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

Role	Patient
Other role	
Location	England
Conflict	no
Notes	I am an ordinary member of OcuMel UK which is a charity that supports ocular melanoma patients. I am an ocular melanoma patient.
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	1.1 "is recommended only in the context of research as part of a clinical study" Although ocular cancer is a melanoma the genetic nature and progression of the disease makes ocular melanoma distinctly different from cutaneous melanoma. And the response to treatments is distinctly different. Chemotherapy has no useful benefit in ocular melanoma. Ipilimumab is the only treatment which has been proven to work. Proven in trials in the US and Europe, excellent results have been shown in the UK and to my personal knowledge Ipilimumab has resulted in years of extra life for a number of patients that would surely have died much earlier without it. The numbers of metastatic ocular melanoma patients are so small that according to my understanding it will never be possible to complete a proper clinical study. And therefore according to this part of the committees recommendation ocular melanoma patients will never be given Ipilimumab. That cannot be correct and I challenge the assertion and the assumptions on which it was made, particularly the fact that no account at all has been taken of ocular melanoma and its particular differences from cutaneous melanoma.
Section 2 (The technology)	Re side effects: Although Ipilimumab has side effects they are typically very much less than other first line treatments. Nevertheless if this decision is upheld, and my disease metastasises I will be forced to take toxic chemicals such as dacarbazine (which are proven not to work in ocular melanoma) in order to access Ipilimumab - which very well might work. Notwithstanding the fact that the spread of metastatic uveal melanoma is often terrifyingly fast, and the time lost being forced to wait for a known useless treatment not to work could prove fatal. Personally I would not treat a dog in such a manner, and in my humble opinion to knowingly put a cancer patient in such a position is cruel and inhumane. Re costs: Simple: Just allow Ipilimumab 1st line for metastatic uveal melamona patients and immediately offset the considerable costs of putting these patients thru useless treatments.
Section 3 (The manufacturer's	I have read section 3 carefully. Although I am not a trained medical person I am intelligent enough to know that I can find

submission)	no mention anywhere of how this applies to ocular melanoma. Indeed I point out again that I find no mention at all of ocular melanoma anywhere in this document. I therefore conclude that Ocular Melanoma has not been taken into consideration in this report and I challenge the recommendation not to allow Ipilimumab as a 1st line treatment. Ipilimumab has been proven to work for ocular melanoma patients. It is licensed by the FDA and European agencies for 1st line treatment in unresectable metastic melanoma. It is the only drug which is known to be of benefit to metastatic ocular melanoma patients and it must be allowed to be used as a first line treatment for sufferers of this rare cancer.
Section 4 (Consideration of the evidence)	In section 4 the committee concludes that: "it could not be confident that the addition of dacarbazine had not enhanced the efficacy of ipilimumab first line" Dacarbazine is widely known to be completely ineffective in respect of metastatic ocular melanoma. Therefore this statement is not true in respect of my melanoma. The last paragraph clearly states the effectiveness of Ipilimumab and explains very well the need for it in certain patient groups. In my opinion ocular melanoma patients fall exactly into that group who should be given Ipilimumab as a first line treatment. Ocular melanoma and cutaneous melanoma are NOT the same and should not be treated the same in this decision. The decision to withdraw Ipilimumab as a 1st line option from all melanoma patients discriminates against metastatic ocular melanoma patients, and I request that metastatic ocular melanoma patients must be exempt from this generic blanket treatment of melanoma.
Section 5 (Implementation)	
Section 6 (Proposed recommendations for further research)	6 Generally: These considerations do not apply to metastatic ocular melanoma 6.2 The committee encourages further use 'patient sub groups, but because of the point I made earlier about the low numbers of patients with metastatic ocular melanoma no trial is ever going to be effective for my disease. 6.3 Re further research: It is already known that dacarbazine is totally ineffective in respect of metastatic ocular melanoma.
Section 7 (Related NICE guidance)	
Section 8 (Proposed date of review of guidance)	
Section 10 (Sources of evidence considered by	I suffer from the rare cancer Ocular Melanoma. I am disabled by my disease, and if it spreads I will become extremely disabled and die. I am represented by the Charity OcuMel UK. OcuMel UK have not been consulted in this process at all. I find

the Committee)	no mention of my disease in this document and I challenge the decision not to allow Ipilimumab as a first line treatment for previously untreated unresectable stage III or IV melanoma on a number of points which I have made above, and particularly the fact that this decision will be applied to me, but the specifics of my disease have not been taken into account in this process and they should have been.
Date	3/18/2014 10:54:00 PM

Role	other
Other role	Mother
Location	England
Conflict	no
Notes	I am the mother of a stage 4 patient who would undoutable be dead if she had not recieved Ipilumumab first line on compassionate grounds. Many friends of her's are now dead as they did not get treatment or waited so long for it that they had progressed too far in to the disease for Ipilimumab to be able to help them.
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	My daughter is continually worrying about how she will get funding for further treatment when requred.
Section 2 (The technology)	I need the guide lines to say that Occular Melanoma patients can have Ipilimumab first Line because there is no other licensed drug recognisedto be of benefit in stage 4 Occular Melanoma.
Section 3 (The manufacturer's submission)	Dacarbazine is known to have no beneficial effect for Occular Melanoma so Ipilimumab should be available. Why should patients be expected to use a drug known to be ineffective for Occular Melanoma.
Section 4 (Consideration of the evidence)	Having had Ipilimumab first line my daughter, some 4 years latter is well and enjoying a good quality of life. This should be available to all Occular Melanoma patients who are well enough to benefit. Which means they need proper treatment to be offer straight away, not just told we see how you get on over the next six months!
Section 5 (Implementation)	
Section 6 (Proposed recommendations for further research)	
Section 7 (Related NICE guidance)	Nice needs to recognise that Occular Melanoma needs a different approach to Melanoma.Treatment is not the same for both.8
Section 8 (Proposed date of review of guidance)	
Section 9	
Date	3/18/2014 9:14:00 PM

