IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

IQWiG Reports – No. 171

Addendum to Commission A13-06 (abiraterone acetate [new therapeutic indication])[1]

Addendum

Commission: A13-22
Version: 1.0
Status: 13 June 2013

[1] Translation of the document "Addendum zum Auftrag A13-06 (Abirateronacetat [neues Anwendungsgebiet])", (Version 1.0; Status: 13 June 2013). Please note: This translation is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

Publishing details

Publisher:
Institute for Quality and Efficiency in Health Care

Topic:
Addendum to Commission A13-06 (abiraterone acetate [new therapeutic indication])

Contracting agency:
Federal Joint Committee (G-BA)

Commission awarded on:
28 May 2013

Internal Commission No.:
A13-22

Address of publisher:
Institute for Quality and Efficiency in Health Care
Im Mediapark 8 (KölnTurm)
50670 Cologne, Germany

Tel.: +49 (0)221 – 35685-0
Fax: +49 (0)221 – 35685-1
E-mail: berichte@iqwig.de
Internet: www.iqwig.de

IQWiG employees involved in the addendum:[1]

- Volker Vervölgyi
- Corinna Kiefer
- Beate Wieseler

Keywords: abiraterone, prostatic neoplasms, benefit assessment

[1] Due to data protection regulations, employees have the right not to be named.

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List of abbreviations

Abbreviation	Meaning
ACT	appropriate comparator therapy
ADT	androgen deprivation therapy
AE	adverse event
BPI-SF	Brief Pain Inventory – Short Form
CI	confidence interval
CSR	clinical study report
FACT-P	Functional Assessment Cancer Therapy – Prostate
G-BA	*Gemeinsamer Bundesausschuss* (Federal Joint Committee)
IQWiG	*Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen* (Institute for Quality and Efficiency in Health Care)
HR	hazard ratio
HRQoL	health-related quality of life
MedDRA	Medical Dictionary of Medical Activities
MMRM	mixed-effects model repeated measures
PT	Preferred Term
RCT	randomized controlled trial
SAE	serious adverse event
SMD	standardized mean difference
vs.	versus

1 Background

On 28 May 2013 the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to conduct a supplementary assessment for Commission A13-06 (benefit assessment of abiraterone acetate [new therapeutic indication], [1]).

In the commenting procedure on the assessment of abiraterone acetate (hereinafter abbreviated to "abiraterone"), the pharmaceutical company (hereinafter abbreviated to "the company") submitted further data to the G-BA on 6 May 2015 going beyond the information in the dossier. These refer to data from Study COU-AA-302 (comparison of abiraterone + prednisone + conventional androgen deprivation therapy [ADT] and placebo + prednisone + ADT). The study was already contained in the company's dossier and was included as relevant by IQWiG in Assessment A13-06. However, on the basis of data presented by the company in the dossier, no data or hardly any evaluable data were available, particularly for the outcomes "health-related quality of life" (HRQoL) and "adverse events" (AEs). The data subsequently submitted mainly comprised new analyses of these outcomes from Study COU-AA-302.

The G-BA commissioned IQWiG with the assessment of the analyses subsequently submitted in the commenting procedure for Study COU-AA-302. In this context the data were to be assessed with regard to the question as to whether, under consideration of the analyses submitted by the company on HRQoL (response criterion), as well as on AEs, an added benefit of abiraterone regarding HRQoL is proven and uncertainties regarding harm have been dispelled.

In the following Chapter 2 the additional results for Study COU-AA-302 are presented and assessed according to the commission. The extent and probability of added benefit of abiraterone are then described under consideration of the analyses subsequently submitted.

The responsibility for the present assessment and the result of the assessment lies exclusively with IQWiG. The assessment is forwarded to the G-BA. The decision on added benefit is made by the G-BA.

