

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

Role	Healthcare Other
Other role	Skin cancer charity
Location	England
Conflict	
Notes	
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	Vemurafenib represents a major breakthrough in treatment for patients with metastatic melanoma, and is the second new melanoma treatment that NICE has not recommended. There have not been any major developments in the treatment of metastatic melanoma for decades and now there is a risk that neither of the two new treatments will be available on the NHS if the draft guidance is not changed. As a patient support charity, we consider this decision to be totally unacceptable if upheld. Patients with metastatic melanoma have a relatively poor prognosis and few other treatment options. NICE has recognised that vemurafenib is a "step-change in the management of malignant melanoma" and so it is important that patients can access this treatment. Major breakthroughs like this need to be available to patients on the NHS
Section 2 (The technology)	It is extremely disappointing that NICE is not recommending routine NHS funding for this new treatment. Although patients can currently get funding through the Cancer Drugs Fund, this has added uncertainty because the Fund operates differently in different parts of the country and it is not clear how funding for treatments will be secured after the Fund comes to an end in 2014
Section 3 (The manufacturer's submission)	The uncertainty that NICE has highlighted around the data on long-term survival is common to many new medicines when they are launched and have not yet been widely used beyond clinical trials. Patients with metastatic melanoma have a poor prognosis and few, if any, other options for treatment. NICE should not deny this group of patients access to a potentially beneficial new treatment on the basis of uncertainty. In addition, vemurafenib is only used in patients who test positive for the BRAF V600 genetic mutation, which means that only those patients who are more likely to benefit are offered treatment
Section 4 (Consideration of the evidence)	
Section 5 (Implementation)	
Section 6 (Proposed recommendations for further research)	
Section 7 (Related NICE guidance)	
Section 8 (Proposed date of review of guidance)	
Date	

Role	
Other role	MD/PhD, wife of a Stage IV Melanoma patient
Location	England
Conflict	
Notes	
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	Considering the recent discussion about the superiority of combined BRAF/MEK inhibition over sole BRAF inhibition- ASCO 2011 and 2012- this decision based on cost is truly disappointing.

Section 2 (The technology)	Missing: BRAF + MM vitally depends on BRAF activity. Blockage of the BRAF/MEK pathway is therefore sufficient to rapidly (usually within days) though only temporarily reduce massive tumor burden and symptoms in Stage IV Melanoma patients. In the context of novel forms of immunotherapy (such as Ipi, a-PD1), a targeted therapy like Vemurafenib has the potential to bridge the typical delay in a potentially long-lasting response to the former and thus represents an essential compound in the new era of Stage IV Melanoma therapy.
Section 3 (The manufacturer's submission)	
Section 4 (Consideration of the evidence)	As widely discussed in the medical community, e.g. ASCO 2012, successful treatment of Stage IV Melanoma with a chance of longer survival will depend on the correct combination of drugs belonging to different families- e.g. immuno- and targeted therapy. By evaluating every drug on its own- such as it happened for Ipilimumab previously and now Vemurafenib- will therefore deny the UK patient the chance to ever come into the benefit of such combined regime.
Section 5 (Implementation)	
Section 6 (Proposed recommendations for further research)	
Section 7 (Related NICE guidance)	
Section 8 (Proposed date of review of guidance)	
Date	

