278P: Plasmid encoding p62/SQSTM1 administered in combination with CMF chemotherapy improves outcomes in metastatic triple negative breast cancer patients

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BACKGROUND

p62/SQSTM1 is a cancer-related protein involved in autophagy and signal transduction. p62-encoding plasmid operates through at least two complementary mechanisms. First, it acts as a classic anti-cancer DNA vaccine. Cancer cells are known to overexpress p62, and, moreover, p62 is indispensable both for tumor formation and metastasis. Second, the plasmid lowers chronic inflammation and renders tumor cells more susceptible to immune response and chemotherapy. In the phase I/IIa clinical trial, p62 plasmid, used as a monotherapy, showed promise in treating patients with advanced disease for whom all standard methods of treatment were exhausted, in particular breast cancer [1]. Also, preliminary studies indicated that p62 plasmid can overcome chemotherapy resistance [1].

AIM

To evaluate safety and efficacy of p62 plasmid in combination with CMF in patients with metastatic triple-negative breast cancer
Primary endpoint: Overall Survival
Secondary endpoints: Progression-free survival, Safety, Overall Response Rate.

MATERIAL AND METHODS

Patient selection: patients with metastatic triple-negative breast cancer (mTNBC).
Design: Prospective randomized study parallel group of patients. Patients randomized 1: 1 to receive either CMF (Cyclophosphamide 600mg/m2 + Methotrexate 40mg/m2 + Fluorouracil 600mg/m^2, IV, day 1 and 8, every 4 weeks) + p62-plasmid (2.5 mg weekly IM) CMF alone.
Expected patients number - 40.
Current analyze: the treatment interim result in 14 patients.
Efficacy: accordance with the RECIST 1.1 criteria.
Toxicity: CT CAE v.4.0.

RESULTS

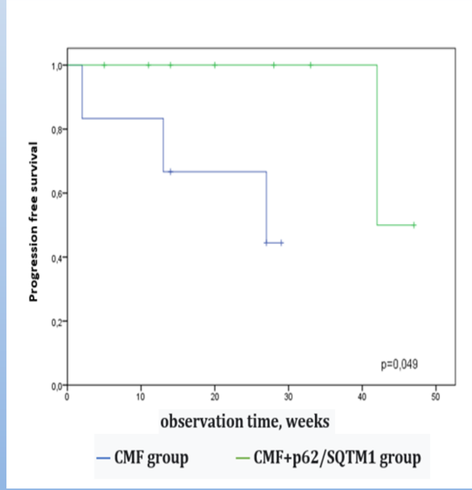
Overall response

	CMF (n=6)	CMF + Plasmid p62 (n=8)
CR	0 (0%)	2 (25.0%)
PR	2 (33.3%)	4 (50.0%)
SD	2 (33.3%)	2 (25.0%)
DP	2 (33.3 %)	0 (0%)

Both CR patients (CMF+plasmid) underwent surgery.
One patient had pCR (pathologic complete response) and another – pCR in tumor and one metastasis (from 20 removed lymph nodes).

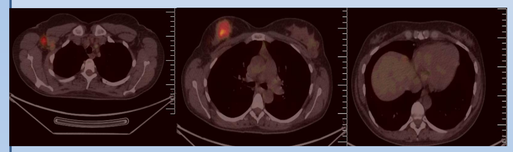
Safety. No Grade 3-4 toxicities were observed.
All adverse effects were managed by conventional medications.

Progression free survival (CMF vs CVF+p62/SQTM1, p<0,049)

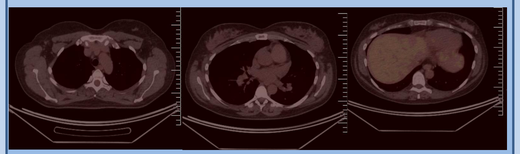


Clinical case

Patient B., 38 years old, right breast cancer, multifocal growth, metastases in the lymph nodes, right lung, and liver.



Received 8 courses of CMF plus plasmid p62.
CR: disappeared metastases in the lungs, liver, lymph nodes, as well as a tumor in the mammary gland.



Radical surgical resection was performed. No tumor cells were found in the removed tumor tissue (PCR).

CONCLUSIONS

- **The interim results of our study showed that adding p62/SQSTM1-encoding plasmid to standard CMF chemotherapy for metastatic triple-negative breast cancer appears to be a safe, well-tolerated and effective.**
- **The study is ongoing.**

Acknowledgements

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References

1. Ponomarenko et al. (2017). Safety and efficacy of p62 DNA vaccine ELENAGEN in a first-in-human trial in patients with advanced solid tumors. Oncotarget 8: 56030-56040