






KDIGO GN Guideline – ERT Feedback

March 6, 2019

Chapter (Lead Author)	Feedback	Action Items for ERT	ERT Response
Chapter 2: General (Dick)	Dick confirmed this chapter did not call for an ERT review.	None	
Chapter 3: SSNS (Keisha and Marina)	Marina: Detailed comments sent in November 2018 are still valid. (please see attached file)	Please check list of missing references and provide rationale for exclusion or if meeting criteria, please add to evidence review [UPDATE: 11.10 has been updated in MAGICApp]	The relevant references has been included and MAGICApp has been updated
Chapter 4: SRNS (Keisha and Marina)	<div style="text-align: center;">  Comments to ERT Data Review for SRN </div> <p>Keisha: One reference for 11.10 in MAGICApp that may be missing:</p> <ul style="list-style-type: none"> Abeyagunawardena AS, Karunadasa U, Jayaweera H, et. al. Short courses of daily prednisolone during upper respiratory tract infections reduce relapse frequency in childhood nephrotic syndrome. <i>Pediatr Nephrol.</i> 2017 Aug;32(8): 1377-1382 		
Chapter 5: MCD (Jai)	No direct feedback for ERT. Note this section will be based mostly on observational data not included in ERT review and extrapolation from childhood nephrotic syndrome.	None	
Chapter 6: FSGS	SRs not performed for 5 of the 6 recommendation	Please confirm whether SR was	An evidence review was


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(Adrian)	statements (please see attached file)  <small>FSGS ERT.docx</small>	conducted and if not, please provide rationale	<p>undertaken to include all RCTs in FSGS and the data presented on MAGICapp is limited by the reporting of RCTs. We were unable to undertake reviews of observational studies given the significant investment of resources required for this work.</p> <p>Recommendations</p> <ol style="list-style-type: none"> 1) There are no RCTs that examine treatment of patients with FSGS without nephrotic syndrome. We have updated the PICO tables in MAGICapp to identify the population as patients with FSGS with nephrotic syndrome. 2) We acknowledge that we have been unable to examine all the observational studies, we did not identify any RCTs that examined dose or duration of 3) As identified, we were unable to review all observational studies in this area, and there were no RCTs examining CNI and corticosteroid in patients with FSGS 4) As stated, we were unable to review observational studies in this area. However, the

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			<p>RCTs that examine the use of cyclosporin in PICO 14.3 – 14.6 were conducted in patients with steroid-resistant FSGS. We have updated MAGICapp to reflect this in the population.</p> <p>“Patients with steroid-resistant FSGS with nephrotic syndrome”</p> <p>5) No action required</p> <p>6) We identified all RCTs that examined treatment of FSGS, unfortunately we did not identify any RCTs examining maintenance therapy in patients with FSGS</p>
Chapter 7: MN (Jack)	<ul style="list-style-type: none"> • The studies with shorter follow-up still included in the meta-analysis and simply downgraded; this was not deemed to be a satisfactory approach as the durations are not long enough to allow conclusions on renal outcomes. • Two recommendations that address therapy, where the authors provide evidence rating based on the manuscripts (and supporting evidence from non RCTs). <ul style="list-style-type: none"> ○ These recommendations need to be discussed in light of the deviations from the judgement of the ERT. (please see attached file) 	Suggested approach: ERT to identify the areas of disagreement and provide arguments to support their rating of the quality of the evidence	Currently underway, two recommendations that can be resolved. Work group has not cited the PICO tables in quality of the evidence. They refer to a handful of trials and observational studies. Looking to how the evidence tables can also be referenced but the caveats also explained in the text.

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	 KDIGO_MN_Guideline_02032019.docx  TabletrialMN guideline.docx		
Chapter 8: Complement (Carla)	<ul style="list-style-type: none"> A number of references were not included (please see attached file)  List of references FB.docx	ERT to review list of references to identify observational studies not included. Please provide rationale for exclusion or if meeting criteria, please add to evidence review	The ERT will review the list of possible included studies and update the evidence summary accordingly. Studies to be included will be: <ul style="list-style-type: none"> Studies focused on treatment Patients with cryoglobulinic GN associated with leukemia or hepatitis C? Fibriallary GN
Chapter 9: Infectious GN (Dick)	Dick is happy with ERT tables.	None	
Chapter 10: IgAN (Jon)	<ul style="list-style-type: none"> 18.1: The evidence tables mix the “control” interventions. <ul style="list-style-type: none"> All forms of steroids (\pm RAS blockade) vs. placebo OR standard of care (control may be \pm RAS blockade) Subsequent tables break down each individual regimen of immunosuppression. TESTING is referenced for RR death and ESKD estimates (It included RASi as comparison) 	Please review feedback and provide comment	Please see updated response to evidence review document (page5-9) for detailed responses to the queries.
Chapter 11: IgAV (Jon)			