Role	Patient
Other role	
Location	England
Conflict	no
Notes	
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	As an Ocular Melanoma patient who has been advised that I am at high risk of developing metastatic disease this recommendation is devastating news. The issues we face as a patient group appear to have been overlooked in that the relatively small patient numbers mean that it is always difficult for traditional clinical trials to be conducted. There are very limited treatment options for secondary disease and I understand that Ocular Melanoma is chemo resistant to Dacarbazine and metastaic disease can progress very rapidly if left unchecked. With the knowledge that Ipilimumab has made a very real difference to some stage IV patients - albeit without formal 'evidence' the intuitive deduction that this is an effective treatment and consequently could be a 'breakthrough' treatment has seemingly been ignored. In my case this means that as a father with two young children my life could be 'sacrificed' instead of being provided the option to extend it for a material period.
Section 2 (The technology)	From an Ocular Melanoma perpsective I feel the provision of the technolgy to assist in building a profile on efficacy would be sensible.
Section 3 (The manufacturer's submission)	As alluded to alreadfrom an Ocular Melanoma perpsctive the challenge our particular patient group will face is small numbers to validate the useage.
Section 4 (Consideration of the evidence)	I understand that for ocular melanoma patients, the distinction between benefit depending on patients genetic (BRAF) mutation, or tumour load has not be considered which it clearly should be.
Section 5 (Implementation)	
Section 6 (Proposed recommendations for further research)	From an Ocular Melaoma perpsctive - as stated earlier given the small patient populations formal clinical trials are always a challenge. We do however know that dacrbazine is not effective. I would ask if Ocular Melanoma which is ditinct from cutaneous melanoma has actually been considered? Consigning a minority patient population to an early death would be wrong and notwithstanding the particular limitations due to the rarity of the condition our interests need to be recognised, failing that it could be argued that the current process is discriminating against Ocular Melanoma patients.
Section 7 (Related NICE guidance)	
Section 8 (Proposed date of review of guidance)	
Section 10 (Sources of evidence considered by the Committee)	Are the Committee able to approach the 3 UK eye centres and more importantly the grwing body of expertise in for instance Southampton University hospitals who have an interest in Ocular Melanoma patients in terms of secondary disease follow

	up?
Date	3/18/2014 8:27:00 PM

Role	other
Other role	Development Director
Location	England
Conflict	yes
Notes	We receive some of our funding for skin cancer awareness activities from a number of drugs companies, including the manufacturers of this technology.
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	Ipilimumab has proved to be a lifesaving treatment for some patients. Where life expectancy would be between six - nine months on average, when treated with ipilimumab some patients live many years longer. Furthermore, ipilimumab offers patients with the chance of quality survival. We hear from many clinicians who are incredibly frustrated at having to initiate their patients onto an ineffective treatment (dacarbazine) before they are able to offer them ipilimumab, which in their clinical opinion should often be given as a first line treatment. With the clinical community calling for this treatment to be made available as a first line option and with the quality survival it can offer some patients, we believe that NICE should reconsider the evidence available. Given the significant rise in the incidence rate of melanoma, it is vital now more than ever that the best possible treatment is available to patients at the right time. As the Appraisal Committee acknowledged, the current first line treatment for this type of advanced melanoma ? dacarbazine ? ?has never been shown to have survival benefit.? The clinical community is unified in this view and both clinicians and patients alike are very aware that this treatment is not effective. This delayed access to ipilimumab means that the patients are less likely to achieve stability in their condition or have the chance of quality survival. Skcin therefore believes that the summaries of clinical and cost effectiveness are not reasonable interpretations of the available evidence. Skcin is very disappointed that the Committee has provisionally recommended that patients must first use a treatment which is clinically recognised as having no survival benefit before they are able to access a treatment which is much more effective in some patients. We believe that money spent on treating these patients with dacarbazine is wasted because the treatment is not effective. Furthermore, whilst ipilimumab is more costly than dacarbazine, the only patients who would be able to receive it (if NICE approves it as a first line treatment) would otherwise still receive it as a second line treatment, should they live long enough.
Section 2 (The technology)	
Section 3 (The manufacturer's submission)	

