DTX on PC3 cell growth inhibition and similar results were recorded after transfection of PC3 cells with shCYR61. In conclusion, it is possible to design new molecular rationale-based therapeutic strategies in androgen-independent prostate cancer.

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DOCETAXEL AND ZOLEDRONIC ACID COMBINATION ADMINISTERED IN TWO DIFFERENT SEQUENCES IN HORMONE REFRACTORY PROSTATE CANCER PATIENTS: PHASE I CLINICAL STUDY – ZANTE

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Background: Docetaxel (DTX) is effective in the treatment of hormone-refractory prostate carcinoma patients (HRPC). *In vitro* data suggest that zoledronic acid (ZOL) and DTX have a synergistic effect on the growth inhibition of prostate cancer cells and that such synergism is sequence-dependent. Therefore, prostate cancer is a suitable target for a pharmacological combination between DTX and ZOL. On the basis of these considerations, a phase I trial on the combination of ZOL and DTX was designed in the treatment of HRPC.

Materials: A dose-escalation of DTX was planned in combination with a fixed dose of ZOL (2 mg), both administered every 14 days. The following two different sequences of the two drugs were explored: Sequence A: DTX at day 1 followed by ZOL at day 2. Sequence B: ZOL at day 1 followed by DTX at day 2. The first dose level of DTX was 30 mg/m^2 with a planned dose escalation of 10 mg/m^2 for each level until 50 mg/m^2. Serum cytokines and PBMC were also collected prior and after the different treatments at each cycle.

Results: Up to now, we have enrolled 22 patients. Six patients at third level (Sequence B) were required due a case of vascular toxicity of grade III (deep thrombo-phlebitis). A different pattern of circulating sangiogenic factors (interleukin 8 and 12, VEGF, PDGF), cytokines (TNF-a, IFN-c, interleukin 6 and 4) and gamma/delta T lymphocyte subpopulation was recorded in the two different sequences. The study is still ongoing and further results will be presented at GOIM meeting.

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INTRAVESCICAL GEMCITABINE VERSUS MITOMYCIN FOR RECURRENT SUPERFICIAL BLADDER TUMOURS (STAGES PTA AND PT1): A RANDOMIZED PROSPECTIVE STUDY

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Background: Approximately, 30–40% of patients with a superficial bladder cancer treated with Bacille Calmette-Guerin(BCG) or epirubicin do not respond and other 35% of initial responders have a relapse within 5 years. We compare the therapeutic efficacy and toxicity of intravescical instillations of Gemcitabine (GEM) with mitomycin C (MMC) in patients with a recurrent superficial bladder cancer.

Methods: Patients with a history of a recurrent Ta-T1, G1-G2 bladder transitional cell carcinoma, previously treated were enrolled in the study. The patients received a 6-week course of GEM instillations or 4-week course of MMC. In both arms, for the initial responders who remained free of recurrences, maintenance therapy consisted of a 10 monthly treatment during the first year. All patients were followed every 6 months by cystourethroscopy.

Results: A total of 120 patients were enrolled and randomly assigned to either the MMC treatment arm or Gemcitabine treatment arm. The remaining 109 patients (55 in MMC arm and 54 in Gemcitabine arm) were evaluable. The median duration of follow-up was (identical for both groups) 34 months.

Of the 54 patients in the Gemcitabine group 42(78%) remained free of recurrence compared to 37 (67%) of the 55 patients treated with MMC ($p = 0.05$). Among patients with recurrences, 10 in the MMC arm and 6 in the Gemcitabine group had progressive disease by stage: either local urothelial spread, or muscle infiltration, in 5 and 3, respectively. Local toxicity in both treatment groups was acceptable. The incidence of. chemical cystitis in MMC arm was statisticantly different from that in GEM group ($p = 0{,}012$).

Conclusions: Gemcitabine for its better clinical activity and favourable toxicity profile than MMC, is a logical candidate for intravescical therapy in refractory transitional cell patients. Final results will be presented at 2008 ASCO Meeting.

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HIGH-DOSE CHEMOTHERAPY AS INITIAL SALVAGE TREATMENT IN RELAPSED TESTICULAR CANCER PATIENTS

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Background: In the last few years, high dose chemotherapy (HDCT) with haematopoietic stem cell transplantation (HSCT) has been increasingly investigated as a therapeutic option for early or late intensification in patients with poor prognosis germ cell tumor (GCT) or in pats who relapse or who have a partial response after a first line chemotherapy.

Methods: Eleven patients were treated with three cycles of VeIP (ifosfamide 1200 mg/m^2, mesna 1200 mg/m^2, cisplatin 20 mg/m^2, days 1–5 and vinblastine 0.11 mg/kg, days 1–2) and one course of HDCT: Carbo-PEC (carboplatin 400–550 mg/m^2/day on day 1, etoposide 450 mg/m^2/day, cyclophosphamide 1600 mg/m^2/day and mesna 3600 mg/m^2 on days 1–4) followed on day 7 by HSCT.

