CHEMOTHERAPY WITH FTORAFUR, EPIRUBICIN, MITOMYCIN C, VINBLASTINE, METHOTREXATE WITH LEUCOVORIN RESCUE (FEMVAL) FOR ADVANCED REFRACTORY METASTATIC BREAST CANCER.

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Metastatic Breast Cancer relapsing after treatment with CMF or Adriamycin containing chemotherapeutic combinations is usually refractory to most attempts to alleviate disease progress. To overcome drug resistance we devised a chemotherapeutic regimen by substituting pro-drugs for drugs and intermediate doses of drugs with rescue together with prolonged infusion for push injections. Treatment schedule starts with Ftorafur 1000mg/m² iv push on days 1 and 2,Epirubicin 25mg/m² given iv over a 6 hour period on days 1 and 8,Mitomycin C 5mg/m² iv push on day 2,Vinblastine 5mg/m² iv push on day 8,and Methotreaxate 500mg given iv over 6 hours on day 14 followed by Leucovorin rescue with 15mg im every 6 hours on day 15 and po on days 16 and 17. Treatment is repeated after a rest of 2 weeks.

Eight patients with far advanced disease and refractory to most chemotherapeutic regimens,including CMF,Adriamycin-Vincristine and Adriamycin-Cytoxan-Methotrexate,have entered the protocol so far. Mean follow up time is 7 months (3+ to 10+ months).Four patents had Lung metastasis,3 Liver,5 Skin,4 Bone,2 infraclavicular lymph node involvement with nerve infiltration and 3 distant soft tissue metastasis. Performane status was 40 to 50%(Karnofsky scale) when entering protocol.Age range was from 42 to 61. Although all patients were heavily pretreated with both Radiotherapy and Chemotherapy we kept timing of treatments strickly on schedule. All patients but one are still alive and enioying very good partial remissions. Treatment was well tolerated without toxicity to bone marrow nessecitating postponement of scheduled drug administration. Gastrointestinal toxicity was minimal,neurotoxicity was acceptable but alopecia was almost universal (one patient was totally unaffected,2 developed complete hair loss,5 patients developed various degrees of alopecia). The one patient that died developed liver insufficiency and died of hepatic coma,while her liver metastasis were in regression,three months after entering the protocol. Best results were seen in skin disease (complete dissappearance of skin lesions in 3 patients lasting for 3 to 6+ months,more than 50% regression in 2 lasting for 2 to 4+ months),liver disease and lung disease.

Our datd,altough preliminary,show that the combination we use is capable of overcoming drug resistance by using pro-drug instead of drug (Ftorafur/Fluorouracil),infusion for 6 hours instead of rapid injection of the drug (Epirubicin,Methotreaxate),higher doses than the conventially used with rescue(Methotrexate) and a very tight time schedule. With these manipullations the "under the curve area" increases (higher concentration of drugs and longer time the drugs are in circulation) and thus they succed to obtain increased cell kill.