LETTERE IN REDAZIONE

# Cancer incidence among petrochemical workers in the Porto Torres industrial area

Dear Sir,

the paper by Budroni et al. (1) evaluates incidence of various cancers among petrochemical workers in the Porto Torres industrial area between 1990-2006. The study results are important as a number of previous studies have demonstrated significantly elevated risks of non-Hodgkin's lymphoma (NHL) in general, or in relation to subtypes of NHL, among petrochemical or refinery workers (4, 9-11, 13), and among workers exposed to benzene or to BTX in general (2, 3, 5, 8, 12). Studies also demonstrate the induction of lymphomas in experimental animals exposed to benzene (6), or to toluene and xylene separately (7).

Budroni et al. (1) concluded that their analyses indicated an increased risk for all cancers and for NHL among these workers, and particularly for NHL among workers potentially exposed to vinyl chloride monomer (VCM). Indeed the study demonstrates significantly elevated risks for these cancers. For NHL overall, the SIR=1.78 (95% CI=1.22-2.62); for VCM, the SIR=4.06 (95% CI=1.52-10.8). The authors also state that no significant increase in risk was observed among workers potentially exposed to styrene, butadiene and to benzene. Yet, the data in Table 3 of their publication appear to indicate a significantly increased risk in the incidence of NHL related to styrene exposure, and an increased risk that falls just short of being statistically significant among workers exposed to butadiene and to the combination of benzene, toluene and xylene (BTX).

For example, the data in the Table 3 for all lymphohematopoietic (LHP) cancers combined in relation to styrene indicate 17 cases with an SIR=1.38 (95% CI=0.86-2.22). If one subtracts from the total LHP cancers, the data for Hodgkin's lymphoma and myeloid leukemia, the remaining cancers are all NHL for a total of 15 vs. 8.27 expected, SIR=1.81 (95% CI=1.01-2.99), which indicates a significantly elevated risk for NHL in relation to styrene exposure. If one does a similar analysis for butadiene, the SIR=1.59 (95% CI=0.88-2.65) and for BTX, the SIR=1.84 (95% CI=0.98-3.15). In addition, the numbers of cases and the SIRs for these NHLs seem virtually identical in the styrene, butadiene and BTX analyses. This observation suggests that the styrene, butadiene and BTX exposures were essentially received in the same exposure situations. Is this the case? If so, the data in Table 3 of their report seem to demonstrate a significant association between styrene exposure and NHL and perhaps between butadiene and BTX exposure and risk of NHL. As Budroni et al. (1) provide important analyses related to NHL risk among petrochemical workers, perhaps they could clarify the issues raised above.

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*Dr. Infante was involved as advisors for workers exposed to benzene in litigation in Courts*

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## Response of the authors

We are delighted receiving comments from Dr Infante and Dr. Huff about our paper on cancer incidence among petrochemical workers in the Porto Torres industrial area (1). As our study was a follow up study of cancer incidence among petrochemical workers based on Cancer Registry data, to properly count the expected events we had to rely on the available reference rates from the Cancer Registry itself. These rates do combine all lymphatic leukemias, acute and chronic, and all myeloid leukemias (acute and chronic); consider separately multiple myeloma and Hodgkin lymphoma; and define non Hodgkin's lymphoma (NHL) as the combination of the ICD9 codes 200.0-200.8 and 202.0-202.9. Such definition would fit the old lymphoma classifications, but not with the Revised European and American (REAL) classification and the subsequent 2001 and 2008 WHO classifications (2), which apparently Dr Infante refers to in his letter. To resume, the old NHL definition excludes CLL and MM, but includes T cell lymphomas, and this is what we reported in Table 3 of our paper (1). Using the most recent classifications, which we couldn't do in absence of proper reference rates, we should consider B lymphomas, including CLL and MM, separately from T lymphomas. However, in our study population, we wouldn't expect more than one T lymphoma and perhaps one acute leukemia cases. So, at the end, Dr. Infante's observation might be correct as it concerns B lymphomas, but we cannot formally test his observation in absence of correspondent reference rates.

Table 1 in our paper (1) is the plant/exposure matrix, in which we infer about exposure based on the knowledge of the specific chemicals manufactured in each plant. As it is clearly explained in the Methods section of the full Italian text, it is a very approximate assessment, as we lack information on the exact job performed by each individual cohort member. Still, it is quite a specific assessment, in the sense that correctly identifies the unexposed subcohorts, for instance to vinyl chloride. The butadiene and styrene subcohorts were largely overlapping and differed only for the exposure in plant # 25, specifically dedicated to styrene manufacture from benzene, which included only 17 persons and 255.5 person-years. Exposure to styrene in this small plant could not be separated from benzene. However, no case of lymphatic cancer occurred among these 17 cohort members during the follow up period, as shown by the absolutely identical number of hemolymphopoietic cancers in the butadiene and styrene subcohorts.

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