development of simple and cost-effective diagnostic assays as an alternative to FISH for such patients.

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References


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Mismatch-repair-deficient metastatic pancreatic ductal adenocarcinoma with a germline PALB2 mutation: unusual genetics, unusual clinical course

A previously healthy 54-year old man was diagnosed with metastatic pancreatic ductal adenocarcinoma (PDAC) in February 2015; the primary tumor was localized in the tail of the pancreas. Histological confirmation of disease was based on a liver biopsy that showed a poorly differentiated adenocarcinoma. The patient had no family history of PDAC; however, two of his paternal aunts died of breast cancer. The patient started chemotherapy with a FOLFIRINOX regimen in March 2015 [1], that was de-escalated to mFOLFOX-6 and finally 5-FU/FA due to toxicity (thrombocytopenia, peripheral neuropathy); maintenance 5-FU/FA was given until June 2016. During this treatment, a very good partial response occurred, with a decline in CA 19-9 levels from 8.149 U/ml (pre-treatment) to a nadir of 5 U/ml in March 2016. On sequential CT imaging studies, the liver metastases as well as the pancreatic primary decreased dramatically in size, and the radiographic finding correlated well with a rapid clinical benefit response (e.g. no further need for analgesics since May 2015).

After the first preliminary data on the role of anti-PD-1 treatment in non-colorectal gastrointestinal cancers harboring a mismatch-repair deficiency (dMMR) were presented [2], and in the light of limited chemotherapeutic options due to persistent (treatment-associated) thrombocytopenia, we decided to determine the MMR status in our patient. At our reference laboratory for molecular pathology, a PCR-based assay found a dMMR status in the microsatellite markers BAT25, DSSS36, and D17S250 of the NCI consensus set. A subsequent human genetic counseling was initiated with the addition of a gene panel diagnostic tool in order to determine germline mutations. Interestingly, this analysis found no mutations in genes associated with a HNPCC syndrome, but a novel—at least to our knowledge not previously described—heterozygous frameshift mutation (c.1725dupG; pSer576Glufs*2) in the partner and localizer of BRCA2 (PALB2) gene [3]. Furthermore, two genetic variants of unknown clinical significance in the BRCA2 gene (c.2459A > G; pAsp820Gly) and in the ATM gene (c.1066-6T > G; p.? were detected.

Upon disease progression in July 2016, an experimental off-label treatment with the anti-PD1 inhibitor pembrolizumab was initiated [2]. Pembrolizumab was given at a dose of 200 mg every 3 weeks in analogy to the ongoing KEYNOTE-177 study in dMMR colorectal cancer (NCT02563002). Treatment was tolerated well; however, after three applications of pembrolizumab, a significant clinical (increase in abdominal pain), biochemical (increase in CA 19-9 levels from 72 to 803 U/ml) and radiographic disease progression occurred. Based on the molecular findings mentioned above, we thus decided to re-introduce the mFOLFOX-6 regimen in September 2016 as platinum-induces DNA double strand breaks are insufficiently repaired in the presence of defect PALB2 [5].

It is well known that a subset of PDAC patients can be characterized by specific molecular alterations (e.g. BRCA mutations)
that might also allow individual treatment decisions (e.g. the use of platinum-containing chemotherapy) [4]. However, PALB2 was mainly investigated for its important role in the biology of breast cancer, with preliminary reports suggesting a role also in PDAC [3, 5]. Based on the case reported here, PDAC patients with a PALB2 mutation may greatly profit from the use of platinum-based chemotherapy [5]. In contrast, the evidence for a predictive role of dMMR in PDAC still should be regarded very preliminary: despite a tumor dMMR status our patient showed no response to pembrolizumab [2].

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References
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Is the pursuit of a higher impact factor fully justified?
J.C. Soria, Editor in Chief of the journal, recently wrote an editorial which resounds like a hymn of praise to the impact factor [1]. Having remarkably reached the objective of raising the impact factor (IF) to 10, the Editor is now setting an even greater challenge by striving for an IF of 12 by 2018. As an author of numerous articles in the journal ever since its foundation, I feel concerned by this editorial strategy, in common, I am sure, with the majority of readers and authors. MB Nielsen, the Editor of the European Journal of Ultrasound (IF = 4.4) recently published an editorial on the same topic which conveyed a very different message while objectively addressing specific problems and concerns regarding the IF [2]. Above all, it must be borne in mind that the principle underlying the IF for a given journal is that it reflects the average number of citations from articles published in the journal during the two previous years. Many articles of high scientific value may in fact generate more citations beyond this relatively short period. A reasonable proposal to enlarge the citation window to a period exceeding 2 years has recently been made [3]. The urge to boost the IF may also induce harmful results by encouraging a “flash-in-the-pan” effect by favoring “hot” topics, while neglecting the long-term impact of articles. As also mentioned by M.B. Nielsen [2], CME articles of major importance may receive fewer citations and thus will likely be judged less acceptable for publication due to a high IF policy. The importance of the greatest educational value conferred by published articles was recently stressed by S.A. Cannistra, the Editor-In-Chief of Journal of Clinical Oncology [4].

The high IF strategy may also place published case-reports at a disadvantage as they tend to receive fewer citations, although they offer a real-life source of information for the reader, especially regarding current developments in cancer treatment. Last but not least, efforts to achieve a higher journal IF may lead to fraud, as recently described in the New England Journal of Medicine [5].

Therefore, the Editorial Board of Annals of Oncology should be encouraged to moderate the drive to eagerly improve the IF. While undoubtedly remaining vital to the life of a journal, a high IF should not be seen as a mandatory aim but rather as the outcome of an editorial policy encompassing complementary aspects of the publication policy in the field of cancer including not only “hot” topic papers but also case-reports and hypothesis-driven articles.

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References