Section 4 (Consideration of the evidence)	Skcin believes that the Committee should give more consideration to the evidence relating to ipilimumab and melanoma. It is important to consider that melanoma incidence has the biggest projected increase of any form of cancer. In the last 30 years, rates of melanoma in the UK have risen five-fold. In 2011, the British Journal of Cancer reported that malignant melanoma had the largest predicted rate of increase of cancers studied and added that it was set to rise by an estimated 52 per cent over the following 20 years. Indeed the study went on to predict that melanoma would become the fourth most common cancer in men and the fifth in women. Other findings state that over the next 25 years melanoma rates in the UK will have risen faster than any of the other top ten common cancers. Cancer ResearchUK also advise that more than 13,300 people (37 a day) are diagnosed with melanoma in the UK, young women appear to be most at risk. Â Like most cancers, skin cancer is more common with increasing age but melanoma rates are disproportionately higher in people aged under the age of 55. Indeed, melanoma is the 2nd most common cancer in young adults, with two young people being diagnosed a day.
Section 5 (Implementation)	
Section 6 (Proposed recommendations for further research)	We believe that ipilimumab has been clearly demonstrated as a highly effective treatment for BRAF-negative patients with advanced melanoma, which would be even more effective if it was given as a first line option. Indeed, the quality of life for patients with advanced melanoma who receive ipilimumab increases significantly when they receive the treatment earlier. Delaying access simply means that patients are more ill when they begin treatment, less likely to be well enough to receive the full course of ipilimumab and have less chance of achieving stability in their condition. The fact that melanoma disproportionately affects young people should also be considered more carefully. Many patients have families to look after and are of a working age. Often, they also contribute significantly to their local community. We believe that NICE should consider the cost to society of allowing these patients to deteriorate on dacarbazine before they are able to have an improved chance of survival with ipilimumab. Melanoma is a very common cancer which has extremely limited median survival time and therefore we believe that it warrants a degree of priority, without delays.
Section 7 (Related NICE guidance)	
Section 8 (Proposed date of review of guidance)	With significant rise in the incidence rate of melanoma, it is vital now more than ever that the best possible treatment is available to patients at the right time. As the Committee acknowledged, the current first line treatment ? dacarbazine ? ?has never been shown to have survival benefit.? The clinical community is unified in this view and both clinicians and patients alike are very aware that this treatment is not effective. This delayed access to ipilimumab means that the patients are less likely to achieve stability in their condition or have the chance of quality survival. Skcin therefore believes that the summaries of clinical

	and cost effectiveness are not reasonable interpretations of the available evidence. Skcin believes that NICE cannot wait until 2017 to review their decision to allow ipilimumab to be used as a first line treatment for advanced melanoma; it is vital that patients with advanced melanoma can have earlier access to ipilimumab now, where clinically appropriate, to improve their chances of quality survival. Skcin suggests that the Committee should act on the clinical evidence available and in line with clinical opinion & recommend for 1st line immediately.
Date	3/17/2014 9:01:00 PM

Role	Carer
Other role	
Location	England
Conflict	no
Notes	n/a
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	My spouse has Ocular (Uveal) Melanoma. This is very distinct from cutaneous melanoma, it behaves differently, has different genetics underlying it, and has a distinct disease pattern. It is a very rare melanoma (only 6 in 1 million people) Is the Appraisal Committee aware that recommendations made in the context of evidence about cutaneous melanoma may have significant adverse or negative consequences if applied to Ocular Melanoma? Specifically, there is evidence ipilimumab has benefits for some metastatic Ocular Melanoma patients. I would urge you to investigate evidence from the US and Europe. It is vital the guideline does not restrict OM patients from accessing ipilimumab only as part of a clinical trial. Because OM is so rare, there are very few clinical trials and the disease progression once metastasised is so quick that time is of the essence. In the time taken to recruit a trial the patient's disease burden will have progressed too much for any treatment to be any longer beneficial.
Section 2 (The technology)	I would urge the Committee in relation to my comments on Ocular Melanoma above, that the numbers of OM patients is so small that the costs involved in treating them with ipilimumab are likely to be marginal
Section 3 (The manufacturer's submission)	
Section 4 (Consideration of the evidence)	Please can the Appraisal Committee consider the unmet needs of Ocular Melanoma patients as a distinct sub-group of 'cutaneous melanoma' patients? There are some clear differences between ocular and cutaneous melanoma, but probably the two most relevant are 1) the absence of benefit from Dacarbazine in OM versus a small

	benefit (c.30%) in cutaneous melanoma and 2) the speed of progression in ocular melanoma, mostly due to the involvement of the liver in 90% of cases. It makes no sense for OM patients to have to be treated with dacarbazine as 'first-line' when there is no evidence of any benefit from it for these patients, when at least there is some evidence of benefit from ipilimumab. Why make OM patients go through dacarbazine as 'first line' when the speed of their disease progression means it would just make the chances of ipilimumab being of any benefit would be smaller?
Section 5 (Implementation)	
Section 6 (Proposed recommendations for further research)	is the committee aware that most of these research proposals are not relevant to Ocular Melanoma? No one in the rest of the world is using dacarbazine as first-line for OM, it has no benefit. Please investigate the evidence on this. BRAF is not a mutation relevant to OM. OM tumours however have a mutation in GNAQ or GNA11 (these are mutually exclusive) in 80% of cases. Please will the guideline NOT apply to Ocular Melanoma for all the reasons above. I believe such a guideline would harm Ocular melanoma patients and their families.
Section 7 (Related NICE guidance)	
Section 8 (Proposed date of review of guidance)	
Section 9 (Appraisal Committee members guideline representatives and NICE project team)	Please enquire of the Appraisal Committee members and NICE project team - how many have any detailed knowledge of rare cancers such as Ocular Melanoma? Has the committee and team researched the DIFFERENT characteristics of Ocular Melanoma in relation to cutaneous melanoma? Has the committee considered any evidence about Ocular Melanoma - with reference to scientific evidence, experienced clinicians and/or patients? has the committee and team considered any ADVERSE EFFECTS of applying this guideline to Ocular Melanoma patients?
Section 10 (Sources of evidence considered by the Committee)	The sources of evidence seem to be almost entirely general melanoma in nature. By this I mean CUTANEOUS MELANOMA Have you got any evidence about Ocular Melanoma specifically? I urge you to do so - the disease has distinct characteristics and many many differences from Cutaneous Melanoma. Therefore if this guideline applied to Ocular Melanoma, it may have bad consequences.
Date	3/17/2014 8:15:00 PM

