117 ORAL

Immediate versus delayed postprostatectomy irradiation

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Purpose: To determine and compare the results of immediate postprostatectomy irradiation in patients with adverse prognostic factors versus observation plus delayed irradiation for clinically/radiographically local-regional recurrence.

Materials and Methods: Eight-one patients with adverse prognostic factors underwent postprostatectomy irradiation, 28 in the postprostactectomy period and 53 a mean of 3.5 years following prostatectomy after clinically localized recurrence.

Results: Only 4 patients developed palpable in-field recurrence; the majority of failures were attributable to the appearance of distant metastases, which appeared a median of 3 years after day 1 of radiation therapy (range, 2–13 years). Both factors were distributed equally between the immediate- and delayed-treatment groups. For the 59 patients treated since 1982, 44 are alive and disease free with a median follow-up of 3.6 years (range, 2–13 years), 5 are alive and receiving hormonal therapy because of metastatic disease and 10 have died, 3 of local recurrence as the 1st sign of failure and 7 with distant metastases and no clinical evidence of local recurrence. Prostate-specific antigen values provided an early indicator of treatment failure but did not alter the ultimate result for patients treated in earlier years versus those treated more recently.

Conclusion: There was no significant difference in the ultimate clinical result for patients treated in the immediate postprostatectomy period versus those for whom irradiation was delayed until local recurrence could be demonstrated.

118 ORAL

Three dimensional conformal radiotherapy in the treatment of localized prostate cancer

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Purpose: The aim of this prospective study is to evaluate the clinical results of three-dimensional conformal radiotherapy (3-D CRT) in the curative treatment of localized prostate cancer.

Methods: From September 1993 to September 1996 92 patients with localized prostate cancer (cT1-3 cN0 cM0) were treated with 3-D CRT using total doses of 68 to 70 Gy. Depending on stage, grade and pretherapeutic PSA level seminal vesicles were included into the target volume. 3D CRT was delivered with four-field axial, six-field axial or four-field oblique non-axial techniques.

Results: The median follow-up was 20 months. At present, there is no local failure. In eight patients a proctitis WHO II with occasional or persistent hemorrhagia was found. No severe side effects occurred (WHO III–IV). Five of eight patients presented vascular diseases, too. On analysis of dose volume histograms of the rectal wall a clear correlation between the amount of normal tissue irradiated and the risk of proctitis could be demonstrated.

Conclusion: Conformal radiotherapy is an effective approach to minimize radiation exposure of the rectum and to reduce the risk of rectal side effects in the radical treatment of prostate cancer.

119 ORAL

Taxotere and cisplatin in metastatic urothelial cancer: A phase II study

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Purpose: Taxotere has documented single agent activity in patients (pts) with metastatic urothelial cancer. We combined Taxotere with Cisplatin in a phase II study evaluating response rate, toxicity and survival.

Methods: Eligibility criteria included locally advanced or metastatic disease, performance status (WHO) < 3, normal bone marrow, liver and renal function, and no symptomatic peripheral neuropathy. The pts received Taxotere 75 mg/m^2 and Cisplatin 75 mg/m^2 day one every third week. Premedication included clemastin and prednisolon.

Results: 24 pts are included in the study. 23 pts are evaluable for response and toxicity. Median age was 64 years (range, 48–72 years), 6 pts had locally advanced disease and 17 pts metastatic disease. Fourteen (61%) pts achieved response including 6 (25%) pts achieving complete response. Six pts had stable disease and 3 pts had progressive disease after 2 courses. Median response duration and survival are 6+ and 10+ months. Eight pts had grade 4 hematological toxicity, but none had neutropenic fever. Gastrointestinal toxicity was moderate. Peripheral neuropathy, myalgia, skin rashes, and fluid retention was mild.

Conclusion: The combination of Taxotere and Cisplatin is effective and feasible in patients with metastatic urothelial cancer. The toxicity of the combination is manageable. (Supported by Rhône-Poulenc Rorer).

120 ORAL

Intravesical BCG-instillation therapy for superficial bladder cancer: A standard beneficial treatment beyond the understanding of its mode of action?

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Purpose: Topic BCG (Bacillus Calmette-Guérin) instillation therapy is the method of choice against superficial bladder cancer recurrences including carcinoma in situ. In order to elucidate the mode of action of BCG, bladder biopsies and the urinary cytokine profile was investigated in patients. In an vitro approach, we set up a model to characterize the cytotoxic effector cells.

Methods: Bladder biopsies were stained for CD4+ and CD8+ cells before, during and after instillation therapy. Urinary secretion of IL-1, TNF and IL-6 was detected by ELISA and bioassay. In vitro, PBMC were co-incubated with BCG or IL-2. The resulting cytotoxicity was measured in different target cell culture systems.

Results: The inversion of the CD4+/CD8+ ratio with predominance of CD4+ cells in the bladder wall after therapy lasted for longer than 1 year. IL-1, TNF and IL-6 secretion in the urine was highly elevated in patients. The in vitro co-incubation of PBMC with BCG resulted in the induction cytotoxic cells termed BCG-activated Killer (BAK-) cells that exhibited a pronounced cytotoxicity towards single bladder tumor cells and multicellular spheroids (MCS).

Conclusion: Our in vitro approach reflects the local activation of immnuno-competent cells detected in vivo playing a crucial role in BCG-instillation therapy.

121 POSTER

Modulating endogenous retinoic acid (En-RA) levels with RAMBAs may produce fewer side-effects (SEs) than exogenous RA (Ex-RA)

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Liazal (LIA), a retinoic acid metabolism blocking agent (RAMBA), promotes cancer cells to differentiate by increasing En-RA. SEs observed in a randomised phase III study (LIA 300 mg bid, n = 160 vs cyproterone acetate 100 mg bid, n = 161) in prostate cancer patients failing first-line androgen ablation, are at least partially similar to hypervitaminosis A. All SEs of LIA were analysed for severity, duration as well as duration relative to the period of drug intake. Although frequent, the SEs were rarely severe. Moreover, most severe SEs lasted for less than one month and/or less than half of the treatment time (Table, % of LIA group). This compares favourably to Ex-RA: mucositis in 48%, dry skin or lips in 100%, rash in 57%, fatigue in 14%, myalgia/arthralgia in 29% (Besa *et al*, 1990).

	Total (%)	Duration			Relative duration		
		≤2 wks	2 wk-1 mo	>1 mo	≤10%	10–50%	>50%
Dry skin	51	3	6	39	3	9	36
Severe	3	1	0	2	0	2	1
Rash	16	4	2	9	3	6	7
Severe	–	–	–	–	–	–	–
Fatigue	22	4	6	11	3	8	10
Severe	7	3	3	1	3	3	2
Naus ± vomit	44	16	6	22	9	18	17
Severe	8	4	1	3	2	5	1

Conclusion: Although side-effects are frequently encountered with Liazal, these are mostly mild to moderate and restricted in time. Nausea and vomiting are known symptoms in late stage cancer patients. This compares favourably to currently used exogenous retinoids.