Role	
Other role	President of Melanoma Independent Community Advisory Board ECPC
Location	England
Conflict	
Notes	
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	1.1 The Committee was satisfied that vemurafenib met all criteria for being a life-extending, end-of-life treatment and that the trial evidence presented for this consideration was robust. Patients urge the committee to review its decision. FOR PATIENTS AND THEIR FAMILIES: Vemurafenib offers significant improvement in quality of life, PFS and OS, and no other existing standard of care provides this. Vemurafenib represents a real breakthrough. It should be recommended on the basis of existing scientific evidence as a life-extending end-of-life treatment drug. Melanoma patients desperately need "options" other than the existing standard of care. You should also consider that in the extension of life strategy of many patients we have seen that though vemurafenib might not be "the cure" it does not need to be "the end" - Often it acts as a "bridge" that allows them to wait or join a clinical trial testing a different strategy (e.g. immunotherapy combination of 2 targeted therapies, or surgery and radiotherapy) In the UK, if vemurafenib is rejected - now that Yervoy has been rejected - what are the real choices you are leaving for end-stage patients and their families?
Section 2 (The technology)	
Section 3 (The manufacturer's submission)	3.11 the manufacturer collected health-related quality of life data in the BRIM3 study using the functional assessment of cancer therapy-melanoma (FACT-M) questionnaire were not presented because completion rates were low. I would like to invite the members to consider the evidence of enhanced quality of life patients themselves can provide, this can be easily organized by patient organizations. Thanks to targeted therapy like this one patients can prolong their lives and fully continue to engage in active, productive lives, with minimal side effects that can be managed by dosage.
Section 4 (Consideration of the evidence)	4.2 The cross-over in this trial was something that patients wanted and fought actively for world-wide, how could we stand seeing a whole arm being "sacrificed"? Current phase III randomized trials need to be adapted for special cases like this where one arm is clearly showing an advantage. The psychological impact of maintaining phase III trial designs like this was considered unethical by patients and we were happy FDA took the decision it did. 4.7 The Committee thinks there was significant uncertainty about the magnitude and duration of the long-term survival benefit attributable to vemurafenib. The patient perspective they have one certainty : Â the quality of life extension obtained

	with vemurafenib offers an incomparable quality of during that period as short as it may be, which also should be taken into consideration.
Section 5 (Implementation)	
Section 6 (Proposed recommendations for further research)	
Section 7 (Related NICE guidance)	
Section 8 (Proposed date of review of guidance)	
Date	

Role	Public
Other role	Mother of Stage 1V melanoma sufferer on Zelboraf
Location	England
Conflict	
Notes	
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	There are patients in the US who have received Zelboraf for over two years with no sign of the drugs efficacy failing
Section 2 (The technology)	
Section 3 (The manufacturer's submission)	
Section 4 (Consideration of the evidence)	It would be helpful if this section which is very technical and difficult for lay people to understand were summarised in a much simpler form which would enable comment from the general public. Â Vemurafenib has been shown to extend life and improve the quality of that life. Â I cannot understand how this drug can be denied to sufferers many of whom are very young Â It is accepted that the patient group is small, you conclude that the extension of life is months not years so by definition this means the cost per person is relatively small
Section 5 (Implementation)	
Section 6 (Proposed recommendations for further research)	
Section 7 (Related NICE guidance)	
Section 8 (Proposed date of review of guidance)	
Date	

