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breast cancer, early stage

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OLYMPIA, NEO-OLYMPIA AND OLYMPIAD: RANDOMIZED PHASE III TRIALS OF OLAPARIB IN PATIENTS (PTS) WITH BREAST CANCER (BC) AND A GERMLINE BRCA1/2 MUTATION (GBRCAM)

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Background: A Phase II study (NCT00494234) showed that the oral PARP inhibitor olaparib (400 mg bid; capsules) exerts antitumour activity in BC pts with a gBRCAm (Tutt *et al Lancet* 2010). Three Phase III trials of olaparib monotherapy have been initiated in BC pts with a gBRCAm: OlympiA (NCT02032823), Neo-Olympia (D081EC00005), OlympiAD (NCT02000622).

Trial design: Trial designs are summarized in the Table. For each trial, eligible pts will have a BRCAm and will undergo gBRCAm testing (Myriad Integrated BRCA*Analysis*®) as part of the trial. For OlympiA, pts must be at high risk of recurrence and have completed local treatment and either neoadjuvant (without pCR) or adjuvant chemotherapy. For Neo-Olympia, pts can have operable, locally advanced or inflammatory BC, must have a tumour >2 cm by clinical exam (or >1 cm by radiological exam) and must have completed four cycles of anthracycline plus carboplatin without disease progression. For OlympiAD, pts can have TNBC or HER2-negative BC, and must have received prior anthracycline and taxane in the adjuvant or metastatic setting, and ≤2 chemotherapy lines for mBC. In OlympiA, pts will receive treatment for up to 12 months; efficacy will be assessed q 3 months up to 24 months, then q 6 months up to 60 months, then q 12 months. In Neo-Olympia, pts will receive treatment for 12 wks pre-surgery and then for 40 wks post-surgery. In OlympiAD, PFS will be assessed by RECIST v1.1; radiologic exams will be performed at baseline, q 6 wks up to 6 months, and then q 12 wks until disease progression. In OlympiA and OlympiAD, IDFS and PFS, respectively, will be analyzed using stratified log-rank tests; for Neo-Olympia, pCR rate will be analyzed with an adjusted logistic regression model. Primary analyses will be undertaken after 330 IDFS events (OlympiA), surgery (Neo-Olympia) and 230 PFS events (OlympiAD). Enrolment began in March 2014 for OlympiAD, April 2014 for OlympiA and is expected to begin in Q3 2014 for Neo-Olympia.

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Table: 331TiP

	OlympiA	Neo-Olympia	OlympiAD
Setting	Adjuvant treatment for high-risk, primary TNBC	Neo-adjuvant treatment for primary TNBC	Metastatic BC (mBC)
Design	Randomized (1:1), double-blind, parallel-group	Randomized (1:1:1), three-arm, parallel-group	Randomized (2:1), open-label
Olaparib monotherapy arm	300 mg bid (tablet)	300 mg bid (tablet) (Arm A)*	300 mg bid (tablet)
Comparator arm(s)	Placebo	Placebo + weekly paclitaxel 80 mg/m^2 for 12 wks (Arm B)* Olaparib 100 mg bid (tablet) + weekly paclitaxel 80 mg/m^2 for 12 wks (Arm C)*	Physician's choice of capecitabine 2500 mg/m^2 (d1-14 q 21d), vinorelbine 30 mg/m^2 (d1, d8 q 21d) or eribulin 1.4 mg/m^2 (d1, d8 q 21d)
Primary endpoint	IDFS	pCR rate	PFS (BICR)
Secondary endpoints	OS, DDFS, incidence of new cancers	OS, EFS, DDFS, ORR at 12 wks	OS, PFS2, ORR
	HRQoL	HRQoL	HRQoL
Other objectives	Safety, tolerability	Safety, tolerability	Safety, tolerability
Target recruitment (pts)	1320	300	310

*Curative-intent surgery to be performed after 12 wks, after which pts will receive olaparib 300 mg bid (Arm A), placebo (Arm B), or either weekly paclitaxel 80 mg/m^2 for 12 wks (followed by olaparib 300 mg bid) or olaparib 300 mg bid (Arm C) BICR, blinded independent central review; d, days; DDFS, distant disease-free survival; EFS, event-free survival; IDFS, invasive disease-free survival; ORR, objective response rate; OS, overall survival; pCR, pathological complete response; PFS, progression-free survival; q, every; PFS2, time to second disease progression or death; TNBC, triple-negative breast cancer; wks, weeks