Bortezomib and Thalidomide for the first-line treatment of multiple myeloma
Janssen-Cilag's response the Appraisal Consultation Document

Thank you for the opportunity to comment on the Appraisal Consultation Document. Our tabulated comments need to be read alongside this cover letter.

1. Preliminary recommendations

1.1. Janssen-Cilag welcomes the fact that the committee has recognised that both thalidomide and bortezomib based combinations are more clinically effective and cost-effective than MP alone.

1.2. We note that the committee's draft recommendation is to restrict the use of bortezomib in combination with an alkylating agent and a corticosteroid to those people who are unable to tolerate or have contraindications to thalidomide. It is on this issue that we would like to focus our response. We will contend that this restriction is inappropriate because it has relied heavily on an assessment report, which is flawed by the omission of key data relevant to and within the scope of this appraisal.

1.3. Before expanding on our main point, we would first like to comment briefly on the wording in section 1 of the ACD. Our interpretation is that the committee's intention was to make bortezomib containing regimens available as an option for patients who are not appropriate for thalidomide, which is consistent with the language that was used in NICE's press release in which Dr Longson states '....*for those people who are unable to take thalidomide, bortezomib was considered an appropriate and cost effective treatment option*'[1]. In our view, the current ACD wording, which defines the group in terms of '*intolerant or contraindicated*', does not adequately convey this intention. Our concern is that unless physicians could prove that the patient has a definitive contraindication or clear evidence of intolerance, people will fall into a significant 'third' group. As a consequence they will be disadvantaged as they will only have the option of receiving MP. This is inequitable and would not be an optimal use of NHS resources.

We appreciate that this 'third' group is somewhat heterogeneous but would include, for example, people who are unsuitable for thalidomide because of co-morbidities e.g. thromboembolic risk, specific disease features such as high risk cytogenetics or patient characteristics. A better terminology would be to define them as 'not considered appropriate for thalidomide'. We note a similar form of wording was used in section 1 of the recent Topotecan NICE guidance (TA 184), where the committee recommended it as an option where retreatment with a first line agent was '*not considered appropriate*'.

[1] http://www.nice.org.uk/newsroom/pressreleases/DraftGuidanceBortezomibThalidomideMultipleMyeloma.jsp

2. Evidence basis for the preliminary recommendations

2.1. The above comments are only relevant considerations if the committee were to accept that SHTAC's analyses were robust and constituted a sound basis for decision making. Our contention is that this is not the case and in our response below, we will demonstrate that the evidence synthesis developed by the SHTAC was flawed. This is because of the omission of key clinical trial data, which were within the scope of the appraisal and which provided data that is crucial in informing an unbiased evaluation of comparative effectiveness. We will demonstrate that the decision to restrict the use of bortezomib regimens to this aforementioned sub population is not supported by the clinical and cost-effectiveness results when all the available evidence is taken into account. Analyses which include all the relevant evidence clearly show that bortezomib is a cost-effective option for front-line patients who are unsuitable for high dose chemotherapy and a stem cell transplant as defined by the product license.

2.2. The relative cost-effectiveness of bortezemib and thalidomide is highly sensitive to the relative efficacy of the products in improving overall survival. These estimates of efficacy are properly derived from a full systematic review of the evidence and meta-analysis as specified in the NICE methods guide. One large registration study comparing VMP with MP was identified and both Janssen-Cilag and the SHTAC also identified one study comparing CTDa with MP and five studies comparing MPT with MP. However, Janssen-Cilag and the SHTAC differed in which evidence from these MPT studies was included in the assessment of efficacy. This difference in study inclusion is pivotal, as it results in estimates of relative cost-effectiveness varying from dominance of thalidomide (based on the SHTAC's approach) to both treatments being similarly cost-effective (based on Janssen-Cilag's approach).

For clarity we set out the differences in study inclusion below, as studies may be referred to differently by different parties.

