Safety analysis, correlation with response and previous treatments of the association of everolimus (EVE) and exemestane (EXE) in 181 metastatic breast cancer patients (MBC)


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The toxicity profile of EVE EXE combination was reported in the Bolero 2 trial in the selected pts population. In order to evaluate the safety in the clinical practice and to evaluate a possible correlation of toxicities with previous treatments, clinical data from 181 pts were retrospectively collected. The hypothesis of a correlation of toxicities with response was also evaluated. Characteristics of pts: median age 65 yrs (range 37-83), 1 site of disease in 27%, 2 or more sites in 73%. Bone was involved in 81%, lymph node 34%, liver 38%, lung 23%, skin 3%, soft tissues 21% of the pts. Overall, median number of previous treatments for advanced disease was 3 (range 0-9): median number of previous chemotherapy (CT) and hormone therapy (HT) was 2 (range 0-9). 96% of the pts started the treatment at 10 mg daily dose, 4% at 5 mg for physician choice. Median time of treatment was 4 months (range 1-48). Results: Distributions of toxicities were: grade (G) 1-3 stomatitis in 65% of pts, G 1-4 hepatic 21%, G 1-4 non-infectious pneumonitis 15%, G 1-3 skin 35%, G 1-3 glucose alteration 25%, G 1-2 lipid alterations 28%, G 1-3 nausea 13%, G 1-2 vomiting 5%, G 1-2 limbs edema in 9%, G 1-2 pleural effusion 4.5%, G 1-2 pericardial effusion 1.2%, G 1-2 diarrhoea 7%, G 1-3 asthenia 51%, G 1-2 arthralgia 21%, G 1-2 myalgia 4%, G 1-2 infections 7%. Treatment was discontinued in 15 pts (8,2%; 11 toxicity, 4 refusal). Due to toxic events, EVE was reduced to 5 mg in 27% of pts. The response rate was as follow: CR 1.8%, PR 24.9%, SD 33.1% PD 34.9%, not evaluable 5.3%, 6% of pts are too early to evaluate. No correlation was found in the analysis between toxicity and number of prior therapies, neither between toxicity and response. In the multivariate analysis, previous exposure to anthracycline for advanced disease represents the only predictive factor of grade > 2 toxicity (OR = 2.85 CI95% 1.07-7.59, p = 0.036). Conclusions: The association of everolimus and exemestane has confirmed to be a safe and effective treatment for endocrine sensitive MBC pts even in routine clinical practice. The rate of treatment discontinuation due to toxicity is low and none correlation between previous number of treatments and response or between toxicity and response was found. Previous anthracycline exposure may represent a predictive factor for developing a higher grade of toxicity and should be taken in account when the EVE EXE combination is chosen in the setting of CT pretreated patients.