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A multicenter, randomized, double-blind, phase II study to evaluate the tolerability of an induction dose escalation of everolimus in patients with metastatic breast cancer (mBC) (DESIREE)

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Background

Everolimus added to exemestane improves the outcome of patients (pts) with HR+/HER2- mBC pretreated with nonsteroidal aromatase inhibitors (NSAI). Mucositis is one of the major causes of everolimus discontinuation. To decrease mucositis, DESIREE investigated the use of a dose escalation schedule of everolimus.

Methods

DESIREE is a phase II, multicenter, randomized, double-blind, placebo controlled trial in pts with HR+/HER2- mBC and progression/relapse after NSAI. Pts were randomized to everolimus 10mg/day (EVE-10mg) for 24 weeks (w) or a dose escalation of everolimus (2.5mg/day, w1; 5mg/day, w2; 7.5mg/day, w3; 10mg/day, w4-24) (EVE-esc) plus exemestane. Primary endpoint was the incidence of first episode of mucositis grade (G)≥2 within 12w of treatment start. Secondary endpoints included clinical benefit rate (CBR), relative total dose intensity (RTDI), safety, quality of life (QoL).

Results

160 pts were randomized (June 2015-October 2020), 156 started therapy (n=80 EVE-esc, n=76 EVE-10mg). Median age was 64 years (33-85). At baseline, 56.3% pts in EVE-esc vs 48.7% in EVE-10mg were overweight/obese (p=0.423), 56.3 vs 42.1% had liver M+ (p=0.081), 62.5% vs 51.3% received >1 therapy line for mBC (p=0.196). In EVE-esc, the incidence of mucositis G≥2 within 12w of therapy was significantly lower (28.8 vs 46.1%, p=0.039). This effect maintained statistical significance in multivariate analysis adjusted for age, ECOG PS, BMI, and number of previous therapy lines for mBC (OR=0.41 [95%CI 0.20-0.82], p=0.012). There was no impact on other non-hematologic toxicities as pneumonitis or rash. Median RTDI was 91.1 vs 80.0% (p=0.329). Discontinuations in the first 3w were more frequent in EVE-10mg (6.3 vs 15.8%, p=0.073). CBR did not significantly differ (32.5% vs 44.7% p=0.139). Prospectively captured QoL was not significantly different.

Conclusions

DESIREE met its primary objective and showed that a dose escalation schema of everolimus over three weeks can be successfully used in pts with HR+/HER2- mBC to prevent the onset of mucositis G≥2 without affecting efficacy.

Clinical trial identification

NCT02387099.

Legal entity responsible for the study

German Breast Group (GBG Forschungs GmbH).

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Disclosure

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