2 Assessment

2.1 Selection of analyses for the benefit assessment

In its comment [2] the company, as proposed in Assessment A13-06 [1], presented on the one hand analyses of AEs on the basis of the time to first event. On the other, the company submitted mixed-effects model repeated measures (MMRM) analyses of HRQoL, measured with the Functional Assessment Cancer Therapy – Prostate (FACT-P) tool. Whereas only results per treatment cycle had been available for Assessment A13-06, as also suggested in Assessment A13-06, in the analyses subsequently submitted the mean values between treatment groups of Study COU-AA-302 were compared over the whole course of the study, so that an assessment of the total effect over the whole course of the study was possible.

In addition to the analyses of AEs and HRQoL described in the G-BA's commission, in the analyses presented by the company in the comment, information was available on change in the worst pain intensity score and pain interference score during the course of the study, in each case measured with the Brief Pain Inventory – Short Form (BPI-SF). As for the FACT-P, the company also compared mean values between the treatment groups over the whole course of the study for the BPI-SF. These outcomes were basically regarded to be patient-relevant and the questionnaire applied was viewed to be sufficiently valid. For this reason the analyses based on BPI-SF are additionally assessed in the present addendum.

For the analyses of AE outcomes presented in the comment, discrepancies were shown compared with the dossier [3] and the clinical study report (CSR) of Study COU-AA 302 [4,5] concerning the number of patients with events considered in the survival time analysis. The cause of these discrepancies could not be inferred from the available information in the comment and in the appendices to the comment. Besides the hazard ratio (HR) with the related confidence interval (CI), the comment provided information on the median time to event per group, as well as on the "events occurred" per group. It could not be inferred from the comment itself whether "events occurred" referred to the number of patients with events or the overall number of events. Only on the basis of the Kaplan-Meier curves provided in the appendix to the comment could it be inferred that this referred to the number of patients with an event. However, it is incomprehensible why these data in the comment deviate from the data on the number of patients with an event reported in the dossier and the CSR of Study COU-AA-302. According to the data in the comment, in part, more patients (but in some cases fewer) experienced an event than was reported in the CSR. This is also implausible because it can be inferred from the data that the analyses are based on the same data cut-off point. For the outcome "overall AE rate" the survival time analysis is based on a markedly lower patient number than the safety population of Study COU-AA-302. This approach is neither explained by the company nor is it comprehensible against the background of the same underlying data cut-off point. The discrepancies are presented in the following Table 1 for clarification.

Table 1: Comparison of data on "events occurred" in the comment and in the dossier and CSR of COU-AA-302

Outcome	**Data according to comment**	**Data according to dossier or CSR**
	Events occurred abiraterone / prednisone / ADT vs. placebo / prednisone / ADT[a] n/N	**Number of patients with at least one event abiraterone / prednisone / ADT vs. placebo / prednisone / ADT[a] n/N**
AEs	522/527 vs. 507/522	538/542 vs. 524/540
Severe AEs (CTCAE-Grade 3 and 4)	268/542 vs. 234/538	267/542 vs. 235/540
SAEs	199/542 vs. 163/539	188/542 vs. 146/540
Treatment discontinuation due to AEs	57/542 vs. 50/540	58/542 vs. 53/540
Fractures	-[b]	-[b]
Fluid retention / oedema	158/541 vs. 122/540	159/542 vs. 130/540
Ischaemic heart disease	26/542 vs. 20/540	25/542 vs. 20/540
Heart failure	12/542 vs. 2/540	12/542 vs. 2/540

a: Operationalization of the watchful waiting approach.

b: It was unclear for the AE "fractures" which operationalization was taken as a basis for the analysis conducted (see text); no reference value is therefore available from the dossier or CSR of Study COU AA-302. For this reason there is no presentation of results here.

ADT: androgen deprivation therapy; AE: adverse event; CSR: clinical study report; CTCAE: Common Terminology Criteria for Adverse Events; n: number of patients with an event; N: number of analysed patients; SAE: serious adverse event.

