Reviewer's report

Title: Polymorphisms in xenobiotic metabolizing genes (EPHX1, NQO1 and PON1) in lymphoma susceptibility: a case control study

Version: 3 Date: 2 April 2013

Reviewer: Kathryn Barry

Reviewer's report:

Major Compulsory Revisions:

1. The Abstract still notes a stronger association for PON1 rs662 in males than females. Even though the p-value for males is lower, the OR point estimates for males and females are relatively similar. In addition, the confidence intervals for males and females are very wide and each includes the point estimate of the other group. Please remove the point about a gender difference from the Abstract and elsewhere in the manuscript as well (Results and Discussion).

2. Now that the focus of the paper is on main effects of genetic variants and NHL risk, please add some citations of genome-wide association studies (GWAS) for NHL in the Background section, for example Smedby et al, PLoS Genet 2011 (for follicular lymphoma specifically) and Vijai et al, PLoS Genet 2013. Were the SNPs studied in the current analysis included in the GWAS scans? If so, could you please add some justification to study these variants again here? One potential justification could be to study these variants in an exposed population, although the limited exposure assessment and potentially heterogeneous nature of the exposures here should again be noted.

3. In the Discussion section, there is currently not enough focus on NHL or hematological outcomes and rather attention on other cancers, for which the etiology may not be relevant to NHL. Please incorporate some mention of the NHL GWAS studies (and any other studies that considered these SNPs with respect to NHL) in the Discussion. Suggest also adding more papers that investigated the SNPs in relation to hematological outcomes, for example, for NQO1 rs1800566: Wan et al, EHP 2002; Chen et al, Xenobiotica 2007; Sun et al, Carcinogenesis 2008; and Lan et al, Science 2004.

Discretionary Revisions:

1. In the concluding sentence of the Abstract, please give the rs number for the PON1 SNP. Even though it is given earlier in the Abstract, it should also be mentioned with the genotype. Please also state the rs numbers for the respective SNPs in Tables 2-4.

2. Suggest presenting only one genetic model in Table 2 and mentioning in the text that results were similar with the recessive and co-dominant models. Suggest presenting recessive here to be consistent with Table 3 (or present the
co-dominant model in both tables). Please also justify in the Statistical Analysis section of the Methods why you chose the recessive model as the main model for the paper.

3. Suggest changing “genetic profile analysis” to “joint effects analysis” in Table 4 and throughout the text of the paper since the term genetic profile has some connotations of a large-scale analysis, whereas here three SNPs were studied.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.