**Supplementary material**

**Explanation of the model and assumptions:**

* The model reflects 1-year outcomes of a patient who undergoes *de novo* treatment and is diagnosed with HER2-positive, HR-negative, advanced-stage (III and IV) breast cancer.
* Patients who do not undergo a liquid biopsy are treated the trastuzumab, pertuzumab, and docetaxel regimen as the first-line treatment, according to the NCCN Clinical Practice Guidelines in Oncology- Breast Cancer Version 1.20181 and the usual clinical practice. Hormone therapy drugs are not considered given that the population under study corresponds to the negative hormonal receptor type.
* The model assumes that all patients receiving this first-line treatment develop clinical resistance,2.3 although not all in the 1st year. Having detected clinical resistance, patients will migrate to a second-line treatment, which in our model consists of trastuzumab emtansine (TDM1).3,4
* If liquid biopsy is included, this may give a positive or negative result in the first measurement for resistance or in a subsequent measurement, which in the model is assumed to be carried out after 4 and 8 months after the first-line treatment has begun, according to the clinical recommendation of experts in this evaluation and the follow-up model reported in literature5.
* The model does not contemplate the performance of liquid biopsy at month 0 because once the patients are typified with HER2-positive cancer, they are placed in a first-line therapeutic regimen, at least for 1 cycle.
* If the liquid biopsy is positive for resistance, patients will migrate to a second-line treatment, which in the case of this study corresponds to the trastuzumab emtansine (TDM1) regimen, according to the ASCO and NCCN guidelines.1,6
* The third line of treatment was not modeled. No evidence was documented regarding the use of liquid biopsy following the second line of treatment.

**References**

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