



Upfront Docetaxel in the Post-STAMPEDE Era – An Analysis of Treatment Population, Toxicities and Outcomes

M. Abdul-Latif, A. Macdonald, K. Ng, C. Alifrangis, J. Shamash
St Bartholomew's Hospital, London, UK

Purpose: To evaluate real-life tolerance and efficacy of upfront docetaxel in patients with castrate-sensitive metastatic prostate cancer.

Methods: We included all patients in St Bartholomew's Hospital with metastatic prostate cancer treated with upfront docetaxel and androgen-deprivation therapy (ADT) since January 2016. Patients were given 6 cycles of chemotherapy at docetaxel 75 mg/m², except the first cycle at 60 mg/m² to assess tolerance. Prophylactic ciprofloxacin was given between days 8 and 18 of each cycle, and steroids were given only as pre-medication.

Results: 78 patients were identified. The median age was 67, all had a performance status of 0–1 and 85% had a Gleason score of 8 or above. 45 (57.7%) had high volume metastasis at presentation, including 9 (11.5%) with visceral metastases. Median PSA at starting docetaxel was 14. The median follow-up time was 423 days. Median PSA after 6 cycles was 2.34, with 5 (7.8%) achieving radiological complete response and 30 (46%) achieving partial response. 3 (4.6%) patients progressed despite upfront docetaxel + ADT. 73.5% of patients remain castrate sensitive at analysis, with 26.5% having progressed and switched to second-line treatment. One patient had died from disease progression. Most patients completed 6 cycles of treatment, but 9 (14%) required dose reductions and a further 4 (7.8%) discontinued treatment because of toxicity. 8 (12.5%) patients experienced severe side-effects (grade 3–4), predominantly diarrhoea (2), neutropenia (2) and fatigue (1). The rate of grade 3 febrile neutropenia was only 2.5%, compared with 8–12% in the 3 large clinical trials. There were 2 (3.1%) treatment-related deaths.

Conclusion: Our patient demographics, tolerance and progression-free intervals are comparable with the GETUG-AFU15, CHAARTED and STAMPEDE trials. This reflects the efficacy and tolerability of this treatment in the real-world population. The lower incidence of febrile neutropenia in our cohort may reflect the use of prophylactic antibiotics and omitting daily steroids.

Patient Reported Toxicity, Quality of Life and Biochemical Control

Following HDR Brachytherapy: Outcomes from the First 2 Years of a New Service at the Sussex Cancer Centre

S. Appleyard, F. Cowtan, A. Johns, A. Robinson, A. Nikapota
Brighton & Sussex University Hospitals NHS Trust, Brighton, UK

Purpose: To measure patient experience following establishment of high-dose-rate (HDR) brachytherapy for prostate cancer at the Sussex Cancer Centre: to inform service development and patient information.

Methods: Patients treated with HDR brachytherapy are asked to complete a combined toxicity and quality of life PROM, including satisfaction with care. Assessment at baseline and by post/telephone at 3 and 6 months and annually thereafter. We report outcomes from 77 patients treated in the first 2 years (2014–2016).

Results: 66 patients received HDR brachytherapy in combination with EBRT to prostate ± pelvis. 11 patients had monotherapy mainly due to inflammatory bowel disease. Patients fulfilled NCCN high-risk criteria (T3a, Gleason 8–10, PSA > 20). Age range 51–78 (median 67) with 24–48 months of follow-up (median 31). 94% are free from biochemical recurrence. 4 patients have metastatic disease and 2 have died (1 each from prostate and bladder cancer). Follow-up PROMS data are available for 94% of patients with data at 24–48 months for 75%. 88% report no GI toxicity, with the remainder reporting

'small' or 'very small' problems. 65% report no GU toxicity, 10% 'small' or 'very small' and 25% 'moderate' problems. 13% have documented urethral strictures. Patients were asked to rate their ability to enjoy life and to conduct their usual activities. 74% and 75%, respectively, reported that this was 'good' or 'very good'. Within the limitation of the small numbers of patients with poor outcomes there was no clear correlation between symptoms and quality of life or association with disease characteristics or treatment. 89% reported that they were 'extremely satisfied' or 'satisfied' with treatment received.

