Is BRCA mutational status a predictor of platinum-based chemotherapy related hematologic toxicity in high-grade serous ovarian cancer patients?

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Objective

To evaluate hematologic adverse effect profiles associated with frontline platinum-based chemotherapy in ovarian cancer patients according to BRCA 1/2 mutational status.

Methods

Patients with high-grade serous ovarian cancer and a known BRCA mutational status who received in frontline 6 cycles of Carboplatin (AUC 5) plus Paclitaxel 175 mg/mq were retrospectively selected from our databases. Hematologic toxicity profiles of BRCA mutated patients were compared to non-mutated patients, according to EORTC Common Terminology Criteria for Adverse Events (CTCAE_4.02)

Results

Totally, 176 women of whom 58 (33%) were BRCA1/2 mutation carriers - 40 BRCA1 (69%) and 18 (31%) BRCA2 mutations carriers - and 118 (67%) non-carriers were identified. A significant higher frequency of thrombocytopenia (24% vs 5%; $p < 0.001$), anemia (21% vs 7%; $p = 0.006$) and neutropenia (62% vs 27%; $p \leq 0.001$) was observed in BRCA mutated patients, resulting in a higher percentage of granulocyte-colony stimulating growth factors injection (12% versus 1%, $p < 0.001$) and dose delay (19% versus 27%, $p = 0.005$). The multivariate analysis confirmed that granulocyte-colony stimulating growth factors injection and dose delay were statistically significantly more frequent in BRCA mutated patients (OR 2.567, 95% CI 1.136–5.798, $p = 0.035$; OR 3.860, 95% CI 1.098–13.570, $p = 0.023$). Finally, the total number of hematologic adverse events compared between the two groups of patients during the entire treatment period showed a substantial higher rate of hematologic adverse events in BRCA mutated population.

Table 2. Haematological toxicity profiles according to BRCA mutational status.

Toxicity	BRCA1/2 mutated (n=58)	BRCA1/2 wild-type (n=118)	P-value
Platelets $<150 \times 10^9/L$	14 (24%)	6 (5%)	<0.001
Hemoglobin <10 g/dL	12 (21%)	8 (7%)	0.006
Absolute neutrophil count $<1.5 \times 10^9/L$	36 (62%)	32 (27%)	<0.001
G-CSFs injection	20 (35%)	6 (5%)	<0.001
Dose reduction	18 (31%)	32 (27%)	0.588
Dose delay	28 (48%)	32 (27%)	0.005

P-value was estimated using a Chi-square Pearson's test.
G-CSFs, granulocyte-colony stimulating growth factors.

Figures show rates of anemia and neutropenia in NACT patients per cycle, according to BRCA mutational status

Conclusions:

Germline BRCA 1/2 mutations are associated with a higher hematologic toxicity in patients with ovarian cancer who underwent platinum-based chemotherapy.