# Synopsis

**NIS Code: NIS-OCN-DUM-2009/2**
**Date: Date：15 Mar 2015**

**Study title：**

A non-interventional study of immediate postoperative adjuvant hormonal treatment in high risk localised or locally advanced Chinese prostate cancer patients

**Participating sites：**

18 sites in the mainland China

**Study duration：**

52 months

Date of Fist Subject Enrolled: 27 April 2010

Date of Last Subject Completing Observation: 2 Aug 2014

**Objectives：**

(1) Primary objective：to assess the efficacy of immediate postoperative adjuvant hormonal treatment according to 2-year PSA relapse rate in high risk localised or locally advanced Chinese prostate cancer patients；

(2) Secondary objectives：

1）To assess the quality of life（QoL）of the high risk localised or locally advanced Chinese prostate cancer patients with immediate postoperative adjuvant hormonal treatment at baseline, 1 year and last visit；

2）To evaluate the use of immediate postoperative adjuvant hormonal treatment (regimen, dosage and duration) at each visit following radical surgery for high risk localised or locally advanced prostate cancer.

**Study design：**

Prospective,single arm,open label, non-interventional study

**Inclusion criteria：**

A patient must have met all of the following criteria to be included into this study：

(1) Localised（T≤pT2, N0M0） with one of any high relapse risk factors(Gleason score≥8 or preoperative serum PSA≥20ng/ml), or locally advanced(T≥pT3, N0M0 and any T, N（+）M0 ) patients within 1 month following radical prostatectomy with either laparoscopy or laparotomy. Before the patient recruitment, the

investigator has decided to prescribe immediate postoperative adjuvant hormonal treatment to the patient according to the Chinese routine practice;

(2) Patients at least 18 years old;

(3) Provision of written informed consent;

**Exclusion criteria:**
Have used neoadjuvant hormonal treatment prior to radical prostatectomy.

**Number of subjects:**
201

**Efficacy variables:**
Not applicable.

**Safety variable:**
Not applicable.

**Efficacy assessment criteria:**
Not applicable.

**Statistical methods:**

Continuous variables were presented by the descriptive statistics including N, mean, SD, median, min and max. Categorical variables were presented by the number and percent of patients in each category. One-way ANOVA with one repeated measure and two-way ANOVA with one repeated measure were treated with the mixed-effect process incorporated in the SAS software, the causal variables in the model being the fixed effect. The analysis results include adjusted mean（LSmeans）, the relevant confidence interval and *p* value. All the statistical analyses were based on two-sided hypothesis test at the $\alpha$=0.05.

**Primary variable:** PSA relapse rate at 2 years following immediate postoperative adjuvant hormonal treatment following radical surgery for high risk localized or locally advanced prostate cancer

Serum PSA cumulative relapse rates at each visit （post-treatment 3 months（baseline -3 months）, 6 months（3-6 months）, 9 months（6-9 months）, 12 months（9-12 months）, 18 months（12-18 months）, 24 months（18-24 months））weredescribed (a patient who discontinued due to relapse was to be treated as a relapse at any visits following discontinuation), calculating the number and percent of patients and treating any discontinued patient without relapse as missing （two definitions of PSA relapse: 1. two consecutive PSA≥0.2ng/ml at anytime within 2 years of baseline for the patients whose baseline serum PSA after surgery is less than 0.2ng/ml [17] or 2. A doubling of PSA versus baseline at

anytime within 2 years after baseline for patients with baseline PSA(≥0.2ng/ml) after surgery）. Kaplan-Meier method was used to estimate the relapse rate. In the absence of relapse, data was to be censored at the date of last PSA examination.

**Secondary variables：**

- FACT-P QoL Questionnaire Score

The total score and each sub-scale score of the FACT-P QoL Questionnaire were described by N, mean, SD, median, min and max . Paired t-test was used for the comparison of QoL at one year visit, last visit and baseline.

- Use of hormonal therapies（regimen, dosage, and duration）

The use of hormonal therapeutic agents was described by the numbers and percents of patients using different agents. The dosage and duration of each hormonal therapeutic agent were described by N, mean, SD, median, min and max (duration of hormonal agent（days） = Date of end of treatment – Date of start of treatment+ 1 ).

Additional analyses：

1）The PSA measurements and their changes from baseline at each visit weredescribed using N, mean, SD, median, min and max.

2）Time to serum PSA relapse estimated by Kaplan-Meier method

Time to PSA relapse (months) = （Date of PSA relapse* -Date of immediate postoperative adjuvant hormonal therapy）/30.44

* Patients with postoperative baseline serum PSA<0.2ng/mL or missing, the later of any two consecutive dates meeting the relapse criteria within two years being the date of relapse.

3）Other explorative analyses:

- Multi-factor analysis for PSA relapse

The influencing factors for the prognostic outcomes（time to PSA relapse and QoL）（visit, age at initial diagnosis, preoperative clinical stage, postoperative TNM stage, preoperative PSA, postoperative GS score, postoperative surgical margin condition, presence of seminal vesicle involvement, BMI, duration of adjuvant therapy, etc.） were analyzed and selected using Cox regression and mixed-effect model, where $\alpha=0.15$ would allow the influencing factor to be retained in the model .

- The associations between PSA relapse and postoperative lymph node examination, postoperative surgical margin and seminal vesicle involvement

The associations between PSA relapse （with or without） and lymph node examination, postoperative surgical margin and seminal vesicle involvement were compared using chi-square test.

