


**A prognostic index model for predicting overall survival in patients with metastatic castration-resistant prostate cancer treated with abiraterone acetate after docetaxel**


1Department of Medical Oncology, BC Cancer Agency, Vancouver, Canada; 2Janssen Research & Development, San Diego; 3Helen Diller Family Comprehensive Cancer Center, University of California San Francisco, San Francisco; 4Janssen Research & Development, Menlo Park; 5Department of Solid Tumor Oncology, Dana-Farber Cancer Institute and Harvard Medical School, Boston; 6Comprehensive Cancer Centers of Nevada, Las Vegas; 7Department of Oncology and Internal Medicine, Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College, New York, USA; 8Groupe Uro-Genitologie, Institut Gustave Roussy, University of Paris Sud, Villejuif, France; 9Johnson & Johnson Medical China, Shanghai, China; 10Tom Baker Cancer Center and University of Calgary, Calgary; 11Department of Medical Oncology, Princess Margaret Hospital and University of Toronto, Toronto, Canada; 12Drug Development Unit, Division of Cancer Therapeutics/Clinical Studies, The Institute for Cancer Research and Royal Marsden Hospital, Sutton, UK; 13Genitourinary Oncology Service, Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College, New York, USA

Received 19 June 2015; revised 25 November 2015; accepted 27 November 2015

**Background:** Few prognostic models for overall survival (OS) are available for patients with metastatic castration-resistant prostate cancer (mCRPC) treated with recently approved agents. We developed a prognostic index model using readily available clinical and laboratory factors from a phase III trial of abiraterone acetate (hereafter abiraterone) in combination with prednisone in post-docetaxel mCRPC.

**Patients and methods:** Baseline data were available from 762 patients treated with abiraterone–prednisone. Factors were assessed for association with OS through a univariate Cox model and used in a multivariate Cox model with a stepwise procedure to identify those of significance. Data were validated using an independent, external, population-based cohort.

**Results:** Six risk factors individually associated with poor prognosis were included in the final model: lactate dehydrogenase > upper limit of normal (ULN) [hazard ratio (HR) = 2.31], Eastern Cooperative Oncology Group performance status of 2 (HR = 2.19), presence of liver metastases (HR = 2.00), albumin ≤ 4 g/dl (HR = 1.54), alkaline phosphatase > ULN.

*Correspondence to: Dr Kim N. Chi, Department of Medical Oncology, BC Cancer Agency, Vancouver, BC, Canada V5Z 4E6. Tel: +1-604-877-6098; E-mail: kchi@bccancer.bc.ca

© Janssen R&D 2015. Published by Oxford University Press on behalf of the European Society for Medical Oncology. This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com.
(HR = 1.38) and time from start of initial androgen-deprivation therapy to start of treatment ≤ 36 months (HR = 1.30). Patients were categorized into good (n = 369, 46%), intermediate (n = 321, 40%) and poor (n = 107, 13%) prognosis groups based on the number of risk factors and relative HRs. The C-index was 0.70 ± 0.014. The model was validated by the external dataset (n = 286).

**Conclusion:** This analysis identified six factors used to model survival in mCRPC and categorized patients into three distinct risk groups. Prognostic stratification with this model could assist clinical practice decisions for follow-up and monitoring, and may aid in clinical trial design.

**Trial registration numbers:** NCT00638690.

**Key words:** castration-resistant prostate cancer, abiraterone acetate, prognostic, risk, survival

**introduction**

Prostate cancer is the second most common cancer and the fifth leading cause of cancer death in men worldwide [1]. Virtually, all patients with advanced prostate cancer respond to medical or surgical castration, but these therapies are not curative and the disease eventually progresses to metastatic castration-resistant prostate cancer (mCRPC) [2, 3]. Several available therapies improve outcomes for patients with mCRPC [4–14].

Abiraterone acetate (hereafter abiraterone) is a prodrug of abiraterone, an inhibitor of CYP17 that blocks androgen biosynthesis [15]. COU-AA-301 (clinicaltrials.gov identifier: NCT00638690) was a multinational, randomized, double-blind, phase III trial comparing abiraterone plus prednisone/prednisolone (hereafter prednisone) with placebo plus prednisone/prednisolone (hereafter prednisone alone) in patients with mCRPC progressing after docetaxel. Abiraterone–prednisone significantly prolonged overall survival (OS) compared with prednisone alone [6, 7]. Abiraterone in combination with prednisone is indicated for the treatment of patients with mCRPC and is considered standard of care [16].

