SPECIALISED COMMISSIONING - CLINICAL EVIDENCE EVALUATION CRITERIA FOR A PROPOSITION FOR A CLINICAL COMMISSIONING POLICY FOR ROUTINE COMMISSIONING

URN: 1748
TITLE: Addition of rituximab to standard chemotherapy for newly diagnosed CD20 positive B-cell precursor acute lymphoblastic leukaemia (ALL)

CRG: Chemotherapy
NPOC: Cancer
Date: 18/07/18

This policy is being considered for:	For routine commissioning	X	Not for routine commissioning	
Is the population described in the policy the same as that in the evidence review including subgroups?	No. The studies did not include children although the phase II Thomas et al paper included adults and adolescents down to age 13. Panel recognised that the outcomes of this disease are significantly worse in adults than children. 80% of children are cured.			
Is the intervention described in the policy the same or similar as the intervention for which evidence is presented in the evidence review?	Yes, the addition of rituximab to first line treatment.			
Is the comparator in the policy the same as that in the evidence review? Are the comparators in the evidence review the most plausible comparators for patients in the English NHS and are they suitable for informing policy development?	Different chemotherapy regimens were used in the control arm. The studies were all open-label with no proper concealment from investigators. The control / comparators arms in the studies appeared to have differences in their exposure to control therapy than the patients receiving rituximab.			
Are the clinical benefits demonstrated in the evidence review consistent with the eligible population and/or subgroups presented in the policy? Are the clinical harms demonstrated in the evidence review reflected in the eligible	No. Panel had concerns regarding use of rituximab in children. There was no evidence presented to demonstrate benefit in this population. In adults it was noted that there could be a benefit in event free survival and complete remission duration. However, there was a lack of evidence regarding benefit in overall survival. There was a suggestion that there may be a subgroup of adults under 60 who may derive greater benefit. However, this was based on post-hoc analysis and this methodology makes the reliability of this finding uncertain. There were harms however these were not significant.			

and /or ineligible population and/or subgroups presented in the policy?			
Rationale Is the rationale clearly linked to the evidence?	The addition of rituximab may have some clinical benefit in adult patients, but this may not extend to older patients. The evidence is not clear. It does appear that the magnitude of benefit is limited in that the main benefit may be delay in relapse. However, the impact on overall survival appears to be insignificant. It may be that overall survival could be improved for a difficult to define subgroup of patients. The Policy Working Group (PWG) are asked to define more specific eligibility criteria based upon the evidence and more specific duration and cessation criteria for treatment. The current policy proposition does not specifically define the eligible population and the stopping criteria also need to specific and clear. The Panel were particularly concerned that this all age policy would be applied to children. There is no evidence in children, for whom the clinical course of this form of ALL differs very significantly from adults. Policy criteria need to be justified by the research evidence and if this is not possible the PWG should consider re-drafting this as a not for routine commissioning policy.		
<u>Advice</u> The Panel should provide advice on matters relating to the evidence base and policy development and prioritisation. Advice may cover: • Uncertainty in the evidence base • Challenges in the clinical interpretation and applicability of policy in clinical practice • Challenges in ensuring policy is applied appropriately • Likely changes in the pathway of care and therapeutic advances that may result in the need for policy review.	We note that outcomes for this condition are generally quite good in children but poor in adults, however the benefits of treatment may be greatest in a group of patients who are under 60, as described in the post-hoc subgroup analysis in the literature review. We noted that some of the research excluded older patients and it would be helpful to understand why they were excluded and whether there are clinical reasons for this that need to be taken into account in the eligibility criteria. The policy proposition is not clear regarding a subgroup who would gain significant additional benefit from treatment. This should be clearly outlined and should be supported by the evidence. In particular, the 'all age' nature of the policy causes concern. The panel would like additional commentary in the policy to explain where rituximab is proposed within the pathway of care. Panel noted that treatment protocols differ by age and the evidence of adding rituximab to these protocols needs to be support by the evidence. Eligibility criteria need to be clear, exclusion criteria may also need to be added. The stopping criteria should be well defined. This policy should be returned to Panel for reconsideration.		
Overall conclusion	This is a proposition for routine commissioning	Should proceed for	

	and	routine commissioning	
		Should reversed and proceed as not for routine commissioning	
	This is a proposition for not routine commissioning and	Should proceed for not routine commissioning	
		Should be reconsidered by the PWG	

Overall conclusions of the panel

Report approved by:
David Black
Clinical Panel Chair
23/09/2018