Immunomodulatory effect of denosumab in early breast cancer: preliminary results of a randomized window-opportunity clinical trial D-Biomark (NCT03691311)

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Methods

Patients with early-stage HER2-negative BC, candidates to tumour excision as first therapeutic approach are included. Patients are randomized 2:1 to denosumab: control (no treatment); experimental arm received 2 doses of 120 mg subcutaneous of denosumab (once per week) before surgery (2-4 weeks later). Tumour cell proliferation by Ki-67 immunohistochemistry (IHC), cell survival by cleaved caspase-3 IHC (primary endpoints) and stromal tumour infiltrating lymphocytes (TILs) were evaluated comparing baseline biopsy sample and surgical specimen. Ki-67 and TILs were quantified according to International guidelines by blinded pathologists.

Results

Table 1. Clinopathological features of 36 patients. Preliminary data from the first patient enrolled out of 60. Clinical and tumour characteristics were well balanced between both groups.

Conclusions and future work

Preliminary data from the D-Biomark clinical trial show that a short treatment of neoadjuvant single agent denosumab does not reduce tumour cell proliferation or survival but increases TILs in early BC. This study will be completed with a histomorpho-immunohistochemical characterization of immune infiltrate and gene expression data. The increase in stromal TILs will be correlated with neoplastic and postmenopausal patients, as well as in TNBC and luminal subtypes.

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Bibliography


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Abstract #384

Denosumab does not reduce tumor cell proliferation or survival

Denosumab increases TILs in early breast cancer

Figure 3. sRANKL mRNA. Table 2. Means of Ki-67 (IMC) and Cleaved Caspase-3 (IMC) increase was associated with an effective antitumoral inhibition of RANK, but not with a reduction in proliferation (Ki67) or survival (Cleaved Caspase-3) primary endpoints.

Figure 2. D-Biomark. The diagram shows the usual route that a patient from the clinical trial NCT03691311 goes through.

Figure 4. Denosumab increases the tumoral inflammatory infiltrate. A. An increase in TILs was observed in the denosumab treated group (p=0.03). Paired t test but not in the control group (p=0.85). B. Patients treated denosumab showed a 210% increase in TILs (33% vs 0% in the control group) (p=0.03). C. Representative picture of H&E showing an increase in stromal TILs after denosumab treatment.