The wide selection of life-prolonging agents for the treatment of mCRPC complicates clinical decision-making [4–13]. Prognostic models estimate risk for clinically significant disease-related morbidity or mortality [17], and can be important for stratification and patient selection in clinical trials. Many prognostic models for prostate cancer have focused on clinically localized disease, and those for mCRPC were developed before the introduction of newer therapies, or focus on markers that can be costly and more difficult to obtain, making them impractical for daily clinical practice [18, 19].

Recognizing the need for a prognostic tool that reflects outcomes from currently available treatments, we explored factors associated with OS in the abiraterone–prednisone arm of the COU-AA-301 study. We report on a tripartite model that defines a meaningful range of risk, based on factors that can be obtained rapidly in routine patient management.

**methods**

**patient population**

The study design and efficacy results of COU-AA-301 are published [6, 7]. Nineteen routinely available and readily assessable clinical and baseline laboratory factors were identified and included in the analysis. Data from 762 of 797 patients in the abiraterone–prednisone arm formed the basis for the modeling. Thirty-five patients with missing relevant baseline data were not included in the modeling. The model was applied to the 398 patients in the prednisone alone arm as a validation to test its discriminative ability in a cohort of patients not treated with abiraterone–prednisone. The external validation set consisted of data from 286 sequentially treated mCRPC patients from 11 centers in Canada who received abiraterone–prednisone as standard therapy after docetaxel. Baseline demographics and disease characteristics for the abiraterone–prednisone arm and the prednisone alone arm were well balanced. The Canadian validation cohort was generally similar, although this cohort had a greater percentage of patients with Eastern Cooperative Oncology Group performance status (ECOG PS) of 2 (36% versus 10–11%) and other apparent differences that reflect a non-clinical trial selected population (summarized in supplementary Table S1, available at Annals of Oncology online).

The review boards at all participating institutions approved the study, which was conducted according to the principles set forth in the Declaration of Helsinki and the Good Clinical Practice guidelines of the International Conference on Harmonisation. All patients provided written informed consent to participate.

**statistical analyses**

Distributions of OS were estimated by the Kaplan–Meier product limit method [6, 7]. Laboratory factors were dichotomized into high or low risk according to the lower and upper limits of normal (LLN and ULN, respectively) or median values. For non-laboratory parameters, the median values were used due to the skewed distribution observed. The factors were dichotomized for ease of interpretation of the results derived from the Cox regression model.

Selected clinically relevant baseline factors previously associated with prognosis were assessed for significant association with OS using a univariate Cox regression model. P ≤ 0.05 was required for inclusion in the subsequent stepwise selection procedure. A multivariate Cox regression model was then used with a stepwise procedure to identify the prognostic factors for OS with a significance level of 0.05 for entry into the model and 0.01 for removal of each factor from the model. The final model was determined based on the Akaike information criterion (AIC) and the model χ² score. The combination of the significance levels for entry and removal and the AIC/χ² score were used to derive a model that is limited to the factors that contribute most to the model. Finally, patients were categorized into risk groups based on the number of baseline risk factors, and the median OS was calculated for each group.

The final model was subjected to several validation steps (supplementary Figure S1, available at Annals of Oncology online). Internal validation of the predictive performance of the final model was assessed by a bootstrap resampling procedure [20]. Five hundred samples were generated randomly, with replacement from the original data (n = 762). Stepwise Cox regression was used in each sample, with the same selection criteria as the original model. The frequency with which each factor was selected in the resulting model was tabulated. Consistency between the most frequently selected factors and
those in the final model was assessed; the model was deemed internally consistent if the factors were common between the two models.

