CUSP9v3

present eight principles that we believe must be considered for more effective treatment of the currently incurable cancers. These are addressed by multidrug adjunctive cancer treatment (MDACT), which uses multiple repurposed non-oncology drugs, not primarily to kill malignant cells, but rather to reduce the malignant cells' growth drives. Previous multidrug regimens have used MDACT principles, e.g., the CUSP9v3 glioblastoma treatment. MDACT is an amalgam of (1) the principle that to be effective in stopping a chain of events leading to an undesired outcome, one must break more than one link; (2) the principle of Palmer et al. of achieving fractional cancer cell killing via multiple drugs with independent mechanisms of action; (3) the principle of shaping versus decisive operations, both being required for successful cancer treatment; (4) an idea adapted from Chow et al., of using multiple cytotoxic medicines at low doses; (5) the idea behind CUSP9v3, using many non-oncology CNS-penetrant drugs from general medical practice, repurposed to block tumor survival paths; (6) the concept from chess that every move creates weaknesses and strengths; (7) the principle of mass-by adding force to a given effort, the chances of achieving the goal increase; and (8) the principle of blocking parallel signaling pathways. Part two gives an example MDACT regimen, gMDACT, which uses six repurposed drugs-celecoxib, dapsone, disulfiram, itraconazole, pyrimethamine, and telmisartan-to interfere with growth-driving elements common to cholangiocarcinoma, colon adenocarcinoma, glioblastoma, and non-small-cell lung cancer. gMDACT is another example of-not a replacement for-previous multidrug regimens already in clinical use, such as CUSP9v3. MDACT regimens are designed as adjuvants to be used with cytotoxic drugs [1)].

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data suggest that Bcl-2/Bcl-xL inhibition enhances the susceptibility of glioblastoma cells towards CUSP9, allowing dramatic dose reduction and potentially decreased toxicity when applied clinically. A clinical trial involving the original CUSP doses (CUSP9v3) is currently ongoing in our institution (NCT02770378). The Bcl-2/Bcl-xL inhibitor ABT263 is in clinical trials and might represent a valuable adjunct to the original CUSP. [2)]

1)
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2)
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