Role	other
Other role	Founder and Key Worker
Location	England
Conflict	yes
Notes	BMS have assisted Melanoma UK in funding small projects.
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	Our response We would like to thank NICE for giving Melanoma UK the opportunity to respond to the Appraisal Consultation Document on ipilimumab as a first line treatment for advanced melanoma. On behalf of patients with advanced melanoma across the country, Melanoma UK strongly disagrees with the Committee?s provisional decision to only allow ipilimumab to be used as a first line treatment for advanced melanoma in clinical trials. This decision is deeply concerning for patients and clinicians and signals a step backwards in terms of the adoption of innovative treatments. We urge the Committee to reconsider the evidence and review this provisional decision.
Section 2 (The technology)	
Section 3 (The manufacturer's submission)	
Section 4 (Consideration of the evidence)	We do not believe there has been a reasonable interpretation of the cinical & Cost effectiveness evidence. Â The only 1st line treatment currently available for advanced melanoma patients who aren't BRAF pos,is dacarbazine, largely considered to be ineffective.Patients are rightly concerned that the committee is recommending such treatment which clinicians agree has no survival benefit as a 1st line option. This is wholly unsatisfactory for patients & against the weight of clinical opinion. Â Ipilimumab can make a real difference to quality of life and survival chances and patients struggle to understand why they can only access a more effective treatment, once the ineffective one has failed them. Â The same patients would receive the drug, but will likely be more ill with a higher burden of disease. Â To allow progression means the patient stands less chance of having the full course of treatment and therefore is less likely to achieve stability following the delay. Â We have spoken with patients, they know that to Â not have the treatment reduces their quality and puts strain on an already burdened NHS.
Section 5 (Implementation)	
Section 6 (Proposed recommendations for further research)	
Section 7 (Related NICE guidance)	
Section 8 (Proposed date of review of guidance)	
Section 10 (Sources of evidence	Melanoma UK believes that the Committee has failed to fully consider the effect that this decision will have on the patient

considered by the Committee)	population with advanced melanoma. Indeed, it is alarming to note that this disease disproportionally affects young people aged between 15 and 34. Melanoma is now the second most common cancer in that age group and the incident rate is rising significantly. To accurately reflect the value that this treatment could bring to the NHS if it was recommended as a first line treatment, it is important that NICE fully considers the value of appropriately treating patients within this age group in a timely manner. Given the extremely aggressive nature of the disease, the age profile of the patient pop becomes even more significant. Having a younger age profile means that patients are often of a working age and many have young families – for these patients the speed of effective treatment is invaluable. More average years of life are lost as a result of melanoma than almost any other tumour type (estimates suggest that, on average, patients lose 22 years). We believe that ipilimumab gives patients with this type of melanoma the best chance of achieving quality survival
Date	3/17/2014 3:17:00 PM

Role	Patient
Other role	
Location	England
Conflict	no
Notes	I am a statistical programmer in the pharmacuetical industry as well as an ocular melanoma patinet. Â I have not worked with this technology or for a sponsor associated with this technology
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	In order for a trial to demonstrate satisfactory results there is always a chance as a patient that you won't be randomised to the YERVOY treatment arm and hence even through a clinical trial you may not be exposed to this treatment which has shown clinical benefit. Â Also by reserving this as a second line treatment we are potenitally risking that the benefits seen may be affected by the baseline status i.e. a different Â metatastic baseline than the point at which mets first are presented. Also if there is enough demonstrated performance that point 1.2 from above seems relevant it seems unfair to limit this treatment from other's that could benefit.
Section 2 (The technology)	
Section 3 (The manufacturer's submission)	In the case of ocular melanoma, it appears here the trials eveidence is limited and hence I would urge more evidence to be presented on this branch of melanoma
Section 4 (Consideration of the evidence)	Although the evidence is not at present conclusive enough as demonstrated above to necessarily warrant first line cost effectiveness it appears we are still exposing patients to a first line treatment where "dacarbazine, although not proven to prolong survival, was a drug that had received a marketing authorisation for the treatment of metastatic melanoma " when a potential drug with some clinical benefit exists. Â As stated above this is also ensuring that some patients are not given

	YERVOY at their true baseline position.
Section 5 (Implementation)	
Section 6 (Proposed recommendations for further research)	It seems very relevant that more research is undertaken in order to validate first line treatment use. Â However I feel definition of those subgroups is important in understanding the effectiveness in more unusual patient groups (e.g. ocular melanoma)
Section 7 (Related NICE guidance)	Please pursue trials in the treatment of ocular melanoma as a subgroup.
Section 8 (Proposed date of review of guidance)	
Date	3/17/2014 2:37:00 PM