The parameter estimates for the final model were also validated by randomly generating 500 bootstrap samples from the original population for the final model. For each sample, a Cox regression model was employed to obtain the parameter estimates using the same factors selected in the final model. Summary statistics were computed and compared with the final model. After the final model was established, patients were assessed for the number of risk factors and categorized into good, intermediate or poor prognosis groups, according to the number of risk factors and the relative hazard ratio (HR). The concordance index (C-index) [21] was computed for the final model. A C-index (0.5 ≤ C-index ≤ 1) of 0.5 suggests no predictive discrimination power, while an index of 1.0 indicates perfect discriminatory power. The final model was applied to patients who received prednisone alone (n = 398) and to an independent, external dataset as validation. Statistical analyses were carried out using SAS® Version 9.2 (SAS Institute Inc., Cary, NC) and the receiver operating characteristic analysis was carried out using R Version 2.15.3 (Comprehensive R Archive Network).

results

univariate and multivariate analyses

Fifteen of 19 baseline clinical and laboratory factors were found to be significantly associated with OS (P ≤ 0.05) through a univariate Cox model and were advanced forward (Table 1). A multivariate Cox regression model with a stepwise procedure identified the following 6 of 15 adverse prognostic factors to be the strongest independent predictors of OS: lactate dehydrogenase (LDH), ECOG PS, presence of liver metastases, albumin, alkaline phosphatase (ALP) and time from start of initial androgen-deprivation therapy to start of treatment (Table 2). They were included in the final model. The C-index was 0.70 ± 0.014.

model checking and bootstrap validation

To avoid overfitting, the independent factors were limited to those that contributed most to the model based on the AIC and the model χ² score. Results from the best subset selection indicated that including additional risk factors was unlikely to improve the model’s predictability (supplementary Table S2 and Figure S2, available at Annals of Oncology online). The six risk factors were selected most frequently via application of the stepwise Cox regression procedure to the 500 bootstrap samples, suggesting robust internal consistency (supplementary Table S3, available at Annals of Oncology online).

risk grouping

Patients were categorized into three risk groups based on the number of baseline risk factors significantly associated with OS and similar HRs (relative to the good prognosis group). Different OS rates were found for each group (Table 3). Patients with zero to one risk factor were in the good prognosis category (n = 369, 46%); the median OS was 21.3 months. Patients with two to three risk factors were in the intermediate prognosis category (n = 321, 40%); the median OS was 13.9 months [HR = 2.3; 95% confidence interval (CI) 1.9–2.8]. Patients with four to six risk factors were in the poor prognosis category (n = 107, 13%), the median OS was 6.1 months (HR = 6.2; 95% CI 4.8–8.0) (Figure 1A and B). The 2-year survival probabilities were 42%, 14% and 4% for the good, intermediate and poor prognosis categories, respectively.

validation cohorts

The model was evaluated for its discriminative ability in patients in the COU-AA-301 study treated with prednisone alone and an external validation cohort. Of the 398 patients treated with prednisone alone, 193 (48%) were in the good prognosis category, the median OS was 19.7 months; 149 (37%) patients were in the intermediate prognosis category, the median OS was 8.7 months (HR = 3.1; 95% CI 2.4–4.1); and 56 (14%) patients were in the poor prognosis category (four to six risk factors), the median OS was 5.3 months (HR = 5.9; 95% CI 4.1–8.4) (Figure 1C and D). The C-index using the prednisone alone treatment arm was 0.72 ± 0.019.

### Table 1. Baseline clinical and laboratory factors assessed for inclusion in the model, and results from univariate analysis

