

## **URACIL MUSTARD (Group 2B)**

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

No epidemiological study of uracil mustard as a single agent was available to the Working Group. Occasional case reports of treatment with uracil mustard, 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<sup>1-5</sup>.

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

Intraperitoneal administration of uracil mustard to mice of three strains induced lung adenomas and adenocarcinomas in a dose-dependent incidence; in one of the strains, liver, ovarian and lymphatic tumours were also observed. In rats, intraperitoneal administration induced peritoneal sarcomas and lymphomas and tumours in the pancreas, ovary and mammary gland<sup>6</sup>.

### **C. Other relevant data**

Uracil mustard is an alkylating agent<sup>7</sup>. No data were available on its genetic and related effects in humans.

Uracil mustard did not induce dominant lethal mutations in mice in one study using low doses. It induced mutation in mouse lymphoma cells *in vitro*, aneuploidy and sex-linked recessive lethal mutations in *Drosophila* and mitotic recombination in yeast. It caused DNA damage and was mutagenic in bacteria<sup>7</sup>.

## References

- <sup>1</sup>Reimer, R.R., Hoover, R., Fraumeni, J.F., Jr & Young, R.C. (1977) Acute leukemia after alkylating-agent therapy of ovarian cancer. *New Engl. J. Med.*, 297, 177-181
- <sup>2</sup>Zarrabi, M.H. & Rosner, F. (1979) Acute myeloblastic leukemia following treatment for non-hematopoietic cancers. Report of 19 cases and review of the literature. *Am. J. Hematol.*, 7, 357-367
- <sup>3</sup>McKenna, R.W., Parkin, J.L., Foucar, K. & Brunning, R.D. (1981) Ultrastructural characteristics of therapy-related acute nonlymphocytic leukemia: evidence for a panmyelosis. *Cancer*, 48, 725-737
- <sup>4</sup>Rosner, F. (1976) Acute leukemia as a delayed consequence of cancer chemotherapy. *Cancer*, 37, 1033-1036
- <sup>5</sup>Zarrabi, M.H. (1980) Association of non-Hodgkin's lymphoma (NHL) and second neoplasms. *Semin. Oncol.*, 7, 340-351
- <sup>6</sup>IARC Monographs, 9, 235-241, 1975
- <sup>7</sup>IARC Monographs, Suppl. 6, 558-560, 1987