4) Subgroup analyses

For this study, subgroup analyses were performed based on 4 subgroups：

- Subgroup with adjuvant hormonal therapy alone
- Subgroup with adjuvant hormonal therapy combined with adjuvant radiotherapy
- Subgroup with duration of adjuvant hormonal therapy≤6 months
- Subgroup with duration of adjuvant hormonal therapy>6 months

PSA relapse rate was estimated by the Kaplan-Meier method, and Logrank test was used for comparison between groups.

An interim analysis was performed when all the patients had been followed up for one year or had unequivocal PSA relapse . The present analyses are the final analyses.

**Study Results：**

**Primary variable：** PSA relapse rate at 2 years following immediate postoperative adjuvant hormonal treatment following radical surgery for high risk localized or locally advanced prostate cancer

Among the 190 patients who received immediate postoperative adjuvant hormonal treatment following radical surgery for high risk localized or locally advanced prostate cancer, the cumulative serum PSA relapse rates at 3 months（baseline -3 months）, 6 months（3-6 months）, 9 months（6-9 months）, 12 months（9-12 months）, 18 months（12-18 months）and 24 months（18-24 months）post-treatment were 3.2%, 6.5%, 8.3%, 11.2%, 13.3%, and 15.4%, respectively；the cumulative relapse rates estimated by Kaplan-Meier method at 3 months, 6 months, 9 months, 12 months, 18 months and 24 months were 3.2 %, 5.9%, 8.2%, 11.0%, 12.1% and 17.9%, respectively.

**Secondary variables：**

- FACT-P QoL Score：

The mean±SD of FACT-P QoL Questionnaire total scores at baseline , 12 months, 24 months were 109.62±21.78, 115.37±20.44 and 117.61±21.64, respectively, and the mean±SD of the increases from baseline at 12 months and 24 months were 5.50±14.04 and 6.40±20.34, respectively, indicating statistically signficant differences from baseline ($p$<0.0001 and $p$=0.0003).

The mean±SD of QoL Questionnaire Physical Well-being scores at baseline , 12 months and

24 months were 21.81±4.75, 23.31±3.94, 24.10±3.66, respectively, and the mean±SD of increases from baseline at 12 months and 24 months 1.44±3.65 and 1.77±4.57, respectively, indicating statistically signficant differences from baseline(both $p$ <0.0001).

The mean±SD of QoL Questionnaire Social/Family Well-being scores at baseline , 12 months and 24 months were 21.34±4.24, 21.75±4.15, 21.35±4.85, respectively, and the mean changes from baseline at 12 months and 24 months were 0.38±3.58 and 0.16±4.70, respectively, indicating no statistically significant difference from baseline.

The mean±SD of QoL Questionnaire Emotional Well-being scores at baseline , 12 months and 24 months were 17.84±3.83, 18.54±3.78, 19.38±3.35,, respectively, and the mean changes from baseline at 12 months and 24 months were 0.62±3.17 and 1.12±3.73, respectively, indicating statistically signficant differences from baseline（ $p$<0.05 and $p$<0.001）.

The mean±SD of QoL Questionnaire Functional Well-being scores at baseline , 12 months and 24 months were 16.56±6.28, 17.46±6.02, 18.29±5.84,, respectively, and the mean changes from baseline at 12 months and 24 months were 0.81±4.53 and 1.42±6.19, respectively, indicating statistically signficant differences from baseline($p$<0.05 and $p$<0.01).

The mean±SD of QoL Questionnaire Additional Concerns scores at baseline , 12 months and 24 months were 32.07±6.71, 34.31±6.47, 34.74±6.92,, respectively, and the mean changes from baseline at 12 months and 24 months were 2.24±4.87 and 2.56±6.08, respectively, indicating statistically signficant differences from baseline（both $p$<0.0001）.

- Use of hormonal therapies（regimen, dosage, and duration）：

Among the adjuvant hormonal agents, Goserelin combined with Bicalutamide were the most commonly used, accounting for 58.9%（112/190） of the patients， 80.4% of whom used Goserelin combined with Bicalutamide for over 12 months.

The most common Bicalutamide dosage was 50mg（81.3%）, and 73.3% patients received over 12 months of Bicalutamide treatment；100% of the patients treated with Goserelin used the 3.6mg dosage; 61.9% patients received over 12 months of Goserelin treatment; and 21.6% patients received 3-6 months of Goserelin treatment.

Through stepwise selection of the factors including postoperative stage-T, postoperative stage-N, preoperative serum PSA, postoperative GLEASON score, postoperative surgical margin, presence of seminal vesicle involvement, BMI, age at initial diagnosis, duration of adjuvant therapy, etc., in the Cox regression model, it was concluded that age at initial

diagnosis（$p$=0.0493） was statistically significant influence on time to PSA relapse, i.e., the relapse risk increased with the age at initial diagnosis（HR：0.946, 95%CI：0.895 ~ 1.000）.

Through stepwise selection of the influencing factors for change from baseline in FACT-P total score including visit, postoperative stage-T, postoperative stage-N, postoperative surgical margin, presence of seminal vesicle involvement, BMI, age at initial diagnosis, and duration of adjuvant therapy, etc., it was concluded that change from baseline in FACT-P total score decreased with the increase of baseline score and age at initial diagnosis; the patients with positive postoperative surgical margin had smaller changes from baseline score than those with negative surgical margin; and patients with duration of adjuvant therapy>6 months had greater changes from baseline than those with duration of adjuvant therapy≤6 months.

Univariant chi-square test showed that PSA relapse was not correlated with postoperative lymph node metastasis, positive postoperative surgical margin or seminal vesicle involvement.