CISPLATIN (Group 2A)

A. Evidence for carcinogenicity to humans (*inadequate*)

No epidemiological study of cisplatin as a single agent was available to the Working Group. Occasional case reports of exposure to cisplatin, especially in the presence of concurrent therapy with other putative carcinogens, such as ionizing radiation, alkylating agents and other potent oncotherapeutic drugs, do not constitute evidence of carcinogenesis[1-3].

B. Evidence for carcinogenicity to animals (*sufficient*)

Multiple intraperitoneal administrations of cisplatin to mice significantly increased the incidence and number of lung adenomas. Similar treatments caused a significant increase in the incidence of skin papillomas in mice given promoting treatment of croton oil applied to the skin. The incidences of epidermoid carcinomas and of both malignant and benign tumours in internal organs were increased by the same treatment, but were not significantly different from those in controls[1,4]. In two studies, multiple intraperitoneal injections of cisplatin to rats induced leukaemia[5,6].

C. Other relevant data

In one study, cisplatin-adriamycin combination chemotherapy induced sister chromatid exchanges in peripheral blood lymphocytes of patients treated with this agent. In another study, antigenicity against cisplatin-DNA adducts was demonstrated in blood cells of treated patients[7].

Cisplatin induced structural chromosomal aberrations and sister chromatid exchanges in cells of rodents treated *in vivo*, but it did not induce dominant lethal mutations in mice. It transformed Syrian hamster embryo cells; it induced chromosomal aberrations, micronuclei and sister chromatid exchanges in both human and rodent cells *in vitro*, and mutation and DNA damage (including DNA cross-links) in rodent cells *in vitro*. In *Drosophila*, cisplatin induced aneuploidy and dominant lethal and sex-linked recessive lethal mutations. It induced chromosomal aberrations and mutation in plants. Cisplatin induced mutation, gene conversion and DNA damage in fungi and mutation and DNA damage in bacteria[7].

References

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