# Podium Session 1: Prostate Cancer
# June 26, 2016 1050-1150

## POD-01.01

### Efficacy and safety of enzalutamide versus bicalutamide in younger and older patients with metastatic castration-resistant prostate cancer in the TERRAIN trial

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**Introduction and Objectives:** The phase 2 TERRAIN trial compared the efficacy and safety of enzalutamide (ENZA) vs. bicalutamide (BIC) in patients (pts) with metastatic castration-resistant prostate cancer who had progressed on luteinizing hormone-releasing hormone agonist/antagonist therapy or after bilateral orchiectomy while maintaining castration therapy during the study. An age effect analysis was pre-specified to investigate the efficacy and safety of ENZA vs. BIC. Results are presented in younger (<75 years) and older (≥75 years) pts in the TERRAIN population.

**Methods:** In this double-blind study in North America and Europe, pts were randomized 1:1 to ENZA 160 mg/day or BIC 50 mg/day. The primary efficacy endpoint was centrally assessed progression-free survival (PFS) and a secondary efficacy endpoint was time to prostate-specific antigen (PSA) progression.

**Results:** 184 pts were randomized to ENZA and 191 pts to BIC. 126 (68.5%) and 119 (62.3%) pts were <75, and 58 (31.5%) and 72 (37.7%) pts were ≥75, in the ENZA and BIC arms, respectively. PFS was significantly improved with ENZA vs. BIC in pts <75 years (median 16.6 vs. 5.8 months; HR 0.38 (95% CI 0.27, 0.52) and pts ≥75 years (median 13.8 vs. 6.4 months; HR 0.59 (95% CI 0.37, 0.92). Median time to PSA progression was similarly significantly improved with ENZA vs. BIC in younger (median 22.1 vs. 8.2 months; HR 0.27 (95% CI 0.18, 0.40) and older pts (median 16.6 vs. 5.8 months; HR 0.33 (95% CI 0.19, 0.57). Adverse events (AEs) with ENZA were more frequent in older pts (98.3%) vs. younger pts (92.8%), but a similar distribution of treatment-related AEs between treatment arms was observed in either age group.

**Conclusions:** ENZA had greater efficacy than BIC regardless of age, with superior PFS and time to PSA progression. ENZA showed safety consistent with its known safety profile in both age subgroups.

## POD-01.02

### A pan-Canadian contemporary analysis of active surveillance uptake for low-risk, localized prostate cancer in Canada

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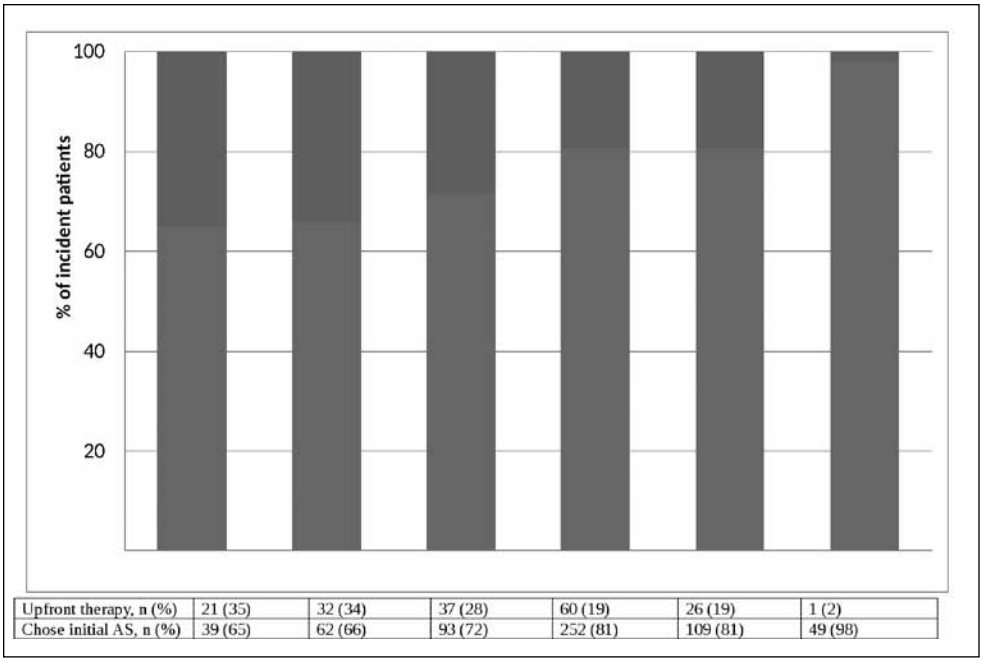
**Introduction and Objectives:** In active surveillance (AS), practitioners delay curative treatment in low-risk patients until there is evidence of disease progression, at which time active treatment is initiated. Although the uptake of AS appears to be increasing, the actual uptake in Canada remains largely unknown. The aim of this study is to examine practice patterns around the use of AS in low-risk prostate cancer in Canada. In addition, we examined regional variations in uptake of AS, as well as predictors of AS uptake and persistent use of AS for 12 months.