Conclusion: Our toxicity and quality of life data are consistent with published data [1]. These real-world data more accurately reflect the local patient population than RCT data and so provide useful estimates to include when counselling patients prior to treatment.

Reference

[1] Hoskin PJ, Rojas AM, Ostler PJ, Hughes RM, Lowe GJ, Bryant L. Quality of life after radical radiotherapy for prostate cancer: longitudinal study from a randomised trial of external beam radiotherapy alone or in combination with high dose rate brachytherapy. *Clin Oncol* 2013;25(5):321–7.

Does Using Choline PET Scans in Patients with Prostate Cancer Alter Management? A South Wales Experience

C. Bowden*, J. Staffurth*, J. Tanguay*, J. Rees†

*Velindre Cancer Centre, Cardiff, UK

†University of Wales Hospital, Cardiff, UK

Purpose: To determine whether using choline-PET scans in patients with prostate cancer changes patient management compared with the use of conventional imaging alone.

Methods: Clinical details of patients who had a choline-PET were sought, including: stage of disease, the clinical scenario (including PSA relapses), past medical history, histopathology results, conventional scan (MRI/CT/bone scan) and PET scan results. The clinical question being asked resulting in each PET scan was documented. It was noted what the management plan would have been without a PET scan. The PET scan result was then reviewed and subsequent management undertaken was documented. These two management strategies were compared leading to three outcomes: 'no change', 'change in management' or 'management influenced' if the PET helped guide treatment or support between two pre-defined options. Two consultant clinical oncologists and a registrar checked these cases, with a rigorous assessment of the management to be undertaken without access to PET.

Results: Between 2013 and 2016, of the 52 patients: 37% demonstrated a 'change' in management as a result of a PET scan, for 23% the PET scan 'influenced' patient management and for 18% there was 'no change' to patient management based on the patient having a PET scan or not.

Conclusion: Although evidence is lacking to show an improved survival using choline-PET scans, there is evidence that they detect disease beyond the resolution of conventional imaging. We suggest that choline-PET scans are useful for men with an initial diagnosis of prostate cancer, confirming ambiguous conventional imaging or on PSA relapse after focal therapy, to guide local treatment options. Our study has shown that in these groups the most common outcome was that the PET scan changed management.

Evaluating the Safety of Up-front Docetaxel in the Treatment of Metastatic and Locally Advanced Prostate Cancer

A. Killean, A. Law, J. Malik, A. Sundaramurthy, D. McLaren

Edinburgh Cancer Centre, Edinburgh, UK

Purpose: To determine the rates of neutropenia, neutropenic sepsis and mortality within 30 days of chemotherapy in patients receiving up-front docetaxel for hormone-naïve metastatic prostate cancer or selected locally advanced prostate cancer at the Edinburgh Cancer Centre (ECC).

Methods: 68 patients received up-front docetaxel at ECC between July 2015 and June 2017 for the indications above. 11 patients had locally advanced disease. Using TRAK and Chemocare software, the date of diagnosis, performance status, TNM staging, Gleason grade and pre-treatment PSA (where available) were recorded. The number of cycles of docetaxel received, number of delayed cycles, dose reductions, rates of hospitalisation within 30 days of chemotherapy, neutropenia, neutropenic sepsis and mortality within 30 days of chemotherapy were recorded.

Results: The median time to starting chemotherapy after ADT was 63 days (IQR = 53–83), 16 patients started after 12 weeks. The full 6 cycles of docetaxel were given to 83.8% ($n = 57/68$) of patients. A dose reduction was required in 26.5% ($n = 18/68$). Neutropenia was recorded in 38.2% ($n = 26/68$) and 20.6% ($n = 14/68$) were treated for neutropenic sepsis. Of these patients, 8 went on to complete the planned 6 cycles of docetaxel. 2.9% ($n = 2/68$) died within 30 days of receiving chemotherapy; both had metastatic disease. Therefore, in our cohort 14.3% ($n = 2/14$) of patients who developed neutropenic sepsis died.