Role	Patient
Other role	
Location	England
Conflict	no
Notes	I was also a GP in NHS till I was told to go home and die in 2010. All advanced Â melanoma patients would benefit from first line Ipilimumab. Although it helps only a small percentage those patients get a sustained response in some cases measured in years. This can not be matched for any other chemotherapeutic option- 4 infusions over 12 weeks then no more treatment for Â 1 or 2 years and sometimes much more. Â This is so much better for the welfare of the patient than going and having a clinic attendance and an infusion and the side effects for as long as your tumour stays under control. Â So in effect you are facing side effects for the rest of your healthy life with regular infusions Â 2-3 weekly and then the decline when you progress come off treatment and die. In contrast those who respond to ipilimumab after 12 weeks leave chemotherapy clinics behind for a long time measured in years. Have the opportunity of returning to normal life. NICE/QUALY points fails to reflect the value of this. Â For those who don?t respond to Ipilimumab but get stable disease it is even more important that they are treated first line. I know this as I was treated first line in 2010. As I had very low levels disease (but a highly progressive sub type) instead of a steady decline to death the disease is held stable. For me this has meant instead of getting symptoms of my disease and dying in 6-12 months in 2010 I am still alive and symptom free. I still run 5miles a day. My friends in the clinic who received it second line alongside of me did not fare as well. They had heavy disease burdens and failed to complete the 4 infusions before their death. Who knows some of them might have had a similar response to me if they had received Ipilimumab earlier. For Braf negative patients there is only traditional chemotherapy which has very poor responses in skin melanoma. The subtype of melanoma Uveal melanoma has even poorer responses to chemo and no progress has been made in my disease for 50 years. It represents only 150 or so patients a year in England so too small for the necessary large

	trials need to prove evidence sufficient for NICE. Many years ago I begged with NICE to consider our unique position- we do not have the same possible treatments as skin Melanoma. NICE replied we are such a small group of patients it would not Â be economically viable to consider our disease. This has happened in this document. NICE has not considered the minority sub group of Uveal melanoma whose Â advanced disease presents and progresses differently to skin melanoma. (Augsberger et al 2009 Effectiveness of treatments for metastatic uveal melanoma19 Am J Ophthalmol; 148: 119?127.)) . Worldwide we are very small numbers. We were allowed Ipilimumab in 2010 when I received it on compassionate grounds. Â Two groups one in US and one in Europe reported on the outcomes retrospectively of Ipilimumab in uveal melanoma. The numbers were small. However it was in keeping with the response rate in skin melanoma10103 Kelderman S, van der Kooij MK, van den Eertwegh AJ, Soetekouw PM, Jansen RL, van den Brom RR, Hospers GA, Haanen JB, Kapiteijn E, Blank CU.(2013) Ipilimumab in pretreated metastastic uveal melanoma patients. Results of the Dutch Working group on Immunotherapy of Oncology (WIN-O). Acta Oncol. 52:1786-1788 1511 Kujala E, Makitie T, Kivela T. Very long-term prognosis of patients with malignant uveal melanoma.(2003). This is such a vast improvement . Bedikan (Â Bedikian AY, Legha SS, Mavligit G, Carrasco CH, Khorana S, Plager C, et al. Cancer 1995; 76:1665?1670.) did a large review of all chemotherapeutic agents they had used in uveal melanoma and found non measurable response rates ? Dacarbazine the alternative suggested by NICE Â had a response rate in their trials of less than 1% in the minority sub group of melanoma ? Uveal melanoma. (Melanoma of the eye.) It is unfair to use a comparison to Dacarbazine in Uveal Â melanoma ? it is used out of tradition without any good evidence of a response rate in Uveal melanoma. This is different to the situation in skin melanoma. There are usually no studies available for uveal melanoma patients in the UK . Â Our disease often progresses faster than skin melanoma as it spreads first by the blood. Â NICE fail to recognise our special needs as we are such a minority amounting to less than 5% of melanoma patients. The incidence of our disease it 6 per million population so approximately of those only 3 per million will go on and get advanced stage IV metastatic uveal melanoma. These tiny numbers mean there are rarely clinical trials available for Uveal melanoma. We are routinely excluded from melanoma trials. So we are left with using a drug that despite 30 years of use has not been shown to be beneficial and hoping to live long enough to get through that and so start Ipilimumab with higher tumour burdens . Thus even if we do get disease stability we will be damaged.

	I was very lucky to get Ipilimumab first line. It makes no sense to make patients wait . They will still want it some may die before they get the drug others will be less likely to respond . There are no 4 year survivors of metastatic uveal melanoma treated with Â Dacarbazine to match me.
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	It is unfair on the rarer subgroups like Uveal melanoma who have poor access to clinical trials. They are routinely excluded from melanoma clinical trials. They are left with no vialbe treatement options. It is wrong to force pateints into a clinical trial of an untried and tested drug when a licensed product exists.
Section 2 (The technology)	
Section 3 (The manufacturer's submission)	
Section 4 (Consideration of the evidence)	They failed to even consider the approx 150 metastatic uveal melanoma patients who are diagnosed in England each year. They excluded the minority .All advanced Â melanoma patients would benefit from first line Ipilimumab. Although it helps only a small percentage those patients get a sustained response in some cases measured in years. This can not be matched for any other chemotherapeutic option- 4 infusions over 12 weeks then no more treatment for Â 1 or 2 years and sometimes much more. Â This is so much better for the welfare of the patient than going and having a clinic attendance and an infusion and the side effects for as long as your tumour stays under control. Â So in effect you are facing side effects for the rest of your healthy life with regular infusions Â 2-3 weekly and then the decline when you progress come off treatment and die. In contrast those who respond to ipilimumab after 12 weeks leave chemotherapy clinics behind for a long time measured in years. Have the opportunity of returning to normal life. NICE/QUALY points fails to reflect the value of this.
Section 5 (Implementation)	Implementing this excludes the minority uveal melanomoa patients from any hope of modern treatment . Their disease progresses more quickly and rarely allows time for a second line treatment. There is no first line drug availble.
Section 6 (Proposed recommendations for further research)	There are very few trials for the rare sub group uveal melanoma in England. There is one trial occaisional but years pass without a trial being availble . It is
Section 7 (Related NICE guidance)	This is never an option for uveal melanoma as it does not have this gene defect
Section 8 (Proposed date of review of guidance)	
Section 9 (Appraisal Committee members guideline representatives and NICE project team)	There was no one with a clinical interest in uveal melanoma
Section 10 (Sources of evidence considered by the Committee)	OcMel Uk was not consulted about Uveal melanoma and Ipilimumab