**Methods:** We evaluated the use of AS in men who underwent a prostate biopsy in 2010 in six centres in four provinces (BC, QC, MB, and ON). For incident cases, clinical and pathological information was collected




| | | | | | | |
|---|---|---|---|---|---|---|
| Upfront therapy, n (%) | 21 (35) | 32 (34) | 37 (28) | 60 (19) | 26 (19) | 1 (2) |
| Chose initial AS, n (%) | 39 (65) | 62 (66) | 93 (72) | 252 (81) | 109 (81) | 49 (98) |

***Fig. 1.*** POD-01.02. Distribution of incident patients by initial active surveillance (AS) vs. upfront active treatment.

via chart review prospectively for 12 months following the last biopsy of 2010. Eligibility for AS and treatment trends by region were compared using chi-square tests for categorical variables and the ANOVA test for continuous variables. Univariate and multivariate logistic regression was used to examine predictors of choosing AS upfront (versus active treatment within six months of diagnosis) and to predict the likelihood of continuing on AS for 12 months.

**Results:** Of 986 patients, 781 patients (mean age 64 years) were incident cases and were eligible for AS. Over three-quarters (77.3%) of patients chose AS at diagnosis. There were significant differences in uptake of AS by region (range 65.0-98.0%; p≤ 0.05). Key multivariate predictors of pursuing AS included age (p=0.044), region (p=0.021), number of cores (p=0.025), number of positive biopsy cores (p<0.001), and percent core involvement (p<0.001). 516 (85.4%) men remained on AS over 12 months. Maintenance with AS over 12 months differed by region, ranging from 64.1-93.9% (p=0.001). Predictors of maintenance with AS over 12 months included age, region, and number of positive cores. In all, 177 (22.7%) patients eligible for AS underwent an active treatment within six months from diagnosis. Among 604 patients who underwent AS for at least six months, 88 (14.6%) received active treatment within 6-12 months after AS.

**Conclusions:** These results suggest that AS is widely practiced across Canada and the majority of men who choose AS remain on it for 12 months, although there are significant differences in practice patterns between and within provinces. More in-depth analyses will be required to understand the root causes of these differences, and also to determine whether AS uptake is changing over time.

## POD-01.03

### The burden of symptomatic skeletal events in castrate-resistant prostate cancer patients with bone metastases at three Canadian uro-oncology centres

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**Introduction and Objectives:** Castrate-resistant prostate cancer (CRPC) patients (pts) with metastatic bone disease (MBD) risk significant morbidity, including symptomatic skeletal events (SSEs) (palliative radiation, pathological fracture, surgery to bone, and spinal cord compression), and require substantial healthcare resource use (HRU). We estimated MBD-related HRU costs at three Canadian (Cdn) uro-oncology centres (UOCs).

**Methods:** A retrospective chart review conducted at Centre hospitalier de l'Université de Montréal (CHUM), Princess Margaret Cancer Centre (PMCC), and Vancouver General Hospital (VGH) estimated MBD-related HRU costs between MBD onset and death in pts dying from or palliated for metastatic CRPC between Jan. 1, 2006 and Jan. 31, 2013. Patterns of SSEs and bone-targeted therapy (BTT) use were analyzed.