Role	Patient
Other role	Retired statistician and, most recently prior to retirement, Corporate Actuarial Manager at AXA Insurance
Location	England
Conflict	
Notes	
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	I have been treated with Verumafenib since 29th March 2012. My primary melanoma was diagnosed and excised in 1992. After a local recurrence in 1993, a wide area excision was carried out, and I was in remission from then until 2004 when, at age 59, I developed local secondaries on the thigh. A year later there was growth in the groin (lymphodectomy in 2005) and since then widespread metastasis in my left leg. In 2011 I had an ILI and two ILPs - the last of these in December 2011. The ILPs were somewhat successful, but by March 2012 there was CT evidence of tumour growth in my leg and also above the groin in the lower abdomen. At that stage my wife and I were fearing the worst, and watching 30 or 40 tumours growing visibly on my leg. I was prescribed vemurafenib. The results have been dramatic. The visible tumours had shrunk noticeably within a week, and after 4 weeks they had halved in size. Now, at 14 weeks, although still visible as pigmented areas about a quarter the original maximum size, they have become almost flat to the skin (from about 3cm circles 1cm proud. To be frank my wife and I feel that there is hope again. The tumours still appear to be receding.
Section 2 (The technology)	I have felt the full weight of the side effects, but I have to say that they have been very effectively managed with steroids (Prednisolone 10mg once a day, a variety of steroid based creams, and removal of various lumps with liquid nitrogen. Not very pleasant, but eminently bearable. I fail to understand why the verumafenib should not be halted pro tem until the tumours regrow - when it could start again. This would save money, and side-effects. Has this approach been adequately tested?
Section 3 (The manufacturer's submission)	It is difficult to comment professionally on the evidence, but my immediate thoughts are: 1. The sample of vmf patients is pretty small, and observed for a short period of time. 2. It is unclear how advance the cancer progression was in sample individuals. Although all were Stage 4, that presumably could cover advanced growths in major organs to relatively minor tumour growth elsewhere (as in my case). 3. I should make it clear that I completely approve of the QALY approach to decisions on use of medicines. 4. However, I think there could be a case for investigating the use of vmf in earlier states of progression.
Section 4 (Consideration of the evidence)	I have not been treated with dacarbazine, but can vouch for the ease of use of vmf (4.1). Unfortunately I am still suffering from severe side effects of my second ILP, but that aside I think that I would indeed have been able to start playing squash again (my measure of real life!) within a month of taking vmf had my leg not still been numb from the knee down. The major unknown, which would presumably have a large effect on calculation of extended life expectancy (and cost of QALY?) is the small sample size, and the absence of real data about long term survivorship. All credit to Roche for attempting virtuoso extrapolation of analogous data, but clearly the committee is right to regard it with some doubt. However, the right way to validate it would be to look again in five years time at those who have been treated in the meantime. As you observe, although the costs are very high, the numbers of suitable candidates is small - so the overall cost would be low. Maybe you should suck it and see for longer. I cannot emphasise too strongly that, for people who have reacted like me, it has been almost miraculous in restoring normality to life simply, and in very short order.
Section 5 (Implementation)	
Section 6 (Proposed recommendations for further research)	
Section 7 (Related NICE guidance)	Presumably it would help to have an adequate sample size to review. This should be achieved at least in part by prescribing the drug to a significant number of people in the meantime, even if you do not consider universal application to be appropriate.
Section 8	

(Proposed date of review of guidance)	
Date	

Role	Patient
Other role	Other
Location	
Conflict	
Notes	

Comments on individual sections of the ACD:

Section 1 (Appraisal Committee's preliminary recommendations)	In your documents you state: "The Committee ... concluded that vemurafenib, although not curative, is an effective treatment option for locally advanced or metastatic BRAF V600 mutation-positive malignant melanoma." "The Committee heard from the clinical specialists and accepted that vemurafenib is a step change in the management of advanced malignant melanoma and that there is a significant need for effective therapies in this patient population." Thus I find that the committee does already accept what I understand to be the facts about this treatment. Not only is Zelboraf a promising treatment for your citizens with melanoma (I am a patient in Canada), but approving it for widespread UK use would contribute to the body of knowledge that will fight this disease worldwide - via the data generated through use in the wider UK patient population. You recognize that this treatment is by no means experimental - its use will absolutely benefit your citizens today, and will assist the refinement of that treatment and related treatments for patients worldwide. Britain may have taken some hits in recent decades but can still be a world leader. Please approve Zelboraf.
Section 2 (The technology)	
Section 3 (The manufacturer's submission)	
Section 4 (Consideration of the evidence)	
Section 5 (Implementation)	
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Role	
Other role	Care Giver
Location	
Conflict	
Notes	

Comments on individual sections of the ACD:

Section 1 (Appraisal Committee's preliminary recommendations)	I have to disagree with the recommendation in section 1.1. A significant portion of the responses that have occurred have been extensive and durable, more so than IL-2. A Data also exist that suggests Vemurafenid in combination or sequenced with IPI may be a very effective treatment.
Section 2 (The technology)	
Section 3 (The manufacturer's submission)	