The numbers differ markedly, in particular for the outcomes "overall AE rate" and "serious adverse events" (SAEs). No statistically significant difference between treatment groups was shown for the outcome "SAEs" in the survival time analysis subsequently provided by the company; however, the lower limit of the CI lay only slightly below the null effect (HR 1.21; 95% CI [0.98; 1.49]). For this outcome it cannot be excluded that the result for statistical significance would change if the discrepancy of the reported numbers between the comment and the dossier and CSR was considered. However, an examination of the influence of discrepancies on the result is not possible on the basis of the survival time analyses.

Furthermore, under consideration of the discontinuation of study medication described in the dossier and the connected discontinuation of the observation of patients, the high number of patients still at risk at a certain time point presented in the Kaplan-Meier curves subsequently submitted by the company in the comment is not plausible. The company does not discuss this point in its comment, so that no information is available that could help solve these ambiguities.

In addition, for the outcome "fractures" it could not be inferred from the information in the comment which operationalization had been taken as a basis for the analysis conducted. In the

CSR of Study COU-AA-302, fractures were not separately analysed as AEs. It was thus unclear whether the results presented were based on a single Preferred Term (PT) according to the Medical Dictionary of Medical Activities (MedDRA) or on a compilation of several PTs defined post hoc.

In summary, the survival time analyses subsequently provided in the comment cannot be used, due to the unexplained discrepancies compared with the dossier and CSR of Study COU-AA-302, as well as to missing information on the operationalization of fractures, and are therefore not considered in the present assessment.

Ambiguities were also shown in the comment and related appendix with regard to the results subsequently provided on the outcomes “pain” and “HRQoL”. Firstly, it was unclear which data cut-off point the analyses were based on. Secondly, it could not be inferred from the information how many patients were actually considered in the analysis. The corresponding results table presented included data only on the number of randomized patients. However, it is improbable that all randomized patients were considered in the analysis, as data were not available for each patient at the start of the study and the number of patients decreased at each time point of observation. For the present assessment it was therefore assumed that the number of patients included in the analysis corresponded to the number of patients for whom values were available for the first time point of observation after the start of the study. Overall, with regard to the results for pain and HRQoL it was not assumed that the ambiguities described had a relevant impact on the result of the analysis, so that the data submitted were considered in the present assessment.

2.2 Risk of bias

Table 2 shows the risk of bias at study level (for reasons see Dossier Assessment A13-06 [1], as well as the risk of bias for results on the outcomes “worst pain”, “pain interference”, and “HRQoL”.

Table 2: Risk of bias at study and outcome level – RCT, direct comparison: abiraterone versus watchful waiting

Study		Outcomes		
	Study level	Worst pain (measured with BPI-SF)	Pain interference (measured with BPI-SF)	Health-related quality of life (measured with FACT-P)
COU-AA-302	l	h	h	h
BPI-SF: Brief Pain Inventory – Short Form; FACT-P: Functional Assessment Cancer Therapy – Prostate; h: high; l: low; RCT: randomized controlled trial				

The risk of bias at study level was low. The outcome-related risk of bias was rated as high for all outcomes considered in the present addendum.

The outcomes for BPI-SF and FACT-P were only recorded until the end of the treatment phase with the study medication. The study medication was continued until occurrence of progression. In the case of progression of disease, patients discontinued randomized treatment. In this context the proportion of patients who discontinued study medication or discontinued the study for other reasons was clearly higher in the placebo group than in the abiraterone group, so that the median treatment periods (and thus the observation period for these outcomes) were markedly different (13.8 versus 8.3 months). Because of the potential relationship between progression and HRQoL or pain it is questionable whether the assumption for an MMRM analysis of "missing at random" is fulfilled. An unbiased estimate of the treatment effect cannot therefore be assumed for the outcomes relating to BPI-SF and FACT-P. Further potential bias may be caused by the ambiguities described in Section 2.1 concerning the patient numbers considered in the analysis.