**Results:** 393 pts (CHUM (130), PMCC (154), VGH (109)) were enrolled, with a mean age of 71 years (yrs) at MBD onset. Median survival from MBD onset was 23.9 months (mos) (no significant difference between sites). 275 (70%) pts experienced 833 SSEs (85 events per 100 pt yrs). Median time to first SSE was 17.6 mos. Pts presented a mean of 2.12 SSEs. Mean MBD-related HRU costs were $31 827 for pts with ≥1 SSE and $14 092 for pts with no SSEs (2014 CAD). 201 (51%) pts received ≥1 BTT, mainly zoledronic acid (ZA) (190/201 (95%)). Median (95% CI) time (mos) to first SSE was longer at CHUM vs. PMCC or VGH (25.0 (18.5-32.6) vs. 14.6 (9.7–16.8) or 17.3 (14.8–24.0)). Fewer pts at CHUM experienced ≥1 SSE vs. PMCC or VGH (71/130 (55%) vs. 121/154 (79%) and 83/109 (76%)). More pts received BTT at CHUM and PMCC than at VGH (83/130 (64%) and 92/154 (60%) vs. 26/109 (24%)). BTTs were used early (in pts with no prior SSEs) for 51%, 32%, and 13% pts at CHUM, PMCC, and VGH respectively. ZA dosing frequency differed substantially between UOCs (Table 1).

**Conclusions:** MBD-related HRU costs for Cdn pts with CRPC are high. Patterns of SSEs and BTT use varied between three Cdn UOCs.

**Table 1. POD-01.03. Frequency of ZA administration**

| | Overall | CHUM | PMCC | VGH |
|---|---|---|---|---|
| Patients receiving ZA | 190 | 77 | 87 | 26 |
| Patients receiving ZA q3w/q4w/qm, n (%) | 78 (41%) | 59 (77%) | 9 (10%) | 10 (38%) |
| Patients receiving ZA ≥q3m, n (%) | 65 (34%) | 3 (4%) | 61 (70%) | 1 (4%) |
| Patients receiving ZA at unknown frequency, n (%) | 47 (25%) | 15 (19%) | 17 (20%) | 15 (58%) |

## POD-01.04

### Prospective comparison of open vs. robot-assisted radical prostatectomy for clinically localized prostate cancer: Results from the University of Alberta radical prostatectomy database

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**Introduction and Objectives:** There are limited prospective data comparing outcomes of open radical prostatectomy (ORP) and robot-assisted radical prostatectomy (RARP) for clinically localized prostate cancer (CLPC). We compared ORP and RARP with respect to surrogate cancer control, functional preservation, perioperative, and healthcare utilization outcomes in men treated at the University of Alberta.

**Methods:** A prospective analysis of data from the University of Alberta Radical Prostatectomy Database was performed. Between September 2007 and January 2013, 1806 consecutive men underwent radical prostatectomy for CLPC. The surgeon selected the surgical approach. Surrogate cancer control outcomes were biochemical recurrence (BCR; prostate-specfic antigen (PSA) ≥0.2 ug/L followed by a subsequent confirmatory value or initiation of salvage therapy) and positive surgical margin (R1) rate. Functional preservation outcomes were one-year urinary and erectile function preservation rates. Perioperative outcomes were 90-day complication and blood transfusion rates. Healthcare utilization outcomes were 90-day return to emergency room and/or readmission to hospital rates. The Kaplan-Meier method and multivariable Cox regression analyses were used to analyze BCR. Statistical tests were two-sided (p<0.05).

**Results:** Complete data were evaluable for 1769 out of 1806 patients. 333 patients underwent ORP and 1436 patients underwent RARP. The median followup duration was 48 months. Baseline age (62 years vs. 61 years; p=0.07) and D'Amico risk stratification score (low-risk: 50% vs. 45%; intermediate-risk: 42% vs. 46%; high-risk: 8% vs. 9%; p=0.15) did not differ in the ORP and RARP groups. The five-year freedom from BCR rate differed between the ORP and RARP groups (79% vs. 86%; log rank p=0.006). Multivariable Cox regression analysis showed that ORP was independently associated with an increased risk of BCR (HR 1.62, 95% CI 1.21–2.18; p=0.001). The one-year urinary function preservation rate (60% vs. 72%; p=0.004), one-year erectile function preservation rate (10% vs. 17%; p=0.007), and blood transfusion rate (4% vs. 1%; p<0.001) differed between the ORP and RARP groups. There were no significant differences between groups for R1 rate (24% vs. 26%; p=0.57), 90-day complication rate (27% vs. 27%; p=0.27), return to emergency room rate (21% vs. 20%; p=0.54), or readmission to hospital rate (3% vs. 4%; p=0.15).

