DACARBAZINE (Group 2B)

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

No epidemiological study of dacarbazine as a single agent was available to the Working Group. Occasional case reports of exposure to dacarbazine, 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].

In a large systematic follow-up of patients with Hogdkin's disease treated with an intensive chemotherapeutic combination including dacarbazine (plus adriamycin [see p. 82], vinblastine [see p. 371] and bleomycins [see p. 134]) but no alkylating agent, preliminary evidence suggested no excess of acute nonlymphocytic leukaemia in the first decade after therapy[2].

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

Following its oral or intraperitoneal administration to rats, dacarbazine produced tumours at various sites, including the mammary gland, thymus, spleen and brain, in as little as 18 weeks after initial exposure[1]. After its intraperitoneal administration to rats at the end of pregnancy, dacarbazine produced tumours, the majority of which were malignant neurinomas, in offspring[3]. Dacarbazine produced tumours at various sites, including lung, haematopoietic tissue and uterus, after intraperitoneal administration to mice[1].

C. Other relevant data

Dacarbazine did not induce sister chromatid exchanges in lymphocytes of treated patients in one study. It gave weakly positive results for induction of sister chromatid exchanges in Chinese hamster cells *in vitro* and was mutagenic to cultured rodent cells and to bacteria[4].

References

[1]*IARC Monographs, 26*, 203-212, 1981

[2]Valagussa, P., Santoro, A., Bellani, F.F., Franchi, F., Banfi, A. & Bonadonna, G. (1982) Absence of treatment-induced second neoplasms after ABVD in Hodgkin's disease. *Blood, 59*, 488-494

[3]Zeller, W.J. (1980) Prenatal carcinogenic action of 5-(3,3-dimethyl-1-triazeno)imidazole-4-carboxamide (DTIC) in the offspring of BD IX rats (Ger.). *Arch. Geschwulstforsch., 50*, 306-308

[4]*IARC Monographs, Suppl. 6*, 208-209, 1987