2.3 Results

Table 3 shows the continuous data on the analyses of pain (measured with the BPI-SF) and HRQoL (measured with the FACT-P).

Table 3: Results (continuous outcomes) on morbidity and quality of life – RCT, direct comparison: abiraterone versus watchful waiting

Study Outcome category Outcome	Abiraterone / prednisone / ADT			Placebo / prednisone / ADT[a]			Abiraterone / prednisone / ADT vs. placebo / prednisone / ADT[a]	
	N[b]	Values at start of study Mean (SE)	Mean values during observation period Mean[c] (SE)	N[b]	Values at start of study Mean (SE)	Mean values during observation period Mean[c](SE)	Difference in means[d] [95% CI]; P-value	Hedges' g[e] [95% CI]; P-value
COU-AA-302[f]								
Morbidity								
BPI-SF								
Worst pain	511	1.11 (0.08)	1.31 (0.06)	502	1.13 (0.08)	1.67(0.06)	-0.36 [-0.53; -0.19]; p <0.001	-0.26 [-0.38; -0.14]; p < 0.001
Pain interference	497	0.68 (0.06)	0.96 (0.05)	493	0.68 (0.06)	1.13 (0.05)	-0.17 [-0.31; -0.02]; p = 0.025	-0.15 [-0.27; -0.02]; p = 0.022
Health-related quality of life								
FACT-P								
Total score	513	123.10 (0.63)	123.64 (0.55)	507	123.23 (0.63)	120.83 (0.61)	2.81 [1.19; 4.42]; p = 0.001	0.21 [0.09; 0.34]; p < 0.001
Physical well-being	512	25.27 (0.13)	24.75 (0.12)	506	25.31 (0.13)	24.17 (0.13)	0.58 [0.24; 0.92]; p = 0.001	0.21 [0.09; 0.33]; p < 0.001
Social/family well-being	512	22.80 (0.17)	22.73 (0.15)	504	22.73 (0.17)	22.78 (0.16)	-0.05 [-0.48; 0.37]; p = 0.802	-0.01 [-0.14; 0.11]; p = 0.816
Emotional well-being	509	18.73 (0.12)	19.74 (0.11)	499	18.83 (0.12)	19.19 (0.12)	0.56 [0.24; 0.87]; p = 0.001	0.22 [0.09; 0.34]; p < 0.001
Functional well-being	509	21.52 (0.17)	21.61 (0.16)	499	21.59 (0.17)	20.90 (0.17)	0.71 [0.26; 1.17]; p = 0.002	0.19 [0.07; 0.32]; p = 0.002
FACT-G	513	88.11 (0.45)	88.34 (0.40)	506	88.17 (0.45)	86.42 (0.44)	1.91 [0.75; 3.08]; p = 0.001	0.20 [0.08; 0.33]; p = 0.001
Prostate cancer subscale	501	35.42 (0.21)	35.83 (0.19)	498	35.50 (0.21)	34.82 (0.21)	1.01 [0.45; 1.56]; p < 0.001	0.23 [0.10; 0.35]; p < 0.001

(continued on next page)

Table 3: Results (continuous outcomes) on morbidity and quality of life – RCT, direct comparison: abiraterone versus watchful waiting(continued)

Study Outcome category Outcome	Abiraterone / prednisone / ADT			Placebo / prednisone / ADT[a]			Abiraterone / prednisone / ADT vs. placebo / prednisone / ADT[a]	
	N[b]	Values at start of study Mean (SE)	Mean values over observation period Mean[c] (SE)	N[b]	Values at start of study Mean (SE)	Mean values during observation period Mean[c](SE)	Difference in means[d] [95% CI]; P-value	Hedges' g[e] [95% CI]; P-value
Trial Outcome Index	513	81.62 (0.48)	81.42 (0.42)	507	81.79 (0.48)	79.29 (0.46)	2.13 [0.91; 3.35]; p = 0.001	0.21 [0.09; 0.34]; p < 0.001

a: Operationalization of the watchful waiting approach.

