weeks, not closely related to PSA changes. Our preliminary data suggest that oral V is a safe and moderately active option in the palliation of elderly HRPC pts. Accrual is ongoing.

429P A phase II study of vinorelbine (NVB) D1+D8 plus prednisone (PDN) for hormone-resistant metastatic prostatic cancer

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Hormone-resistant prostate cancer has few effective drugs, and the vinca alkaloids and taxanes are emerging drugs for this treatment. We studied 30 actually available pts with 2 or more cycles of NVB, with a mean age 68 years (46 - 87), with metastatic and hormone-resistant prostate cancer. 18/30 (60%) completed 3 or more cycles of NVB. Median PSA at baseline was 252,9 ng/mL. Schedule of treatment: NVB 30 mg/m^2 intravenous D1+D8 (21 days cycle), plus PDN 10 mg PO daily, continuously.
Objectives: PSA response (stable, up to 50% and more than 50% and 75%), clinical response for pain (intensity and reduce of analgesic consumption), asthenia and anorexia, variation of PS (ECOG); toxicity; time to progression and overall survival were not evaluated.
Results: Response of PSA- 50% of the pts completed 2 cycles, with 12/15 excluded by elevation of PSA. Therefore, 18 pts completed 3 or more cycles (3 - 11+ cycles) with 11/18 PSA responses (61,1%), 4 stable PSA (22,2%) and only 3/15 progression of PSA. *Clinical evaluation:* (Analogic scales varies from 0 - 5). Mean pain intensity score fall from 3,9 to 2,3; at baseline 9 pts were without pain, and after 2 cycles, 12 pts were without pain. Asthenia falls from 2,2 to 1,1, and anorexia from 2,1 to 1,0. PS variation - 0 to 0 =4 pts; 1or 2 to 0 = 4; 1 to 1 = 12 pts; 0 to 1= 3 pts; PS worsted in 6 pts. It was observed a positive correlation between PSA response and clinical response at 5th cycle: from 15 alived and well pts in the 5th cycle, 7 of them demonstrated a PSA response, and 3 a stable PSA. *Toxicity:* G3 toxicity: neutropenia - 1 pt; phlebitis G3 - 3 episodes; neurotoxicity G1+G2 = 5 pts; 1pt with varicella-zoster; 1 pt developed diabetes mellitus. NVB weekly dosis varies from 34 - 55 mg.
Conclusions: the association of NVB + PDN is a safe and appropriated treatment for these special pts, and our results (with D1+D8 NVB) confirms others similars studies (with weekly NVB). Final reports will be done after analysis of data obtained with the actual 51 included pts by this research group.

430P Early undetectable serum PSA is an independent predictive factor of progression-free survival (PFS) in patients with localized prostate cancer treated by androgen deprivation and radiotherapy

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Background: Patients with locally-advanced prostate cancer are currently managed by androgen deprivation (AD) and radiation (RT). We attempted to identify early predictors of outcome in a retrospective series.
Methods: From 1991 to 1998, 92 patients with locally-advanced prostate cancer were treated by AD and RT. Median pretreatment PSA level was 19 ng/mL (1.6-148). Clinical stage was T1 (4%), T2 (60%), and T3 (36%). Gleason score was 4-6 (46%), 7 (32%) and 8-10 (22%). Prognosis was classified as high risk (T3 and/or PSA>20 ng/mL and/or Gleason score > 7) (n= 59) or intermediate risk (n= 33). AD consisted in a complete androgen blockade (GnRH agonist and anti-androgen) (55 pts) or an anti-androgen as a single agent (37 pts) and was given for a median duration of 6 months (3-18). AD was usually initiated 3 months before RT. The prostate was to receive 65 Gy (2.5 Gy/day) (74 pts) or 70 Gy (2 Gy/day) (18 pts). The median follow-up (from Day 1 AD) was 70 months (14-126).
Results: The 5-year PSA PFS rate was 41% (95% CI: 30-52) and 57% (95% CI: 47-67) according to the ASTRO definition and the MDACC definition, respectively. The 5-year metastases-free survival and the 5-year cause specific survival rates were respectively 81% (95% CI: 73-89) and 93,5% (95% CI: 88-99). The median PSA level assessed 3 to 6 months after the start of AD and before RT was 1.3 ng/mL (0.08-31). In multivariate analysis, significant predictors for PSA-PFS included high-risk disease (HR=3.3, 95% CI=1.7%-6.2%; p<0.01) and an undetectable (<0.2 ng/mL) serum PSA after 3 months of neo-adjuvant AD (HR=13.4, 95% CI=1.8%-97%; p=0.01). High-risk disease was the only significant predictor of distant metastases (HR=3.7, 95% CI=1.1%-12.6%; p=0.04). The 5-year metastases-free survival rates were 79% for the patients who had detectable PSA after 3 months of neo-adjuvant AD and 100% who had undetectable PSA (p=0.11).
Conclusion: Undetectable serum PSA 3 months after AD is an independent predictor of PSA-PFS. Metastases rate may be also be lower in case of undetectable PSA. Therefore, this factor may be a useful early surrogate endpoint in clinical trials using neo-adjuvant treatments.

