available at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejconline.com

Abstracts

Genitourinary cancer

SUNITINIB IN ADVANCED CLEAR CELL RENAL CANCER: A SINGLE CENTRE EXPERIENCE

G.S. Bruni, G. Facchini, V.R. Iaffaioli, C. Pisano, S. Pignata. *Uro-Gynecologic Department, National Cancer Institute of Naples, Italy*

Renal cell carcinoma represents 2–3% of all cancer. New systemic therapies have reached the market in the last 2 years. Sunitinib was found to be superior to IFN-a in a phase III trial in metastatic renal cancer patients (mRC). Fatigue, gastrointestinal and skin are the most frequently reported toxicities. Most of them are easily solved with medical intervention or dose changes. In our center we evaluated the sunitinib compliance and activity in an unselected series of consecutive patients. In the first year after sunitinib availability in Italy, 17 consecutive patients (13 male, 4 female, median age 62 years, range 40–81) with intermediate/poor risk mRC were treated in our institution. Most frequent metastatic sites were lung, pleura, bone, nodes and liver. Six out of 17 patients were pretreated with cytokines. Overall 68 cycles of sunitinib were given (range 1–11). Objective responses were observed in 5 patients (29%), while stable disease was observed in 4 patients (23%) (overall clinical benefit 52%). Toxicity was as follows:

	G1–2 (%)	G3 (%)
Gastrointestinal	75	0
Skin	29	11
Mucositis	17	23
Hypotirodism	23	0
Anemia	11	0
Leukopenia	11	0
Hearth	6	6
Fatigue	35	6

Results: Dose reductions were done in 9/17 patients (skin 1, mucositis 4, hearth 2, fatigue 1, anemia 1), and in 3 cases treatment was temporaneously interrupted due to toxicity. In conclusions, sunitinib was confirmed to have significant activity in mRC. G3 toxicities are unfrequent, but often require dose modifications. Self-training and internal guidelines in side effects medical treatment and dose reduction rules seems crucial for an optimal use of sunitinib in unselected patients out of clinical trials.

doi:10.1016/j.ejcsup.2008.06.046

CYR61 DOWN-MODULATION SENSITIZES PROSTATE CANCER CELLS TO ZOLEDRONIC ACID AND DOCETAXEL: A NEW ANTI-CANCER STRATEGY

M. Caraglia [a], M. Marra [a], G. Meo [a], S. Zappavigna [a], B. Vincenzi [b], A. Baldi [c], M. Rosolowski [d], M. Loeffler [d], G. Tonini [b], D. Santini [b], A. Budillon [a]. [a] *Department of Research, Experimental Pharmacology Unit, National Institute of Tumours Pascale, Naples, Italy.* [b] *Medical Oncology, University Campus Bio-Medico, Rome, Italy.* [c] *Second University of Naples, Italy.* [d] *Institute for Medical Informatics, Statistics and Epidemiology, University of Leipzig, Germany*

We have analysed the gene modulation induced by zoledronic acid (ZOL) in androgen-resistant prostate cancer PC3 cells with cDNA microarray platform to identify new molecular targets of ZOL in prostate cancer. The gene coding for cysteine-rich, angiogenic inducer, 61 (CYR61), often over-expressed in tumour cells, resulted highly down-regulated with a fold-change of 5.58. Therefore, we have studied the effects of different concentrations of ZOL on CYR61 protein product and we have found that CYR61 protein expression was significantly decreased after exposure to ZOL. The effect of ZOL on CYR61 expression was dose and time-dependent and was due to a reduced transcriptional activity of CYR61 promoter as demonstrated by transfection with a plasmid encoding for luc-CYR61 promoter. Interestingly, other signal transduction inhibitors or cytotoxic agents did not induce or induced less effect on CYR61 modulation if compared to ZOL. Moreover, ZOL reduced CYR61 expression through decreased activation of ras-raf-1-dependent pathway that was dependent from isoprenylation inhibition since they were antagonized by the addition of either farnesol or geranilgeraniol. Finally, we have investigated the role of CYR61 in the regulation of growth inhibition and invasion/motility of PC3 cells using a shRNA for CYR61 in order to down-regulate the expression of CYR61 protein. We have found that shCYR61 enhanced inhibition of proliferation and motility/invasion induced by ZOL by S-phase accumulation. In the same experimental conditions, CYR61 protein down-regulation potentiated the inactivation of the ras-dependent proliferation pathway. Since CYR61 was reported to be involved in the resistance to taxanes we have evaluated if ZOL could sensitize PC3 cells to Docetaxel (DTX). We have found a sequence-dependent synergism induced by the combination between ZOL and

doi:10.1016/S1359-6349(08)00111-0