COMMITTEE ON CARCINOGENICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

Consideration of recent meta-analysis investigating the effect of alcohol on Non-Hodgkin lymphoma (NHL) and Hodgkin Lymphoma (HL) cancer risk

1. During discussions at the previous COC meeting in November on the role of alcohol consumption and cancer risk, it was suggested that the COC should consider the recently published meta-analysis on alcohol consumption and non-Hodgkin lymphoma (NHL) (Tramacere et al., 2012a, Annex A) and Hodgkin lymphoma (HL) (Tramacere et al., 2012b, Annex B). In 2007 (published IARC 2010), IARC reviewed the epidemiological evidence on the possible association between alcoholic beverage consumption and cancer at 27 anatomical sites, including NHL and HL. IARC concluded that there was evidence suggesting lack of carcinogenicity in humans for alcoholic beverages and non-hodgkin lymphoma (NHL). The results of cohort studies and evidence from some very large case–control studies showed an inverse association or no association between the consumption of alcoholic beverages and the risk for NHL. The evidence for an association between consumption of alcoholic beverages and risk for Hodgkin lymphoma was sparse (IARC, 2010) (Annex C). Following another IARC review in 2009 (IARC 2012), IARC reached similar conclusions and reaffirmed their position for the aforementioned cancers (NHL and HL) (Annex D).

HL and NHL Cancer Statistics for the UK

2. NHL (all subtypes combined) was the sixth most common cancer in the UK in 2010, accounting for 4% of all new cases. NHL was the fifth and seventh most common cancer among men and women, respectively, in the UK in 2010 accounting for 4% of all new cases of cancer. In 2010, there were 12,180 new cases of NHL in the UK (6,538 men and 5,642 women) giving a male:female ratio of 12:10. In 2011, there were 4,646 deaths (2,490 men and 2,156 women) from NHL in the UK giving a male:female ratio of around 12:10. In 2011, the crude mortality rate showed that there were 8 NHL deaths for every 100,000 males in the UK and 7 for every 100,000 females. Risk factors for NHL include age, male sex, HIV/AIDS and immune dysfunction such as autoimmune diseases. The role, if any, played by lifestyle factors including alcohol is still largely unknown.

3. Hodgkin lymphoma accounted for less than 1% of all cancers in the UK in 2010. In 2010, there were 1,866 new cases of Hodgkin lymphoma in the UK: 1,072 in males and 794 in females, giving a male:female ratio of more than 13:10. Hodgkin lymphoma accounts for 0.2% of all male deaths from cancer, and 0.2% of all female cancer deaths (2011). In 2011, there were 303 deaths from Hodgkin lymphoma in the UK: 171 in men and 132 in women, giving a male:female ratio of around 13:10. The risk factors, in particular the role of lifestyle factors, of Hodgkin lymphoma are largely undefined and the disease remains poorly characterised at a cellular and molecular level (Cancer Research UK). Parkin (2011) estimated that around 45% of Hodgkin lymphomas in the UK are related to infection with the Epstein-Barr virus (EBV).

Meta-Analysis on Alcohol Drinking and the risk of NHL and HL

4. Two recently published meta-analyses are considered here. Both analyses were carried out by the same group of researchers.

5. Tramacere et al. (2012a) carried out a meta-analysis of 29 studies (21 case-control and 8 cohort studies) on the effect of alcohol consumption and NHL risk. The meta-analysis included a total of 18759 cases of NHL. For the exposure assessment and in order to have a uniform variable of alcohol consumption for the meta-analysis, the authors used the amount of alcohol consumed in terms of grams of ethanol per day as standard measurement unit, defining 1 drink as 12.5 g of ethanol. The reference group was non-drinkers where possible but the authors noted that several studies used occasional drinkers as the reference category. Alcohol consumption was stratified into three categories: light drinkers of ≤ 1 drink per day, moderate drinkers of > 1 to < 4 drinks per day, and heavy drinkers of ≥ 4 drinks per day. The relative risks were estimated from the odds ratio in case control and by the hazard ratio in the cohort studies using random-effects models. Dose-response analysis was performed using a meta-regression model in a non-linear dose–response relationship framework, choosing the best fitting two-term fractional-polynomial model In their analysis of drinkers versus non-drinkers, the overall RR was 0.85 (95% CI 0.79 – 0.91), with estimates for case-control studies 0.80 (95% CI 0.74 – 0.91) and 0.96 (95% CI 0.88 – 1.04) for cohort studies. When the data was stratified by level of alcohol consumption and compared to non-drinkers, they report overall RRs of 0.88 (95% CI 0.81 – 0.96) for light drinking, 0.87 (95% CI 0.79 – 0.95) for moderate drinking, and 0.84 (95% CI 0.70 – 1.00) for heavy alcohol drinking, based on 23, 21, and 7 estimates, respectively. In their dose-response analysis, they reported a downward trend with increasing grams of ethanol consumed per day (RRs of 0.91 (95% CI 0.87–0.94) for 10g ethanol/day, 0.85 (95% CI 0.80–0.90) for 25 g ethanol/day, 0.80 (95% CI 0.74–0.87) for 50g ethanol/day, 0.80 (95% CI 0.70–0.91) for 75g ethanol/day, and 0.81 (95% CI 0.66–1.00) for 100g ethanol/day). In their stratified analysis, the observed association was stronger in studies conducted in Asia compared to studies conducted in non-Asian countries but no significant differences were found across strata of sex, type of controls or subtypes of NHL. The overall RR presented in the paper represents a 15 % reduction of NHL risk among drinkers compared with non-drinkers but the authors do suggest that some caution is required in the interpretation of the findings. Issues may include misclassification of drinkers among cases, cancer sub-type diagnosis and under-reporting of alcohol consumption.