<table>
<thead>
<tr>
<th>Baseline risk factor</th>
<th>P-value</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDH &gt; ULN (250 IU/l) versus ≤ ULN</td>
<td>&lt;0.0001</td>
<td>3.01 (2.51–3.60)</td>
</tr>
<tr>
<td>ECOG PS (2 versus 0–1)</td>
<td>&lt;0.0001</td>
<td>2.55 (1.98–3.28)</td>
</tr>
<tr>
<td>Liver metastases (present versus absent)</td>
<td>&lt;0.0001</td>
<td>2.53 (1.98–3.24)</td>
</tr>
<tr>
<td>ALP &gt; ULN (160 IU/l) versus ≤ ULN</td>
<td>&lt;0.0001</td>
<td>2.02 (1.69–2.41)</td>
</tr>
<tr>
<td>Hemoglobin ≤ LLN (12.5 g/dl) versus &gt; LLN</td>
<td>0.0001</td>
<td>1.76 (1.44–2.16)</td>
</tr>
<tr>
<td>Albumin ≤4 g/dl versus &gt;4 g/dl</td>
<td>0.0001</td>
<td>1.71 (1.43–2.04)</td>
</tr>
<tr>
<td>Presence of pain (BPI-SF item 3 ≥4 versus &lt;4)</td>
<td>0.0001</td>
<td>1.64 (1.38–1.96)</td>
</tr>
<tr>
<td>PSA &gt;131.4 ng/ml versus ≤131.4 ng/ml</td>
<td>&lt;0.0001</td>
<td>1.59 (1.33–1.90)</td>
</tr>
<tr>
<td>Visceral metastases (present versus absent)</td>
<td>&lt;0.0001</td>
<td>1.46 (1.21–1.75)</td>
</tr>
<tr>
<td>Start of androgen-deprivation therapy to initiation of abiraterone–prednisone (≤36 versus &gt;36 months)</td>
<td>&lt;0.0001</td>
<td>1.46 (1.21–1.76)</td>
</tr>
<tr>
<td>Prior radiation therapy (yes versus no)</td>
<td>0.0014</td>
<td>1.40 (1.14–1.72)</td>
</tr>
<tr>
<td>End of chemotherapy to initiation of abiraterone–prednisone (≤3 versus &gt;3 months)</td>
<td>0.0012</td>
<td>1.54 (1.12–1.61)</td>
</tr>
<tr>
<td>Radiographic progression (with or without PSA progression)</td>
<td>0.0061</td>
<td>1.31 (1.08–1.59)</td>
</tr>
<tr>
<td>Start of chemotherapy to initiation of abiraterone–prednisone (≤12 versus &gt;12 months)</td>
<td>0.0035</td>
<td>1.30 (1.09–1.56)</td>
</tr>
<tr>
<td>Prior duration of docetaxel treatment (≤6 versus &gt;6 months)</td>
<td>0.0101</td>
<td>1.27 (1.06–1.52)</td>
</tr>
<tr>
<td>Gleason score (≥8 versus &lt;8)</td>
<td>0.1653</td>
<td>1.14 (0.95–1.38)</td>
</tr>
<tr>
<td>Bone and soft-tissue metastases (present versus absent)</td>
<td>0.0661</td>
<td>1.19 (0.99–1.43)</td>
</tr>
<tr>
<td>Age (≥69 versus &lt;69 years)</td>
<td>0.2722</td>
<td>0.91 (0.76–1.08)</td>
</tr>
<tr>
<td>Prior prostatectomy (yes versus no)</td>
<td>0.1576</td>
<td>0.88 (0.74–1.05)</td>
</tr>
</tbody>
</table>

ALP, alkaline phosphatase; BPI-SF, Brief Pain Inventory-Short Form; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; LDH, lactate dehydrogenase; LLN, lower limit of normal; PSA, prostate-specific antigen; ULN, upper limit of normal.

*Factors with P-values >0.05 were excluded from modeling.
patients was 0.69 ± 0.023.

respectively (Figure 1E and F). The groups, the median OS was 16.2 months (relative HR = 1.9; 95% CI 1.3–2.9) and 8.2 months (relative HR = 4.1; 95% CI 2.7–6.4), respectively (Figure 1E and F). The C-index using the 286 patients was 0.69 ± 0.023.

The external validation cohort was an independent cohort of 286 patients with mCRPC who were sequentially treated in a routine clinical care setting with abiraterone at 11 centers in Canada. Sixty-three patients (22%) were categorized as having a good prognosis, 146 patients (51%) an intermediate prognosis and 77 patients (27%) a poor prognosis. Analysis of the validation set confirmed the ability of the model to prognosticate for OS: for the good prognosis group, the median OS was 23.9, and for the intermediate and poor risk groups, the median OS was 16.2 months (relative HR = 1.9; 95% CI 1.3–2.9) and 8.2 months (relative HR = 4.1; 95% CI 2.7–6.4), respectively (Figure 1E and F). The C-index using the 286 patients was 0.69 ± 0.023.

### discussion

A prognostic index model was developed for post-docetaxel mCRPC using six factors that are highly associated with OS. The factors are available during routine patient treatment and enable patients to be categorized into three distinct risk groups (poor, intermediate and good prognosis). The model was validated with an external cohort of 286 patients treated with abiraterone–prednisone outside of a clinical trial and, notably, the model enabled similar stratification of the prednisone alone group. The diversity of the patient populations studied suggests that our findings are generalizable. Ravi et al. [22] have provided further external validation of the model by applying the prognostic index to an independent cohort of 94 patients treated with abiraterone–prednisone after docetaxel [C-index = 0.71 (95% CI 0.60–0.80)].

