WHEN AND HOW TO TREAT PELVIC LYMPH NODES

Professor David Dearnaley set the scene for the following discussion by asking whether pelvic lymph nodes should be treated in prostate cancer. Most studies in advanced localised disease have involved the treatment of lymph nodes, but when the phase 3 Scandinavian Prostate Cancer Group-7 (SPCG-7) trial, which did not involve pelvic radiotherapy, is compared with the Medical Research Council (MRC) PR07 trial, in which pelvic radiotherapy was recommended, the results are strikingly similar (12 and 11 per cent prostate cancer deaths in SPCG-7 and MRC PR07, respectively, after 10 and 7 years of follow-up).

In terms of randomised trials, the Radiation Therapy Oncology Group (RTOG) 9413 trial in 1279 patients with clinically localised adenocarcinoma of the prostate and prostate-specific antigen (PSA) <100ng/ml showed no difference in progression-free survival (PFS) between patients treated with whole pelvic radiotherapy and those treated with prostate-only radiotherapy.

The smaller French study, Genito-urinary Tumor Group-01 (GETUG-01), in 444 patients with T1b-T3, N0 pNx, M0 prostate carcinoma, also showed no benefit in PFS with pelvic node irradiation.4

These observations raise a number of important questions:

- Were the appropriate patient groups recruited?
- Were the prostate and pelvic lymph node doses adequate?
- Was the pelvic lymph node target volume appropriate?
- Was the RTOG trial confounded by the second randomisation?
- Were the trial sizes adequate?

Professor Dearnaley then asked the audience a series of questions pertinent to the implementation of a new trial into pelvic lymph node radiotherapy. The keypad responses are summarised in Table 1.

Professor Dearnaley commented that the responses are useful in helping shape future trials into pelvic lymph node treatment, particularly given the large
differences in the design of existing studies in this area, notably RTOG 09245 and Prostate and pelvis Versus proOsTate Alone treatment for Locally advanced prostate cancer (PIVOTAL). A similar observation can be made among patients with extensive metastases and rising PSA (9–12 months for both asymptomatic and symptomatic patients).

In terms of PSA doubling time, several clinical trials have confirmed the intuitive expectation that a longer PSA doubling time tends to lead to longer survival than a shorter PSA doubling time. As survival is therefore somewhat predictable, this raises the question of whether intervention can impact on survival time.

Guidance from the Prostate Cancer Clinical Trials Working Group on the role of PSA as an endpoint in clinical trials of patients with castration-resistant prostate cancer does not make any distinction between asymptomatic and symptomatic patients. This guidance states that, in the absence of clinically compelling indicators of disease progression, early changes in PSA should be ignored, while in the pre-chemotherapy or first-line chemotherapy setting, treatment should continue for at least 12 weeks, irrespective of PSA. Furthermore, patients with a rising PSA should remain on therapy until radiographic or symptomatic progression.

Discussion

The responses to a series of questions posed by Professor Clarke are shown in Table 2.

Among participants who responded that they would intervene based on PSA-based parameters, this was felt to be in the absence of any other information relating to disease progression in the patient. The reason for such an intervention would be to attempt to delay the onset of symptoms, even though it was acknowledged that there are currently no data to support this. It was felt among these responders that PSA-based parameters are currently the

tables
best way of deciding when to intervene in asymptomatic patients.

The absolute PSA level was not generally considered to be relevant to the management of a patient, even if the value was particularly high. The rate of PSA increase was considered to be more informative. It was commented that it is psychologically important for the patient to try to reduce the PSA doubling time, as many patients are familiar with PSA and fear a rapidly rising level.

Declaration of interests
The British Uro-oncology Group seminar ‘Hot topics for debate in prostate cancer’ was sponsored by Takeda. Takeda selected and briefed the speakers on the content of the session and they were paid an honorarium by Takeda. Takeda have had no editorial control over any publications arising from the meeting.

REFERENCES


6. Prostate and pelvis Versus prostate Alone treatment for Locally advanced prostate cancer (PIVOTAL). http://rrtrialsqa.dmsalias.org/Pivotal/Pivotal%20Trial%20Website%20Summary.htm

