## EVIDENCE FOR AN ASSOCIATION BETWEEN ALCOHOL INTAKE AND AN INCREASED RISK OF NON-MELANOMA SKIN CANCER

Non-Melanoma Skin Cancer (NMSC), which includes basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), is the most common malignancy in mainly fair-skinned populations <sup>1</sup>. Registered NMSC incidence has increased over the past decades in various areas of the world, but valid estimates are difficult to obtain <sup>1</sup>. The World Health Organization estimated that between 2 and 3 million diagnoses of NMSC occur yearly worldwide <sup>2</sup>. A recent report showed that the NMSC incidence rate is expected to double by 2030 in Germany, with no tendency for leveling-off <sup>3</sup>. This causes a significant burden to health systems and at the same time highlights the importance of primary prevention. Beyond ultraviolet (UV) radiation from sun or sunbeds exposure <sup>4</sup>, the strongest risk factor for NMSC, little is known about the role of dietary <sup>5</sup> and modifiable lifestyle factors on NMSC risk.

In this issue of the *BJD*, Yen and colleagues <sup>6</sup> report the results of a systematic review and meta-analysis to quantify the relationship between alcohol intake and NMSC risk. After an accurate review process, the authors included in their meta-analysis a total of 8 case-control (7 on BCC and 1 on both BCC and SCC) and 5 cohort (2 on BCC, 1 on SCC, and 2 on both BCC and SCC) studies, leading to a total of over 90,000 BCC and 3,000 SCC cases. The meta-analysis shows slightly significant increased risks for BCC and SCC in a dose-dependent fashion. For each alcoholic drink per day, the risk of BCC increased by 7%, and that of SCC by 11%. The risk did not significantly differ by sex for both BCC and SCC, and a positive association was observed only in cohort studies, and for studies located in the United States <sup>6</sup>.

Interpretation of such small excess risk from observational studies remains open to discussion. Confounding by UV exposure should be accounted for when evaluating the relationship between alcohol intake and skin cancer risk. In fact, excessive alcohol drinking during outdoor leisure activities can lead to risky behaviors such as an excessive sun exposure and an infrequent sunscreen use, that in turn lead to sunburn <sup>7</sup>, an established risk factor for skin cancer. Notably, meta-analytic results showed that a positive association between alcohol intake and NMSC risk was more frequently observed among studies adjusting for UV exposure-related factors <sup>6</sup>.

Other potential mechanisms underlying the increased NMSC risk related to alcohol drinking are unclear.

Alcohol is converted to acetaldehyde, a carcinogen which can inhibit the DNA repair system and bind to

DNA to form DNA adducts. In combination with UV exposure, alcohol metabolites may also have a

photosensitizing effect that can enhance cellular damage leading to the generation of reactive oxygen

species and related intermediates 8.

The results by Yen et colleagues <sup>6</sup> are consistent with those published in a meta-analysis investigating the

relationship between alcohol drinking and melanoma risk 9,10. However, current evidence is insufficient to

conclude for a causal association between alcohol intake and skin cancer, both melanoma and NMSC, as

residual confounding by UV radiation and other unknown factors cannot be completely ruled out <sup>6,9</sup>. Still, it

is more clear that limiting alcohol drinking – a risk factor for several neoplasms <sup>10</sup> - can help lower risk of

NMSC and reduce the global burden of the disease.

Matteo Rota, Ph.D.

Department of Biomedical and Clinical Sciences, University of Milan, Italy

Via G.B Grassi 74, Milan 20157, Italy

Email: matteo.rota85@gmail.com

Acknowledgments

I wish to thank Prof Carlo La Vecchia for the helpful comments on a draft of this commentary.

**Conflicts of interests** 

None to declare. MR is supported by a fellowship from the Italian Foundation for Research on Cancer

(FIRC).

2

## References

- 1. Lomas A, Leonardi-Bee J, Bath-Hextall F. A systematic review of worldwide incidence of nonmelanoma skin cancer. Br J Dermatol 2012;**166**:1069-80.
- 2. http://www.who.int/uv/faq/skincancer/en/index1.html Accessed on 02/06/2017.
- 3. Leiter U, Keim U, Eigentler T et al. Incidence, Mortality and Trends of Non-Melanoma Skin Cancer in Germany. J Invest Dermatol 2017; DOI: 10.1016/j.jid.2017.04.020.
- 4. Leiter U, Garbe A. Epidemiology of melanoma and nonmelanoma skin cancer--the role of sunlight. Adv Exp Med Biol 2008;**624**:89-103.
- 5. Payette MJ, Whalen J, Grant-Kels JM. Nutrition and nonmelanoma skin cancers. Clin Dermatol 2010;**28**:650-62.
- 6. Yen H, Dhana A, Okhovat JP et al. Alcohol intake and risk of non-melanoma skin cancer: a systematic review and dose-response meta-analysis. Br J Dermatol 2017 [in press].
- 7. Mukamal KJ. Alcohol consumption and self-reported sunburn: a cross-sectional, population-based survey. J Am Acad Dermatol 2006;**55**:584-9.
- 8. Saladi RN, Nektalova T, Fox JL. Induction of skin carcinogenicity by alcohol and ultraviolet light. Clin Exp Dermatol 2010; **35**:7–11.
- 9. Rota M, Pasquali E, Bellocco R et al. Alcohol drinking and cutaneous melanoma risk: a systematic review and dose—risk meta-analysis. Br J Dermatol 2014;**170**:1021-8.
- 10. Bagnardi V, Rota M, Botteri E et al. Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. Br J Cancer 2015;**112**:580-93.