Conclusion: Up-front docetaxel for the management of metastatic and selected locally advanced prostate is generally well-tolerated, with most patients completing 6 cycles of treatment; however, 26.5% required a dose reduction and 16.2% did not complete chemotherapy. A significant proportion developed neutropenic sepsis, with 2 deaths related to treatment. Pending cost analysis, prophylactic G-CSF for this cohort of patients should be considered. We intend to evaluate progression-free survival to compare our data with that of the published trials.

Variability Analysis of Clinical Target Volume Outlining for Prostate Stereotactic Body Radiotherapy within the Multicentre PACE Trial

K. Morrison, O. Naismith, N. van As
Royal Marsden Hospital, London, UK

Purpose: The PACE trial is a randomised multicentre trial comparing stereotactic body radiotherapy (SBRT) with conventional treatment in low- and intermediate-risk prostate cancer. SBRT is associated with a small margin for error, and it is therefore vital to ensure accuracy of clinical target volume (CTV) delineation. As part of the PACE trial quality assurance programme, centres are required to successfully complete a benchmark planning exercise using CT and MRI from a set intermediate-risk cases. The aim of this study was to analyse CTV outlining variability between centres.

Methods: Imaging and structure sets from 21 centres were uploaded using VODCA (Visualisation and Organisation of Data for Cancer Analysis) software. The investigational CTV, prostate and proximal seminal vesicles (pSV) contours were compared with reference PACE volumes using conformity indices [1–3]: DICE similarity coefficient; Geographical Miss Index (GMI); and Disconcordance Index (DI).

Results: The median volumes of the investigational CTV, prostate and pSV contours were greater than the reference contours by 9.7 cm³, 7.7 cm³ and 1.7 cm³, respectively. The median DICE coefficient (ideal value 1) was 0.72 (0.39–0.86) for pSV contouring, compared with 0.88 (0.82–0.91) for CTV and 0.905 (0.87–0.93) for prostate contouring, demonstrating that pSV contours had the least similarity to reference contours. The level of geographical miss was relatively low, reflected by low median GMI: CTV 0.06 (0.01–0.15), prostate 0.03 (0.01–0.09), pSV 0.15 (0.03–0.66). Median DI values were higher: CTV 0.17 (0.07–0.23), prostate 0.15 (0.04–0.22), pSV 0.31 (0.03–0.62), demonstrating that, overall, investigational contours were excessive compared with reference contours, particularly for pSV contouring.

Conclusion: The use of conformity indices has shown that CTV contouring variability between centres in the PACE trial is most evident with regard to pSV delineation. This highlights the need for a standard pSV delineation method to improve consistency in further prostate SBRT trials.

References

- [1] Hanna GG, Hounsell AR, O'Sullivan JM. Geometrical analysis of radiotherapy target volume delineation: a systematic review of reported comparison methods. *Clin Oncol* 2010;22(7):515–25.
- [2] Holyoake DLP, Robinson M, Grose D, McIntosh D, Sebag-Montefiore D, Radhakrishna G et al. Conformity analysis to demonstrate reproducibility of

target volumes for Margin-Intense Stereotactic Radiotherapy for borderline-resectable pancreatic cancer. *Radiother Oncol* 2016;121(1):86–91.

[3] Gwynne S, Spezi E, Wills L, Nixon L, Hurt C, Joseph G et al. Toward semi-automated assessment of target volume delineation in radiotherapy trials: the SCOPE 1 pretrial test case. *Int J Radiat Oncol Biol Phys* 2012;84(4):1037–42.

