: Serious. Inadequate/lack of binding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up; Imprecision: Serious. Only data from one study, Low number of patients;
10. Risk of bias: Serious. Inadequate/lack of binding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up; Imprecision: Serious. Only data from one study, Low number of patients;
12. Risk of bias: Serious. Inadequate/lack of binding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up; Imprecision: Serious. Only data from one study, Low number of patients; Upgrade: Large magnitude of effect.
14. Risk of bias: Serious. Inadequate/lack of binding of participants and personnel, resulting in potential for performance bias, Incomplete data and/or large loss to follow up; Imprecision: Serious. Only data from one study, Low number of patients; Upgrade: Large magnitude of effect.

References
[24] Immunosuppressive therapy for anti GBM.