Applications of the model include the homogenization of the risk of death of patients to be enrolled in clinical trials and may be a useful tool in addition to treatment guidelines to help physicians determine appropriate follow-up and monitoring of patients with poor prognosis. The St Gallen conference guidelines recommend baseline examinations that measure the readily available factors that were included in our analysis. Some factors, such as duration of initial androgen-deprivation therapy and established prognostic factors, like hemoglobin, LDH and ALP, could potentially aid in prognostic stratification of patients with mCRPC, but their value in guiding treatment decisions is not well established [23]. Prospective studies are needed to determine the utility of the model for selecting therapies for patients with mCRPC and poor prognostic factors.

We purposefully developed this model using continuous variables dichotomously and weighting each risk factor equally in order to facilitate ease of use in the clinic. Prognostic models employing an index design similar to that developed here have seen widespread application in patients with metastatic renal cell cancer to classify patients into prognostic risk groups and in patients with non-Hodgkin’s lymphoma to classify risk of death, complete response and relapse risk [24, 25]. These prognostic indices have evolved over time to incorporate changes in treatment and contemporary outcomes [26, 27]. Armstrong et al. [28] and Halabi et al. [29, 30] developed prognostic nomograms in the post-docetaxel and first- and second-line chemotherapy mCRPC settings, and identified several similar pretreatment clinical prognostic factors that are associated with survival. More recent studies of docetaxel for mCRPC report greater survival than previous studies; however, these do not account for the introduction of recent life-prolonging therapies. Other prognostic factors warranting further study include bone-associated biomarkers [31], bone-specific ALP and urinary N-telopeptide, although these factors are not usually obtained in routine practice [28, 32–34]. Enumeration of circulating tumor cells with the Veridex system [19] and of androgen levels as determined by ultrasensitive assays have also been identified as independently prognostic in patients with mCRPC treated with abiraterone–prednisone [18]; these tests were not included in the development of this model because they are not routinely carried out or widely available.

### conclusion

We have developed a contemporary prognostic index model, composed of six routinely available and readily assessable factors, that categorizes patients with mCRPC treated with abiraterone–prednisone into distinct risk groups. Further external...
validation of our model is required. This model could be useful in clinical practice to aid in the determination of patient prognosis so that follow-up and monitoring may be planned accordingly, and may aid in patient stratification in clinical trials.

acknowledgements

Presented in part at the 49th American Society for Clinical Oncology Annual Meeting, Chicago, IL, 31 May–4 June 2013.
Writing assistance was provided by Lashon Pringle, PhD, of PAREXEL and was funded by Janssen Global Services, LLC.

funding
This work was supported by Ortho Biotech Oncology Research & Development, unit of Cougar Biotechnology (now Janssen Research & Development). No grant number is applicable.

