KDIGO GN Guideline update – Evidence summary

Anti-glomerular basement membrane (anti-GBM) antibody glomerulonephritis

Immunosuppressive therapy of HSP nephritis

PICO question
In patients with biopsy-proven anti-glomerular basement membrane (anti-GBM), what immunosuppressive agents compared to no treatment/placebo or other immunosuppressive therapies improve 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
Keywords for anti-glomerular basement membrane (anti-GBM), and immunosuppressive therapy were used to search the Cochrane Kidney and Transplant Specialized Register for all randomized controlled trials (RCTs) published up to May 2018.

Search results
Two relevant citations from the Cochrane Kidney and Transplant Specialized Registry of studies were identified. Studies were excluded if they were not RCTs and included patients without biopsy-proven Anti-GMB. One primary study (two reports) with 17 participants was included in the 2018 review for the KDIGO glomerulonephritis guideline update

One comparison was included:
1. Plasma exchange vs. Standard of care (one study, 17 participants)

Summary of the main findings

Plasma exchange vs. standard of care
• This has only been examined in one small RCT (Johnson 1985). Either critical or important outcomes were not examined in this RCT or due to the very low certainty of evidence (study limitations and very serious imprecision) the effects of treatment are unclear.

Effect modifiers
The following effect modifiers were considered:
• Kidney function (GFR, presence of proteinuria, presence of albuminuria)
• Relapse or resistant disease
• Age (adults vs. pediatrics)
• Initial presentation requiring dialysis

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 anti-GBM chapter for the 2012 KDIGO GN guideline.
**PICO (22.1)**

Population: Anti-glomerular basement membrane antibody glomerulonephritis  
Intervention: Plasma exchange  
Comparator: Standard of care

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<th>Outcome</th>
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<th>Study results and measurements</th>
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| All-cause mortality | Relative risk: 2.7  
(CI 95% 0.13 - 58.24)  
Based on data from 17 patients in 1 studies  
Follow up Mean 17 weeks | Plasma of care: 110 per 1000  
Plasma exchange: 297 per 1000  
Difference: 187 more per 1000  
(CI 95% 96 fewer - 6296 more) | Very Low  
Due to serious risk of bias, Due to serious indirectness, Due to very serious imprecision | We are uncertain whether plasma exchange compared to standard of care improves or worsens all cause mortality |
| End-stage kidney disease | Relative risk: 2.19  
(CI 95% 0.6 - 7.93)  
Based on data from 15 patients in 1 studies  
Follow up Mean 17 weeks | Plasma of care: 286 per 1000  
Plasma exchange: 626 per 1000  
Difference: 340 more per 1000  
(CI 95% 114 fewer - 1982 more) | Very Low  
Due to very serious imprecision, Due to serious indirectness, Due to serious risk of bias | We are uncertain whether plasma exchange compared to standard of care improves or worsens end stage kidney disease |
| ≥ 50% loss of GFR | (CI 95% -) | Difference: fewer | No studies were found that looked at ≥ 50% loss of GFR |
| Malignancy | (CI 95% -) | Difference: fewer | No studies were found that looked at malignancy |
| Complete remission | (CI 95% -) | Difference: fewer | No studies were found that looked at complete remission |
| Infection | Relative risk: 0.67  
(CI 95% 0.21 - 2.12)  
Based on data from 17 patients in 1 studies  
Follow up Mean 17 weeks | Plasma of care: 500 per 1000  
Plasma exchange: 335 per 1000  
Difference: 165 fewer per 1000  
(CI 95% 395 fewer - 560 more) | Very Low  
Due to serious risk of bias, Due to very serious imprecision, | We are uncertain whether plasma exchange compared to standard of care improves or worsens infection |
| Annual GFR loss 3 years | Measured by: Scale: - Lower better | Difference: null lower | No studies were found that looked at annual GFR loss |

1. **Risk of bias**: Serious. Unclear randomisation process, allocation concealment and blinding of assessors. Trial was open-label.; **Indirectness**: Serious. The outcome time frame in studies were insufficient, the duration of therapy ranged from two to 36 weeks; **Imprecision**: Very Serious. Wide confidence intervals, Low number of patients, Only data from one study;  
2. **Risk of bias**: Serious. Unclear randomisation process, allocation concealment and blinding of assessors. Trial was open-label.; **Indirectness**: Serious. The outcome time frame in studies were insufficient, the duration of therapy ranged from two to 36 weeks; **Imprecision**: Very Serious. Wide confidence intervals, Low number of patients, Only data from one study;  
3. Primary study Johnson 1985 Baseline/comparator: Control arm of reference used for intervention  
4. **Risk of bias**: Serious. Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision**: Very Serious. Wide confidence intervals, Only data from one study, Low number of patients;