The American Society of Clinical Oncology (ASCO) Genitourinary Cancers Symposium 2013

Highlights from the The American Society of Clinical Oncology (ASCO) Genitourinary Cancers Symposium 2013, 14-16 February, Orlando FL, USA

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The The American Society of Clinical Oncology (ASCO) Genitourinary Cancers Symposium 2013 held from the 14th - 16th of February, 2013, in Orlando, Florida, focused on multidisciplinary approaches to the prevention, screening, evaluation, and management of genitourinary (GU) cancers.

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One-third of localised prostate cancers Gleason upgraded during active surveillance

During long-term active surveillance, approximately one-third of localised prostate cancers will be pathologically upgraded, according to new findings from a prospective registry of active surveillance. These findings underscore the importance of repeat prostate biopsies to detect early progression on active surveillance and, if necessary, to switch to active treatment.

The study at hand examined repeat biopsy data in a prospective database of 862 patients on active surveillance at the University of Toronto. Active surveillance was open to patients of any age with Gleason scores ≤6 and prostate-specific antigen (PSA) levels ≤10 ng/dL. Patients older than age 70 were required to have favourable intermediate disease, defined as Gleason scores ≤3+4 and PSA levels ≤15 ng/mL.[1]

During the median follow-up of 76 months, 592 patients had repeat biopsies. Of these, 185 (31.3%) were Gleason upgraded. Most cancers (60%) were Gleason score ≤3+4 at the time of upgrading. The remaining tumours were Gleason score 4+3 (25.4%), 8 (9.2%), or ≥9 (5.4%). In a multivariate analysis, three baseline factors predicted Gleason upgrading: T2 versus T1 disease, higher PSA, and greater percentage of cores involved at diagnostic biopsy (*Table 1*). Certain dynamic factors also increased the risk of upgrading, including PSA velocity >2 ng/mL/yr (OR, 3.274; p<0.001), and shorter time from registration biopsy to first positive repeat biopsy (OR, 1.437; p=0.0102).[1]

Based on these results, investigators suggested that patients who met any of the following reclassification criteria could be considered for a switch to active treatment: PSA doubling time <3 years, histological upgrading, clinical progression, or patient preference. Overall, 62% of patients had active treatment during the study.

Duration of hormone therapy for high-risk prostate cancer can be shortened without compromising treatment efficacy

Phase III data show that androgen blockade can be

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safely reduced from 36 to 18 months in combination with standard pelvic radiotherapy without compromising outcomes in patients with localised high-risk prostate cancer.

In the PCS IV trial 630 patients with high-risk, node-negative (localised) prostate cancer were randomly assigned to receive either 36 or 18 months of androgen blockade therapy (bicalutamide and goserelin) before, during, and after pelvic and prostate radiotherapy. At a median follow-up of 77 months, comparable numbers of patients were still alive in the two treatment groups (77.1% in the 36-month group and 76.2% in the 18-month group). Five- and 10-year overall survival (OS) rates were also comparable in the 36-month and 18-month groups (92.1% versus 86.8% and 63.6% versus 63.2%, respectively). Moreover, assessment of cancer-specific survival showed that halving the duration of androgen blockade therapy did not affect the odds of dying of prostate cancer (10-year disease-specific survival was 87.2% in both groups).[2]

Prolonged suppression of testosterone production causes a wide range of physical, mental, and emotional side-effects in men, including hot flashes, loss of libido, erectile dysfunction, weight gain, loss of bone density, loss of muscle mass, and depression. Many of those side-effects worsen over the duration of the androgen blockade therapy. It is therefore expected that shorter-course treatment will result in improved quality of life. A quality of life analysis for this study, still in progress, marks the longest quality of life follow-up among patients with prostate cancer to date.

Adjuvant radiotherapy following radical prostatectomy improves long-term biochemical control with few late side-effects

Radiation therapy following radical prostatectomy safely improves long-term biochemical control compared to a wait-and-see approach in men with pathologic T3 (pT3) prostate cancer, according to new findings that add to a growing evidence base in support of adjuvant radiotherapy.

