

Supplemental Files

Supplemental Table 1. Classification scheme of the strength of evidence. (Adopted from: Shekelle P, Woolf S, Eccles M, Grimshaw J. Clinical guidelines: developing guidelines. *BMJ* 1999;318:593–596.)

Supplemental Table 2. Overview of available RCTs on the effect of TAC-based regimens in lupus nephritis.

Supplemental Table 1.

Classification schemes

Category of evidence:

- Ia Evidence for meta-analysis of randomised controlled trials
- Ib Evidence from at least one randomised controlled trial
- IIa Evidence from at least one controlled study without randomisation
- IIb Evidence from at least one other type of quasi-experimental study
- III Evidence from non-experimental descriptive studies, such as comparative studies, correlation studies, and case-control studies
- IV Evidence from expert committee reports or opinions or clinical experience of respected authorities, or both

Strength of recommendation:

- A Directly based on category I evidence
 - B Directly based on category II evidence or extrapolated recommendation from category I evidence
 - C Directly based on category III evidence or extrapolated recommendation from category I or II evidence
 - D Directly based on category IV evidence or extrapolated recommendation from category I, II or III evidence
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Supplemental Table 2.

| Reference | No. of patients | Type of study* | Duration | Study protocol † | Remission criteria ‡ | Outcome (CR/PR/NR) |
|-------------------------------|-----------------|----------------|----------|---|---|--|
| Chen et al 2011 ¹⁸ | 81 | RCT | 6 months | <p><u>TAC-based regimen (n=42):</u> Pred: initial dose 1 mg/kg/d tapered until 10 mg/d TAC: initially 0.05 mg/kg/d (through 5-10 ng/ml)</p> <p><u>Control arm IVCYC (n=39):</u> Pred: initial dose 1 mg/kg/d tapered until 10 mg/d IVCYC: 0.75 g/m² for the 1st month, then adjusted to 0.5-1 g/m²</p> | <p><u>CR:</u> proteinuria <0.3 g/24h, normal urinary sediment, serum albumin ≥3.5 g/dl, stable kidney function (normal range or not >15% more than baseline)</p> <p><u>PR:</u> proteinuria 0.3-2.9 g/24h and a decrease of at least 50% of baseline level, serum albumin ≥3 g/dl, stable kidney function</p> <p><u>NR:</u> proteinuria >3 g/24h or 0.3-2.9 g/24h, serum albumin <3 g/dl, increase in serum creatinine >30% of baseline</p> | <p>TAC-based regimen: 52/22/26</p> <p>Control arm IVCYC: 38/43/19</p> |
| Li et al 2012 ¹⁹ | 60 | RCT | 6 months | <p><u>TAC-based regimen (n=20):</u> Pred: initial dose 1 mg/kg/d tapered until 10 mg/d TAC: 0.08-0.1 mg/kg/d (through 6-8 ng/ml)</p> <p><u>Control arm MMF (n=20):</u> Pred: initial dose 1 mg/kg/d tapered until 10 mg/d MMF: 1.5-2 g/d</p> <p><u>Control arm IVCYC (n=20):</u> Pred: initial dose 1 mg/kg/d tapered until 10 mg/d IVCYC: 0.5-0.75 g/m² monthly</p> | <p><u>CR:</u> proteinuria <0.3 g/24h with normal urine sediment, serum albumin >3.5g/dl and stabilization (±15%) or improvement of serum creatinine</p> <p><u>PR:</u> proteinuria 0.3-2.9 g/24h, having decreased by at least 50% from baseline values, with a serum albumin of at least 3 g/dl and relative stabilization (±30%) in serum creatinine</p> | <p>TAC-based regimen: 45/30/25</p> <p>Control arm MMF: 30/30/40</p> <p>Control arm IVCYC: 45/30/25</p> |

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|------------------------------|-----|-----|----------|--|---|--|
| Mok et al 2014 ⁸ | 150 | RCT | 6 months | <p><u>TAC-based regimen (n=74):</u> Pred: initial dose 1 mg/kg/d tapered until 10 mg/d TAC: initially 0.1 mg/kg/d to 0.06 mg/kg/d if clinical response was satisfactory at month 3</p> <p><u>Control arm MMF (n=76):</u> Pred: initial dose 1 mg/kg/d tapered until 10 mg/d MMF: 2-3 g/d</p> | <p><u>CR:</u> proteinuria <1 g/24h or uP/Cr <1 with stabilization (within 25%) or improvement in serum creatinine, resolution of urinary sediment abnormalities, persistent improvement in C3 and anti-dsDNA levels</p> <p><u>PR:</u> reduction of proteinuria; if nephrotic at baseline, a 50% decrease but <3 g/24h or uP/Cr <3; if non-nephrotic, a decrease to ≤50% of pre-treatment value but >1 g/24h (or uP/Cr >1), with stabilization (within 25%) or improvement in serum creatinine, improvement of urinary sediment abnormalities (>50% reduction in haematuria and urine RBC (<10/HPF)</p> <p><u>NR:</u> deterioration of serum creatinine (>25%), an increase in proteinuria, or a reduction in proteinuria but not to the extent of CR or PR</p> | <p>TAC-based regimen: 62/27/11</p> <p>Control arm MMF: 59/21/20</p> |
| Bao et al 2008 ²⁰ | 40 | RCT | 6 months | <p><u>TAC-based regimen (n=20):</u> Methylprednisone 0.5 g/d for 3d + pred taper until 10 mg/d TAC: 4 mg/d BID (through 5-7 ng/ml) MMF: 1.5-2 g/d (through AUC 20-45 mg*h/l)</p> <p><u>Control arm IVCYC (n=20):</u> Methylprednisone 0.5 g/d for 3d + pred taper IVCYC: 0.75 g/m² for the 1st month, then adjusted to 0.5-1.0 g/m² monthly</p> | <p><u>CR:</u> proteinuria 0.4g/24h, normal urinary sediment, serum albumin ≥3.5 g/dl, normal serum creatinine or no more than 15% above baseline</p> <p><u>PR:</u> normal or at least a 50% improvement in proteinuria and haematuria, serum albumin ≥3 g/dl, normal serum creatinine or no more than 15% above baseline</p> | <p>TAC-based regimen: 50/40/10</p> <p>Control arm IVCYC: 5/40/55</p> |

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| Liu et al 2015 ⁹ | 362 | RCT | 6 months | <u>TAC-based regimen (n=181):</u> Methylprednisone 0.5 g/d for 3d + pred taper until 10 mg/d TAC: 4 mg/d MMF: 1g/d | <u>CR:</u> proteinuria <0.4 g/24h, normal urinary sediment, serum albumine ≥3.5 g/dl, normal serum creatinine <u>PR:</u> proteinuria <3.5 g/24h and ≥50% reduction, serum albumin ≥3 g/dl, normal or ≤25% increase in serum creatinine from baseline | TAC-based regimen: 46/38/17 |
| | | | | <u>Control arm IVCYC (n=181):</u> Methylprednisone 0.5 g/d for 3d + pred taper until 10 mg/d IVCYC: 0.75 g/m ² for the 1st month, then adjusted to 0.5-1 g/m ² | Control arm IVCYC: 26/37/37 | |

* RCT = randomized controlled trial; † TAC = tacrolimus; IVCYC = intravenous cyclophosphamide; MMF = mycophenolate mofetil; pred = prednisone; ‡ CR = complete response; PR = partial response; NR = no response