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索拉非尼联合AS 2O 3对 FLT3-ITD 突变白血病细胞MV-4-11的抑制作用 点此下载全文

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摘要：

目的：观察FLT3抑制剂索拉非尼(sorafenib)联合三氧化二砷(AS 2O 3)对FLT3-ITD突变的人类急性双表型（B、单核）髓细胞白血病MV-4-11细胞增殖、细胞周期和凋亡的作用，为该联合用药方案的临床应用提供实验依据。方法：将对数生长期的 MV-4-11细胞分为4组：空白对照组（不加药），索拉非尼单药（1、10、100、1 000、5 000、10 000 nmol/L）组，AS 2O 3单药（0.125、0 25、0.5、1.0、2.0 μmol/L）组，索拉非尼+AS 2O 3联合用药（10 nmol/L+1.0 μmol/L）组。CCK-8法检测索拉非尼和AS 2O 3单用或联用对MV-4-11细胞增殖的抑制作用，流式细胞术检测MV-4-11细胞的凋亡及细胞周期。结果：索拉非尼和AS 2O 3单用对MV-4-11细胞的增殖均有抑制作用，且均呈浓度依赖性；两药联用对MV-4-11细胞增殖的抑制率显著高于两药的单用\[（ 70.72±1.03）% vs （47.24±1.27）%、（20.28±0.70）%；均 P <0.01），两药相互作用指数(coefficient of drug interaction，CDI)为0.696，表现出协同作用。索拉非尼可使MV-4-11细胞周期阻滞于G 0/G 1期，两药联用阻滞得更严重。两药联合作用于MV-4-11细胞48 h后，MV-4-11细胞早期凋亡率显著高于两药单用（89.06% vs 68.27%、78.71%；均 P <0.05）。结论：索拉非尼联合AS 2O 3能够协同抑制MV-4-11细胞的增殖，并且比单药作用更有效地阻滞细胞周期于G 0/G 1，更明显地促进细胞凋亡。

关键词：急性髓细胞白血病 FLT3 索拉非尼 三氧化二砷

Inhibitory effect of sorafenib and arsenic trioxide on the FLT3ITD -mutated myelomonocytic leukemia MV-4-11 cells Download Fulltext

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Abstract:

Objective : To determine the effect of the FLT3-specific inhibitor sorafenib in combination with arsenic trioxide on the proliferation, cell cycle and apoptosis of leukemia MV-4-11 cells, a biphenotypic B myelomonocytic leukemia cell line with FLT3-ITD mutations, as a model in vitro . Methods: Logarithmic phase MV-4-11 cells were cultured in the absence (control) or presence of sorafenib (1, 10, 100, 1 000, 5 000, 10 000 nmol/L), arsenic trioxide (0.125,0.25,0.5,1.0,2.0 μmol/L), and sorafenib (10 μmol/L) and arsenic trioxide (1.0 μmol/L) in combination, respectively, for 48 h cell proliferation was assessed by CCK-8 assay, apoptosis and cell cycle progression by flow cytometry. Results: Sorafenib and arsenic trioxide, each alone, inhibited MV-4-11 cell proliferation in a concentration dependent manner. However, the inhibitory effect was more significant (P <0.01) when 10 nmol/L sorafenib and 1.0 μmol/L arsenic trioxide were used in combination (\[70.72±1.03\]%) than each alone (\[47.24±1.27\]% and \[20.28±0.70\]%); the interaction coefficient for these two drugs was 0.696. Sorafenib alone resulted in cell cycle arrest in G 0/G 1 phase and sorafenib in combination with arsenic trioxide increased cell cycle arrest. Similarly, both sorafenib and arsenic trioxide induced MV-4-11 cell apoptosis, but they were more effective in combination than each in itself (89.06% vs 68 27%, 78 71%; P <0.05). Conclusion: Sorafenib and arsenic trioxide, each in itself, are capable of inhibiting proliferation, blocking cycle progression, and induing apoptosis in FLT3 -mutated myeloid leukemia cells.

Keywords:acute myeloid leukemia FLT3 sorafenib arsenic trioxide

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