Aspirin for *PIK3CA*-mutated colorectal cancer

Regular aspirin use after diagnosis could significantly increase survival of patients with colorectal cancer with mutated *PIK3CA*, the gene encoding the α catalytic subunit of phosphoinositide-3-kinase in the PI3K signalling pathway. *PIK3CA* mutations occur in almost 20% of colorectal tumours.

In a recent study, data were analysed for 964 patients with colorectal cancer from the Nurses' Health Study and the Health Professionals Follow-up Study, including information about aspirin use, *PIK3CA* mutation, and survival. Post-diagnosis use of aspirin prolonged both colorectal cancer-specific survival and overall survival among patients with *PIK3CA*-mutated tumours, but not among patients with wild-type *PIK3CA* tumours.

Author Shuji Ogino (Dana-Farber Cancer Institute, Boston, MA, USA) said, "we cannot conclude that there is no effect on *PIK3CA* wild-type cases; there may be a small effect… we would still recommend aspirin for *PIK3CA* wild-type cases given [the] high risk of cancer mortality compared to typically mild side-effects. But you can expect a lot more effect if the tumour has a *PIK3CA* mutation." Ogino continued, "It is necessary to replicate our findings in independent datasets. However, there are very few studies that can even do this analysis with reasonable statistical power… even though we started with almost 1000 cases, after subgrouping, the sample size of each subgroup was getting smaller and smaller. This is the challenge we are facing."

He elaborated, "we need to make [the] world's cancer registries more sophisticated by incorporating data from clinical molecular testing which is increasingly routine…given [the] inherent heterogeneity and complexity in human cancers, the future of epidemiology will depend on this type of integrative science—molecular pathological epidemiology."

Boris Pasche (University of Alabama at Birmingham, Birmingham, AL, USA) commented, "this finding is very intriguing and has the potential to be a game changer". He cautions, "the study is small, with 403 patients in the aspirin treatment group and only 66 with mutated *PIK3CA*; and only a few had died. We may not be seeing the exact effect. I would like to have these findings replicated in one or two additional studies; I would expect results of these validation studies to be released in the next 2 years. We'll [then] have a firm answer to the question of 'is this something we should apply, yes or no?'"

Judith A Gilbert

Envision/Corbis

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Positive results for ibrutinib in B-cell malignancies

Ibrutinib (PCI-32765)—a small molecule that irreversibly inhibits Bruton's tyrosine kinase (BTK)—has been shown to affect a complete response in eight of 50 patients with relapsed or refractory B-cell malignancies, including B-cell lymphoma and chronic lymphocytic leukaemia. A further 22 patients had a partial response. "These findings emphasise that patients with chronic lymphocytic leukaemia and mantle cell lymphoma are particularly sensitive to this new drug and they also highlight ibrutinib's benign side-effect profile", commented Jan Burger (MD Anderson Cancer Center, Houston, TX, USA).

David MacEwan (University of East Anglia, UK) reports that other studies are also showing that ibrutinib is working well in patients with chronic lymphocytic leukaemia. "Trials involving B-cell non-Hodgkin lymphomas, diffuse large B-cell lymphoma, and mantle cell lymphoma are underway and ibrutinib is producing promising results even in multiple myeloma, where BTK expression had been thought to be too low for an inhibitor to prove beneficial", he noted. Evidence is emerging that BTK inhibitors might also be useful for other lymphomas and for autoimmune disorders such as lupus, rheumatoid arthritis, and multiple sclerosis. "Possibly even some myeloid leukaemias" could benefit, he added.

Burger points out that "head-to-head comparisons with established therapies in the ibrutinib registration trials will broaden our early experience of this new drug and provide us with more robust guidance about its optimal use". He believes that a logical extension of the single-agent experience will be investigation of the use of ibrutinib combination treatments and to compare them against single-agent ibrutinib in terms of efficacy and safety. "Combinations of ibrutinib with other targeted agents (antibodies, proteasome inhibitors, and others) are promising and reflect our longing for chemotherapy-free regimens for patients with B-cell malignancies", he stressed.

MacEwan agrees but says that showing that BTK inhibitors can prolong survival when used in combination with chemotherapeutics is only the first step. "Bearing in mind the diverse and heterogeneous nature of these diseases, our next goal will be to discover specific combinations, including perhaps different BTK inhibitors and different chemotherapeutic regimens that can target subtypes of B-cell malignancy much more effectively", he said.

Kathryn Senior

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