

Latest news about drug repurposing in oncology #5

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[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 story

[Mitochondrial Inhibitor Atovaquone Increases Tumor Oxygenation and Inhibits Hypoxic Gene Expression in Patients with Non-Small Cell Lung Cancer](#)

Published in Clinical Cancer Research

A UK window of opportunity trial that sequentially allocated 15 patients to receive the anti-malaria drug atovaquone, a known mitochondrial inhibitor (for a median of 12 days), and 15 patients to not receive the drug before NSCLC surgery. Atovaquone treatment strikingly reduced hypoxia as measured on hypoxia PET-CT. Analysis of the surgical specimen confirmed hypoxia reduction at the transcriptomic level. Because hypoxia is a major issue in resistance to radiotherapy, these results support the use of atovaquone in future radiotherapy trials in NSCLC as well as in other cancers primarily treated by radiotherapy. The next trial is ongoing ([NCT04648033](#)).

Clinical data

Clinical trials

[The Effect of Metformin vs Placebo on Sex Hormones in Canadian Cancer Trials Group MA.32](#)

Published in JNCI

While waiting for the survival endpoint, results continue to emerge from the large Canadian/US adjuvant metformin trial in breast cancer. Here, authors report an independent and large effect of metformin on oestradiol levels in post-menopausal patients with oestrogen receptor negative cancers. While not immediately relevant for this population, these findings may inform future work with metformin in oestrogen-sensitive tumours.

[Auranofin improves overall survival when combined with standard of care in a pilot study involving dogs with osteosarcoma](#)

Published in Vet Comp Oncol

Building on previous research showing improved survival in mouse osteosarcoma xenografts treated with auranofin – a gold compound approved for rheumatoid arthritis – dogs with osteosarcoma were treated with standard of care (surgery + carboplatin) and auranofin in this single-arm Australian trial. Compared to historical controls, dogs treated with auranofin had an improved survival. Though limited by the absence of a control arm, these results support continuing the development of auranofin in osteosarcoma.

Observational studies

[Digoxin treatment reactivates in vivo radioactive iodide uptake and correlates with favorable clinical outcome in non-medullary thyroid cancer](#)

Published in Cell Oncol

A thorough investigation of the potential role of digoxin in non-medullary thyroid cancer in combination with radioactive iodide. The most notable findings were the increased accumulation of radioactive iodide in tumours in mice when digoxin was added and an association between response and digoxin treatment in a retrospective analysis of Dutch patients.

[Improved survival in several cancers with use of H1-antihistamines desloratadine and loratadine](#)

Published in Transl Oncol

A nationwide Swedish observational study reporting a positive association between cancer survival and the use of H1-antihistamines at the time of diagnosis, mainly driven by a positive association in 'immunogenic' cancers.

Desloratadine and loratadine are the best candidate drugs to be tested in various cancers (eg melanoma, breast, pancreas, ovarian) in future research.

[Effects of beta-blocker therapy on mortality after elective colon cancer surgery: a Swedish nationwide cohort study](#)

Published in BMJ Open

In this nationwide Swedish study of all patients undergoing elective colon cancer surgery, preoperative use of beta-blockers was associated with significant reductions in postoperative short-term and long-term mortality. The difference in 90-day mortality was important (3.9% vs 1.9%, incidence rate ratio of 0.29, 95% CI 0.24 to 0.35). This, however, doesn't tell us whether pre-operative use of betablockers in beta-blocker naïve patients would have a similar effect.

Preclinical data

[Exploiting Gangliosides for the Therapy of Ewing's Sarcoma and H3K27M-Mutant Diffuse Midline Glioma](#)

Published in Cancers

An interesting set of results around ganglioside GD2 in paediatric cancers other than neuroblastoma. First, authors report that GD2 is highly expressed in diffuse mid-line glioma (DMG) and Ewing's sarcoma. A patient with refractory Ewing's sarcoma responded to dinutuximab (used off-label) given with irinotecan and temozolomide. In DMG cells, a drug approved for Gaucher's disease called eliglustat was used to disrupt ganglioside metabolism, which resulted in the inhibition of H3K27M-mutant DMG cells proliferation in vitro.

[Abnormal dopamine receptor signaling allows selective therapeutic targeting of neoplastic progenitors in AML patients](#)

Published in Cell Reports Medicine

Using samples from patients they included in their phase I trial of thioridazine, authors show that dopamine receptor D2 (DRD2) is a relevant target in a subset of AML patients and confirm that thioridazine is a potent DRD-directed therapy. They also suggest that the positive thioridazine enantiomer is more potent and could be prioritized in future trials targeting DRD-positive AML and other tumours.

[Local blood coagulation drives cancer cell arrest and brain metastasis in a mouse model](#)

Published in Blood

In a series of elegant experiments, this German team shows how blood clot formation and von Willebrand factor deposition determine the arrest of circulating cancer cells and subsequent brain colonization in mice. The most clinically relevant finding of this comprehensive article is that dabigatran, a direct

thrombin inhibitor, strongly reduced brain metastases formation confirming the role of cancer cells-derived thrombin and the plasmatic coagulation system for brain colonisation of cancer cells.

[Pyrvinium Pamoate Induces Death of Triple-Negative Breast Cancer Stem-Like Cells and Reduces Metastases through Effects on Lipid Anabolism](#)

Published in Cancer Res.

In this Italian study, authors selected pyrvinium pamoate, an anti-helminthic drug, as a drug to affect triple-negative breast cancer stem-like cells. Through lipid anabolism inhibition, pyrvinium pamoate was cytotoxic to cancer stem cells, which are strongly dependent upon activation of lipid biosynthetic pathways. In a TNBC mice model, the drug prevented metastases formation at dose compatible with human dosage. However, knowing that pyrvinium pamoate is an 'endangered' drug only available in very few countries, clinical translation of this work may not be straightforward.

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

<http://www.redo-project.org/db/>

We have updated our Repurposing Drugs in Oncology (ReDO) database. The ReDO database now contains 335 non-cancer drugs with at least one scientific article supporting a possible anticancer effect of the drug. This list is our primary source for the scientific work the Anticancer Fund conducts with many collaborators around the world. Feel free to send us suggestions of drugs to add to this list.