Testing the second-generation MDM2 inhibitor, RG7388, in patient-derived chronic lymphocytic leukemia cells and its effect on the induction of p53-transcriptional targets

Untreated normal and chronic lymphocytic leukemia (CLL) cells

Mouse double-minute-2 homolog → Tumor suppressor → p53 → MDM2 → p53 → Proteasomal degradation

Treatment with RG7388

p53 functional-CLL cells

RG7388 → MDM2(RG7388) → p53

Apoptotic genes: PUMA, BAX, TNFRSF10B, FAS

• ↓ viability
• ↑ caspase-3/7
• ↑ cleaved PARP → Tumour death

Normal blood progenitors

RG7388 → MDM2(RG7388) → p53

Cell cycle genes: MDM2, CDKN1A

• ↑ viability
• ↓ caspase-3/7 → No cellular death Cell cycle arrest

MDM2 inhibitor, RG7388, is a novel potential treatment option for patients with p53-functional CLL

Ciardullo et al., Haematologica, 2019