MELPHALAN (Group 1)

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

Epidemiological studies of patients with ovarian carcinoma[1-3], multiple myeloma[4,5] or breast cancer[6] have consistently shown very large excesses of acute nonlymphocytic leukaemia in the decade following therapy with melphalan. The relative risk was consistently estimated to be in excess of 100, to increase with increasing dose, and to be roughly the same with and without radiotherapy[7].

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

Melphalan has been tested in mice and rats by intraperitoneal injection, producing lymphosarcomas and a dose-related increase in the incidence of lung tumours in mice and peritoneal sarcomas in rats[8].

C. Other relevant data

Melphalan is a bifunctional alkylating agent. Patients treated therapeutically with melphalan had increased frequencies of chromosomal aberrations and sister chromatid exchanges in their peripheral lymphocytes[9].

Melphalan induced chromosomal aberrations in bone-marrow cells of rats treated *in vivo*. The compound induced chromosomal aberrations, sister chromatid exchanges and DNA damage in human cells *in vitro*. It induced transformation of C3H 10T1/2 cells. In cultured rodent cells, it induced chromosomal aberrations, sister chromatid exchanges, mutation and DNA damage. It induced aneuploidy and sex-linked recessive lethal mutations in *Drosophila* and mutation in bacteria[9].

References

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