b: Number of patients at the first observation time point (assuming that this is the number of patients considered in the estimate of mean values during the whole observation period); values at the start of the study may be based on different patient numbers.

c: Mean values (least square means) over the whole observation period from the MMRM model with the following explanatory variables: baseline value, treatment cycle, treatment, treatment-treatment cycle interaction (fixed effects) and patients (random effect).

d: Difference in mean values over the whole observation period from the MMRM analysis.

e: Institute's calculation from mean values over the whole observation period, the corresponding SEs, and the number of patients in the two groups.

f: The information on values at the start of the study are based on the 2nd data cut-off point (20 December 2011). No data were available on the data cut-off point used for the mean values over the course of the study as well as the effect estimates.

ADT: androgen deprivation therapy; BPI-SF: Brief Pain Inventory – Short Form; FACT-G: Functional Assessment Cancer Therapy - General; FACT-P: Functional Assessment Cancer Therapy – Prostate; MMRM: mixed-effects model repeated measures; RCT: randomized controlled trial; SE: standard error

Morbidity

Pain, measured with the BPI-SF

The BPI-SF comprises 4 questions on pain intensity, 2 on use of pain medication, and 7 on pain interference. In its comment the company subsequently submitted analyses firstly on the worst pain in the previous 24 hours (question 3 of the BPI-SF) and secondly on pain interference in the previous 24 hours (questions 9 A to G of the BPI-SF). These analyses were in each case predefined in the statistical analysis plan of Study COU-AA-302. Each question is rated by the patient on a scale of 0 (no pain or no interference) to 10 (strongest imaginable pain or complete interference). For pain interference, in each case a mean value is formed from the 7 questions. As displayed in Table 3, in the available analyses the mean values were compared between treatment groups over the whole course of the study.

Both with regard to the worst pain in the previous 24 hours and also with regard to pain interference the analyses subsequently submitted for Study COU-AA-302 in each case showed a statistically significant difference to the advantage of abiraterone versus watchful waiting. As no adequate responder analyses or scale-specific validated or established relevance criteria were available for the group difference, the standardized mean difference (SMD in the form of Hedges' g) was used in the assessment of relevance. In each case the 95% CI of the SMD did not lie completely below the irrelevance threshold of −0.2. An irrelevant effect could therefore not be excluded with certainty.

Overall, the analyses subsequently submitted in the comment provide no proof of an added benefit of abiraterone versus watchful waiting under continuation of conventional ADT for the outcomes "worst pain" and "pain interference", in each case measured with the BPI-SF. As pain is only recorded with the BPI-SF until progression of disease, the results exclusively describe this period.

Health-related quality of life measured with the FACT-P

FACT-P is a disease-specific instrument for measurement of HRQoL. It consists of the FACT-G, as well as a subscale specific to prostate cancer. The patients provide an answer to each of the 39 items on a 5-point Likert scale. The FACT-P has a total score that was mainly used for the assessment. As presented in Table 3, in the available analyses the mean values are compared between treatment groups over the whole course of the study.

Both with regard to the total score of the FACT-P and most of the subscales, the analyses subsequently submitted showed a statistically significant difference to the advantage of abiraterone versus watchful waiting. As no adequate responder analyses or scale-specific validated or established relevance criteria for the group difference were available, the SMD (in the form of Hedges' g) was used for the assessment of relevance. For the total score of the FACT-P and also for all subscales, the 95% CI of the SMD in each case did not lie completely above the irrelevance threshold of 0.2. An irrelevant effect could therefore not be excluded with certainty.

Overall, for HRQoL measured with the FACT-P, the analyses subsequently submitted in the comment provide no proof of an added benefit of abiraterone versus watchful waiting under continuation of the existing conventional ADT. As HRQoL is only measured with the FACT-P up to progression of the disease, the results exclusively describe this period.

