NICE National Institute for Health and Care Excellence

Fluorouracil plasma monitoring the My5-FU assay for guiding dose adjustment in patients receiving fluorouracil chemotherapy by continuous infusion

Diagnostics Assessment Report (DAR) - Comments

Stakeholder	Comment no.	Page no.	Section no.	Comment	Response
Royal College of Physicians	1.	**General**		The NCRI/RCP/RCR/ACP/JCCO are grateful for the opportunity to comment on the above DAR. Our experts believe that there are significant issues with the review on the 5FU PK assessment assay. These are outlined below and covered in more detail later. • The authors admit that the level of evidence for a comparison of 5FU administered by BSA vs. PK is extremely low. Therefore we should be justifiably sceptical of any conclusions. • Analysis (including economic evaluation) has only been performed for patients treated with infused 5FU. However, many GI patients are treated with oral capecitabine making the analysis less clinically relevant. • It is stated that clinical trials are ongoing. As such, the analysis is felt to be premature.	We appreciate these useful comments. The comment accurately highlights our concerns reflected in the report. My5-FU is not valid for use with oral capecitabine preparations. The comment accurately highlights our concerns reflected in the report.
		16	**Results**	***"Quality and quantity of evidence were very weak for PK versus BSA dosing for all cancers"*** This statement emphasises the substantial weaknesses of this document, which is freely acknowledged by the authors. Unfortunately, despite significant efforts in review and synthesis of the	The comments accurately highlight our concerns reflected in the report.

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				literature on the topic, the level of evidence is low and therefore it is necessary to remain somewhat sceptical of any conclusions reached.	
		18	**1.2 E**	The authors have collected data on 5FU administration by infusion. However, most clinicians now prefer oral 5FU administration with capecitabine tablets. These are more convenient, do not require indwelling venous catheter placement or administration and disconnection of chemotherapy by a medical professional in each cycle. The financial implications for this are substantially different than for infused 5FU. Therefore, the economic analysis presented is unrepresentative of most patients treated with 5FU (in particular in GI cancers).	Thank you for the clarification. The comments accurately highlight our concerns reflected in the report.
		25	**1.6.1**	***"Well conducted RCTs of PK versus BSA dosing.. and... research on the QALY impact of adverse events of 5-FU which would be of benefit in any further economic assessments.."*** The authors state that these are future research recommendations. In fact these are pre-requisites before making a recommendation for use of any commercially available 5FU PK assessment model.	Thank you for the clarification.
		49	**2.4.3**	The authors state that the My5-FU assay is currently being evaluated in several clinical trials. As the current level of evidence has been identified as low	The comment accurately highlights our concerns reflected in the report.

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				quality, this report may be considered premature pending publication of these trial results.	