Studies (alternative descriptions)	Janssen Cilag's evidence synthesis for survival	SHTAC's evidence synthesis for survival
Facon 2007 (IFM-99-06)	Included	Included
Hulin 2009 (IFM-01-01)	Included	Included
Palumbo 2008 (GIMMEMA)	Included	Excluded due to maintenance phase
Wijermans 2009 (HOVON, Wijermans 2010)	Included	Excluded due to availability only as abstract and maintenance phase
Gulbrandsen 2008 (NORDIC, Waage 2010)	Included	Excluded due to availability only as abstract and maintenance phase

2.3. With this in mind, we would be grateful if the committee would consider the following two major issues that we believe require their attention.

2.3.1. The approach to the evidence synthesis undertaken by the SHTAC was not systematic.

The NICE methods guide states that 'The analysis of clinical effectiveness should be based on data from all relevant studies of the best available quality…..' and that 'The process of assembling evidence for health technology assessment needs to be systematic. That is, evidence must be identified, quality assessed and, when appropriate, pooled using explicit criteria and justifiable and reproducible methods'. We contend that the SHTAC's evidence synthesis was not conducted in accordance with these principles. As described above Janssen-Cilag and the SHTAC identified the same five studies assessing the efficacy of MPT, however the SHTAC's approach to study inclusion for evidence synthesis was neither systematic nor justifiable. It is not scientifically valid to exclude critically important studies simply because they have only been published in abstract form, especially when it seems that no attempt has been made to obtain further details (Wijermans 2009 and Gulbrandsen 2008). As we indicated in our response to the assessment report, the investigators of both studies were willing to share further details on these studies, which have both now been published online in peer reviewed journals (Wijermans, 2010; Waage, 2010). In addition, there was an inconsistency in their approach in that the reviewers did seek and obtain additional information for another study that was also published in abstract form only (the MRC Myeloma IX trial). In accordance with NICE's principles therefore, failure to include the full relevant evidence base means that the evidence synthesis is open to selection bias and is not fit for purpose. Furthermore, our results presented below demonstrate that the inclusion of the relevant studies results in a significantly improved estimate of the cost-effectiveness of VMP compared to MPT.

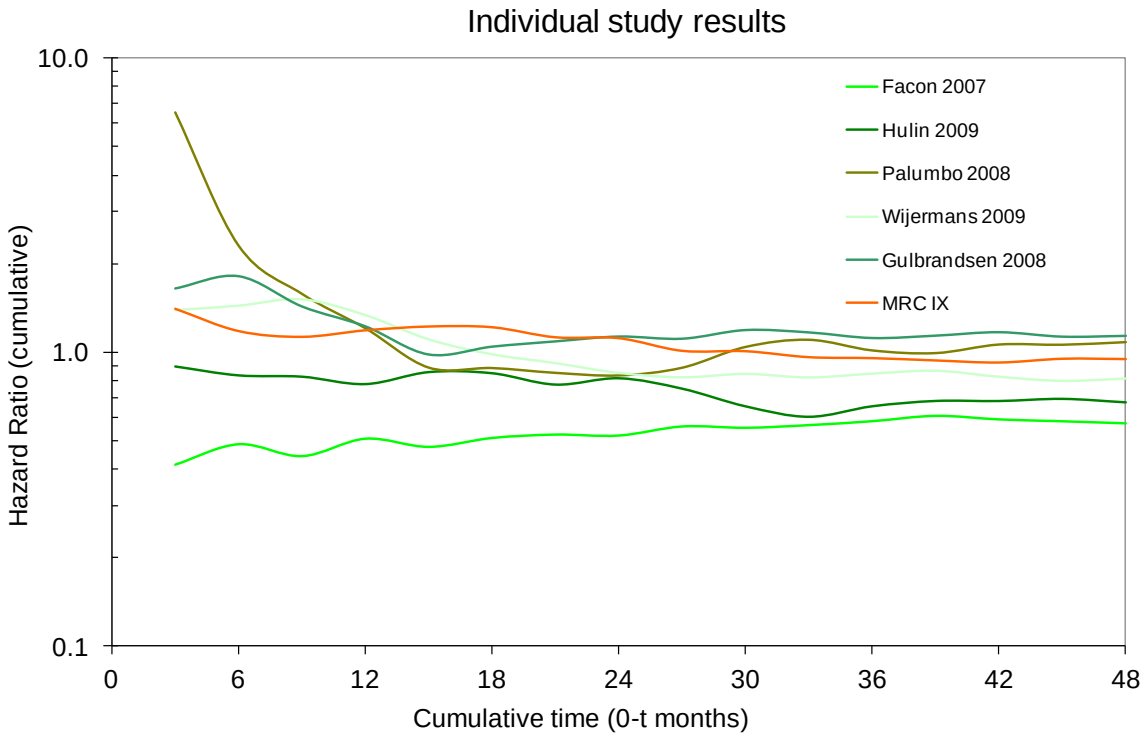
2.3.2. Exclusion of overall survival from studies including a 'maintenance' phase is inappropriate

