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Cell culture drug resistance testing (CCDRT) in platinum-resistant ovarian cancer (OC)

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Objectives: We obtained background data required for the design of a clinical trial to determine the efficacy of CCDRT-directed therapy of platinum-resistant OC.
Methods: 680 fresh surgical specimens (SPC) of OC were submitted from outside hospitals for the purpose of obtaining CCDRT data to assist in the choice of chemotherapy on a non-investigational basis. Virtually all SPC were tested with two separate Medicare-approved CCDRT assays (DISC and MTT) having cell death endpoints.
Results: Validation of CCDRT for identifying platinum resistance was as follows: (1) SPC from platinum-treated patients(PTS) had significantly greater in vitro resistance to platinum(IVRP) than SPC from untreated(UnRxd) PTS. (2) Untreated PTS without IVRP had significantly better long-term, overall survival(LTOS) than PTS with IVRP (2775 vs 713 days, P2=0.0066). (3) SPC obtained within 6 months of platinum-based therapy ("early relapse"/ER) had significantly greater IVRP than SPC obtained more than 6 months after the last platinum-based therapy ("late relapse"/LR). (4) In LR PTS, IVRP predicted for significantly inferior LTOS (950 days vs median not reached, P2<0.05). Comparing ER SPC with UnRxd SPC, the following regimens showed significantly inferior activity in ER SPC: cisplatin, carboplatin, oxaliplatin, melphalan, thiotepa, mitomycin, paclitaxel, and the topotecan/cisplatin combination. The following did *not* show significantly inferior activity in ER SPC: gemcitabine, etoposide, vinorelbine, fluorouracil, epirubicin, pegylated doxorubicin, topotecan, irinotecan, docetaxel, and all 3 gemcitabine/platinum (G/P) combinations. Although G/P was the only active regimen in 25% of the ER SPC, in 30% there was at least one active single agent, and in another 20%, other drug combinations were superior to G/P, some of these being irinotecan/mitomycin, paclitaxel/CTX, CTX/etoposide, platinum/topotecan, and gemcitabine/melphalan. With a *minimum* follow-up of 3 years post-assay, ER (primary refractory and 1st relapse) PTS had a median LTOS of 849 days, while all ER PRTS (including multiple relapse) had a median survival of 612 days. ALL LR PTS had a median LTOS of 1244 days.
Conclusions: These results support a 3-armed, prospective randomized trial in ER PTS to compare (1) "physician's choice" chemotherapy, (2) G/P, and (3) CCDRT-directed therapy.

Category (Complete): Ovary