Scand J Work Environ Health 2005;31(3):236
Issue date: Jun 2005

Response to Swaen & Duijts on the epidemiologic evidence for the carcinogenicity of vinyl chloride monomer

by Boffetta P, Mundt KA, Dell LD

Affiliation: International Agency for Research on Cancer, 150 cours Albert-Thomas, 69008 Lyon, France. boffetta@iarc.fr

Refers to the following texts of the Journal: 2005;31(3):233-235
2003;29(3):220-229

Key terms: angiosarcoma of the liver; brain cancer; carcinogenicity; epidemiologic evidence; hematopoietic neoplasms; letter to the editor; liver cancer; lung cancer; occupational exposure; vinyl chloride monomer

Print ISSN: 0355-3140 Electronic ISSN: 1795-990X

Response to Swaen & Duijts on the epidemiologic evidence for the carcinogenicity of vinyl chloride monomer

We thank Gerard Swaen & Saskia Duijts for allowing us to clarify a few issues on our interpretation of the available evidence on the carcinogenicity of vinyl chloride, and we would like to reply to the three criticisms they raise in their letter on the meta-analysis we recently published in the *Scandinavian Journal of Work, Environment & Health* (1).

Risk of hepatocellular carcinoma

We think that the issue of an increased risk of hepatocellular carcinoma among workers exposed to vinyl chloride is not solved. In such circumstances, it is not unusual that different reviewers reach different conclusions. In our view, the strongest argument in favor of an increased risk is the dose–response relationship found in the European multicenter study when the analysis was restricted to cases of histologically confirmed hepatocellular carcinoma (2), and thus ruled out possible misclassification of liver angiosarcomas.

Swaen & Duijts state that we used the argument of decreased mortality from liver cirrhosis as supportive evidence for an increased risk of hepatocellular carcinoma, since "benign processes in the liver may have become malignant in the presence of VCM [table 1 of their letter]" (3). In fact, we suggested "that vinyl chloride enhances carcinogenesis in an otherwise chronically damaged liver [p 225]" (1) as an explanation of the decrease in liver cirrhosis mortality, not as argument to support a causal association between vinyl chloride and hepatocellular carcinoma, our hypothesis being that common mechanisms, for example, the chronic proliferation of hepatocytes, may underline both processes. Swaen & Duijts, on the other hand, offer no explanation for the decreased mortality from liver cirrhosis among these workers.

Risk of soft-tissue sarcoma

Contrary to Swaen & Duijts' statement, the four cases of angiosarcoma identified among the 12 deaths from soft-tissue sarcoma in the North American cohort study were not confirmed cases of liver angiosarcoma (4), and this lack of confirmation explains our reluctance to exclude them from the numerator in our meta-analytic estimate for soft-tissue sarcoma. We think that, in our review, we presented arguments both in favor and against an increased risk of soft-tissue sarcoma, and we did not conclude that a such link can be established on the basis of the current evidence. In fact, in the final part of our review, we mentioned the results on soft-tissue sarcoma as an example of a situation in which diagnostic misclassification of rare conditions can generate false associations.

Meta-analysis when heterogeneity is present

Different approaches are used for dealing with the opportunity and way to conduct a meta-analysis in the presence of heterogeneous results, and we are not convinced that the one proposed by Swaen & Duijts (fixed-effects model when the P-value of test of heterogeneity is ≥0.1, random-effects model otherwise) is superior to the one we used (random-effects model when the P-value of the test of heterogeneity is ≥0.01, no summary estimate otherwise). In any case, the point estimates and confidence intervals reported in table 2 of their letter are very similar to those reported in our paper.

References

1. Boffetta P, Matisane L, Mundt KA, Dell LD. Meta-analysis of studies of occupational exposure to vinyl chloride in relation to cancer mortality. Scand J Work Environ Health 2003; 29(3):220–9.
2. Ward E, Boffetta P, Andersen A, Colin D, Comba P, Deddens JA, et al. Update of the follow-up of mortality and cancer incidence among European workers employed in the vinyl chloride industry. Epidemiology 2001;12:710–8.
3. Swaen GMH, Duijts SFA. Epidemiologic evidence for the carcinogenicity of vinyl chloride monomer [letter to the editor]. Scand J Work Environ Health 2005:31(3);233–235.
4. Mundt KA, Dell LD, Austin RP, Luippold RS, Noess R, Bigelow C. Historical cohort study of 10 109 men in the North American vinyl chloride industry, 1942-72: update of cancer mortality to 31 December 1995. Occup Environ Med 2000;57:774–81.

Paolo Boffetta,[1] Kenneth A Mundt,[2] Linda D Dell[2]

[1] International Agency for Research on Cancer, 150 cours Albert-Thomas, 69008 Lyon, France.
[2] Applied Epidemiology, Inc; Amherst, Massachusetts, United States.