The evidence base for MPT includes some studies that were designed such that thalidomide was administered to progression up to a maximum dosage period, whilst others were designed such that thalidomide was dosed to progression for a shorter period (induction), and then continued only in those reaching some defined indicator of benefit, normally without a maximum duration. Studies of this latter design have been termed 'maintenance' studies and have been excluded from consideration for overall survival in the ACD. There appears to be two justifications for this exclusion, which we address in turn below:

- Overall survival data from studies including a maintenance phase with thalidomide is not considered relevant to the decision problem, as these studies presumably do not reflect clinical practice or the licensed indication for thalidomide. However, we contend that the distinction of 'maintenance' and 'non-maintenance' studies is a false dichotomy given the length of maximum treatment that was allowed in the 'non-maintenance' studies. To illustrate this we can compare the Facon 2007 study, which allowed for treatment to progression of all patients up to a maximum of 72 weeks, with the Palumbo 2008 study which allowed for 24 weeks of treatment followed by maintenance. The reported median doses (217mg in the Facon study, not reported in the Palumbo study but the protocol dose was 100mg daily) and median durations of treatment (11 months in the Facon study and 8 months in the Palumbo study) are consistent with those specified by the SMPC (up to 200mg per day for a maximum number of 12 cycles of 6 weeks (or approximately 18 months)) and therefore relevant to the decision problem. A similar conclusion holds for the other excluded studies.

- During the open session of the first appraisal committee meeting it was suggested to the committee that 'maintenance' treatment may worsen overall survival outcomes and that this could explain the heterogeneity of results between those studies that included a maintenance phase and those which did not. Hence this would justify the exclusion of this data from the decision making process. If this was the case we would expect an increase in the heterogeneity between the 'maintenance' and 'non-maintenance' studies over the follow-up period as the maintenance treatment lengthened and its effect became more pronounced on overall survival outcomes. The data does not support this conclusion; in fact the greatest heterogeneity between the 'non-maintenance' and 'maintenance' studies in terms of overall survival is evident early in follow-up before initiation of the maintenance phase (see figure 1 below and Appendix 1).

Figure 1. Cumulative hazard ratio for overall survival in individual studies



Each point on the above graph represents the hazard ratio when the analysis is restricted to a shorter follow up time. That is to say the hazard ratio is derived using all deaths up to that point but excluding further follow up. It can be seen that in all studies excepting the Facon study (Facon 2007) the hazard ratio improves as follow up increases - this pattern is evident regardless of whether the studies included a maintenance phase or not. In the four studies including a maintenance phase, out of the six studies considered, an excess of deaths is seen in the thalidomide arm early in treatment, rather than later in follow up as would be expected if the poor outcome in these studies was due to resistance to subsequent treatments caused by prolonged use of thalidomide as stated in the ACD. Therefore the evidence does not suggest that continued maintenance treatment worsen survival outcomes, but that there is heterogeneity between studies in survival during the induction period.

The assumption that these studies should be excluded from the appraisal is therefore scientifically flawed.