The phase III ARO 96-02 trial included 385 men with pT3 prostate cancer with no evidence of metastasis following radical prostatectomy. Before achieving an undetectable PSA level, patients were randomly assigned to treatment with adjuvant radiotherapy or a wait-and-see approach. The intent-to-treat analysis included 114 patients treated with adjuvant radiation therapy and 159 patients managed with wait-and-see methods.[3]

After ten years of follow-up, biochemical progression-free survival (PFS) was 61% for patients in the adjuvant radiation therapy group, compared to 40% for those in the wait-and-see group ($p=0.000022$). The analysis found no differences between treatment arms in terms of metastasis-free survival ($p=0.56$) or OS ($p=0.59$). However, in the subgroup of patients with positive surgical margins after prostatectomy, adjuvant radiation therapy was associated with a significant improvement on metastasis-free survival compared to wait-and-see (55% versus 27%; $p<0.0001$). Few patients reported late side-effects in the radiation therapy group, suggesting that adjuvant radiotherapy immediately following radical prostatectomy is safe in the long run.[3]

Together with the EORTC 22911 trial and the SWOG 8794, ARO 96-02 is the third large phase III trial evaluating the role of adjuvant radiation following prostatectomy for men with pathologic T3 disease or positive surgical margins at high risk of local failure. All three trials met their primary endpoint of reducing biochemical evidence of disease, suggesting a role for adjuvant radiation therapy after radical prostatectomy in patients with similar risk features.

Surveillance is a safe alternative to surgery for older patients with small kidney tumours

A large retrospective study of older patients diagnosed with small kidney tumours (less than 3.8 cm in diameter) showed that patients who undergo surgery to remove these tumours have the same risk of dying of kidney cancer over a five-year period as those who undergo surveillance. Additionally, elderly patients treated with surgery for these small masses may be at greater risk for suffering a cardiovascular event and an earlier death from any cause. The findings suggest that surveillance with imaging, such as MRI, ultrasound, and CT, is a safe option for the management of small renal masses in the elderly. In three out of four cases, small renal tumours are detected incidentally when a patient undergoes ultrasound, CT, or MRI imaging for an unrelated condition, such as gallstones, abdominal pain, or back pain. Currently, the majority of patients diag-

nosed with a small renal mass receives surgery, which entails removal of either part of the kidney or the entire kidney.

In the study at hand, researchers analysed SEER registry data linked to Medicare claims for patients aged 66 years or older who were diagnosed with small renal masses. Out of the 8,317 patients, 5,706 (70%) underwent surgery and 2,611 (30%) underwent surveillance. During a median follow-up of 4.8 years, overall 2,078 (25%) patients died of whom 277 (3%) of kidney cancer.[4]

Interestingly, the rates of kidney cancer-related death were the same among patients who received surgery and those who underwent surveillance. Moreover, surveillance was associated with a markedly lower risk of death from any cause as well as a lower risk of having a cardiovascular event, such as chronic heart failure, ischaemic stroke, and vascular disease.[4]

Targeted therapies miss the mark for prostate cancer

The phase III READY trial tested the use of dasatinib in combination with docetaxel/prednisone versus docetaxel/prednisone alone in 1,522 patients with metastatic castration-resistant prostate cancer with progressive disease.

Preclinical trials of dasatinib indicated that the drug-inhibited osteoclast function in the tumour micro-environment, and, in combination with docetaxel/prednisone, it was well tolerated and showed anti-tumour activity as indicated by PSA decline and partial tumour response. However, results of the phase III trial showed that dasatinib did not improve OS compared to standard care. The OS for dasatinib was 21.5 months compared to 21.2 months for patients given placebo. Furthermore, subgroups analyses indicated no advantage of dasatinib over the entire population in any of the subgroups analysed. Neither were there any meaningful changes between the two arms with regard to response rates for urinary N-telopeptide, PFS or pain reduction.[5]

The VENICE trial enrolled 1,224 patients. All patients were randomly assigned treatment with docetaxel/prednisone with or without aflibercept. At a median follow-up of three years there was no difference between the arms for the primary endpoint of overall survival, or the secondary endpoint of PFS. Median overall survival was 22.1 months in the aflibercept group versus 21.2 months in the placebo group.[6]

When looking at some of the secondary response endpoints, patients assigned aflibercept had a slightly greater rate of PSA response and tumour response. However, patients assigned aflibercept had a higher rate of grade 3/4 adverse events compared to patients assigned placebo (76.9% versus 48.5%), including a higher rate of fatal adverse events.[6]

As such, aflibercept and dasatinib are now both among a growing list of targeted agents that researchers have unsuccessfully tried to combine with standard treatment to improve survival for men with metastatic castration-resistant prostate cancer.

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