CDK7 has recently emerged as an attractive target in cancer since its inhibition decreases the transcript levels of oncogenic transcription factors, especially those driven by super- enhancers (SEs). Oncogenic transcription factors, with a role in the regulation of cell proliferation, survival, and apoptosis, are abnormal in a majority of cancer patients.

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SY-1365 induces unique transcriptional signature compared to other transcriptional inhibitors

Conclusions

SY-1365, a first-in-class selective CDK7 inhibitor, demonstrated antiproliferative and apoptotic effects in solid tumor models, including negative breast, ovarian, and small cell lung cancers.

SY-1365 inhibited tumor growth in TNBC and PDX mouse models with minimum body weight change.

Twice weekly regimen planned for clinical trial showed substantial anti-tumor effect in vivo.

SY-1365 induced a distinct, more selective transcriptional response compared with other transcriptional inhibitors.

In AML, in vivo models, SY-1365 demonstrated synergistic activity with venetoclax; this data provides a rationale for further investigating the combination of SY-1365 with inhibitors targeting apoptotic pathways.

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