Date	3/16/2014 9:13:00 PM

Role	Carer
Other role	
Location	England
Conflict	no
Notes	My father was diagnosed with ocular melanoma and feel the differences between ocular and cutaneous melanoma should be addressed in this guidance.
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	There are no clinical studies for people with ocular melanoma so where does this leave patients? Â Are you including all types of melanoma in this proposal. Â Doctors will need clarity or it could mean someone is denied treatment when it should be given to them. Â Ocular melanoma patients are finding this treatment is helping them but there has been no formal trial as it's such a rare cancer.
Section 2 (The technology)	
Section 3 (The manufacturer's submission)	These studies have not included ocular melanoma patients. Â Dacarbazine has a 1% success rate with Ocular Melanoma patients and so should not be given over a treatments which is helping more people.
Section 4 (Consideration of the evidence)	This makes no reference to the different types of melanoma, how they spread, how they react to current treatments. Â Ocular & Cutaneous are two very different conditions and so cannot be grouped together. Â Studies so far indicate that we need treatments to trigger the immune system such as ipilimumab.
Section 5 (Implementation)	
Section 6 (Proposed recommendations for further research)	We need some research to be carried out which includes ocular melanoma patients. Â However well this treatment is working for patients, it will never be given routinely until a study is carried out to prove it's effectiveness. Â Ocular melanoma patients need support from NICE as too many families are losing loved ones as we have done. Â My dad was not offered any treatment other than Decarbazine which only helps 1% of patients. He ended up having treatment in Germany which gave him more time. Â If he had been treated sooner in the UK, I may still have my dad with me or at least let him spend more time with us. Â Please don't look just at costs. Â Germany were swift & efficient in handling my fathers condition but it took us too long to realise the UK were not geared up to treating a rare cancer such as Ocular Melanoma. Â I miss my dad every moment of every day, so please help other families have less of a struggle to gain treatment.
Section 7 (Related NICE guidance)	
Section 8 (Proposed date of review of guidance)	
Section 10	Why are OcuMel UK not included on the above list of

(Sources of evidence considered by the Committee)	patient/carer groups. Â They are the only UK based charity helping people with Ocular Melanoma. We need clarity, does any of the above include Ocular Melanoma patients? As no trials exist, can I doctor give this treatment to their patients as a first line treatment if they believe it will help them?
Date	3/12/2014 10:26:00 PM

Role	Patient
Other role	
Location	England
Conflict	no
Notes	
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	I have ocular melanoma. I am requesting that NICE will recommend that Ipilimumab will be available for people with advanced metastisis even if they have not had any other treatment. Â This is because, if they delay using Ipilimumab until after they have tried something else, (and most other treatments are unsuitable) they might die before they are eligible for the drug. Ocular melanoma is different to cutaneous melanoma and, if there is advanced metasis, it Â is essential that it is treated as early as possible.
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)	
Section 8 (Proposed date of review of guidance)	
Date	3/12/2014 6:06:00 PM

Role	Patient
Other role	
Location	England
Conflict	no
Notes	Trustee of OcuMelUK charity.
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	This effectively means ocular melanoma patients will not be able to receive Ipilimumab without first having something else. Â Given ocular melanoma patients have no viable pre-treatment options they are then forced to have a drug which we know doesn?t work (eg dacarbazine) before they can have a drug which might work. Â This will cause dangerous, potentially fatal,

	delay especially for those with fast progression. Ocular melanoma is not the same as cutaneous melanoma
Section 2 (The technology)	
Section 3 (The manufacturer's submission)	There is a complete lack of evidence concerning ocular melanoma
Section 4 (Consideration of the evidence)	This seems to say that patients without the BRAF mutation have no viable treatment options and that if they have small volume disease they could benefit from receiving Ipilimumab first-line. Â This is the same situation for ocular melanoma patients, yet the committee has not separated out the recommendations for those with and without the BRAF mutation, or made a distinction on size.
Section 5 (Implementation)	
Section 6 (Proposed recommendations for further research)	How can the committee consider ocular melanoma patients to be within in this guideline when they have been completely ignored in every section?
Section 7 (Related NICE guidance)	
Section 8 (Proposed date of review of guidance)	
Section 10 (Sources of evidence considered by the Committee)	I would ask the Committee to consider/comment: 1. Has all of the relevant evidence been taken into account? For ocular melanoma patients? 2Â· Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence - for ocular melanoma? 3. Are the provisional recommendations sound and a suitable basis for guidance to the NHS? For ocular melanoma patients?
Date	3/11/2014 7:01:00 PM

