Background: Neo-adjuvant (NA) chemotherapy (CT) +/- anti-Her2 treatment of operable breast cancer (BC) is considered a standard option in the management of BC. However, pathologic complete response (pCR) rates with CT in hormonal receptor +/- Her2 negative BC are usually low: 7% (Luminal A) to 16% (Luminal B). Alternatively, NA endocrine therapy (ET) has not been established as a standard treatment because of low pCRs (i.e. 5% using 8 months of ET).

Trial design: This is a multicenter phase III, 3rd generation neo-adjuvant trial performed in 34 centers and 8 countries of Middle-East and Maghreb with the objective to investigate the potential role of the addition of a CDK 4/6 inhibitor (Palbociclib) to ET (Fulvestrant +/- Gosereline) compared to ET alone as neo-adjuvant therapy of HR +/- Her2- operable BC sensitive to ET. The question Is whether or not ET plus CDK 4/6 inhibitor would yield high enough pCR rates to establish this strategy as a reasonable therapeutic option in this group of patients (pts) with luminal HER2- BC. A total of 400 pts with stage II and IIIA are planned to be recruited in this trial. OncoType DX will be performed upfront in order to eliminate CT candidates. All pre/peripost and -menopausal pts with a recurrence score < 31 will be treated with 4 months of Fulvestrant (500 mg Day (d.) 1, 14, 28 then q. 28 d. (+/- Gosereline 3.6 mg q.28 d.). Patients with responding/stable disease will then be randomized in double blind fashion to Fulvestrant (+/- Gosereline) either with Palbociclib 125mg po daily 3 weeks/4 or placebo. No additional cycles will be delivered before surgery. The study primary endpoint is pCR while clinical/radiological response, rate of conservative surgery, safety, disease-free and overall survival are secondary endpoints. Exploratory endpoints encompass biomarker serial analysis of liquid biopsies with Quantum Optic and DNA methylation technologies. The SAFIA trial aims to identify a new neo-adjuvant standard with ET plus CDK 4/6 inhibitor in luminal - Her2 negative operable BC. 

Clinical trial identification: SAFIA Study (ICRG 1201); NCT03447132.

Legal entity responsible for the study: International Cancer Research Group (ICRG).

Funding: AstraZeneca, Pfizer and Genomic Health.

Disclosure: J-M. Nabholtz, F. Dabouz, S. Kullab: Research grants: AstraZeneca, Pfizer, Genomic Health. All other authors have declared no conflicts of interest.