

Euro Cancer 2019: Hydrogen/deuterium ratio is a key regulator of energy production and cell proliferation – submolecular dimensions of drug development

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The concentration of deuterium (D) is about 150 ppm (over 16 mM/L) in surface waters and 12-14 mM/L in living organisms, which is clearly a biologically relevant ion considering that circulating Ca^{2+} is only 2.24-2.74 mM/L. In order to reveal the possible role of naturally occurring D in living organisms, the replacement of normal tap water with deuterium depleted water (DDW) in a range from 25 ppm to 135 ppm was investigated in cell cultures, animal studies, as well as in prospective blinded and retrospective clinical trials. DDW inhibited cell growth of multiple cancer cell lines in in vitro culturing studies and readily induced tumor xenograft regression in mice [1-3]. Double blind, controlled, human Phase II clinical trial with prostate cancer, in compliance with GCP principles exhibited a significant difference between the control (n=22) and DDW treated (n=22) patients with respect to end point parameters and confirmed significant antitumor efficacies [4].

To gain additional information on DDW efficacy, the data matrices of 1827 cancer patients consuming DDW were evaluated in an open label retrospective study. The cumulative follow-up period of patients covers over 6881 years from the diagnosis of the disease, with DDW consumption of 2265 cumulative years. Median survival time (MST) of the 1827 control patients treated with standard oncotherapy, which represent all major tumor types, was 121.2 months (10.1 years). MST correlated with the length of DDW consumption in treated groups. The MST of small, homogenous prostate-, breast-, lung- and pancreas cancer populations was also calculated. The MST was 64.8 months in prostate cancer patients (n=20) having bone metastases within one year after diagnosis, which is a 3-fold increase when compared to 15-20 months in patients with

standard oncological care without DDW [4]. The 74 breast cancer patients with stage IV disease with distant metastases in 135 cumulative number of organs the DDW treated group showed an MST of 4.3 years in comparison with ~2.0 years MST [5] of control patients. The MST was 25.9 months in male patients (n=78) and 74.1 months in female patients (n=51) with lung cancer which is a 3 to 7-fold increase in comparison with control patients receiving conventional oncotherapy [6]. Unresectable pancreatic cancer patients entering DDW trial within or after 60 days of diagnosis were also evaluated. The MST for patients starting the DDW treatment within 60 days after diagnosis (n=18) achieved 39 months MST. In contrast, patients joining the DDW trial 60 days or later after diagnosis (n=14) showed a 16 months' MST [7]. The basic concepts of dosing DDW as part of standard oncotherapy will be discussed. Thirty volunteers with decreased glucose tolerance underwent 90 days long DDW treatment. Fasting glucose decreased significantly after 90 days DDW treatment (6.06 ± 0.66 mmol/L at day 0 and 5.74 ± 0.94 mmol/L at day 90, $p=0.029$). Evaluation of individual cases showed that glucose uptake increased in 11 volunteers (6.9 ± 2.4 mg/kg/min at day 0, 8.6 ± 2.5 mg/kg/min at day 90, $p=0.0014$).

We suggest that the cells can regulate the D/H ratio and the changes in the D/H ratio trigger certain molecular mechanisms having key role in cell cycle regulation, metabolism. The decrease of D concentration can intervene in the signal transduction pathways.

Deuterium depletion opens new perspectives in drug development offering a completely safe and non-invasive treatment modality.