Comments on the ACD Received from the Public through the NICE Website

Name	[redacted]
Role	NHS Professional
Other role	Health Professional (Private Sector)
Location	England
Conflict	No
Notes	Afilbercept in addition to chemotherapy with Irinotecan and 5FU (FOLFIRI)is proven effecacious second line treatment for metastatic colorectal cancer.
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	I do not agree with this recommendation.
Section 2 (The technology)	This is a novel treatment technology.
Section 4 (Consideration of the evidence)	There is good evidence from a well designed phase 3 clinical trial to support the use of the drug for patients with metastatic colorectal cancer with FOLFIRI chemotherapy as second line treatment after Oxaliplatin based chemotherapy.

Name	[redacted]
Role	NHS Professional
Other role	
Location	England
Conflict	No
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	The concept of continuing anti VEGF blockade has been proven to extend overall survival in patients with metastatic colo-rectal cancer in the TML study (Treatment througt mulitiple lines) using a different agent Bevacizumab. Aflibercept has extended survival for the same group of patients in 2nd line in combination with Irinotecan and 5FU. This group had a patients who recieved avastin and who did not in first line setting. This offers a valuble option of colo-rectal cancer patients who had progressed on first line agent in combination with Bevacizumab/or without, especially the patients harboring the K-ras mutation. This particular group have no other biological option available. I believe using Aflibercept give our patients and clinicians muliple options to maximise the benefit from therapy and extend their lives.
Section 2 (The technology)	This combination accentuates the toxicity of chemotherapy, so patients selection is vital.
Section 3 (The manufacturer's submission)	The Velour study was a well conducted study which met it's primary endpoint. I agree that patient selection is vital with this combination, but it offers a real choice for patients

Name	[redacted]

Role	NHS Professional
Other role	
Location	England
Conflict	No
Notes	I do support availability of aflibercept for my colorectal cancer patients
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	I would like to support availability of aflibercept for selected group of patients

Name	[redacted]
Role	NHS Professional
Other role	
Location	England
Conflict	Yes
Notes	I have used aflibercept in the VELOUR clinical trial and in patients with colorectal cancer funded by the CDF (now Cancer Reference Group).
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	The decision not to recommend aflibercept is obtuse. Aflibercept is a unique technology in a sense that it is a not a monoclonal antibody, but a genetically engineered fusion molecule incorporating VEGF receptors 1 and 2 leading to a VEGF 'trap'. It binds VEF-A but unlike bevacizumab also VEGF-b and placental growth factor. Alflibercept incombination with FOLFIRI produces a prolonged survival because the survival curve is biphasic and a group of around 20% have survival of over 2 years. This is not seen with bevacizumab. It is reminiscent of ipilimumab where some patients get substantial benefit and this has not been taken account of.
Section 2 (The technology)	Aflibercept is unique technology, it is a soluble fusion molecule and represents a new chapter in applied genetically engineered targeted medicines
Section 3 (The manufacturer’s submission)	The manufacturers submission is well written. The time line of 15 years for survival projection is probably not reasonable. However the survival curve for VELOUR is biphasic and around 20% of patients get substantial benefit. The modelling of these curves needs to take into account this phenomenon.
Section 4 (Consideration of the evidence)	This is by and large reasonable but you must react to new evidence. Here because those patients progressing within 6 months of completing adjuvant therapy did so badly (actually harmed) I would not treat this group of patients. We have known that this group do badly since the ACCENT group published a retrospective analysis of around 10 000 patients relapsing at different periods after completing adjuvant therapy and this trial VELOUR, provides new evidence on this point. Doing this does improve the utility of aflibercept considerably. The other point is single agent irinotecan is really not used ay all in the NHS, is nearly always FOLFIRI
Section 5	no comment

(Implementation)	
Section 6 (Related NICE guidance)	TA 242 was very flawed because it really didn't review all the available RCT evidence for bevacizumab or the EGFR monoclonals. NICE technology and methods unravel when multiple trials need analysis.
Section 7 (Proposed date of review of guidance)	No comment

Name	[redacted]
Role	NHS Professional
Other role	
Location	England
Conflict	No
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	I don't understand the logic. FOLFIRI-Aflibercept is an effective and well tolerated regimen. It's at the very least non inferior to similar studies using Bevacizumab.
Section 2 (The technology)	I believe this makes the drug slightly cheaper than Bevacizumab
Section 3 (The manufacturer’s submission)	I think the clinical data speaks for itself. It is in my understanding cost beneficial over bevacizumab. I cannot follow the logic in the QALY or ICER calculations at all. For CDF purposes it is unlikely that maintenance therapy will be approved, what is the QALY / ICER using 12 cycles FOLFIRI-Af with no maintenance?
Section 4 (Consideration of the evidence)	There are defined groups of patients for whom a 3 month improvement in survival is possible, I am disappointed at the negative guidance. This drug, for certain patient groups, should be available via the NHS. We can discuss the patient groups I feel would benefit most