Adding plasmid encoding p62/SQSTM1 to gemcitabine chemotherapy increases PFS for patients with platinum-resistant ovarian cancer (updated data)

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Background

Here we report the results of the second interim analysis of a randomized prospective multi-center clinical study aimed to evaluate safety and efficacy of p62/SQTM1-encoding plasmid applied as an adjuvant to chemotherapy in patients with advanced platinum-resistant ovarian cancer (PROC). These results are a very important update of the first intermediate analysis we presented at 2021 ESMO congress. [1].
p62/SQSTM1 is a cancer-related protein involved in multiple processes including autophagy and signal transduction. p62-encoding plasmid appears to operate through at least two complementary mechanisms. First, it acts as a classic anti-cancer DNA vaccine, and second, it lowers chronic inflammation and renders tumor cells more susceptible to immune response and chemotherapy. Preliminary clinical studies indicated that p62 plasmid can enhance the effects of chemotherapy.

Material and Methods

Patient selection: Advanced platinum-resistant ovarian cancer without previous Gemcitabine treatment.
Design: Prospective randomized study of 2 parallel group of patients was started in 2020.
Patients randomized 1: 1 to receive either Gemcitabine (1000 mg/m2 days 1,8 every 3 weeks) + p62-plasmid (2.5 mg weekly) or Gemcitabine alone. Expected patients number was 40 (enrollment completed) with 20 patients in each arm.
Endpoints. Primary: Overall Survival. Secondary: Progression-free survival, Safety, Overall Response Rate.

Results

Patients characteristics

Median age was 54.6 and 53.4 in chemo and plasmid arms. Most of patients (more than 90% in both arms) received 1st line treatment in PROC setting.

Safety.

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

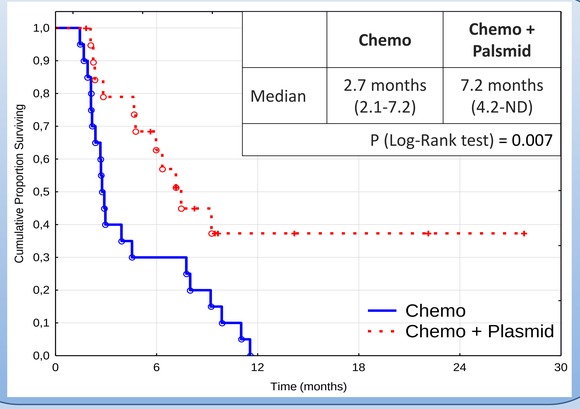
Table 1. Overall response

	Chemo	Chemo + Plasmid
CR	0 (0.0 %)	1 (5.0 %)*
PR	1 (5.0 %)	3 (15.0 %)
SD	8 (40.0 %)	12 (60.0 %)
DP	11 (55.0 %)	4 (20.0 %)

* Complete resection was performed after registered CR

Progression free survival

To data cut-off, the median follow-up was 11.1 months. In the plasmid group 7 of patients (35%) did not progress for more than 12 mo with the longest PFS recorded so far is 24 mo. In Chemo arm all patient has been progressed (range 1.4 – 11.5 mo)



Overall survival

14 deaths were registered (8 in chemo arm and 6 in chemo+plasmid arm). One death in chemo+plasmid arm was without evidence of progression (OS 1.8 months).

OS in chemo and plasmid arms

	6 months	12 Months	18 Months
Chemo	89.5 ± 7.1	63.1 ± 14.0	37.0 ± 16.6
Chemo + Palsmid	84.6 ± 8.2	77.8 ± 9.9	57.1 ± 14.5

The differences are not statistically significant yet.
The study is ongoing

Conclusions

The interim results of this study show that adding p62/SQSTM1-encoding plasmid to standard Gemcitabine chemotherapy for advanced platinum-resistant ovarian cancer is a novel treatment approach which is safe, well-tolerated and very effective: it improves ORR, DCR, and PFS. The long-lasting PFS in some patients is typical for immunotherapeutic agents. The study is ongoing.

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References

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