National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Avelumab with axitinib for untreated advanced or metastatic renal cell carcinoma

Response to consultee and commentator comments on the draft remit and draft scope

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit

Section	Consultee/ Commentator	Comments [sic]	Action
Wording	Merck/Pfizer	The proposed wording is adequate.	Comment noted.
	Kidney Cancer UK (KCUK)	Yes.	Comment noted.
	Bristol Myers Squibb	N/A	Response noted.
	Ipsen	No comment.	Response noted.
	EUSA Pharma	The wording does not reflect the cost effectiveness about the technology. It stipulates the unmet need of combined approach of Immune-therapy/ VEGFR inhibition.	Comment noted. The draft remit is “To appraise the clinical and cost effectiveness of avelumab in combination with axitinib within its

Section	Consultee/ Commentator	Comments [sic]	Action
			marketing authorisation for untreated, advanced or metastatic renal cell carcinoma." This wording reflects consideration of the cost effectiveness of the technology. No action required.
Timing Issues	Merck/Pfizer	No comment.	Response noted.
	Kidney Cancer UK (KCUK)	From the point of view of the patient population we are representing, it is imperative this treatment is made available, since it is different to others available and has significantly greater benefit in progression free survival for a large number of Renal cancer patients including a favourable prognosis which is not included with other immunotherapy combinations.	Comment noted. NICE schedules technology appraisals so that guidance to the NHS is timely. For cancer drugs, NICE aims to publish final guidance within 90 days of marketing authorisation wherever possible. No action required.
	Bristol Myers Squibb	N/A	Response noted.
	Ipsen	No comment.	Response noted.

Section	Consultee/ Commentator	Comments [sic]	Action
	EUSA Pharma	No response.	Response noted.
Additional comments on the draft remit	Merck/Pfizer	No response.	Response noted.
	Kidney Cancer UK (KCUK)	No response.	Response noted.
	Bristol Myers Squibb	N/A	Response noted.
	Ipsen	No comment.	Response noted.
	EUSA Pharma	No response.	Response noted.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Merck/Pfizer	The background information is accurate and comprehensive.	Comment noted.
	Kidney Cancer UK (KCUK)	This background gives a good representation of the current picture of Renal cancer.	Comment noted.
	Bristol Myers Squibb	Update to include the recommendation for nivolumab + ipilimumab providing this is published by the time the final scope is released	Comment noted. The background section of the scope will reflect the current technology appraisal guidance at

Section	Consultee/ Commentator	Comments [sic]	Action
			the time the final scope is issued.
	Ipsen	The phrase 'The aim of treatment is to prevent the growth and survival of cancer cells within the tumour' is correct for axitinib only. For avelumab, the aim is to modulate the immune system to attack the tumour.	Comment noted. The sentence has been removed.
	EUSA Pharma	Accurate. Epidemiology data inconsistent with that of CRUK which suggests 12547 new kidney cancer cases in 2015. Similarly 5 year survival rate for stage IV disease is 10% as per the National Cancer Intelligence Network.	Comment noted. Data on incidence is derived from ONS statistics for number of new cases in England in 2016 (10,609 new cases). This is consistent with CRUK data in England from 2015, which reports 10,507 new cases. No action required.
The technology/ intervention	Merck/Pfizer	The description of the technologies is accurate.	Comment noted.
	Kidney Cancer UK (KCUK)	This is accurate	Comment noted.
	Bristol Myers Squibb	N/A	Response noted.
	Ipsen	No comment.	Response noted.

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	EUSA Pharma	Yes.	Comment noted.
Population	Merck/Pfizer	The population is defined appropriately.	Comment noted.
	Kidney Cancer UK (KCUK)	The word locally may not need to be included. No groups that should be considered separately.	Comment noted. The word 'locally' has been removed.
	Bristol Myers Squibb	N/A	Response noted.
	Ipsen	No comment.	Response noted.
	EUSA Pharma	Yes, the population is well defined.	Comment noted.
Comparators	Merck/Pfizer	The comparators are defined appropriately.	Comment noted.
	Kidney Cancer UK (KCUK)	Yes, Sunitinb and Pazaopnaib are the standard treatments for first line treatment. Tivozanib is rarely used in practice for first line treatment. Carbozantinib usage in first line is increasing but is obviously for a specific group of patients, intermediate to poor Nivolumab and Ipilimumab with be the best alternative care, when it has finished being appraised but does not include or benefit favourable patients which avelumab and axitinib would , as shown in the results of the clinical trial Javelin 101	Comment noted.
	Bristol Myers Squibb	N/A	Response noted.
	Ipsen	The comparators listed are appropriate.	Comment noted.

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	EUSA Pharma	Yes.	Comment noted.
Outcomes	Merck/Pfizer	The outcomes are defied appropriately.	Comment noted.
	Kidney Cancer UK (KCUK)	Yes	Comment noted.
	Bristol Myers Squibb	N/A	Response noted.
	Ipsen	No comment.	Response noted.
	EUSA Pharma	Yes.	Comment noted.
Economic analysis	Merck/Pfizer	No comment.	Response noted.
	Kidney Cancer UK (KCUK)	No comment	Response noted.
	Bristol Myers Squibb	N/A	Response noted.
	Ipsen	No comment.	Response noted.
	EUSA Pharma	No response.	Response noted.
Equality and Diversity	Merck/Pfizer	No comment.	Response noted.
	Kidney Cancer UK (KCUK)	Includes all	Comment noted.