disclosure
KNC has served as a consultant/advisor to Amgen, Astellas Pharma, Bayer, ESSA, Janssen Pharmaceuticals, Lilly/ImClone, Sanofi and Takeda; has received honoraria from Astellas Pharma, Janssen Pharmaceuticals and Sanofi; and has received research funding from Amgen, Astellas Pharma, Bayer, Exelixis, Janssen Pharmaceuticals, Novartis, Oncogenex, Sanofi, Teva and Tokai Pharmaceuticals. TK and AM are employees of Janssen Research & Development and own stock in Johnson & Johnson. CJR has served as a consultant/advisor to Bayer and Millennium Pharmaceuticals and has received honoraria and research funding from Janssen Research & Development. JB has served as a consultant/advisor to Astellas Pharma, Pfizer and Pierre Fabre; has received research funding from Millennium Pharmaceuticals and Sanofi; and has received funds for travel/accommodations/ expenses from MSD Oncology and Pfizer. NJV is an employee of US Oncology; owns stock in Caris Life Sciences; has served as a consultant/advisor to Amgen, AVEO, BIND Biosciences and Janssen Biotech; has received honoraria from AbbVie, Bavarian Nordic, DAVA Oncology, Endocyte, Mannkind and UpToDate; has received research funding from Endocyte, Exelixis, GlaxoSmithKline, PAREXEL International, Progenics, US Oncology and Viatrum Pharmaceuticals; has served on speakers’ bureaus for Bayer, Caris MPI, Dendreon, GlaxoSmithKline, Medivation, Millennium Pharmaceuticals and Sanofi; and has received funds for travel/accommodations/expenses from Bayer/Onyx, Celgene, Dendreon, Exelixis, Genentech/Roche, Novartis, Pfizer and US Oncology. DER has received research funding from Celgene, Ferring Pharmaceuticals, Janssen Research & Development, Medivation/Avastin, Millennium/Takeda and Novartis. KF has served as a consultant/advisor to and has received honoraria from Janssen Research & Development. PWK has served as a consultant/advisor to Amgen, Aragon Pharmaceuticals, Archimedes, Bavarian Nordic, Bayer, Celgene, Dendreon, Exelixis, Genetech, Genomic Health, GTx, Janssen-Ortho, Millennium/Prometrika, MorphoSys, Pfizer and Teva; and has received research funding from Astellas Pharma and Sanofi. JL is an employee of Johnson & Johnson and owns stock in Johnson & Johnson. AAA has served as a consultant/advisor to and has received research funding from Astellas Pharma; and has received honoraria from Janssen Research & Development. BJE has received honoraria from Astellas Pharma and Pfizer. DYCH has a consultant/advisory role at Astellas Pharma and Janssen. AMJ has received research funding from Astellas Pharma and Janssen. JdB has served as a consultant/ advisor to Astellas Pharma, AstraZeneca, Genentech/Roche and Sanofi; has received honoraria from Astellas Pharma, AstraZeneca, Genentech/Roche, Pfizer and Sanofi; and has received research funding from Armo Therapeutics, AstraZeneca, Genentech, Sanofi and Tokai Pharmaceuticals. HIS has served as a consultant/advisor to AstraZeneca, Astellas Pharma, BIND Therapeutics, Bristol-Myers Squibb, Celgene, Chugai Academy for Advanced Oncology, Endocyte, Exelixis, Ferring Pharmaceuticals, Foundation Medicine, Medivation, Millennium Pharmaceuticals, Oncology STAT, Palmetto GBA, Pfizer, Roche/Ventana Medical Systems, Sanofi-Aventis and WCG Oncology; has received honoraria from Chugai Academy for Advanced Oncology; and has received research funding from BIND Therapeutics, Exelixis, Janssen Diagnostics, Janssen Pharmaceuticals and Medivation.

references
Association between PSA kinetics and cancer-specific mortality in patients with localised prostate cancer: analysis of the placebo arm of the SPCG-6 study

F. B. Thomsen1*, K. Brasso1, K. D. Berg1, T. A. Gerds2, J.-E. Johansson3, A. Angelsen4, T. L. J. Tammela5 & P. Iversen1 on behalf of the Scandinavian Prostate Cancer Group

1Copenhagen Prostate Cancer Center, Department of Urology, Rigshospitalet, University of Copenhagen, Copenhagen; 2Department of Biostatistics, University of Copenhagen, Copenhagen, Denmark; 3Department of Urology, Faculty of Medicine and Health, Örebro University, Örebro, Sweden; 4Faculty of Medicine, Norwegian University of Technology and Science, Trondheim, Norway; 5Department of Surgery, Tampere University Hospital and School of Medicine, University of Tampere, Tampere, Finland

Received 23 June 2015; revised 8 October 2015, 9 November 2015 and 3 December 2015; accepted 4 December 2015

Background: The prognostic value of prostate-specific antigen (PSA) kinetics in untreated prostate cancer (PCA) patients is debatable. We investigated the association between PSA doubling time (PSAdt), PSA velocity (PSAvel) and PSAvel risk count (PSAvelRC) and PCA mortality in a cohort of patients with localised PCA managed on watchful waiting.

Patients and methods: Patients with clinically localised PCA managed observationally, who were randomised to and remained on placebo for minimum 18 months in the SPCG-6 study, were included. All patients survived at least 2 years and had a minimum of three PSA determinations available. The prognostic value of PSA kinetics was analysed and patients were stratified according to their PSA at consent: ≤10, 10.1–25, and >25 ng/ml. Cumulative incidences of PCA-specific mortality were estimated with the Aalen-Johansen method.

Results: Two hundred and sixty-three patients were included of which 116, 76 and 71 had a PSA at consent ≤10, 10.1–25, and >25 ng/ml, respectively. Median follow-up was 13.6 years. For patients with PSA at consent between 10.1 and 25 ng/ml, the 13-year risks of PCA mortality were associated with PSA kinetics: PSAdt ≤3 years: 62.0% versus...