Reviewer’s report

Title: Lack of association between screening interval and cancer stage in Lynch syndrome may be accounted for by over-diagnosis; a Prospective Lynch Syndrome Database report

Version: 0 Date: 04 Feb 2019

Reviewer: Evgeny Imyanitov

Reviewer's report:

This is a very interesting epidemiological paper suggesting that MSI-H cancer may spontaneously regress due to high immunogenicity and actually putting into question the guidelines for surveillance of Lynch syndrome mutation carriers.

There is an apparent controversy between the presented data and a relatively well-established clinical benefit from a regular colonoscopy in Lynch syndrome mutation carriers. This controversy needs to be discussed in an explicit way.

The Summary is missing an important data. It is stated that the numbers of cancers detected within <1.5, 1.5-2.5, 2.5-3.5 and at >3.5 years since last colonoscopy were 36, 93, 56 and 33, respectively. To my understanding, the absolute number do not matter much. The proportion between the number of detected cancers and the number of analyzed patients is essential. One would expect that longer interval since the last examination will result in higher proportion of subjects detected to have a cancer.

There is a number of inaccuracies. For example, see the phrasing in the lines 14/15 of the Conclusions of the Summary; the line 7 of the Background section; references in the line 53/54 of the 2nd page of the Discussion.

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