Adverse events

As described in Section 2.1, the survival analyses subsequently submitted by the company for AE outcomes could not be used because of incomprehensible discrepancies in the data and were therefore not considered in the present assessment. Consequently, for the assessment of AEs, results are still only available that were already available in Dossier Assessment A13-06.

Subgroup analyses

The company provided no additional subgroup analyses in its comment. As a result, for the present benefit assessment of abiraterone, subgroup analyses for the relevant subgroup characteristics described in Assessment A13-06 are still only available for the outcome "overall survival".

2.4 Extent and probability of added benefit

The following text presents the derivation of the extent and probability of added benefit at outcome level, under consideration of different outcome categories and effect sizes. The methods used for this purpose are explained in Appendix A of Benefit Assessment A11-02 [6].

The approach for deriving an overall conclusion on added benefit based on the aggregation of conclusions derived at outcome level is a proposal by IQWiG. The decision on added benefit is made by the G-BA.

2.4.1 Assessment of added benefit at outcome level

The overall assessment of data presented in Section 2.4 of Assessment A13-06 [1] and Section 2.3 of this addendum provided in each case an indication of an added benefit (outcomes: "overall survival" and "severe pain measured by means of initiation of opiate therapy") of abiraterone versus the ACT (watchful waiting under continuation of existing conventional ADT). On the basis of these results the extent of the added benefit in each case was assessed at outcome level. The following tables (Table 4 and Table 5) represent an update of Tables 12 and 13 of Assessment A13-06, which were supplemented with the results considered in this addendum.

Table 4: Extent of added benefit at outcome level (benefit outcomes): abiraterone versus watchful waiting

Outcome	**Effect estimates [95% CI]** **P-value** **Time to event:[a] abiraterone / Prednisone / ADT vs. placebo / prednisone / ADT[b] (months)** **Probability[c]**	**Derivation of extent[d]**
Mortality[e]		
Overall survival	HR: 0.79 [0.66; 0.96] p = 0.015 Median: 35.3 vs. 30.1 Probability: "indication"	Outcome category: "survival time" $0.95 \leq CI_u < 1$ Added benefit; extent: "minor"
Morbidity		
Severe pain measured by means of initiation of opiate therapy[e]	HR: 0.71 [0.59; 0.85] p < 0.001 25% quantile[f]: 14.8 vs. 12.0 Probability: "indication"	Outcome category: serious/severe/late complications $0.75 \leq CI_u < 0.90$ Added benefit; extent: "considerable"
Worst pain (measured with BPI-SF)[g]	MD: -0.36 [-0.53; -0.19] p <0.001 SMD:[h] -0.26 [-0.38; -0.14] p < 0.001	Lesser benefit/added benefit not proven
Pain interference (measured with BPI-SF)[g]	MD: -0.17 [-0.31; -0.02] p = 0.025 SMD:[h] -0.15 [-0.27; -0.02] p = 0.022	Lesser benefit/added benefit not proven
Health-related quality of life		
FACT-P total score[g]	MD: 2.81 [1.19; 4.42] p = 0.001 SMD:[h] 0.21 [0.09; 0.34] p < 0.001	Lesser benefit/added benefit not proven

a: If applicable.
b: Operationalization of the watchful waiting approach.
c: Probability provided, if statistically significant differences or relevant effects exist.
d: Estimates on effect size were performed according to outcome category with different limits using the upper limit of the CI (CI_o).
e: 3rd data cut-off point (22 May 2012).
f: The median time to event could not be estimated in at least one treatment arm due to the high proportion of censored data. The 25% quantile provides the time at which the Kaplan-Meier estimate of the survival function falls below 75% for the first time.
g: No information provided on the underlying data cut-off point.
h: SMD in the form of Hedges' g for assessment of the relevance of the statistically significant difference. If the 95% CI does not lie completely below the irrelevance threshold of −0.2 or above the irrelevance threshold of 0.2, an irrelevant effect cannot be excluded with certainty.

