Also, greater credence should be given to a well-controlled study of drug resistance in actual human subjects, than to a well-controlled study with cultured cells. The ultimate arbiter of appropriate trial design is whether the therapy actually works – many attempts to use drug sequences that were configured to avoid resistance have often failed to be effective (84).

c. A tumor's genetic expression can provide guidance on drug resistance

Gene expression data from a tumor can determine if the tumor is likely to be resistant to a given drug (85).

1. Doxorubicin

According to Munoz et al. (86) Grant et al. (87) and Di Nicolantionio et al. (88) doxorubicin induces the expression of ABCC1, a multi-drug transporter that transports doxorubicin and methotrexate. Hence, it might be expected that, where patients receive doxorubicin, and where their tumors respond by up-regulating ABCC1, the tumors will acquire resistance to both doxorubicin and methotrexate. Doxorubicin is in the anthracycline class of drugs. This drug targets an enzyme used for DNA metabolism, namely, topoisomerase II.

2. Paclitaxel

Paclitaxel is in the taxane class of drugs. Taxanes can be eliminated from tumors by way of the ABC drug transporters, ABCB1 or ABCB4 (89). Where a cancer patient is treated with a taxane, and where the tumors acquire resistance, for example by overexpression of ABCB1 or ABCB4, the physician can change the drug. For example, tumors of breast cancer patients treated with taxanes often develop resistance to this drug. In this context, the FDA has specifically approved switching to another drug, namely, ixabepilone (90). In a clinical study of breast cancer, Thomas et al. (91)

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