

Cell Culture Drug Resistance Testing (CCDRT) in Cancer Treatment

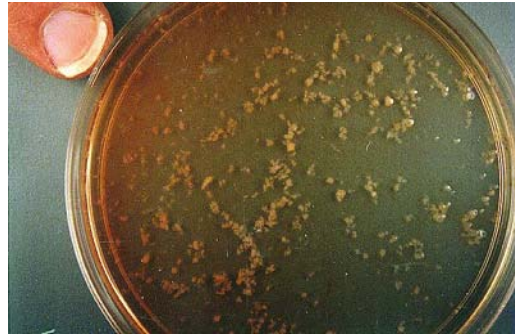
Your doctor is considering referring a biopsy specimen (or fluid specimen) for cell culture drug resistance testing (CCDRT). This pamphlet answers some of the more frequently asked questions.

What is the purpose of CCDRT?

There are about 40 drugs and thousands of potential drug combinations which are used to treat cancers and related blood disorders. In most cases, there is no single “best” treatment which will dependably work for all patients. CCDRT is carried out to improve the odds of selecting the best drug or drug combination.

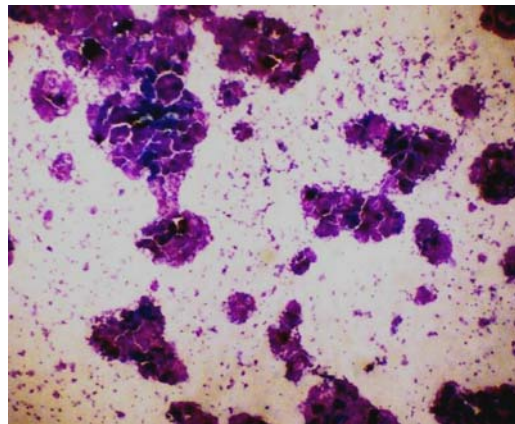
How does CCDRT work?

Your doctor sends a tissue biopsy specimen or body fluid containing cancer cells to the Weisenthal Cancer Group (WCG) laboratory, in Huntington Beach, CA via either local courier or FedEx. WCG tests the cancer cells for sensitivity and resistance to the most important drugs and drug combinations. The drugs are selected for testing based on a knowledge of the patient’s clinical diagnosis (type of cancer), prior treatment history, and available knowledge from the medical literature and clinical experience. On average, 20 different drugs and/or drug combinations are tested. The number tested depends upon the number of cells available from the tissue or fluid submitted.



Above: Appearance of solid tumor biopsy, after preliminary mincing, prior to enzymatic digestion.

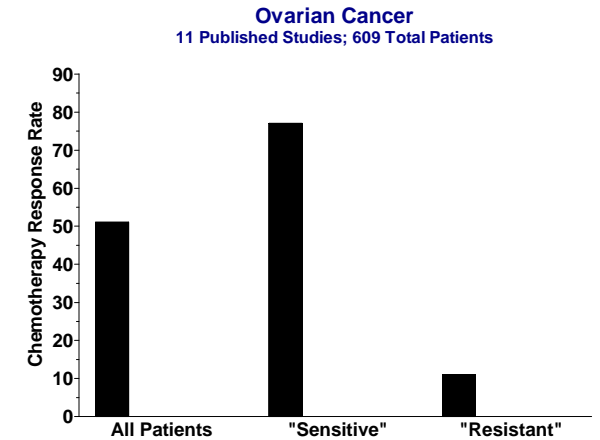
If the specimen is small, or in poor condition, then a more limited number of drugs may be tested



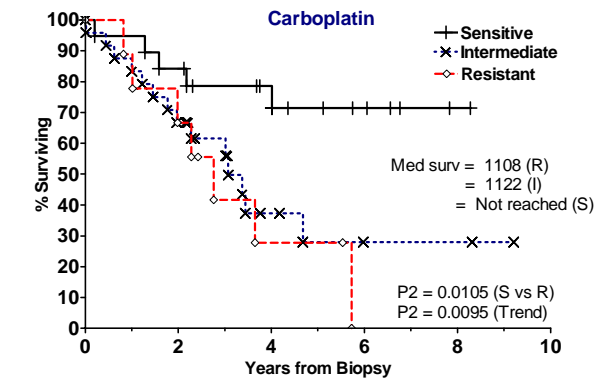
Above: Appearance of tumor cells following cell culture for 96 hours, magnified 100 times.

How accurate is CCDRT?

On average, drugs and drug combinations testing in the “sensitive” range are 7-fold more likely to produce a clinical response (shrinkage of the patient’s tumor) than are drugs testing in the resistant range.



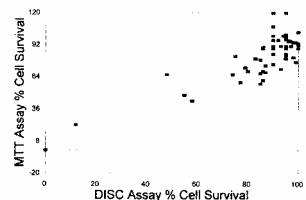
Patients treated with drugs testing in the “sensitive” range have also been found to have longer durations of survival than patients with drug “resistant” tumors, in several types of cancers.



