Latest news about drug repurposing in oncology #4

5 February 2021

Drug repurposing is a strategy for identifying new uses for approved drugs, outside the scope of the original indication. It is one of the focus areas of the Anticancer Fund.

Below, we have listed recent findings about the repurposing of generic drugs in oncology. Our intention is to help bring these findings to the attention of the broader cancer research community.

Being listed is no endorsement of the results and conclusions of the article. All articles need to be critically assessed and viewed in their broader research context.

Please get in touch if you're interested in discussing research based on the findings presented below (info@anticancerfund.org).

Top stories

Arsenic Trioxide Rescues Structural p53 Mutations through a Cryptic Allosteric Site
Published in Cancer Cell
Arsenic trioxide reactivates mutant p53 for tumour suppression in vitro and in vivo. This investigation uses a range of clinically important p53 variants. Arsenic trioxide stabilized most p53 mutants but not all were transcriptionally rescued. A phase I trial in AML/MDS is ongoing in China (NCT03855371).

Dipeptidyl Peptidase 4 Inhibition for Prophylaxis of Acute Graft-versus-Host Disease
Published in NEJM
High-dose sitagliptin (600mg twice a day) for 16 days starting the day before allogeneic stem cell transplantation was well tolerated and resulted in a low

incidence (5%, CI95% 1-16) of acute graft-versus-host disease in this phase 2 non-randomized trial.

Clinical trial

Phase 2 trial comparing sorafenib, pravastatin, their combination or supportive care in HCC with Child-Pugh B cirrhosis
Published in Hepatol int
No role for pravastatin in HCC patients with Child-Pugh B cirrhosis either alone or in combination with sorafenib. Overall survival was very short in all 4 groups.

A phase I trial evaluating the effects of plerixafor, G-CSF, and azacitidine for the treatment of myelodysplastic syndromes
Published in Leuk Lymphoma
Plerixafor 560 mg/kg D1-5, G-CSF 5 mcg/kg D1-5 and azacitidine 75 mg/m2 D1-5 was determined safe and had a good level of efficacy in this phase I trial. That G-CSF and plerixafor enhance sensitivity to azacitidine in MDS should now be confirmed in a next efficacy trial.

Case series

The use of anakinra in the treatment of secondary hemophagocytic lymphohistiocytosis
Published in Pediatr Blood Cancer
Six paediatric patients with hemophagocytic lymphohistiocytosis, including 2 cancer-related, were treated for 2 months with anakinra. All responded. Because of the very good tolerance and high response rate, authors propose a treatment algorithm starting with anakinra as soon as hemophagocytic lymphohistiocytosis is suspected.

Observational studies

Concurrent Aspirin Use Is Associated with Improved Outcome in Rectal Cancer Patients Who Undergo Chemoradiation Therapy
Published in Cancers
Aspirin use at the time of diagnosis associated with improved outcomes in rectal cancer patients undergoing chemo-radiation, mainly due to fewer distant recurrences in patients on aspirin. Not subject to immortal-time bias. Benefit not associated with PI3KCA or KRAS mutational status but indication that the effect may be mediated by adaptive immunity and suppression of epithelial to mesenchymal transition.

Beta-blockers have no impact on survival in pancreatic ductal adenocarcinoma prior to cancer diagnosis
Published in Sci Rep
In this study using Medicare data for drug exposure, beta-blockers usage was not associated with improved survival (HR 1.04, 95% CI 0.98–1.1) in pancreatic cancer patients. This lack of association persisted when stratification on receptor selectivity of the beta-blockers was done.

Preclinical data

Therapeutic targeting of pancreatic cancer stem cells by dexamethasone modulation of the MKP-1-JNK axis
Published in Journal of Biological Chemistry
In vitro & in vivo study showing clinically relevant doses of dexamethasone can prevent tumour formation by cancer stem cells in a mouse model of pancreatic cancer.

Metoclopramide treatment blocks CD93-signaling-mediated self-renewal of chronic myeloid leukemia stem cells
Published in Cell Rep
A very thorough investigation to confirm that CD93 is a relevant target for CML stem cells. Followed by the search for drugs targeting CD93, eventually leading to the validation of metoclopramide, in vitro and in vivo. Making metoclopramide an interesting candidate for trials aiming to allow CML patients to stop tyrosine kinase inhibitors.

Hydroxychloroquine can impair tumor response to anti-PD1 in subcutaneous mouse models
Published in iScience
A detrimental effect of hydroxychloroquine in 3 GI tumour models in combination with anti-PD-1. Hydroxychloroquine offsets MHC-1 expression and T-cell cytotoxicity. Important findings knowing the existing publication bias against negative results.

Other drug repurposing news (soft repurposing, non-oncology late-phase trials, regulations ...)

Repurposing existing drugs for new uses: a cohort study of the frequency of FDA-granted new indication exclusivities since 1997
Published in J Pharm Policy Pract
Using FDA exclusivity data for 197 drugs that later became generic, the authors show 64 (32%) had at least one new indication added. The probability of a new indication addition peaked 7-8 years prior to generic entry and then dropped to

near zero 15 years after FDA approval. This paper provides hard data to document the problem of new uses of off-patent drugs.