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IN BRIEF

TARGETED THERAPY

Sunitinib modulates MCL-1 and mTOR signalling

Despite improvements in overall survival being achieved with the use of targeted therapies, the onset of resistance to treatment is virtually inevitable. In a translational study, researchers demonstrated enhanced stability of the antiapoptotic protein MCL-1, which resulted in an increase in mTORC1 activity in cancer cells exposed to clinically relevant doses of the tyrosine-kinase inhibitor sunitinib. Exposure to doses of sunitinib higher than those used clinically resulted in a decline in MCL-1 levels and inhibition of mTOR signalling. Further investigations revealed that the effects of sunitinib are mediated by proteasomal degradation of MCL-1. Analysis of MCL-1 and mTORC1 expression in tumour samples from patients with renal cell carcinoma, or neuroendocrine tumours revealed a significant association between MCL-1 expression and resistance to sunitinib.

ORIGINAL ARTICLE Elgendy, M. *et al.* Dual modulation of MCL-1 and mTOR determines the response to sunitinib. *J. Clin. Invest.* http://dx.doi.org/10.1172/JCI84386 (2016)

IMAGING

Solid stress indicates tumour pathology

Both mouse and human fibrotic tumours are known to have elevated levels of solid stress, and the presence of solid stress has been linked with several aspects of tumour pathology, including invasiveness and metastatic potential. Now, in a basic study, investigators have developed three methods for the measurement of solid stress: 2D imaging of spatial distribution; release of solid stress by creating thin tumour slices; and release of solid stress by core biopsy sampling. These methods will enable the development of therapeutics specifically designed to release the mechnical forces exerted on tumours by blood vessels, which partly explains the effectiveness of the repurposed angiotensin receptor inhibitor losartan. These methods might also provide insight into the complex interplay between tumours, fibroblasts and their microenvironment, in addition to facilitating tumour prognosis on the basis of solid stress and elastic energy, both of which can be used as prognostic and diagnostic markers.

ORIGINAL ARTICLE Nia, H. T. *et al.* Solid stress and elastic energy as measures of tumour mechanopathology. *Nat. Biomed. Eng.* http://dx.doi.org/10.1038/s41551-016-0004 (2016)

HAEMATOLOGICAL CANCER

Rituximab enhances responses to lenalidomide

Data from a phase II clinical trial reveal impressive responses to rituximab when used in combination with lenalidomide in patients with mucosa-associated lymphoid tissue (MALT) lymphoma. A total of 46 patients, of which 30% had gastric MALT lymphoma, received a maximum of eight courses of rituximab (375 mg/m^2 on day 1) plus lenalidomide (20 mg on days 1–20) every 4 weeks. Overall, 80% of patients had a response to treatment, with 54% entering complete remission, compared with 60% in a previous phase II study of lenalidomide monotherapy in patients with MALT lympoma. Investigators reported no unexpected toxicities. The effectiveness of this combination was unaffected by the type of MALT lymphoma (gastric versus extragastric), or whether or not patients had received previous lines of therapy. These data indicate a need for further investigation of the efficacy of this combination in a pilot clinical trial.

ORIGINAL ARTICLE Kiesewetter, B. *et al.* A phase II study of rituximab plus lenalidomide for mucosa-associated lymphoid tissue lymphoma (MALT lymphoma). *Blood* http://dx.doi.org/10.1182/blood-2016-06-720599 (2016)

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