Role	NHS Professional
Other role	Consultant in Medical Oncology
Location	England
Conflict	no
Notes	I am a clinician involved in care of patients with metastatic melanoma
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	Moving from 2nd line ipilimumab to 1st line ipilimumab means that patients who are currently denied ipilimumab (due to deterioration on futile 1st line Dacarbazine) would potentially benefit. Costs associated with futile Dacarbazine use would be avoided. The real-world cost of Ipilimumab is less than modelled because the actual number of cycles received is lower than originally estimated (due to treatment-suspension for toxicity, and early deaths)
Section 2 (The technology)	Moving from 2nd line ipilimumab to 1st line ipilimumab means that patients who are currently denied ipilimumab (due to deterioration on futile 1st line Dacarbazine) would potentially benefit. Costs associated with futile Dacarbazine use would be avoided. The real-world cost of Ipilimumab is less than modelled because the actual number of cycles received is lower than originally estimated (due to treatment-suspension for

	toxicity, and early deaths)
Section 3 (The manufacturer's submission)	Moving from 2nd line ipilimumab to 1st line ipilimumab means that patients who are currently denied ipilimumab (due to deterioration on futile 1st line Dacarbazine) would potentially benefit. Costs associated with futile Dacarbazine use would be avoided. The real-world cost of Ipilimumab is less than modelled because the actual number of cycles received is lower than originally estimated (due to treatment-suspension for toxicity, and early deaths)
Section 4 (Consideration of the evidence)	Moving from 2nd line ipilimumab to 1st line ipilimumab means that patients who are currently denied ipilimumab (due to deterioration on futile 1st line Dacarbazine) would potentially benefit. Costs associated with futile Dacarbazine use would be avoided. The real-world cost of Ipilimumab is less than modelled because the actual number of cycles received is lower than originally estimated (due to treatment-suspension for toxicity, and early deaths)
Section 5 (Implementation)	Moving from 2nd line ipilimumab to 1st line ipilimumab means that patients who are currently denied ipilimumab (due to deterioration on futile 1st line Dacarbazine) would potentially benefit. Costs associated with futile Dacarbazine use would be avoided.
Section 6 (Proposed recommendations for further research)	Collect real-world data on true number of cycles of ipilimumab received / patient
Section 7 (Related NICE guidance)	Urgent review of nivolumab data required
Section 8 (Proposed date of review of guidance)	
Date	3/11/2014 5:52:00 PM

Role	Patient
Other role	
Location	England
Conflict	no
Notes	
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	This means that ocular melanoma patients will not be able to have ipilimumab treatment as it is a rare cancer and there are no trials and pretreatment with other drugs has been shown to be a waste of time as they have been shown not to be effective.
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)	How can you include occular melanoma patients in your guidance when you have ignored them all the way through this appraisal. We need to be recognised as having different needs

	to other melanoma patients and to receive ipilimumab as a first line treatment.
Section 7 (Related NICE guidance)	
Section 8 (Proposed date of review of guidance)	
Date	3/10/2014 6:04:00 PM

Role	other
Other role	Professional rugby coach
Location	Wales
Conflict	no
Notes	Ocular melanoma patient
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	This treatment should be available to OM sufferers until consultants consider it appropriate to stop.
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)	
Section 8 (Proposed date of review of guidance)	
Date	3/5/2014 9:46:00 AM

Role	Patient
Other role	
Location	England
Conflict	no
Notes	I am a sufferer of OM (Ocular Melanoma) not CM (Cutaneous Melanoma). I am currently and fortunately, Stage I, i.e. no metastases as yet. The deliberations in this consultation document have not reflected the different genetic nature of OM vs CM and have not requested any input from the OM community. A large degree of the conclusions drawn will have a major impact on the potential use of Ipilimumab for Stage IV OM patients. Dacarbazine is known to offer no benefit for OM patients and would dramatically diminish the potential for Ipilimumab if that were to be used as second line of treatment. Please identify OM as a distinct and separate community and appraise it in that context.
Comments on individual sections of the ACD:	

Section 1 (Appraisal Committee's preliminary recommendations)	Advanced OM (Ocular Melanoma) has not been considered. It is genetically different to CM (Cutaneous Melanoma). The OM community is extremely small. Recruiting for statistically relevant trials would be difficult. Offering Ipilimumab as a second line form of treatment only after use of an acknowledged ineffective chemo drug such as Dacarbazine would a) delay the potential benefit of Ipilimumab b) increase the tumour burden c) decrease the period of effectiveness All leading to an accelerated and earlier death.
Section 2 (The technology)	No comment other than to say that it is extremely difficult to comment blindly without a knowledge of the actual price of Ipilimumab to the NHS and the separate cost of delivering it within the NHS when compared with alternative, ineffective drugs.
Section 3 (The manufacturer's submission)	There is a complete absence of any reference to Advanced Ocular Melanoma, which is genetically different to Cutaneous Melanoma. It is extremely unlikely that there will ever be any trials involving Advanced OM patients as the population is so small. For Advanced OM patients, comparing Ipilimumab with Dacarbazine, a universally acknowledged ineffective chemo drug, is an absolute nonsense.
Section 4 (Consideration of the evidence)	"The Committee understood that Ipilimumab would be valuable as a first-line treatment option for people with advanced (unresectable or metastatic) malignant melanoma." BRAF mutation is not relevant to Advanced Ocular Melanoma. Hence, Ipilimumab should be available as a first line treatment option to those patients. This should be made absolutely and unequivocally clear. Patients with Advanced Ocular Melanoma are classified as disabled. As such, this consultation document has failed absolutely to consider Advanced OM and the benefit to those patients of first line treatment with Ipilimumab and is discriminating against those disabled by the disease. You need simply, straightforwardly and rapidly to acknowledge Advanced OM as a relevant and genetically different sub-group eligible for first line use of Ipilimumab. People are dying.
Section 5 (Implementation)	
Section 6 (Proposed recommendations for further research)	It would be interesting to see some research on the existing evidence and relevance of this form of treatment for Advanced Ocular Melanoma as distinct from Cutaneous Melanoma which this consultation is focussed on.
Section 7 (Related NICE guidance)	
Section 8 (Proposed date of review of guidance)	
Section 10 (Sources of evidence	This report has obviously only considered Advanced Cutaneous

considered by the Committee)	Melanoma when reviewing the various issues with adopting Ipilimumab. No-one with any knowledge of Advance Ocular Melanoma was consulted. Why not?
Date	3/4/2014 11:10:00 PM

