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American Society of Clinical Oncology Clinical Practice Guideline Update on the Use of Chemotherapy Sensitivity and Resistance Assays

The Bottom Line

- **Intervention**

  Use of Chemotherapy Sensitivity and Resistance Assays to determine chemotherapy

- **Target Audience**

  Medical Oncologists

- **Recommendation**

  Chemotherapy sensitivity and resistance assays to select chemotherapeutic agents for individual patients are not recommended outside of the clinical trial setting

- **Methods**

  Systematic review and analysis of the medical literature by an Update Committee

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Introduction

- The ASCO Technology Assessment (Guideline) on the Use of Chemotherapy Sensitivity and Resistance Assays was first published in 2004
- This Update, like the original Guideline, focuses only on assays using in-vivo measures of chemotherapy resistance or sensitivity

Guideline Methodology Systematic Review

- The Update Committee completed a review and analysis of the medical literature available from December 2003 to May 2010
- Databases searched:
  - ✓Medline
  - ✓Cochrane Collaboration Library

Guideline Methodology Systematic Review cont'd

- Data Supplement 1 includes an evidence table with data from new studies
- Data Supplement 2 includes an Overview of Chemotherapy Sensitivity and Resistance Assays reproduced from the original guideline with the addition of ChemoFX
- Data supplements available at www.asco.org/guidelines/csra

Guideline Methodology Systematic Review cont'd

The Update Committee addressed the same clinical questions as did the original Guideline:

1. Is there a clear definition of what constitutes a successful assay?
2. Do assay results depend on the particular lesion biopsied?
3. Does the assay-guided therapy affect the choice of chemotherapy agent?
4. Does the assay yield clinically useful results?

Summary of Literature Review Results

- Data Supplement 3 and Data Supplement 4 include details about the search terms and the number of excluded and included publications
- Data were extracted for the following CSRAs: adenosine triphosphate bioluminescence (ATP), extreme drug resistance (EDR[A]), methyl thiazolyl-diphenyl-tetrazolium bromide (MTT), and ChemoFX
- Data supplements available at www.asco.org/guidelines/csra

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Recommendations – Table 1

The Update Committee determined that no changes to the 2004 recommendations are warranted.

Recommendation Category	2011 Recommendations
Use of Chemotherapy Sensitivity and Resistance Assays	The use of chemotherapy sensitivity and resistance assays to select chemotherapy agents for individual patients is not recommended outside of the clinical trial setting.
Chemotherapy Treatment Decisions	Oncologists should make chemotherapy treatment recommendations on the basis of published reports of clinical trials and a patient's health status and treatment preferences.
Future Research Evaluating CSRAs in Clinical Trials	Because the *in vitro* analytic strategy has potential importance, participation in clinical trials evaluating these technologies remains a priority.

Overview of Chemotherapy Sensitivity and Resistance Assays

Assay Name	Target Tumor Types	Assay Description
Methylthiazolyl-diphenyl-tetrazolium bromide[9] (MTT)	Breast Cancer	Tumor cell suspensions are cultured with various chemotherapy agents for 4 days. MTT is then added; because it is reduced intracellularly to a blue dye, the intensity of uptake yields permits an estimate of the number of viable cells.
Adenosine Triphosphate Bioluminesence (ATP)	Epithelial ovarian cancer	Tumor cells are cultured in the presence/absence of test drugs and then cells are lysed. The amount of ATP – a reflection of the number of viable cells–is measured by adding luciferin (the compound which causes fireflies to glow). Low ATP concentration manifests as low luminescence to identify efficacious test drugs.

Overview of Chemotherapy Sensitivity and Resistance Assays cont'd

Assay Name	Target Tumor Types	Assay Description
Extreme Drug Resistance (EDR) Assay	Epithelial ovarian cancer	After successful culture, tumor cells obtained from fresh biopsy specimens are labeled with tritiated thymidine. The level of uptake is tracked after exposure to chemotherapy concentrations that approximate the peak level achieved clinically. Extreme resistance is identified when thymidine incorporation is inhibited in the presence of the drug by less than one standard deviation of the median cell inhibition measured for several hundred reference tumor samples.

Overview of Chemotherapy Sensitivity and Resistance Assays cont'd

Assay Name	Target Tumor Types	Assay Description
ChemoFX **	Ovarian, Breast, Endometrial, Cervical, Lung and Colorectal Cancer	The test requires a small tissue sample from surgery or as little as two core needle biopsies (≥35 mg) or ascites or pleural fluid (≥100 cc). Cancer cells grown in vitro are treated with a number of chemotherapies. A report that measures chemosensitivity and resistance is sent to a physician that details how cancer cells responded to each type of chemotherapy.

Guideline Methodology: Update Committee Members

Update Committee Members	Affiliation/Institution
Harold J. Burstein, MD, PhD, Co-Chair	Dana Farber Cancer Institute, Boston, MA
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Additional ASCO Resources

- The Full Text guideline is published in JCO and can also be found online, as is this slide set, at www.asco.org/guidelines/csra

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