IN VITRO CHEMOTHERAPEUTIC DRUG ASSAYS  
MED203.005

COVERAGE:

The chemotherapeutic drug sensitivity assay (human tumor stem cell assay) is not eligible for coverage as it is considered investigational.

The chemotherapeutic drug resistance assay (nonclonogenic cytotoxic drug resistance assay), including but not limited to extreme drug resistance assays, is not eligible for coverage as it is considered investigational.

DESCRIPTION:

In Vitro Chemotherapeutic Drug Assays or In Vitro Chemoresistance-sensitivity Assays (CR-SAs) are intended to provide oncologists with information that assists in the selection of chemotherapy drugs for an individual patient. CR-SAs have been used to select potentially more effective chemotherapy regimens and to avoid the toxicity of potentially ineffective chemotherapy drugs. A variety of assays have been developed that differ in their processing and in the technique used to measure sensitivity or resistance. However, all involve the same basic four steps:

1. isolation of cancer cells,
2. incubation of cells with drugs,
3. assessment of cell survival, and
4. interpretation of results.

The results are reported as either drug sensitive, drug resistant, or intermediate.

There are two general types of in vitro assays:

1. The TUMOR CHEMOSENSITIVITY ASSAY, also known as the human tumor stem cell assay, is an in vitro technique designed to test the sensitivity of antineoplastic agents on cells from tumor specimens obtained from patients. The response of the tumor cell line in the laboratory is used to predict the effectiveness of the agent in the patient. More than one commercial method is available.

2. The TUMOR CHEMORESISTANCE ASSAY, also known as the nonclonogenic cytotoxic drug resistance assay (NCDRA), is intended to identify cancer patients who are not likely to respond to a specific chemotherapeutic agent. The NCDRA is intended to provide information that allows patients to avoid the adverse effects of chemotherapy from which they would not benefit medically. In the absence of assay results, patients would generally receive the first-line chemotherapy of choice for their disease. The assay is performed by first culturing a tumor sample in vitro. Once viable tumor colonies have been established, each culture is exposed to a selected chemotherapeutic agent. After a standard period of time, the test cultures are analyzed for the number of remaining viable...
tumor cells. The relative decrease in number of viable cells in the test cultures compared to control cultures is taken as an indicator of tumor cell resistance. If the in vitro tumor-cell sample is resistant to a particular agent, then the agent may not be recommended for treating the patient.

An additional refined chemoresistant assay technique has been identified that predicts extreme drug resistance (EDR). In this assay, tumor cells are cultured in soft agar medium and then exposed to high concentrations of selected chemotherapeutic agents for prolonged periods of time (far exceeding the time used in NCDRA). Cells that survive this exposure are characterized as showing EDR. The negative predictive value associated with this assay has been reported as greater than 99%. As a result, potentially ineffective drugs can be eliminated from the patient's drug regimen.

RATIONALE:

Studies suggest that in terms of improved patient survival, the clinical role of chemosensitivity and chemoresistance assays is unproven. There have not been any clinical trials showing that either of these assays is associated with improving patient survival.

For chemosensitivity assays, the intent is to select the most effective treatment; the key statistic is the positive predictive value. In other words, what is the likelihood that drugs shown to be effective in vitro will produce a positive clinical response? The enthusiasm for chemosensitivity assays has diminished over the years, due to the poor positive predictive values. This is due in part to a variety of host factors, such as tumor vascularity or technical challenges and inconclusive results.

In contrast, the clinical utility of chemoresistance assays will depend upon the prior probability of response to a given chemotherapy. Since chemoresistance assays are used to deselect potential chemotherapies, the negative predictive value is the key statistical measure. In other words, what is the likelihood that chemoresistance as measured in vitro will correspond to a lack of clinical effect. Unless the negative predictive value is high, there is a chance that clinical decision-making based on a chemoresistance assay could inappropriately exclude an effective therapy.

The EDR assay was specifically designed to produce a very high negative predictive value (greater than 99%) such that the possibility of inappropriately excluding effective chemotherapy is remote in all clinical situations. However, there is still inadequate clinical data to determine whether the use of EDR assays to deselect ineffective chemotherapies results in improved health benefits.

DISCLAIMER:

State and federal law, as well as contract language, including definitions and specific inclusions/exclusions, takes precedence over Medical Policy and must be considered first in determining coverage. The member's contract benefits in effect on the date that services are rendered must be used. Any benefits are subject to the payment of premiums for the date on which services are rendered. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically. HMO Blue Texas physicians who are contracted/affiliated with a
capitated IPA/medical group must contact the IPA/medical group for information regarding HMO claims/reimbursement information and other general polices and procedures.

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