Section 4 (Consideration of the evidence)	Again, no consideration of vemurafenid in combination with existing IPI or emerging PD-1 inhibitors.
Section 5 (Implementation)	
Section 6 (Proposed recommendations for further research)	
Section 7 (Related NICE guidance)	
Section 8 (Proposed date of review of guidance)	
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Role	
Other role	Carer
Location	US
Conflict	
Notes	
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	Please reconsider your recommendations. My wife is alive today because she is on this drug. She has been taking Vemurafenib for 9 months. Makes no sense to me why you would not approve in your country.
Section 2 (The technology)	
Section 3 (The manufacturer's submission)	
Section 4 (Consideration of the evidence)	
Section 5 (Implementation)	
Section 6 (Proposed recommendations for further research)	
Section 7 (Related NICE guidance)	
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Role	
Other role	Patient
Location	US
Conflict	
Notes	
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	
Section 2 (The technology)	
Section 3 (The manufacturer's	

submission)	
Section 4 (Consideration of the evidence)	In 2009 I was diagnosed with metastatic melanoma in my lungs two large tumors 8.9 x 6.8 cm and 5.2 x 2.5 cm. I started Zelboraf on 3-March-2010 and in December 2010 PET scans showed no activity and tumor shrinkage of 98% and 85% respectively. (My doctor believes the remainder that shows on the CT scan is either dead or scar tissue.) I had scans on 18-June-2012 and everything remains stable. I wanted you to be aware that there are people who are long term Zelboraf responders.
Section 5 (Implementation)	
Section 6 (Proposed recommendations for further research)	
Section 7 (Related NICE guidance)	
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Role	
Other role	Patient
Location	US
Conflict	
Notes	Currently taking Zelboraf which has reduced a cardiac melanoma tumor.
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	Although this drug is not perfect, it is helping extend my life so that I can care for my 3 young children. My father died from malignant melanoma 2.5 years ago and he wouldve gladly taken the drug, even with side effects, if given the chance.
Section 2 (The technology)	
Section 3 (The manufacturer's submission)	I have found that side effects do lessen over time. Its sickening that because it was working so well they switched people over from. Dacarbazine to HELP them, now you are holding this against them.
Section 4 (Consideration of the evidence)	I agree it is too expensive. It is not right for Roche to charge so much.
Section 5 (Implementation)	
Section 6 (Proposed recommendations for further research)	
Section 7 (Related NICE guidance)	
Section 8 (Proposed date of review of guidance)	
Date	

Role	
Other role	
Location	England
Conflict	
Notes	I am currently taking the drug Vemurafenib as treatment for stage 4 Melanoma.
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's	

preliminary recommendations)	
Section 2 (The technology)	Before Vemurafenib the treatment options for Stage 4 Melanoma patients were limited. This new drug, suitable for use in approximately 60% of melanomas where the BRAF mutation is present, represents an effective treatment where before there were none without awful side effects (E.g. Interferon) that limited patients ability to get on with daily life. Vemurafenib may have side effects but these can be controlled with a combination of treatment and dose adjustment.
Section 3 (The manufacturer's submission)	
Section 4 (Consideration of the evidence)	Vemurafenib acts more quickly than the standard Dacarbazine treatment and is more effective but does not require patients to attend hospital to have the treatment administered because of its oral formulation. This allows patients to carry on their lives as normal, in my own case, this means continuing with working and being able to support my family financially as well as having an improvement in my health that allows me to enjoy my life much as I did before my diagnosis.
Section 5 (Implementation)	
Section 6 (Proposed recommendations for further research)	
Section 7 (Related NICE guidance)	
Section 8 (Proposed date of review of guidance)	
Date	

Role	Patient
Other role	
Location	US
Conflict	
Notes	To withhold access of this drug to late stage melanoma patients seems cruel. It is some patients last hope for some extra time with their loved ones. I would urge you to reconsider this matter as if it was one of your family members suffering from melanoma.
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Section 2 (The technology)	
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