2.4. Unfortunately the SHTAC's report does not present estimates of cost-effectiveness including all survival data whilst also correcting for their error regarding the number of bortezomib vials used in the VISTA trial. Therefore to provide the committee with cost-effectiveness estimates for this scenario we have adjusted our model to include the assumptions used by SHTAC for other parameters (see footnote of Table 1b). We have replicated the SHTAC's cost-effectiveness estimates for their base case and the

alternative scenarios as well as providing an ICER for this new scenario (table 1b, column entitled Scenario 4). The close agreement between the two models is demonstrated by comparing the results of Scenario 1 in the SHTAC and Janssen models in tables 1a and b. As reported in column 'Scenario 4' of table 1b, when all the available evidence is used and the correct number of doses is used, the cost-effectiveness ratio for VMP vs. MP is similar to that for MPT vs. MP, and the ratio between VMP and MPT (£14,426) is within the conventionally acceptable range. When the distribution of second line therapies is as observed in the VISTA trial, the ICER for VMP vs. MPT (£21,565) remains within the conventionally acceptable threshold (Scenario 5, Table 1b).

Table 1. Comparison of the ICERs estimated using the SHTAC's model and Janssen-Cilag's model

To ease the comparison of estimates between Tables 1a and b, we have numbered each scenario in Tables 1a and b.

1a. ICERs estimated by the SHTAC (as provided in the SHTAC's report or as presented at the 1st appraisal committee meeting)

Scenarios from SHTAC #	**Scenario 1 (SHTAC Base case)** - 52 vials of bortezomib - MPT studies included: Hulin and Facon*	**Scenario 2 (Scenario C in SHTAC report)** - 52 vials of bortezomib - Inclusion of 5 MPT studies **	**Scenario 3 (Scenario B in SHTAC report, corrected at 1st appraisal committee meeting)** - 31.5 vials of bortezomib - MPT studies included: Hulin and Facon*
MPT vs. MP			
Incremental cost	£11,207	Not available	£11,207
Incremental QALYs	1.22	Not available	1.22
ICER	***£9,174***	***£24,390***	***£9,174***
VMP vs. MP			
Incremental cost	£35,749	£35,749	£23,947
Incremental QALYs	1.20	1.20	1.26
ICER	***£29,837***	***£29,837***	***£18,996***
VMP vs. MPT			
Incremental cost	£24,542	Not available	£12,490
Incremental QALYs	-0.02	Not available	0.04
ICER	***VMP dominated by MPT***	***£32,739***	***£319,923***

*Meta-analysis of studies by Hulin and Facon performed by the SHTAC: HR=0.62 (95% CI 0.50-0.77)

** HR from the meta-analysis of the 5 MPT studies performed by Janssen-Cilag: HR=0.83 (95% CI 0.71-0.97)

All scenarios are based on the distribution of 2nd line therapies as per SHTAC's report

Data in blue are not available in the SHTAC's report. They come from the presentation 'cost-effectiveness' by Peter Jackson at the 1st appraisal committee meeting (slide 15).

Data in green were not explicitly presented in the SHTAC's report or in the slides presented at the 1st appraisal committee meeting but were deduced by Janssen-Cilag.

1b. ICERs estimated based on Janssen-Cilag's model using the SHTAC assumptions*

Replication of SHTAC scenarios using JC model with similar assumptions to SHTAC*	**Scenario 1** - 52 vials of bortezomib - MPT studies included: Hulin and Facon** - Distribution of 2nd line therapies as per SHTAC's report	**Scenario 2** - 52 vials of bortezomib - Inclusion of 5 MPT studies *** - Distribution of 2nd line therapies as per SHTAC's report	**Scenario 3** - 31.5 vials of bortezomib - MPT studies included: Hulin and Facon** - Distribution of 2nd line therapies as per SHTAC's report	**Scenario 4** *Scenario performed by Janssen-Cilag only:* -31.5 vials of bortezomib -Inclusion of 5 MPT studies*** -Distribution of 2nd line therapies as per SHTAC's report	**Scenario 5** *Scenario performed by Janssen-Cilag only:* -31.5 vials of bortezomib -Inclusion of 5 MPT studies*** -Distribution of 2nd line therapies as observed in the VISTA trial #
MPT vs. MP					
Incremental cost	£12,104	£8,706	£12,104	£8,706	£9,509
Incremental QALYs	1.32	0.55	1.32	0.55	0.55
ICER	***£9,138***	***£15,873***	***£9,138***	***£15,873***	***£17,337***
VMP vs. MP					
Incremental cost	£33,244	£33,244	£17,615	£17,615	£22,827
Incremental QALYs	1.17	1.17	1.17	1.17	1.17
ICER	***£28,510***	***£28,510***	***£15,107***	***£15,107***	***£19,576***
VMP vs. MPT					
Incremental cost	£21,140	£24,538	£5,512	£8,909	£13,318
Incremental QALYs	-0.16	0.62	-0.16	0.62	0.62
ICER	***VMP dominated by MPT***	***£39,733***	***VMP dominated by MPT***	***£14,426***	***£21,565***

