

BASOPHIL CELL ACTIVATION TEST BY FLOW CYTOMETRY IN THE MANAGEMENT OF IMMEDIATE DRUG HYPERSENSITIVITY TO CARBOPLATIN IN OVARIAN CANCER PATIENTS.

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Hypersensitivity reactions (HSRs) to carboplatin (CARB) chemotherapy are becoming increasingly frequent in the clinical practice of ovarian cancer (OC). Longer survival time of patients and availability of ancillary treatments make it possible administration of multiple treatment cycles of CARB, thus facilitating presentation of HSRs that typically occur after 5/6 therapy cycles. Discontinuation of treatment and standardized protocols of desensitization represent the standard of care for OC patients after HSRs to CARB, since alternative drugs for OC treatment are not available. The basophil activation test (BAT) is considered useful in the diagnosis of HSRs to several chemotherapeutics. Thus, we set out to verify whether BAT might help in the management of OC patients who had presented HSR to CARB and had to receive desensitization to this agent. Eleven patients with diagnosed HSR to CARB were enrolled in the study. Patients were free from steroid treatment in the last 2 wks. We optimized a BAT protocol to detect sensitivity/desensitization to CARB. Peripheral blood was obtained from patients after at least 2 wks from HRS. Blood samples (100µl) were incubated for 20 min in Ca⁺⁺ activation solution (Beckman Coulter) with three different concentrations of CARB, anti FcεR (positive control) or PBS (negative control). A drug (taxol) was also included for comparison, with which patients had no history of previous HSR. All the experimental conditions were run in the presence/absence of IL-3. Cells were then stained with previously titrated BV-421 anti-CD63 and APC anti-CCR3 (BioLegend), FITC anti-CRTH2, PE anti-CD203c, APC-AF750 anti-CD45 and KO anti-CD3 (Beckman Coulter) for 20 mins at room temperature. One ml Fix and Lyse solution (Beckman Coulter) was added to lyse erythrocytes and fix samples. Flow cytometry run was performed on Cytotflex LX (Beckman Coulter). Positive reactions were evaluated by computing the stimulation index (SI) for CD63 and CD203c expression. Both CD63 and CD203c SI increased in a CARB dose-dependent fashion, but not in the presence of taxol. The SI was further increased in the presence of IL-3. Interestingly, we observed a relationship between extent of CD63 SI and HSR severity grading. Conversely, no correlation was found between CD203c SI and severity grading. CD63 and CD203c SI were larger in patients tested after at least 21 days from HSR.

In conclusion, the BAT seems to be a feasible and minimally invasive assay to monitor risk of HSR to CARB in OC patients who had HSR in response to previous treatment with this agent. These preliminary results are based on a limited number of patients and may not be extrapolated to the general population. Introduction of BAT in the range of assays performed in OC patients referred for desensitization protocol for HSR to CARB is currently being investigated.