The IGCCCG stage was III A in 1, III B in 3 and III C in 7. The median age was 24 years (range 17–33).

Results: Ten patients were assessable for response: 3 CR, 4 PR, 2 SD and 1 PD were observed. One patient died due to brain hemorrhage (on day 10 from Carbo-PEC). Four patients underwent to surgery and two were pCRs. Six patients (54%) are still alive with a median follow up of 100 months (range 78–148). Four patients progressed after chemotherapy and died from disease at 5, 10, 32 and 34 months from the date of the start of the first chemotherapy cycle. Event free survival rates (defined as time to disease progression, relapse or death, whatever the cause) were measured from the date of the start of the first chemotherapy cycle at 1 and 3 years and resulted 72% and 54%, respectively.

Conclusions: Our experience showed that early intensification HDCT is an effective and tolerable regimen in patients relapsing after a standard first line chemotherapy. Further clinical trials of HDCT should analyze predictive factors for treatment outcome.

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TAMOXIFEN IN THE TREATMENT OF RECURRENT, ADVANCED BORDER LINE OVARIAN CANCER: A SINGLE CENTRE EXPERIENCE

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Background: Treatment of borderline ovarian tumours is based on surgery while chemotherapy is poorly effective. Advance border line ovarian tumours are rare nad response to chemotherapy is poor. Border line cancer frequently express estrogen receptors and few cases responding to hormonal treatments have been reported.

Methods: We describe three cases of recurrent serous disease out of 42 newly diagnosed border line cancer observed at our institution in 5 years. In all three cases estrogen receptor was determined by immunohistochemistry and was found positive. Patients were treated with 20 mg/daily tamoxifen until progression.

Results: In no case we observed a complete remission, but in all a clinical and serological Ca 125 response was observed. In one patient a control was maintained for 3 years. In another, after progression, a new response was obtained doubling tamoxifen dose. Two of 3 patients are alive continuing tamoxifen and in response from 10 and 15 months, respectively.

Conclusions: Our data support the hypothesis that hormonal treatment represents an option for recurrent borderline ovarian tumours.

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REDISCOVERING IMMUNOTHERAPY IN COMBINATION WITH MOLECULARLY TARGETED AGENTS IN RENAL CELL CANCER

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Renal cell carcinoma accounts for approximately 2–3% of all malignancies and includes different histological subtypes.

Prognosis of metastatic disease (mRCC) still remains unfavourable and patients survival depends on well known prognostic factors, as defined by the MSKCC score. Overall, the median survival in advanced disease is about 14 months.

Cytokine-based immunotherapy with interferon-alfa (IFN-alfa) and interleukin-2 (IL-2), alone or in association, is considered the standard care for mRCC.

From 2005, in the targeted therapies era, some significant clinical trials showed the promising activity and efficacy of new drugs like Sorafenib, Sunitinib, Temsirolimus, Everolimus and Bevacizumab. These biomolecular agents have improved disease control in patients with mRCC.

In particular, Sorafenib is an orally available multikinase inhibitor that demonstrated, as single agent, an improvement of progression-free survival in cytokine-refractory mRCC.

Some clinical trials explored the efficacy and safety of the association between biomolecular agents such as Sorafenib itself, Bevacizumab or Temsirolimus and immunotherapy with IFN-alfa and IL-2.

The rationale of bio-immunotherapy of mRCC with targeted agents in combination with cytokines is represented by their different mechanisms of action and possible synergistic effects in blocking cancer growth.

The ROSORC trial is a phase II italian study of first line therapy with Sorafenib *plus* low dose IL-2 administered subcutaneously versus Sorafenib alone in unresectable and/or metastatic RCC. The accrual target is set at 128 patients and the main endpoints are the progression-free survival, the overall survival, the response rate and the safety in both arms of therapy.

In our experience the association between cytokines and targeted therapies is feasible and we purpose to choose this combination regimen in the upfront treatment of particular subgroups of patients, according to risk stratification and objectives of clinicians.

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IMAGE GUIDED RADIATION THERAPY (IGRT) IN THE TREATMENT PLANNING OF PROSTATE CANCER: ACCURACY AND PRECISION OF RADIATION THERAPY THROUGH MODERN IMAGING TECNOLOGIES

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The objective principal of the radiotherapy it is the control local or locoregional to curative purpose with saving of the normal tissues. In the last decades the possibility to have available software able to integrate diagnostic data coming from images of Computerized Tomography (CT), of Magnetic Resonance Imaging (MRI) and nuclear medicine (NM) with algorithms of calculation of doses able to calculate the dose in more dimensions have allowed to realise the radiotherapy conformal (3D-CRT) to the purpose to realise of radiant treatments more and more individualised and with smaller late effects.

Advances in the delivery of radiotherapy treatment such as the 3D-CRT and Intensity Modulated Radiation Therapy (IMRT)