*SHTAC assumptions: distribution of 2nd line therapies as per SHTAC's report page 126, only the costs of 2nd line treatments are included, no cost nor outcome for the 3rd line and subsequent treatment, cost of progression = £121.11 as per SHTAC's report page 127

**HR from the meta-analysis of studies by Hulin and Facon performed by the SHTAC was used: HR=0.62 (95% CI 0.50-0.77).

*** HR from the meta-analysis of the 5 MPT studies performed by Janssen-Cilag: HR=0.83 (95% CI 0.71-0.97)

For scenario 5 only: distribution of 2nd line therapies as observed in the VISTA trial – Table 33 page 62 of Janssen-Cilag's submission

2.5. Below we provide the committee with further reassurance that a worsening effect of maintenance treatment is not responsible for improved outcomes and cost-effectiveness of bortezomib vs. thalidomide when all studies are included. We have conducted additional analyses based on the same model as in Table 1b, where we have repeated our evidence synthesis whilst attempting to exclude any effect of maintenance on survival. To achieve this we have based our hazard ratio estimates for survival only on the early phases of these 'maintenance' studies, before maintenance could have any effect on outcomes. The results, based on the most conservative assumptions (see footnote # in Table 2), are presented in table 2 (NB/ as the length of 'induction' in the Gulbrandsen study was not available, two alternative plausible scenarios (24 and 32 weeks) are presented. These are based on the duration of the 'induction' period in the studies by Palumbo (24 weeks) and Wijermans (32 weeks)). These analyses show that the estimates of overall survival are insensitive to the inclusion (base case scenario) or exclusion (alternatives 1 and 2) of the maintenance phases of the three MPT studies (Wijermans 2009, Gulbrandsen 2008, Palumbo 2008). In each of the three scenarios the point estimate for the HR overall survival of MPT vs. MP is between 0.83 and 0.84 and the upper bound of the 95% CI MPT vs. MP is either close to or crossing 1. Details of these analyses are presented in Appendix 1.

Table 2. Impact of inclusion/exclusion of maintenance phase on the overall survival and ICER estimates (based on the most conservative assumptions #)

Scenarios (all based on 31.5 vials of bortezomib)	**SHTAC** MPT studies included: Hulin and Facon	**Base case** Whole duration of the 5 MPT studies included	**Alternative 1 (JC):** Exclusion of the maintenance phase of the 3 MPT studies ***– assumptions in footnote a***	**Alternative 2 (JC):** Exclusion of the maintenance phase of the 3 MPT studies ***– assumptions in footnote b***
OS : HR (95% CrI)*				
VMP vs. MP	0.653 (p=0.0008)**	0.68 (0.51-0.90)~	0.67 (0.51-0.88)~	0.68 (0.51-0.89)~
MPT vs. MP	0.62 (0.50-0.77)	0.83 (0.71-0.97)	0.84 (0.66-1.02)	0.83 (0.66-1.00)
CTDa vs. MP	Not available	0.94 (0.66-1.29)	0.96 (0.68-1.35)	0.94 (0.69-1.27)
Incremental OS (discounted – in years)				
VMP vs. MP	Not available	1.48	1.54	1.48
MPT vs. MP	Not available	0.67	0.63	0.67
CTDa vs. MP	Not available	0.21	0.14	0.21
VMP vs. MPT	Not available	0.81	0.92	0.81
VMP vs. CTDa	Not available	1.26	1.40	1.26
Incremental QALYs				
VMP vs. MP	1.20	1.17	1.21	1.17
MPT vs. MP	1.22	0.55	0.52	0.55
CTDa vs. MP	0.26	0.16	0.11	0.16
VMP vs. MPT	-0.02	0.62	0.69	0.62
VMP vs. CTDa	0.94	1.01	1.10	1.01
ICER based on the above HR vs. MP for OS				
VMP vs. MP	£18,996	£19,576	£19,008	£19,576
VMP vs. MPT	VMP dominated by MPT	£21,565	£19,676	£21,565
VMP vs. CTDa	Not estimated	£13,669	£12,830	£13,669