**Conclusions:** In men treated at a Canadian academic centre, RARP provided superior cancer control, functional preservation, and blood product transfusion rates compared to ORP. Further analyses designed to examine mechanisms of differences in outcomes is underway.

## POD-01.05

### Cardiovascular and skeletal-related complications among patients treated with surgery or radiotherapy for clinically localized prostate cancer: A population-based cohort study

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**Introduction and Objectives:** Complications, including cardiovascular disease and skeletal-related events (SREs), from androgen-deprivation therapy (ADT) in the treatment of prostate cancer are well-described, but the role of primary therapy and its interaction with ADT is unknown among patients treated for clinically localized prostate cancer. We examined long-term rates of cardiovascular and SREs for these patients.

**Methods:** We conducted a population-based, retrospective cohort study using the Surveillance, Epidemiology and End-Results (SEER) Medicare-linked databases for men aged 65-79 years who underwent radical prostatectomy or radiotherapy between 2001 and 2008 for cT1/T2 prostate cancer. We categorized treatment exposure according to primary treatment and receipt of ADT. We measured the cumulative incidence of cardiovascular and skeletal-related complications.

**Results:** Among 60 156 men, 14 403 underwent primary surgery and 45 753 underwent radiotherapy. A higher proportion of patients treated with radiotherapy received ADT (52%) than did those treated with surgery (12%; p<0.0001). After a median followup of 6.0 years, patients treated with radiotherapy had an increased risk of coronary heart disease, myocardial infarction, sudden cardiac death, fracture, and fracture requiring hospitalization (adjusted hazard ratios 1.16-1.28; p<0.0001-0.04) compared to those treated with surgery. Patients receiving ADT had an increased risk of coronary heart disease, sudden cardiac death, fractures, and fractures requiring hospitalization (adjusted hazard ratios 1.18-1.32; p<0.0001-0.008), but not myocardial infarction (adjusted hazard ratio 1.04; p=0.5). We did not find evidence of significant interaction between local and systemic treatments.

**Conclusions:** Cardiovascular disease and SREs are important complications for the treatment of clinically localized prostate cancer. The risk is higher among those treated with radiation or ADT and should be considered when discussing the risks and benefits of treatment for localized prostate cancer.

## POD-01.06

### Expressed prostatic secretion (EPS) biomarkers for the pre-surgical prediction of early biochemical recurrence

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**Introduction and Objectives:** Biochemical recurrence within 2.5-3 years after surgery is associated with higher risk of prostate-specific death. Consequently, predicting the likelihood that biochemical recurrence would not occur within 2.5 years would indicate a favorable surgical outcome. Our objective was to develop biomarkers in non-invasive specimens that would improve the prediction of early biochemical recurrence (BCR), defined as prostate-specific antigen (PSA) greather than 0.2 ng/ml detected within 2.5 years of surgery.

**Methods:** Prospectively collected 855 expressed prostatic secretion (EPS) specimens prior to robot-assisted radical prostatectomy. 378 specimens have now been followed for biochemical recurrence over 2.5 years. We used quantitative reverse transcriptase polymerase chain reaction to quantify RNA expression from PSA, Thioredoxin Reductases 1 and 2, PCA3, and TMPRSS2:ERG fusions, along with a novel assay for the determination of PSA proteolytic activity (PPA). The data was modeled using logistic regression, random forests and cross-validated.

**Results:** A baseline model using biopsy Gleason sum and serum PSA value was constructed with logistic regression. receiver operating curve (ROC) analysis gave an area under the curve (AUC) value for the absence of biochemical recurrence within 2.5 years of 0.8176. A model containing the PCA3 RNA level normalized to the input RNA value, and PPA, improve the AUC of the model to 0.8820. The difference in the values is statistically significant, with a p value of 0.0046. Random forest analysis was also applied to the data using all variables available, however, a statistical comparison showed that the logistic regression classifier was preferred. At 5% fixed false negative rate, adding PPA and PCA3 lab values to Gleason sum and serum PSA improved the false positive rate by 33%.

**Conclusions:** PPA and PCA3 RNA are effective biomarkers in EPS specimens for the pre-surgical prediction of early biochemical recurrence after surgery, which should have use in counselling patients prior to prostatectomy.