431P Cell growth inhibition in PC-3 human prostate cancer cells after treatment with gamma-radiation and 8-Cl-cAMP

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Prostate cancer is the most frequent malignant disease in men. The advanced cancer is mostly treated by radiation, sometimes in combination with hormone therapy. However, such therapy often leads to selection of hormone resistant cells and necessity to include chemotherapy.
In this study the individual or combined effects of 8-Cl-cAMP (1-50 μM) and gamma-radiation (2-20 Gy) on hormone resistant PC-3 human prostate cancer were followed. In the combined treatment experiments cells were exposed to 8-Cl-cAMP 24 h previous to 10 Gy irradiation. All cells were assayed for their membrane integrity preservation (trypan blue exclusion assay, TBE), DNA synthesys rate (BrdU uptake assay) and the metabolic activity (MTT assay). The results demonstrated that either 8-Cl-cAMP or gamma-radiation, inhibited proliferation and metabolic activity of PC-3 cells in the dose dependant manner. Both treatment showed significant inhibition of PC-3 cell proliferation with IC_{50} of 12.5 μM and 11.9 Gy, respectively, according to BrdU test. The inhibition of metabolic activity was also dose dependant, but the IC_{50} values were not reached within the dose ranges used in this study. The TBE assay showed that cell viability remained rather high after treatment with either 8-Cl-cAMP or gamma-radiation (>90%), but the number of viable cells in treated *vs.* control cells (i.e. Viability index) decreased, with IC_{50} values of 15 μM and 10.4 Gy, respectively. The Viability index was further decreased from 77% (1 μM 8-Cl-cAMP) and 52% (10 Gy) to 26% when combined treatment was applied. The combination index (CI) of 0.7 suggested moderate synergism. On the contrary, BrdU assay showed antagonism (CI 3.5) in the combined treatment, indicating that 72 hours after irradiation and pre-treatment with 8-Cl-cAMP, the effect of combination disappears.
Thus, although the pretreatment of PC-3 cells with relatively low concentration of 8-Cl-cAMP significantly enhances cell growth inhibition of successive gamma-radiation, this effect is short-term. Further preclinical tests should be introduced to show if 8-Cl-cAMP added after gamma-irradiation could successfully control growth of hormone-refractory prostate-cancer.

432P Preliminary report of a multicenter Spanish trial (GICOR-05) of risk-adapted androgen deprivation vombined with dose-escalation 3D conformal therapy for prostate cancer: Impact on PSA outcome

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Purpose/Objective: A multicenter prospective study was conducted to determine the impact on biochemical control and survival of risk-adapted androgen deprivation (AD) in combination with dose escalation 3D conformal radiotherapy (3DCRT) for localized prostate cancer. Preliminary results of biochemical control are reported.
Materials/Methods: Between October 1999 and October 2001, 416 eligible localized prostate cancer patients were enrolled in a prospective multicenter study. 181 low risk patients (defined as having T1c stage or T2 stage with PSA <20 ng/ml and Gleason score <7) were treated with 3DCRT alone. 73 intermediate risk patients (T2 stage with PSA 20-40 ng/ml or Gleason score = 7) were allocated to receive neoadjuvant AD (NAD) 2 to 6 months prior