Most conservative assumptions include the following SHTAC's assumptions: only the costs of 2nd line treatments are included, no cost or outcome for the 3rd line and subsequent therapies, cost of progression = £121.11 as per SHTAC's report page 127. In addition the distribution of 2nd line therapies observed in the VISTA trial was used – Table 33 page 62 of Janssen-Cilag's submission

*Cumulative HR for OS at 48months for alternatives 1 and 2

** Mateos. ASH 2009

a: Alternative 1: length of the induction period. Hulin and Facon: whole duration; Palumbo = first 24 weeks; Wijermans = first 32 weeks; Gulbrandsen first *24 weeks*

b: Alternative 2: length of the induction period. Hulin and Facon: whole duration; Palumbo = first 24 weeks; Wijermans = first 32 weeks; Gulbrandsen first *32 weeks*;

~ HR for OS of VMP vs. MP are different because each result comes from a different run of the model with solutions obtained by means of simulation in Winbugs.

2.6. We also note that the ACD concludes clinical equivalence of CTDa and MPT and therefore the outcomes of the Myeloma IX study are also relevant to the overall assessment of efficacy of thalidomide. Further comment on the handling of survival from this study is provided in the tabulated comments.

2.7. The ACD also rejects the cost-effectiveness of bortezomib vs. thalidomide due to the inclusion of differential second line therapy costs in the estimation of cost-effectiveness. These arguments are not justified. A lifetime time horizon has been adopted based on the NICE's methods guide to '*reflect all important differences in costs or outcomes between the technologies being compared*'. As the effect of second line therapies on outcomes are already incorporated into the overall survival estimates the cost of these second line therapies should be captured in the modelling. These costs are based on the differential use of second line therapies in the VISTA trial which was supported by clinical experts' opinion and NICE guidance for bortezomib (TA127) in the absence of published data. In addition the effect of these assumptions on estimates of cost-effectiveness supported by scenario analyses presented by both ourselves and SHTAC did not alter the conclusions. We discuss this issue further in the comment template. It may be argued that the extent of differential use should be limited to that seen in the study as it is this use which generated the observed effects. For that reason we have provided scenario 5 in table 2 which is based on the distribution of use of second line therapies observed in the VISTA trial.

3. In summary, Janssen-Cilag believes that when the appropriate clinical evidence base is considered, both bortezomib and thalidomide containing regimens are clinically effective and superior to MP, and are similarly cost-effective to each other. We therefore believe that it would be appropriate to recommend 1) both treatments as options for patients with front line multiple myeloma within the licensed indication and 2) for clinicians to have the ability to chose the treatment which best meets the needs of the individual.

References

Facon,T., Mary,J.Y., Hulin,C., Benboubker,L., Attal,M., Pegourie,B., Renaud,M., Harousseau,J.L., Guillerm,G., Chaleteix,C., Dib,M., Voillat,L., Maisonneuve,H., Troncy,J., Dorvaux,V., Monconduit,M., Martin,C., Casassus,P., Jaubert,J., Jardel,H., Doyen,C., Kolb,B., Anglaret,B., Grosbois,B., Yakoub-Agha,I., Mathiot,C., & Avet-Loiseau,H. (2007) Melphalan and prednisone plus thalidomide versus melphalan and prednisone alone or reduced-intensity autologous stem cell transplantation in elderly patients with multiple myeloma (IFM 99-06): a randomised trial. *Lancet*, **370**, 1209-1218

Gulbrandsen,N., Waage,A., Gimsing,P., Turesson,I., Juliusson,G., Abildgaard,N., Bjorkstrand,B., Carlson,K., Dahl,I.M., Forsberg,K., Knudsen,L.M., Lanng Nielsen,J., Mellqvist,U.H., Nesthus,I., Strandberg,M., Wisloff,F., & Fayers,P. (2008) A RANDOMISED PLACEBO CONTROLLED STUDY WITH MELPHALAN/PREDNISONE vs MELPHALAN/PREDNISONE/THALIDOMIDE: QUALITY OF LIFE AND TOXICITY. *13th Congress of the European Hematology Association*, p.84.

