

## Safety of assisted reproductive techniques in young BRCA carriers with a pregnancy after breast cancer: results from an international cohort study

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**Background:** Very limited evidence is available on the safety of assisted reproductive techniques (ART) in breast cancer (BC) patients harboring *BRCA1/2* pathogenic variants (PVs). Hence, concerns remain among physicians counseling young *BRCA* carriers with BC on the safety of ART use.

**Methods:** This is an international, multicenter, hospital-based, retrospective cohort study including women harboring known *BRCA1/2* PVs and diagnosed at  $\leq 40$  years with stage I-III BC between January 2000 and December 2020 (NCT03673306). This analysis explored safety of ART to achieve a pregnancy. Maternal and fetal outcomes were compared between patients achieving a pregnancy spontaneously (spontaneous pregnancy group) vs. using ART (ART group).

**Results:** Out of 4732 patients included across 78 centers worldwide, 543 with a pregnancy after BC entered the present analysis. Among them, 436 conceived naturally and 107 using ART. In the ART group, 45 (42.1%) underwent oocyte/embryo cryopreservation at BC diagnosis, 33 (30.8%) ovarian stimulation following use of anticancer therapies, 21 (19.6%) embryo transfer following oocyte donation and for 8 ART type was missing. As compared to the spontaneous pregnancy group, patients in the ART group were significantly older at the time of conception (37.1 vs. 34.3 years), had more often hormone receptor-positive BC (43.4% vs. 30.8%) and a longer median time from BC diagnosis to conception (4.2 vs. 3.3 years). No statistically significant differences in pregnancy complications were observed between cohorts ( $p=0.382$ ). However, patients who conceived with ART had more miscarriages (11.3% vs. 8.8%) and less induced abortion (0.9% vs. 8.3%) than those who conceived spontaneously. At a median follow up of 9.1 years (IQR 6.4-13.4), no detrimental effect of ART on disease-free survival (DFS) was observed

with 13 and 118 DFS events in the ART and spontaneous pregnancy groups, respectively (log-rank  $p=0.147$ ; HR 0.64, 95% CI 0.36-1.14; adjusted HR 0.72, 95% CI 0.38-1.33).

**Conclusions:** This global study showed that ART to have a pregnancy appears to be safe in BC survivors harboring *BRCA1/2* PVs, with no apparent worsening of maternal prognosis or fetal outcomes.

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