Less to Hold – a Comparison of Bowel and Bladder Toxicities in Patients Undergoing Prostate Radiotherapy between those Treated with an Empty Bladder and those Following a Bladder Filling Protocol

S. Morrison*, T. Ellis*, E. Fillingham*, Y.P. Song†, A. Birtle*

*Lancashire Teaching Hospitals NHS Foundation Trust, Preston, UK

†Christie Hospital NHS Foundation Trust, Manchester, UK

Purpose: Radical radiotherapy to the prostate is conventionally treated with a full bladder to minimise dose to bladder and bowel. Patients' tolerance of the bladder filling protocol varies and 'accidents' during treatment can cause undue distress to patients and increased pressure on the radiotherapy department. Several UK centres report treating with an empty bladder. We carried out a feasibility study of full bladder versus empty bladder to ascertain if we can safely change our practice.

Methods: 50 patients receiving radical radiotherapy to the prostate were randomised in a 1:1 manner to control and empty bladder groups. The control group followed the conventional drinking protocol at our centre (200 ml pre-treatment) and the empty bladder group was instructed to void prior to treatment. Baseline, end of treatment and 6 week follow-up scores were prospectively collected for IPSS, LENT SOMA bowel toxicity and quality of life questionnaires. Bowel and bladder DVH achievements were assessed.

Results: 50 patients were enrolled between March 2017 and January 2018. The mean increase in IPSS score from baseline to end of treatment was 2.12 for patients on the drinking protocol and 3.22 for those on the empty bladder protocol; this was not statistically significant ($P = 0.68$). At 6 weeks of follow-up, mean IPSS scores improved compared with baseline in the control group (–0.33) but worsened (+2.86) in the empty bladder group. This was once again not statistically significant ($P = 0.08$). No difference was seen in bowel toxicity, quality of life or dose to OARs between the 2 groups.

Conclusion: An empty bladder approach in prostate radiotherapy has no significant difference on acute bowel and bladder toxicity or OAR dose constraints. Empty bladder treatment can improve patient comfort and efficiency in our department. We continue to monitor patients in order to determine impact on long-term toxicity.

A Phase II Trial of Triamcinolone with Hormone Therapy for Prostate Cancer (TRICREST) in Chemotherapy Naïve Metastatic Castration Resistant Prostate Cancer

K. Ng, S.-J. Sarker, M. Greenwood, E. Gjafa, C. Alifrangis, J. Shamash
St Bartholomew's Hospital, London, UK

Purpose: To evaluate the efficacy of intramuscular triamcinolone in chemotherapy-naïve metastatic castration resistant prostate cancer (CRPC).

Methods: We conducted a phase II study of intramuscular triamcinolone administered monthly in metastatic CRPC. Triamcinolone has putative advantages over commonly used steroids, including lack of weight gain and an inability to stimulate mutated androgen receptors. 55 patients were recruited over 2012–2016. Imaging was performed every 3 months. The primary end point was radiological and symptomatic progression-free survival (PFS). Secondary end points included PSA progression, weight changes and toxicity. Steroid androgenic precursors, cortisol and circulating tumour cells were assessed prior to and 1 month after triamcinolone to see if they correlated with PFS.

Results: Median follow-up time was 21.3 months (95%CI: 13.2–24.5). The median radiological PFS was 9.4 months (95%CI: 7.0–20.1) and the 6 month PFS rate was 67.3% (95%CI: 0.53–0.78). The 50% PSA response rate was 31/55 = 56% (95%CI: 42–70%). There were no treatment-related deaths. The most common grade 3 toxicity was hypertension 40%, but only 5 patients (11%) required concomitant medication. Proximal myopathy (grade 2) was seen in 22 patients (40%). Skin toxicity (grade 2; bruising) was seen in 7 patients (12%). One patient had a gastrointestinal bleed. Hyperglycaemia developed in 3 patients (5%) There was no evidence of weight gain (mean weight 83.5 kg pre-study and 79.4 kg post-study).