Lifetime carcinogenicity studies in the CD-1 mouse: historical data for survival and neoplasms

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SUMMARY

The availability of historical data for survival and tumor incidences can be a key element in the overall interpretation of lifetime carcinogenicity bioassays. Survival data and incidences of neoplastic lesions were compiled for CD-1 mice from the same supplier used in nine carcinogenicity studies of two years duration. All the studies were performed between 2003 and 2011 in our facility with standardized environment, housing, feeding, necropsy, tissue sampling and trimming procedures, application of common diagnostic criteria and peer review.

INTRODUCTION

Although concurrent controls are the most relevant controls when evaluating potential drug-related increases in tumors during a study, there are situations in which historical control data from previous comparable studies can be useful in the overall evaluation of the study results. Comparison to historical control data is useful to ensure that a marginally increased finding is really drug-related and not purely due to a chance variation. These data can also be used to provide a quality control for factors that may have compromised the survival of the control or treated animals (Desch et al. 2002; van Zwieten et al. 1986). The objective of this retrospective analysis was to provide the survival, cause of death and incidence rates of neoplasms in Swiss CD-1 mice maintained for up to 106 weeks at CiToxLAB in France.

MATERIAL AND METHODS

Data were collected from nine carcinogenicity studies performed in mice at CiToxLAB in France initiated between 01 January 2003 and 31 December 2009. The information was gathered from twelve (males) or thirteen (females) control groups of 50 to 79 animals (each study had one or two control groups, the control groups being considered individually). The duration of the studies was approximately 104 weeks (85 weeks for one group and up to 106 weeks for the others). The Swiss CD-1 mice were obtained from Charles River France (Arbresle). The results in this compilation were acquired from diet ad libitum, oral gavage or subcutaneous injection studies, where the mice were 6 or 7 weeks-old at study initiation. The control animals were given one of the following vehicles: purified water, 0.9% NaCl, Cremophor EL/PEG 300, 1% w/v Hydroxyethylcellulose, 1% carboxymethylcellulose, solvent (zinc chloride solution), PEG 400 or untreated diet. A complete macroscopic post-mortem examination was performed on all animals. The tissues were preserved in 10% buffered formalin (except for the eyes with optic nerves and Harderian glands, and the testes and epididymides, which were fixed in Davidson’s fixative). A microscopic examination was performed on the following tissues: macroscopic lesions, most common tumors in male and female Swiss CD-1 mice (with incidence above 5%)

RESULTS

Survival data

The terminal mean survival rates of male and female mice were similar (respectively 45% and 43% at terminal sacrifice). The longest studies, and the subcutaneous injection study, had the lowest terminal survival, as expected.

Most common tumors in Swiss CD-1 mice

In males, the most common neoplasms were found in lungs (adenoma and carcinoma; >25%), liver (adenoma and carcinoma; >25%) and the lymphoreticular system (10% malignant lymphoma). Females had principally malignant lymphoma (>25%). Other common tumors seen with an incidence above 1% were found in various organs, i.e. Harderian gland, uterus, ovary, adrenal gland, pituitary gland, mammary gland, testis and kidney. In addition to systemic tumors (mainly histiocytic sarcoma and hemangiosarcoma), the incidences of the principal tumors were compared to published data. There were no marked differences with the exception of the higher incidence of malignant lymphomas in the males and females in our facility. This may be due to the difference of duration of studies (especially when compared to Charles River data with termination of studies in week 78). Comparable historical control information is used to define rare tumors with a background incidence rate of less than 1%; these tumors can be tested at higher levels of significance.

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CONCLUSION

These data, compiled from 9 recent internal studies, will provide survival, tumor incidences and causes of death in Swiss CD-1 mice after different treatment periods. This will allow comparisons for tumor incidences and causes of death. The mouse Swiss CD-1 strain was considered to be stable over the considered period (2005-2011) for tumor incidence.

BIBLIOGRAPHICAL REFERENCES

Introductions and Results

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