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	Bristol Myers Squibb	N/A	Response noted.
	Ipsen	There are no equality issues to raise at this stage.	Comment noted.
	EUSA Pharma	No response.	Response noted.
Other considerations	Merck/Pfizer	None.	Response noted.
	Kidney Cancer UK (KCUK)	No response.	Response noted.
	Bristol Myers Squibb	N/A	Response noted.
	Ipsen	No comment.	Response noted.
	EUSA Pharma	No response.	Response noted.
Innovation	Merck/Pfizer	The avelumab + axitinib combination is a step change in therapy. It has the potential to achieve rapid and high rates of responses through axitinib and the possibility of durable responses with avelumab, resulting in patients across all risk groups having longer disease-free periods than with standard of care. Sources: 1) TK Choueiri, BI Rini, J Larkin, et al. Avelumab plus axitinib vs sunitinib as first-line treatment of advanced renal cell carcinoma: phase 3 study (JAVELIN Renal 101) Proc Am Soc Clin Oncol, 35 (2017), p. TPS4594	Comment noted. The appraisal committee will consider the innovative nature of avelumab with axitinib during the appraisal.

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		2) Motzer RJ, Penkov K, Haanen J, et al. Avelumab plus axitinib versus sunitinib for advanced renal-cell carcinoma. N Engl J Med. 2019 Feb; DOI:10.1056/NEJMoa1816047	
	Kidney Cancer UK (KCUK)	Progression free survival is good for all groups (favourable, intermediate and poor) on this treatment and is 5 months longer than its comparator (current standard of care) in the clinical trial. This is very significant in renal cancer and a need for patients to be able to prolong the time until their cancer worsens is significant. Patients known to our organisation who have been on this treatment have had significantly better quality of life and although they may have had side effects specifically related to the axitinib, it was quickly resolved and they were able to live a fairly norm al life including being able to work. There is data available from the phase 1B (javelin 100) clinical trial and the Phase 3 (javelin 101) clinical trial. There are also patients who have been on this clinical trial who are willing to tell about their experience. Regarding QALY calculation, the prolonged extension of life beyond a ten-year period in a proportion of patients will make the health economic evaluation more complex. There is no phase III RCT data available at this time that we are aware of.	Comment noted. The appraisal committee will consider the innovative nature of avelumab with axitinib during the appraisal
	Bristol Myers Squibb	N/A	Response noted.
	Ipsen	No comment.	Response noted.
	EUSA Pharma	Axitinib is associated with improved outcome in 2nd line setting as per demonstrated in AXIS pivotal trial. Avelumab is a checkpoint inhibitor (mAb)	Comment noted.

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		that has shown single agent activity in advanced RCC and is approved for treatment of other malignancies. Avelumab is currently being investigated in Phase III programme JAVEIN 101.	
Questions for consultation	Merck/Pfizer	Have all relevant comparators for avelumab with axitinib been included in the scope? • All relevant comparators have been included within the Comparators section of the scope Which treatments are considered to be established clinical practice in the NHS for untreated advanced renal cell carcinoma? • The treatments included in comparators are those which are established in clinical practice. Are the outcomes listed appropriate? • The outcomes listed are appropriate. Are there any subgroups of people in whom avelumab with axitinib is expected to be more clinically effective and cost effective that should be examined separately? • No additional subgroups are relevant for separate examination. Where do you consider avelumab with axitinib will fit into the existing Renal Cancer NICE pathway? In line with its proposed indication, avelumab with axitinib will be available for untreated patients with advanced or metastatic renal cell carcinoma.	Comments noted. No action required.

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	Kidney Cancer UK (KCUK)	No response.	Response noted.
	Bristol Myers Squibb	N/A	Response noted.
	Ipsen	1. Have all relevant comparators for avelumab with axitinib been included in the scope? Yes. 2. Which treatments are considered to be established clinical practice in the NHS for untreated advanced renal cell carcinoma? Sunitinib, pazopanib, tivozanib and cabozantinib are currently reimbursed for untreated RCC patients. 3. Are the outcomes listed appropriate? Yes. 4. Are there any subgroups of people in whom avelumab with axitinib is expected to be more clinically effective and cost effective that should be examined separately? No comment.	Comments noted. No action required.

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		5. Where do you consider avelumab with axitinib will fit into the existing Renal Cancer NICE pathway? It is expected that avelumab with axitinib will be a treatment option for untreated advanced and metastatic RCC patients. 6. Do you consider avelumab with axitinib to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)? No comment. 7. Do you consider that the use of avelumab with axitinib can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation? No comment. 8. To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly. No comment.	
	EUSA Pharma	No response.	Response noted.
Additional comments on the draft scope	Merck/Pfizer	No response.	Response noted.
	Kidney Cancer UK (KCUK)	No response.	Response noted.

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	Bristol Myers Squibb	N/A	Response noted.
	Ipsen	No response.	Response noted.
	EUSA Pharma	No response.	Response noted.

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope:

None