Above: Long term survival of patients with advanced, poorly-differentiated ovarian cancer, as a function of whether or not the tumor cells were “sensitive,” “intermediate,” or “resistant” to carboplatin, an important drug of the type often used in the treatment of ovarian cancer.

The estimated probability of a given drug providing clinical benefit is provided on the assay report.

| | |
|--------------------------------------|------------------------|
| Date Rpt | |
| Date Rcvd | |
| Patient | |
| Case No. | 85134 |
| Path Ref# | BC-98-2816 |
| Physician | |
| Diagnosis | Ovarian Cancer |
| Prior ChemRx | Carb/Taxol;HiDose/ABMT |
| DISC Assay | |
| Viable tumor cell ratio, Day 4/Day 0 | 0.90 |
| % tumor cells, Day 4 | 98 |
| MTT Assay | |
| O.D. Negative Control-Pos Control | 0.81 |
| Comments | |
| DISC/MTT Correlation Coefficient | 0.86 |
| Technical Quality: Excellent | |



| Drug or Combination | Expected (Pre-Test) ResponseRate | Assay Result | Assay Predicted Response Probability |
|-----------------------------|----------------------------------|-----------------|--------------------------------------|
| Cyclophosphamide(4HC) | 10 | Resistant | 2 |
| Ifosfamide(4HI) | 10 | Resistant - EDR | 2 |
| Ifosfamide(4HI) | 10 | Resistant - EDR | 2 |
| Melphalan | 10 | Resistant - EDR | 2 |
| Thiotepa | 10 | Resistant | 2 |
| Carboplatin | 15 | Resistant - EDR | 2 |
| Carboplatin+Ifosfamide(4OH) | 15 | Resistant | 3 |
| Cisplatin | 15 | Resistant | 3 |
| Cyclophos(4HC)+Carboplatin | 15 | Resistant - EDR | 2 |
| Doxil | 15 | Resistant | 3 |
| Doxorubicin | 15 | Resistant - EDR | 2 |
| Etoposide | 15 | Resistant - EDR | 2 |
| Fluorouracil+Leucovorin | 15 | Resistant | 3 |
| Fluorouracil+Carboplatin | 15 | Resistant | 3 |
| Gemcitabine (Gemzar) | 15 | Intermediate | 15 |
| Gemcitabine+Carboplatin | 15 | Sensitive | 38 |
| Pentamethylmelamine | 15 | Resistant | 3 |
| Docetaxel (Taxotere) | 15 | Resistant | 3 |
| Taxol (Paclitaxel) | 15 | Resistant | 3 |
| Taxol+Carboplatin | 20 | Resistant | 3 |
| Thiotepa+Fluorouracil | 15 | Resistant | 3 |
| Topotecan (Hycamtin) | 15 | Intermediate | 15 |
| Topotecan+Carboplatin | 20 | Intermediate | 20 |
| Vinorelbine (Navelbine) | 15 | Resistant | 3 |
| Vinorelbine+Thiotepa | 15 | Resistant | 3 |

Above: Sample assay report. The above patient had far advanced ovarian cancer, which had failed to respond to initial treatment with carboplatin plus Taxol. The patient was then treated with very high dose chemotherapy and two separate stem cell transplants, costing more than \$200,000. There was also no response. At a time when she had massive, unresectable abdominal and pelvic tumor, the surgical oncologist sent tissue for CCDRT, with the above result. The tumor cells were resistant to virtually all drugs, save for a single drug combination, to which the tumor cells were "sensitive." The patient was treated with this combination and had a complete disappearance of cancer, which remained controlled for more than 4 years.

What is the cost of CCDRT? Is it covered by insurance?

The cost is related to the number of drugs tested. There is a base charge for isolating the cancer cells from the specimen and a per drug surcharge. There is also a professional fee charged by Larry Weisenthal, MD, a board-certified medical oncologist. On average, Dr. Weisenthal devotes 3 hours of his own personal time to each assay. This is in addition to an average of 8 hours of California-licensed medical technologist time. The fee for typical assays ranges from \$1,800 to \$2,800. Health insurance plans (including managed care plans) often provide partial to complete payment for the testing, although some health care plans continue to deny payment on the grounds that the companies consider the testing to be "not medically necessary" (WCG vigorously disagrees, as explained on our website (<http://weisenthal.org>) and WCG has been very successful in supporting appeals and legal actions against the insurance companies to ultimately obtain payment). Unfortunately, Medicare will reimburse only a total of \$620 for this testing, and the balance must be paid by the patient (or by the medical center from where the specimen is submitted).



Larry M. Weisenthal, M.D., Ph.D. received his medical and doctoral (in Pharmacology) degrees from the University of Michigan. He received fellowship training in oncology at the National Cancer Institute and is Board Certified in Medicine and Medical Oncology. Curriculum vitae listed at <http://weisenthal.org>

How may I obtain additional information and have my questions answered?

1. Visit our website: <http://weisenthal.org>
2. Call our laboratory, 714-894-0011.

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Cancer Group

15140 Transistor Lane
Huntington Beach, CA 92649
714-894-0011