

CIRG/TORI 010: first analysis of a randomized phase II trial of motesanib plus weekly paclitaxel (P) as first line therapy in HER2-negative metastatic breast cancer (MBC)

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Background: Motesanib (M) is an oral tyrosine kinase inhibitor of VEGF, PDGF and Kit receptors. We assessed, in an ongoing double-blinded placebo-controlled trial, the effect of adding M to P as first line treatment of patients (pts) with MBC. A P plus bevacizumab (B) arm was included. The CIRG/TORI 010 study was supported by Amgen.

Methods: 282 pts with HER2-negative and measurable MBC were randomly assigned treatment with P 90mg/m² on days 1, 8 and 15 in combination with blinded placebo (P: arm A), blinded M 125mg once daily (PM: arm B) or open label B 10mg/kg on days 1 and 15 (PB: arm C). Treatment was administered in 28-day cycles until disease progression, toxicity or consent withdrawal. The primary objective was to determine the difference in response rate (RR) between P and PM. Treatment efficacy was assessed every 8 weeks according to RECIST and scans were independently centrally reviewed.

Results: 277 pts received the assigned treatment. Pts characteristics at entry were balanced: median age was 55, 80% had hormone receptor positive tumors and 66% had received prior chemotherapy with curative intent. At the first planned analysis, 16 weeks after last patient enrolment, the median treatment duration was 6 cycles. The median cumulative dose of P was similar across the arms: 1328, 1282 and 1438 mg/m² in arm A, B and C, respectively. Pts received a median cumulative dose of B=133 mg/kg (arm C) and an averaged daily dose of M=111mg (arm B). The table displays the efficacy results and relevant differences in toxicities incidences (all grade).

	Arm A (P)	Arm B (PM)	Arm C (PB)
Efficacy (all pts)	n=94	n=91	n=97
RR (95% CI)	35% (26-46)	48% (38-59)	45% (35-56)
Progression-Free Survival (95% CI)	8.0mo (6.6-9.6)	9.1mo (8.1-11.6)	10.1mo (9.0-15.3)
Toxicity Incidence (% treated pts)	n=90	n=91	n=96
Nausea	44	60	48
Diarrhea	33	69	42
Vomiting	24	40	23
Abdominal Pain	21	44	16
Stomatitis	11	15	29
Alopecia	63	59	71
Infections	54	55	66
Hypertension	13	57	30
Anorexia	16	35	25
Left Ventricular dysfunction	1	8	3
Hepatobiliary disorders	6	17	3
Back Pain	14	15	23
Peripheral Neuropathy	42	48	54

The RR favored PM and PB as compared with P but the differences were not statistically significant (p=.09, adjusting for stratification factors). The distributions of times to progression or death did not significantly differ between the three arms.

Conclusion: The administration of M in combination with weekly P is feasible with no unexpected toxicities. This regimen is efficacious in the treatment of pts with Her2-negative MBC.