Role	Patient
Other role	
Location	England
Conflict	no
Notes	
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	As a ocular melonoma patient this means that i would have to under go treatments that are known not to work for ocular melonama suffers before having access to something that might work. This is unfair in the extreme.
Section 2 (The technology)	
Section 3 (The manufacturer's submission)	
Section 4 (Consideration of the evidence)	"The Committee heard from clinical specialists that for patients who are BRAF V600 mutation negative, dacarbazine is the only first-line treatment option currently available, and it has never been shown to have survival benefit. For patients who are BRAF V600 mutation positive, the Committee heard that vemurafenib was likely to remain the standard first-line treatment option especially in those with a high disease burden, but understood that ipilimumab would be valuable as a first-line option in approximately 20-30% of patients with small-volume indolent disease for whom vemurafenib could be reserved as rescue treatment later in the pathway.? It is essentially saying that patients without the BRAF mutation have no viable treatment options and that if they have small volume disease they could benefit from receiving Ipilimumab first-line. Â That is the same for ocular melanoma patients, yet the committee haven?t separated out the recommendations for those with and without the BRAF mutation, or made a distinction on size. Â You may decide to flag that up if you agree. "The Committee heard from clinical specialists that for patients who are BRAF V600 mutation negative, dacarbazine is the only first-line treatment option currently available, and it has never been shown to have survival benefit. For patients who are BRAF V600 mutation positive, the Committee heard that vemurafenib was likely to remain the standard first-line treatment option especially in those with a high disease burden, but understood that ipilimumab would be valuable as a first-line option in approximately 20?30% of patients with small-volume indolent disease for whom vemurafenib could be reserved as rescue treatment later in the pathway."

	It is essentially saying that patients without the BRAF mutation have no viable treatment options and that if they have small volume disease they could benefit from receiving Ipilimumab first-line. Â That is the same for ocular melanoma patients, yet the committee haven?t separated out the recommendations for those with and without the BRAF mutation, or made a distinction on size. Â You may decide to flag that up if you agree.
Section 5 (Implementation)	
Section 6 (Proposed recommendations for further research)	Where/when/how is ocular melanoma condition going to be incorporated into future trials as it doesnt appear thatr this hashappened before
Section 7 (Related NICE guidance)	
Section 8 (Proposed date of review of guidance)	
Date	3/4/2014 2:23:00 PM

Role	Patient
Other role	
Location	England
Conflict	no
Notes	I am an Allied Health Professionl
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	1.1 I suffer from a rare form of chorodial melanoma with rare clinical trials .I am not elligable for these trials due to not having had a biopsy,this reccomendation would deny me and other OM sufferers acess to treatment. I need the guidelines to say Ipilimumab is available through my local medical oncologist on discression not just for clinical trials.
Section 2 (The technology)	
Section 3 (The manufacturer's submission)	
Section 4 (Consideration of the evidence)	The committie has not considered occular melanoma for which there is no other effective treatment other than ippilimumab. Dicarbazide has only a 1% sucess rate in the treatment of OM.By recomending Ippilimumab is only used in the end stagees of the disease you have deprived OM sufferers from any effective treatment.I need the guidelines to allow OM sufferers access to Ipiliummab as a first line treatment.
Section 5 (Implementation)	
Section 6 (Proposed recommendations for further research)	Occular melanoma is very rare ,Clinical trials invloving OM patients are therefore rare by limiting Â use of Ippilimumab to trials you are depribing OM sufferers from an effective first line treatment.Ineed the guideines to say OM patients can have Ipilimumab as a first line treatment because there is no other

	effective treatment.
Section 7 (Related NICE guidance)	
Section 8 (Proposed date of review of guidance)	
Section 10 (Sources of evidence considered by the Committee)	There was no documented consultation with a representative from Occumel UK ,
Date	3/4/2014 2:23:00 PM

Role	NHS Professional
Other role	Consultant Plastic Surgeon
Location	England
Conflict	no
Notes	I am an Allied Health Professionl
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	As a group of health care professionals treating patients with advanced melanoma, we want the best treatments for patients at the best time. We agree that ipilimumab is an important part of the treatment for melanoma and so there is much debate about whether this should move from second line treatment to first line or even as an adjuvant treatment. We know that ipilimumab takes time to work and so it makes most sense to give it to fitter patients, with lower tumour burden, earlier in their treatment pathway. NICE has delayed the Committee discussion by one month after BMS requested to submit new evidence and analyses as part of the ACD consultation. We think this is a positive move and hope that this increased data will confirm that first line treatment with 3mg/kg ipilimumab as a single agent is the best treatment. Â Â Â Â Â Â Â Â Â Â Â Â Â Â Â Â Â Â Entered by Karen Leivers, Yorks & Humber Strategic Clinical Network supporting the Skin Network Site Specific Group on behalf of AJ Stephenson Chairman, North Trent Cancer Network Skin Site Specific Group
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)	
Section 8 (Proposed date of review of guidance)	
Section 10 (Sources of evidence	

considered by the Committee)	
Date	19/03/2014: 13:14