6. Tramacere et al. (2012b) carried out a meta-analysis of 10 studies (8 case-control and 2 cohort studies) on the effect of alcohol consumption and HL risk. The meta-analysis included a total of 1488 cases of HL. This meta-analysis used the same exposure assessment measurements and statistical analyses as described above for Tramacere et al. (2012a). The reference group was non-drinkers where possible but the authors noted that one study (Willett et al. 2007) used light drinkers as the reference category. Alcohol consumption was stratified into two categories: light drinkers of ≤ 1 drink per day and moderate to heavy drinkers of > 1 drinks per day. In their analysis of drinkers versus non-drinkers, the overall RR was 0.70 (95% CI 0.60 – 0.81), with estimates for the 8 case-control studies 0.66 (95% CI 0.56 – 0.78) and 0.92 (95% CI 0.63 – 1.33) for the 2 cohort studies. When the data was stratified by

level of alcohol consumption and compared to non-drinkers, they report overall RRs of 0.71 (95% CI 0.57 – 0.89) for light drinking, with estimates of 0.65 (95% CI, 0.51–0.81) among the five case–control studies and 1.00 (95% CI 0.53–1.90) among the two cohort studies. The overall RR was 0.72 (95% CI 0.59 – 0.88) for moderate to heavy alcohol drinking, with estimates of 0.72 (95% CI, 0.59–0.88) among six case–control studies and 0.76 (95% CI, 0.45–1.27) among the two cohort studies. Similar findings were obtained when the authors considered moderate alcohol consumption (> 1 to < 3 drinks per day), and heavy alcohol consumption (≥ 3 drinks per day) separately (data was not shown). In their dose-response analysis, they reported a non-significant inverse dose-response relationship with increasing grams of ethanol consumed per day (RRs of 0.95 (95% CI 0.89 – 1.02) for 10g ethanol/day, 0.87 (95% CI 0.72 – 1.05) for 20 g ethanol/day and 0.82 (95% CI 0.0.64 – 1.04) for 30g ethanol/day). This meta-analysis found a significant decrease in HL cancer risk among alcohol drinkers compared to non-drinkers but this result was restricted to case-control studies only. They also did not observe a significant dose-response relationship. The authors suggest some caution is required in the interpretation of the findings and outline a number of limitations of their analysis. Limitations include the small number of cohort studies available, the reliance on case-control studies and the misclassification of drinkers among cases.

Conclusions

7. For both NHL and HL, the meta-analyses suggest a decrease in risk among drinkers compared to non-drinkers but a significant dose response was not observed for both cancers types. The authors themselves suggest caution in interpretation of the findings.

Questions for the Committee

1) What are the views of the Committee on the recently published meta-analysis on alcohol consumption and NHL and HL cancer risk?

2) Do these meta-analyses add further weight to the statement by IARC (2012) on alcohol consumption and these cancer types?

3) Do members think there is sufficient data to come to a conclusion about the amount of alcohol and nature of drinking i.e. cumulative per week, daily intake, type of alcohol and NHL and HL?

4) Thus far, does the data provided enable the Committee to make any definitive conclusions on the role of alcohol and NHL and HL?

PHE Toxicology Unit
March 2014

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Extract from IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 96: Alchol Consumption and Ethyl Carbamate
Pages: 871-907.

Full document is available here:
http://monographs.iarc.fr/ENG/Monographs/vol96/mono96.pdf

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Extract from IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 100E: Personal Habits and Indoor Combustions
Pages: 406-410, 446-449, 472 and Tables 2.63 and 2.64.

Full document is available here:
http://monographs.iarc.fr/ENG/Monographs/vol100E/mono100E.pdf
Tables are available here:
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