When neoadjuvant therapy is not effective in triple negative breast cancer, are there any weapons available?
DISCLOSURE OF INTEREST

- No disclosure of interest
Case clinic presentation

39 years old woman with a 4.5 x 4 cm mass in the lower inner quadrant of the right breast.

18/10/18: Tru-cut biopsy: Metaplastic breast carcinoma Er<2% PgR 30% Ki67 50% c-erb B2 1+

25/10/18: PET-TB with FDG: no secondary lesions in other districts

Program proposed to the patient after multidisciplinary meeting:

- Neoadjuvant chemotherapy with epirubicin plus cyclophosphamide for 4 cycles, followed by weekly paclitaxel plus carboplatin for 12 cycles.
- BRCA 1-2 test
Lack of response to anthracycline

- **30/11/18:** BRCA1 mutation c.53T>C (p. Met18Thr) class 4
- **21/12/18:** After 4 cycles with anthracycline plus cyclophosphamide:
  - Right breast appears hyperemic, with tight and thin skin.
  - Raise of CA 15.3
  - Breast ultrasound: intrammary edema with necrotic areas inside the tumoral mass that showed increased dimensions (5.2X5 cm).
  - PET-CT scan: no secondary lesion in other districts.

- **11/01/2019:** 1°cycle of Neoadjuvant CT with carboplatin + paclitaxel
Initial response…

- Patient referred pain in the right breast, therefore she received local drainage of the intrammary edema every week, with benefit.

- After 4 cycles of CT with weekly paclitaxel and carboplatin:
  - clinical and radiological response (4X3.5cm mass)
  - neither hyperemic nor tight skin
  - significantly reduced intrammary gland edema
  - patient didn’t feel any pain
  - lowering of CA 15.3 at the blood examinations.
...but then another progression

- During the 10\textsuperscript{th} infusion of carboplatin, patient referred rhinorrhea, swelling of the face and throat, wheezing, nasal congestion and itching in the mouth. Corticosteroids and antihistamines were infused, with benefit.

- 24/04/19: after 10 cycles of CT with weekly paclitaxel and carboplatin right nipple secretion started to appear, with increasing edema and raising of CA 15.3.

- Breast Ultrasound confirmed an enlargement of the tumoral mass, that now spreaded in all the inner quadrants and in the retroareolar region. Still no pathologic lymph-nodes.
Early surgery after PD

Because of the lack of response to every treatment performed, we decided, after a multidisciplinary discussion, to anticipate the surgical procedure.

05/19: Bilateral mastectomy was performed. Histopathological examination confirmed a ductal cell carcinoma with squamous metaplastic foci, low TILs:
- pT3 (7X6.5X5,5 cm, mass infiltrating the muscle)
- N 0/5
- G3
- ER 0 PgR 0 Ki67 60% c-erb B2: score 1+
- p63 positive CKAE1/AE3 positive CK5/6 positive CEA negative
How should we proceed next?

- Chest radiotherapy?
- Adjuvant Capecitabine: yes or no?
- Clinical trial if available?

**How we proceeded:** The patient couldn’t be enrolled in the OLYMPIA trial because it ended its recruiting. Also, Olaparib was not available in the expanded access programme for our patient. Therefore, after a multidisciplinary meeting, we decided to propose chest radiotherapy and discuss with the patient the possible benefits of starting an adjuvant chemotherapy with Capecitabine. What about BRAVE trial?
Between May and June the patient received chest and supraclavicular RT (total dose of 50.4 Gy in 28 fractions).

06/2019: starts Capecitabine 1250mg/m² bid g1–14 q3w for 6/8 cycles.

25/09/2019: after the fourth cycle of capecitabine…
Conclusions

- Triple negative breast cancer (TNBC) is a heterogeneous disease with distinct molecular subtypes that differentially respond to chemotherapy and targeted agents.
- Many patients with a TNBC, who receive neoadjuvant chemotherapy, do not achieve a pCR or sometimes they don’t respond to the CT at all.
- We surely need active treatments that can improve their prognosis. CREATE-X is the only trial that demonstrated a clinical benefit for these patients by using Capecitabine as an adjuvant therapy.
- Carboplatin has become a standard of care in TNBC neoadjuvant treatment, especially in BRCA1/2 mutated patients. CREATE-X trial didn’t evaluate the efficacy of adjuvant Capecitabine in patients who received a neoadjuvant CT with carboplatin, therefore we don’t know if this therapy truly improves the prognosis of these kind of patients nowadays.
- OLYMPIA trial will hopefully give us a new “weapon” (Olaparib) in order to improve the prognosis of patients with a TNBC BRCA1/2 mutated.
Thank you for your attention!