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	<ul style="list-style-type: none"> ○ Manno study (NDT 2009) is not included: <ul style="list-style-type: none"> ▪ Has combined ESKD/doubling creatine as the primary endpoint, also rate of renal function decline ▪ It is only referenced in table 18.4 which is oral steroid plus RASi vs. RASi alone ○ Lv 2009 not included, but in 18.4, the TESTING study is not included. ○ STOP-IgAN study (JASN Jan 2018) should be included in this table. <ul style="list-style-type: none"> ▪ Only 27 patients received combo immunosuppression, but data allows separation of the patients into steroid-only group. ▪ Please review to 18.7 below for additional information on the inclusion of this study • 18.2: TR-Budesonide should not be included as it is the targeted release formulation and it is not yet commercially available. • 18.5: Steroid plus RAS vs. steroid: Please include study reference for complete remission and GFR. • 18.7: Mixed of studies that may be inappropriately pooled: <ul style="list-style-type: none"> ▪ STOP study is considered as “CYC then AZA + steroid vs. supportive therapy”; yet only a subset of intervention patients received CYC/AZA 		

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	<ul style="list-style-type: none"> • The count in the forest plots for cytotoxic is 82 but 82 patients did not receive this regimen in STOP, only 27. • STOP is compared to Ballardie which did not have a steroid only group and did not include uniform RAS blockade. • Similar issues for STOP in 18.1 - referenced as "Stop-IgAN 2008" <ul style="list-style-type: none"> ▪ In the complete remission section of 18.7, there are multiple forest plots for studies that do not fit into this category. • 18.10: Forest plots refer to multiple regimens that are in other categories/tables. <ul style="list-style-type: none"> ○ Locatelli study referenced in table but no mention of the 2010 Pozzi/Locatelli pub (JASN 2010) of AZA plus steroid vs. steroid (and RASi) which is the largest study and included several endpoints in the chart. <p>WCN GN Guideline Slide Deck Feedback:</p>		

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	 <p data-bbox="447 334 575 383">WCN19-IgAN KDIGO.pptx</p> <ul style="list-style-type: none"> <li data-bbox="464 440 1073 781">• Slide #16: STOP-IgAN – cyclophosphamide then AZA plus steroids (1 study) Increases complete remission (RR 3.41, 95%CI 1.17, 9.93) (Moderate certainty) <ul style="list-style-type: none"> <li data-bbox="558 578 1073 675">○ Cyclophosphamide then AZA in STOP-IgA demonstrated no effect on complete remission. <li data-bbox="558 683 1073 781">○ An increase in remission rate was only seen with corticosteroid monotherapy in patients with a GFR >60 ml/min. <li data-bbox="464 789 1073 1065">• Slide #17: The statement that steroids decrease ESRD is true based on the studies selected; however, many of the studies are flawed since RAS-blockade was insufficient. <ul style="list-style-type: none"> <li data-bbox="558 935 919 959">○ STOP-IgAN is not included. <li data-bbox="558 967 1062 1065">○ Long-term data will be presented this summer and may ultimately affect the conclusions. <li data-bbox="464 1073 1073 1317">• Slide #17: Overall the studies suggest there is a modest increase in infections only; however, there is a concern regarding the under-reporting in past trials. <ul style="list-style-type: none"> <li data-bbox="558 1219 1062 1317">○ Both STOP-IgAN and TESTING demonstrated a significant increase in infections 		
Chapter 12: Lupus nephritis	<ul style="list-style-type: none"> <li data-bbox="422 1333 1062 1403">• Authors do not disagree with the ERT’s summaries; yet, the strength of a recommendations will not 	None	

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(Daniel)	<p>mirror the strength of ‘scientific evidence’ which is dependent primarily on the quality of clinical trials included in the evidence analysis while ‘expert opinion’ takes into consideration the clinical impact of the findings in addition to the quality of research methodology.</p> <ul style="list-style-type: none"> • Authors have been advised that “the strength of a given recommendation is determined not only by the quality of the evidence, but also by other, often complex judgments regarding the size of the net medical benefit (potential risks vs. benefit), values, and preferences, and costs. For this reason, a recommendation statement could be upgraded or downgraded based on these additional considerations. That is all the more reason why these other determinants will need to be explicitly and transparently stated in the rationale so that the readers can fully appreciate our line of thinking.” 		
Chapter 13: ANCA (Vladimir)	Jan-Stephan & Vladimir are happy with ERT tables.	None	
Chapter 14: Anti-GBM (Vladimir)	Jan-Stephan & Vladimir are happy with ERT tables.	None	