invariant over the same time period. Ser15-p53 foci were not observed in ATM-/- fibroblasts (GM05823) cells, but are present in Nijmegen Breakage Syndrome fibroblasts (GM07166). Current experiments are underway to correlate the number of ser15-p53, rad51 and rad50 foci in a panel of fibroblasts with biochemical DNA rejoining assays (CFGE) and overall cell survival and may possibly provide a predictive assay for mammalian cell radiosensitivity.

Genitourinary cancer

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Bicalutamide ('casodex') 150 mg as adjuvant to radiotherapy in localised or locally advanced prostate cancer

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Objectives: The efficacy and tolerability of bicalutamide ('Casodex') 150 mg (a non-steroidal antiandrogen) as immediate therapy or as adjuvant to therapy of curative intent in localised or locally advanced prostate cancer has been evaluated in the world's largest randomised, double-blind clinical trial programme in prostate cancer.

Patients and Methods: Prostate cancer patients (n=8113) with negative bone scans were enrolled from N. America (n=3292), Scandinavia (n=1218), and Europe, S. Africa, Australia and Mexico (n=3603). Patients were randomised to receive bicalutamide 150 mg/day (n=4052) or placebo (n=4061), plus standard care of radical prostatectomy (55%), radiotherapy (17%) or watchful waiting (28%). Objective disease progression was determined by bone scan, CT scan, ultrasound or MRI. Deaths from any cause in the absence of progression were counted as objective progressions. PSA progression was not a criterion for objective progression. A planned, pooled analysis of all 3 trials was performed on an intent-to-treat basis using a Cox proportional hazards regression model for progression-free survival.

Results: At a median follow-up of 3 years, bicalutamide 150 mg plus standard care significantly reduced the risk of disease progression by 42% compared with standard care alone (HR 0.58; 95% CI 0.51, 0.66; $p<<0.0001$). Of 922 patients with objective progression, 363 progressed on bicalutamide and 559 on standard care alone. Reductions in risk were seen across the entire patient population, regardless of underlying therapy (radical prostatectomy, radiation therapy or watchful waiting) or disease stage. Of the 1,358 patients who received radiotherapy, 178 patients progressed (75 bicalutamide; 103 standard care alone). The most frequently reported side effects of bicalutamide were gynaecomastia and breast pain. Survival data were immature with 6% overall mortality and <2% of patients dying due to prostate cancer.

Conclusions: Radiotherapy with adjuvant bicalutamide 150 mg, in men with localised or locally advanced prostate cancer, reduces the risk of disease progression. These findings are consistent with those reported by Bolla, showing that adjuvant hormonal treatment with goserelin ('Zoladex') and radiotherapy reduced disease progression and significantly improved overall survival compared with radiotherapy alone.

'Casodex' and 'Zoladex' are trade marks of the AstraZeneca group of companies

References

[Bolla M et al. Eur Urol 1999;35:23-25.]

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A randomised trial of two radiotherapy schedules in the adjuvant treatment of stage I seminoma (MRC TE18)

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Background: Adjuvant post-orchidectomy radiotherapy (RT) cures the majority of patients (pts) with stage I seminoma, but as approximately 80% would remain relapse-free on surveillance alone, minimising RT - and hence morbidity and second cancer risk - is a worthwhile aim.

Methods: Pts were randomised within 8 weeks (wks) of orchidectomy to receive 20 Gy in 10 fractions over 2 wks or 30 Gy in 15 fractions over 3 wks. They were asked to complete a symptom diary card daily for 4 wks after starting RT and weekly for a further 8 wks, and quality of life forms (EORTC QLQ-C30+testis cancer module) at 0,3,6,12 and 24 months. The primary endpoint was the relapse-free rate.

Results: Between Jan 1995 and Jan 1998, 625 pts were randomised from 45 centres worldwide. The groups were well balanced with respect to baseline characteristics and 98% of pts in each treatment group received their allocated treatment. Four wks after the start of RT significantly more 30Gy patients reported moderate or severe lethargy (20% vs 5%) and an inability to carry out normal work (46% vs 28%), however by 12 wks, levels in the randomised groups were similar. With a median follow-up time of 37 months, 8 relapses have been reported in the 30 Gy group and 10 in the 20 Gy group (HR=1.27, 90% CI (0.58, 2.8)). The difference in 2 year relapse rates is 0.3%, 90% CI (-1.9%, 2.5%) i.e. the probability that true difference exceeds 2.5% is < 5%. A further 393 patients have been randomised with respect to the same RT doses within a subsequent trial (MRC TE19) of whom 6 (30Gy 5;20Gy 1) have relapsed; analysing all 1018 patients the difference in relapse rates at 2 years is 0.8% in favour of the 20 Gy group, with the upper 90% CI excluding differences of more than 1.3%.

Conclusions: This randomised trial has confirmed that 20 Gy in 10 fractions is unlikely to produce relapse rates more than 2% higher than for standard 30Gy RT and reductions in morbidity enable patients to return to work more rapidly.

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Quality of life (QL) in patients with good prognosis metastatic malignant germ cell tumour (MGCT): comparison of 4 chemotherapy schedules (EORTC 30941/MRC te20)

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Aim: To compare by a 2x2 factorial design QL after 3 or 4 cycles BEP (Bleomycin/Etoposide/Cisplatin) chemotherapy, being applied over 3 or 5 days. Methods: In 30941/TE20 (JCO, 19; 1629, 2001) QL was evaluated by the EORTC QLQ C-30 questionnaire (version 2.0) and a testicular cancer (TC) module prior to chemotherapy and at 3, 6 and 12 months thereafter. A mixed model was applied for statistical analysis of QL patterns during the first year. Statistically significant changes of ~10 effect points were defined as clinically significant.

Results: 666 of 812 patients were evaluable for QL. Global QL is significantly decreased at month 3 in all groups relative to baseline, the impact is less for 3-cycle regimens and is more for 3-day regimens. The best tolerated regimen appears to be 3 cycles/5days. There was a significant worsening at 3 months for physical, role and social functioning and for fatigue, dyspnoea and appetite loss. Nausea/vomiting at 3 months was worst for the 4 cycles/3days regimen and was best for the 3cycles/5days regimen. Tinnitus was much increased at 3 months with the 4 cycles/3days regimen. Sexual problems were more frequent during treatment on the 4 cycle regimens. Recovery of side effects was rapid after discontinuation of chemotherapy except for peripheral neuropathy (PN) and Raynaud phenomena (RP) which were worst at the 6 months assessment. One year after treatment start, QL was generally slightly better than at treatment start without differences between the 4 schedules. Role and emotional function were even better than at diagnosis, whereas PN and RP remained clinically relevant problems, as was tinnitus, if 4 cycles were given during 3 days.

Conclusion: If 4 BEP cycles are needed, chemotherapy should be given during 5 days per cycle to maintain optimal QL during chemotherapy and up to 1 year after treatment. Problems with nausea/vomiting and tinnitus at 3 months can be reduced if BEP chemotherapy is applied as a 3 cycles/5 days regimen.

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Favourable psa outcome in patients with large prostates or moderate risk prostate cancer treated by a combination brachytherapy and neoadjuvant hormonal therapy

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Purpose: Patients with localized prostate cancer electing permanent brachytherapy may have an inferior outcome if they present with a large