Hulin,C., Facon,T., Rodon,P., Pegourie,B., Benboubker,L., Doyen,C., Dib,M., Guillerm,G., Salles,B., Eschard,J.P., Lenain,P., Casassus,P., Azais,I., Decaux,O., Garderet,L., Mathiot,C., Fontan,J., Lafon,I., Virion,J.M., & Moreau,P. (2009) Efficacy of Melphalan and Prednisone Plus Thalidomide in Patients Older Than 75 Years With Newly Diagnosed Multiple Myeloma: IFM 01/01 Trial. *J.Clin Oncol.*

Mateos MV., Richardson PG., Schalg R., et al. Bortezomib Plus Melphalan–Prednisone Continues to Demonstrate a Survival Benefit Vs Melphalan–Prednisone in the Phase III VISTA Trial in Previously Untreated Multiple Myeloma After 3 Years' Follow-up and Extensive Subsequent Therapy Use. *Blood* (ASH Annual Meeting Abstracts) 2009 114: Abstract 3859 and recently fully published: *J Clin Oncol 28:2259-2266.*

Owen,R.G., Morgan,G.J., Jackson,H., Davies,F.E., Drayson,M.T., Ross,F.M., Navarro-Coy,N., Gregory,W.M., Szubert,A.J., Rawstron,A.C., Bell,S.E., Heatley,F., & Child,J.A. (2009) MRC Myeloma IX: Preliminary Results from the Non-Intensive Study. *XII International Myeloma Workshop*, p.79. Clinical Lymphoma & Myeloma.

Palumbo,A., Bringhen,S., Liberati,A.M., Caravita,T., Falcone,A., Callea,V., Montanaro,M., Ria,R., Capaldi,A., Zambello,R., Benevolo,G., Derudas,D., Dore,F., Cavallo,F., Gay,F., Falco,P., Ciccone,G., Musto,P., Cavo,M., & Boccadoro,M. (2008) Oral melphalan, prednisone, and thalidomide in elderly patients with multiple myeloma: updated results of a randomized controlled trial. *Blood*, **112**, 3107-3114.

Wijermans,P.W., Schaafsma,M., van Norden,Y., Ammerlaan,M., Sonneveld,P., Wittebol,S., Sinnegen,H., Huijgens,P., van Marwijk Kooy,M., & van der Griend,R. (2008) Melphalan prednisone versus melphalan prednisone thalidomide in induction therapy for Multiple Myeloma in elderly patients: first interim results of the Dutch Cooperative Group Hovon. *13th Congress of the European Hematology Association*.

Wijermans,P.W., Zweegman,S., van Marwijk Kooy,M., an der Griend,R., okhorst,H., Schaafsma,M., van Norden,Y., Ammerlaan,M., Wittebol,S., Sinnegen,H., & Sonneveld,P. (2009) MP versus MPT in Elderly Myeloma Patients: The Final Outcome of the Hovon-49 Study. *12th International Myeloma Workshop*.

Wijermans P. et al. Phase III study of the value of thalidomide added to melphalan plus prednisolone in elderly patients with newly diagnosed multiple myeloma.: the HOVON 49 study. J Clin Oncol. 2010. Published ahead of print on June 1, 2010 as 10.1200/JCO.2009.26.1610

Waage A. et al. Melphalan and prednisolone plus thalidomide or placebo in elderly patients with multiple myeloma. Blood 2010. Prepublished online May 6, 2010; DOI10.1182/blood-2009-08-237974

Waage A et al. MP versus MPT for previously untreated elderly patients with multiple myeloma: a meta-analysis of survival of 1682 individual patient data from 6 randomized clinical trials. Haematologica. 2010;95(s2): 235