Study: **OlympiA / D081CC00006 / BIG 6-13 / NSABP B-55**

Date: **July 28, 2021**

To: **OlympiA Investigators**

OlympiA: A randomised, double-blind, parallel group, placebo-controlled multi-centre Phase III study to assess the efficacy and safety of olaparib versus placebo as adjuvant treatment in patients with germline BRCA1/2 mutations and high risk HER2 negative primary breast cancer who have completed definitive local treatment and neoadjuvant or adjuvant chemotherapy.

Dear OlympiA Investigator,

As you are aware, earlier this year, OlympiA trial met the pre-specified criteria for superiority for the primary endpoint of invasive disease–free survival (IDFS), at which time the IDMC recommended primary analysis to be conducted. In the interim IDFS analysis presented at ASCO 2021 and published at the NEJM, adjuvant olaparib was associated with significantly longer invasive and distant disease-free survival compared to placebo. The safety profile of olaparib was consistent with that previously reported, with no excess of serious adverse events or adverse events of special interest in the olaparib group (N Engl J Med 2021; 384:2394-2405).

Given the interim nature of this analysis, final survival analysis are still not available, and "longer blinded follow-up is required to assess the effect of olaparib on overall survival", as stated in the NEJM publication. Thus, with respect to ongoing study conduct, the IDMC recommended that all assessments for all patients should continue as defined in the study protocol and no unblinding of patients was endorsed by the committee following the presentation of the aforementioned data.

All patients included in OlympiA were randomized within a maximum of 12 weeks of completion of their last treatment (surgery, chemotherapy or radiotherapy). At this time, delayed initiation of olaparib beyond this time frame should not be encouraged due to the absence of evidence supporting the benefit of such approach.

Systematic unblinding of patients and investigators in situations not foreseen in the study protocol (e.g., disease recurrence) could introduce significant bias into the interpretation of OlympiA's final safety and efficacy results. Investigators and patients will remain blinded to treatment, so the trial can continue to collect patient outcomes to assess the important key secondary endpoints of overall survival and distant disease-free survival and continue to monitor for any late safety signals.

Yours sincerely,

OlympiA Study Principal Investigators, on behalf of the Olympia Steering Committee