LANDMARKS  Reports of recent research

Report from the Innovative Therapies in Prostate Cancer conference

The Innovative Therapies in Prostate Cancer conference, chaired by Dr. Franck Bladou, Professor of Urology and Oncology at McGill University and Chief of Urology at the Jewish General Hospital, invited Canadian and international experts to discuss the latest research and evidence in the treatment of prostate cancer. Oncology Exchange reports here on three sessions devoted to the treatment of metastatic disease.

Prostate cancer

METASTATIC DISEASE: IS THERE A RATIONALE FOR LOCOREGIONAL TREATMENT?

Andrew Loblaw, MD, FRCPC, Sunnybrook Health Sciences Centre

Dr. Andrew Loblaw, Professor in the Department of Radiation Oncology at the University of Toronto and Radiation Oncologist at Sunnybrook Health Sciences Centre, looked at emerging evidence supporting the use of stereotactic body radiation therapy (SBRT) for oligometastatic disease; discussed how docetaxel’s role may change in prostate cancer; and reviewed evidence around the management of M1 castrate-resistant prostate cancer.

SUMMARY: Dr. Loblaw raised the concern that US and Canadian task force recommendations would decrease rates of prostate specific antigen (PSA) screening and result in the appearance of more metastatic or advanced disease. However, a 2015 study by Drazer et al showed only a slight decrease in screening between 2006 and 2013. Dr. Loblaw compared attitudes to PSA screening to political party affiliations: most are firmly entrenched in one camp or the other, with only a small minority undecided and susceptible to influence. He also pointed to Welch et al’s 2015 study showing that in prostate cancer, unlike breast cancer, screening really has reduced metastatic disease, from a rate of 70 per 100,000 when PSA screening began in the early 1990s, to under 30 per 100,000 in the last decade. “We’re not,” he said, “going to see a tidal wave of metastases.”

MANAGEMENT OF N1 DISEASE

The 2006 Messing study showed large differences in overall and cause-specific survival with the early use of androgen deprivation therapy (ADT), while the study by Schroder et al in 2004 did not. Dr. Loblaw pointed to a significant difference, in that patients in the first underwent radical prostatectomy prior to starting ADT, thereby debulking the disease, while those in the second did not. These and other studies find a small difference of around 17% in cause-specific mortality with the early use of ADT, but no difference in overall survival (OS), though a study presented at ASCO 2015 looking at the timing of ADT post radiotherapy or surgery showed a trend toward survival advantage with the early use of ADT. Dr. Loblaw remarked on Canada’s strong work on intermittent androgen blockade (IAB), which has contributed to showing that it performs as well as continuous ADT in terms of OS, time to progression and cause-specific survival. His take home messages were that:

1. ADT is the standard of care and should be offered;
2. Early ADT appears to bring a cause-specific survival, but not OS, advantage; and
3. IAB is equally effective and favours the early use of ADT.

He recommended starting ADT when the relapse PSA is between 10 and 15: “The longer you wait to start ADT, the less likely you are to be able to offer an IAB approach. I think it is better to start earlier and get the PSA down and then take them off treatment, and get the benefits in terms of quality of life.”

LOCOREGIONAL TREATMENT IN N1 DISEASE

Some retrospective data sets suggest that the more treatment one gets to the pelvis, the better the patient does in terms of cause-specific survival and possibly OS. Dr. Loblaw cautioned about interpreting OS data, but pointed out that patients who receive no local therapy may have inferior prostate-specific survival compared with patients who receive some form of local therapy, be it radiation and surgery, or radiation alone.
ADT +/- RADIOTHERAPY
The STAMPEDE study, presented at ASCO 2015 included 6 arms. All patients were either metastatic node-positive or M0 with any 2 high-risk factors, and were managed with ADT +/- other experimental interventions. Patients may have relapsed after prostatectomy, and it was left to physician discretion to give radiotherapy. A subset analysis of N1 patients from this study enabled them to see that patients who received radiotherapy alongside ADT had better survival. Other randomized controlled trials of M0 patients have confirmed that radiotherapy and hormones are better than either one alone.

DOCETAXEL
Dr. Loblaw considers the ASCO analysis especially valuable for its findings regarding the advantage of docetaxel: “If you look at results for standard of care plus docetaxel vs standard of care alone in the entire group of metastatic patients in STAMPEDE, there is a massive difference in failure-free survival and OS, about 10 months median, which is very impressive.” No real difference in OS was seen in N0 patients, though there was a benefit in terms of failure-free survival.

For N1 disease, Dr. Loblaw concluded, ADT should be offered as the standard of care since it improves disease-specific survival, while IAB is an option, and locoregional therapy can be considered, preferably in the context of a clinical trial.

METASTATIC DISEASE
The subset of patients in the STAMPEDE study who were M1 saw a significant benefit in OS with the addition of docetaxel to standard of care, with median survival approaching 2 years. The advantages of locoregional treatment for metastatic disease are cloudier, and Dr. Loblaw cautioned against relying on observational and retrospective studies in assessing the benefits of radical prostatectomy, brachytherapy, and no local treatment in this group. “It was observational studies that led women to be advised to take hormone replacement therapy (HRT) to lower the risk of cardiovascular disease,” he stated. “Then they did the proper randomized controlled trial and actually found it was harmful to use HRT.”

Dr. Loblaw recognized that the current era presents a significant change for urologists and radiation oncologists, as fewer radical prostatectomies are performed, fewer men undergo intensive workup following PSA testing, and brachytherapy takes over from external beam radiation. Dr. Loblaw developed a collaboration between the Sunnybrook radiation oncologists and community urologists to determine the absolute minimum aims for treating these men in a multidisciplinary prostate cancer clinic. “We agreed,” Dr. Loblaw told the conference, “that all patients should be seen by a urologist and a radiation oncologist before deciding on treatment, and that all side effects, even if unusual or unlikely, should be described to the patient.” He presented Cancer Care Ontario data showing that less than a third of patients in Ontario get treatment with radical prostatectomy without first seeing a radiation oncologist (Figure 1).

Dr. Loblaw described “a wave of prostate cancer coming our way.” The Canadian Cancer Society has stated that prostate cancer will be the number-one diagnosed tumour and will increase the most between now and 2030. Data from Ontario centres collected by the Canadian Institute for Health Information (CIHI) examined the number of
patients managed in each centre by quartile of volume: “About 25% of patients are managed with radical prostatectomy in centres that do less than 2 cases a month. I think we will see a concentration in centres of excellence, which is a good thing for patients,” said Dr. Loblaw.

References:

TAKE-HOME MESSAGES
• Androgen deprivation therapy (ADT) and docetaxel is the standard of care and should be offered to patients for N1 disease.
• Not all patients, including those with oligometastatic disease, have to have chemotherapy and ADT, however the option should be discussed.
• Locoregional therapy may be considered after multidisciplinary consultation, or if the patient refuses chemotherapy, but is best offered in the context of a clinical trial.