ADT: androgen deprivation therapy; BPI-SF: Brief Pain Inventory – Short Form; CI: confidence interval; CI_u: upper limit of confidence interval; FACT-P: Functional Assessment of Cancer Therapy-Prostate; HR: hazard ratio; MD: mean difference; SMD: standardized mean difference

Table 5: Extent of added benefit at outcome level (harm outcomes): abiraterone versus watchful waiting

Outcome	**Effect estimates [95% CI]** **P-value** **Proportion of events:[a] abiraterone / prednisone / ADT vs. placebo / prednisone / ADT[b]** **Probability[c]**	**Derivation of extent[d]**
Adverse events[e]		
Overall rate AEs	No evaluable data available	Greater/lesser harm not proven
Severe AEs (CTCAE grades 3 and 4)[f]	RR: 1.06 [0.82; 1.37] p = 0.652 18.1% vs. 17.0%	Greater/lesser harm not proven
SAEs	No evaluable data available	Greater/lesser harm not proven
Treatment discontinuations due to AEs	IDR: 0.77 [0.53; 1.11] p = 0.160 58 (8.2) vs. 53 (10.7)[g]	Greater/lesser harm not proven
Fractures	No evaluable data available	Greater/lesser harm not proven
Fluid retention/oedema	No evaluable data available	Greater/lesser harm not proven
Ischaemic heart disease	IDR: 0.87 [0.49; 1.57] p = 0.655 25 (3.5) vs. 20 (4.0)[g]	Greater/lesser harm not proven
Heart failure	IDR: 4.20 [0.94; 18.76] p = 0.060 12 (1.7) vs. 2 (0.4)[g]	Greater/lesser harm not proven

a: Unless otherwise stated.
b: Operationalization of the watchful waiting approach.
c: Probability provided, if statistically significant differences exist.
d: Estimates on effect size were performed according to outcome category with different limits using the upper limit of the confidence interval.
e: 3rd data cut-off point (22 May 2012).
f: Severe AEs (CTCAE grades 3 and 4) within 3 months after start of study treatment.
g: Number of patients with event (n/100 patient years).
ADT: androgen deprivation therapy; AE: adverse event; CI: confidence interval; CTCAE: Common Terminology Criteria for Adverse Events; HR: hazard ratio; IDR: incidence density ratio; RR: relative risk; SAE: serious adverse event

2.4.2 Overall conclusion on added benefit

Table 6 summarizes the results considered in the overall conclusion on extent of added benefit.

Table 6: Positive and negative effects from the assessment of abiraterone versus watchful waiting

Positive effects	**Negative effects**
Indication of added benefit – Extent: “minor” (mortality: overall survival)	
Indication of added benefit Extent: “considerable” (morbidity, serious/severe symptoms/late complications: severe pain measured by means of initiation of opiate therapy	

On the basis of the available and evaluable results, exclusively positive effects remain in the overall assessment at outcome level. These consist of an indication of a minor added benefit in the outcome category “mortality” (overall survival) and an indication of considerable added benefit for an outcome in the category “serious/severe symptoms/late complications” (severe pain measured by means of initiation of opiate therapy). In the aggregation of these positive effects the data initially provide an indication of considerable added benefit of abiraterone versus watchful waiting under continuation of conventional ADT. For a large proportion of outcomes on harms, particularly SAEs, there are still no adequate analyses due to the ambiguities in the survival analyses subsequently submitted in the comment as described in Section 2.1; therefore still no final conclusion on harm can be drawn. Due to this fact, the downgrading of the probability of the added benefit of abiraterone to a “hint”, as performed in Assessment A13-06, is still effective.

In summary the data provide a hint of a considerable added benefit of abiraterone versus the ACT (watchful waiting under continuation of existing conventional ADT) for treatment of metastatic castration-resistant prostate cancer in adult men with asymptomatic or mild symptomatic course of disease after failure of ADT and for whom chemotherapy is not yet clinically indicated.

3 References

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