Radium-224 Injections - Radiobiological Impact of an Abandoned Therapy for Ankylosing Spondylitis

R. Wick[a] and E. Nekolla[b]

[a] *Helmholtz Center Munich, German Research Center for Environmental Health, Institute of Radiation Biology, D-85764 Neuherberg, Germany;* [b] *Federal Office for Radiation Protection, Department Radiation Protection and Health, Ingolstaedter Landstr. 1, D-85764 Neuherberg, Germany*

wick@helmholtz-muenchen.de

At the Helmholtz Center Munich, formerly GSF - National Research Center for Environment and Health, since 1971 an epidemiological study has been carried out on 1471 ankylosing spondylitis patients treated with repeated intravenous injections of the short lived α-emitter ^{224}Ra between 1948 and 1975. The then usual therapeutic plan consisted of a total of 10 to 12 injections of about 1 MBq of ^{224}Ra each, given at weekly intervals. This results in a cumulative α-dose of 0.56 to 0.67 Gy to the marrow-free skeleton (bone surface dose: $\sim$5.5 Gy) of a standard man (70 kg). These patients have been followed together with a control group of 1324 ankylosing spondylitis patients not treated with radioactive drugs and/or X-rays. Until now causes of death have been ascertained for 1006 exposed patients and 1072 controls (mean follow-up time 26.3 yr in the exposed or 24.6 yr in the control group). In particular, in the exposed group we observed 18 cases of kidney cancer (vs. 9.1 cases exp., p=0.006), 7 liver carcinomas (vs. 3.5 cases exp., p=0.06), and 4 malignant thyroid tumours (vs. 1.2 cases exp., p=0.03). In the control group the observed cases for these tumours were in the expected range, apart from a non-significant increase of kidney cancers. The most striking observation, however, were the 19 cases of leukaemia in the exposed group (vs. 6.8 cases exp., p<0.001) compared to 12 cases of leukaemia in the control group (vs. 7.5 cases exp.). Further sub-classification of the leukaemia cases demonstrated a high increase of myeloid leukaemia in the exposed group (11 cases obs. vs. 2.9 cases exp., p<0.001), and especially a high excess of acute myeloid leukaemia (7 cases obs. vs. 1.8 exp., p=0.003), whereas in the controls the observed cases are within the expected range (4 cases of myeloid leukaemia vs. 3.1 cases exp.). The number of myeloid leukaemia cases in the exposed group is also significantly increased in direct comparison with the control group on basis of a modified Fisher-test (p<0.05). It is rather unlikely that the negligibly lower purity of earlier ^{224}Ra preparations compared to those used until very recently plays an important role for the increased rates of myeloproliferative diseases in the exposed group of this study. The enhanced leukaemia incidence in the exposed group is in line with results from animal experiments in mice having been injected with varying amounts of ^{224}Ra.

Article published by EDP Sciences and available at http://www.radioprotection.org or http://dx.doi.org/10.1051/radiopro:2008633