Is intraductal papillary mucinous neoplasm associated with extrapancreatic malignancies? Which is the true, prevalence or incidence?

We read with great interest the article by Larghi et al. [1], a multicenter cohort study about prevalence and risk factors of extrapancreatic malignancies (EPMs) in patients with intraductal papillary mucinous neoplasm (IPMN) of the pancreas. They concluded that their prevalence was high, especially for colorectal carcinoma, renal cell and thyroid cancers. IPMN harbored some genetic mutations in the pancreas and was significantly associated with both synchronous and metachronous pancreatic cancer development [2, 3]. However, the relationship between IPMN and EPM still remained to be solved. There were some retrospective studies evaluating the prevalence of EPM in patients with IPMN and all of them, including the article by Larghi A et al., concluded that their prevalence was high. On the other hand, we reported the prospective study and concluded that the incidence of EPM in patients with IPMN was not high compared with that in general population in contrast to the high incidence of pancreatic cancers [4]. Prevalence is the proportion of a population found to have a disease, whereas incidence is a measure of the risk of developing a disease within a special period of time. The object to be measured was different between them, so it should be interpreted carefully. In focusing on the prevalence, overestimation of EPM could not be eliminated due to the diagnostic bias. As described in the article by Larghi et al. [1], incidence of EPM in their cohort was expected.

Some patients with IPMN may have some germline mutations, like BRCA2 in the article by Lubezky et al. [5], but the majority did not. There were no significant risk factors for developing IPMN. Therefore, if IPMN was really associated with EPM, both the prevalence and incidence should be high. Until the high incidence of EPM in patients with IPMN or genetic mutations for developing EPM was to be elucidated, systemic surveillance should not be justified without certain specific risk factors for developing EPM.

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Concern on quality-of-life analysis in the OPTIMAL study

We read with interest the paper by Chen et al. investigating the quality of life (QoL) in a planned secondary analysis of the ‘OPTIMAL’ study, a randomized trial comparing erlotinib treatment with chemotherapy by gemcitabine/carboplatin (G/C) in patients harboring sensitizing EGFR mutations [1]. The authors used the Functional Assessment of Cancer Therapy-Lung (FACT-L) questionnaire, a well-established validated instrument to measure the QoL [2]. It consists of a series of questions resulting in a score ranging from 0 to 144. In the methods section of their paper, Chen et al. stated that an improvement of six points in the FACT-L total score can be considered clinically relevant, a threshold based on the methodology used in previous studies [3, 4]. Chen et al. state that each patient who showed at least once an elevation of six points (or higher) in its FACT-L score during the study (at any cycle) was considered as clinically improved, which can introduce bias since the number of cycles is different for the two arms.

Indeed, supplementary Table S1 showed that there is a great imbalance between the two arms regarding the number of patients who completed the QoL questionnaires throughout the duration of the study. Patients in G/C arm completed their questionnaires up to cycle 4 (the usual cycle number for...