759P: Adding dosing of plasmid encoding p62/SQSTM1 to Gemcitabine chemotherapy may provide clinical benefits to patients with platinum-resistant ovarian cancer

S. Polyakov[1], S. Krasny[1], E. Zhavrid[1], Y. Baranau[2], O. Sergeeva[1], K. Zharkova[1], A. Filimonava[2], A. Khorau[1], S. Kozlovskaya[1], V. Gabai[3] and A. Shneider[3]

[1]N. N. Alexandrov National Cancer Centre of Belarus, [2]Minsk City Clinical Cancer Center (Belarus), CureLab Oncology, Inc. (USA).

PARIS 2021 ESMO congress
PARIS FRANCE
17-21 SEPTEMBER 2021

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 ovarian 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 Gemcitabine in patients with platinum-resistant ovarian cancer

Primary endpoint: Overall survival

Secondary endpoints: Progression free survival, safety, Overall Response Rate.

Material and Methods

Patient selection: Advanced platinum-resistant ovarian cancer without Gemcitabine exposure.

Design: Prospective randomized study parallel group of patients. Patients randomized 1: 1 to receive either Gemcitabine 1000 mg/m^2 days 1, 8 every 3 weeks) + p62-plasmid (2.5 mg weekly) or Gemcitabine alone. Expected patients number - 40.

Current analyze: the treatment interim result in 24 Patients.

Results

Patients characteristic

		Chemo (n=12)	Chemo + Plasmid (n=12)
Age (median, years)		53.3	56.6
ECOG	0	11 (91.7%)	11 (91.7%)
	1	1 (8.3%)	1 (8.3%)
Stage at fist diagnose	3	9 (75.0%)	8 (66.7%)
	4	3 (25.0%)	4 (33.3%)
Treatment's line (platinum-resistant setting)	1	0 (0 %)	1 (8.3%)
	2	12 (100%)	11 (91.7%)

Overall response

	Chemo (n=12)	Chemo + Palsmid (n=11)*
CR	0 (0%)	1 (9.1%)**
PR	1 (8.3%)	2 (18.2%)
SD	5 (41.7%)	7 (63.6%)
DP	6 (50.0 %)	1 (9.1%)

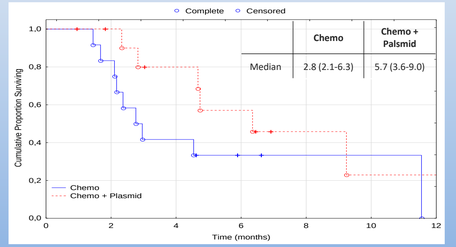
* Response was not assessed in 1 patient

** Complete resection was performed after registered PR

Overall survival. 4 death were registered (2 in each group). One death in Chemo + Plasmid arm without evidence of progression (OS 1.8 months)

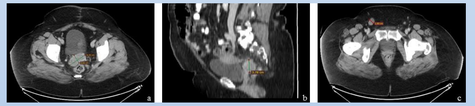
Safety. No Grade 3-4 toxicities were observed. All adverse effects were managed by conventional medications.

Progression free survival

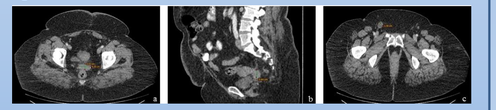


Clinical Case

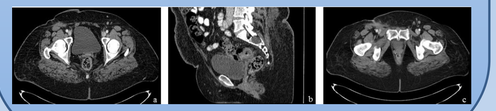
Patient TS, 53 years old female. The Gemcitabine+Plasmid in platinum resistance serous ovarian carcinoma G3, setting was started on 12.10.2020. The Target lesions at baseline were: the pelvic tumor up to 65 mm and the inguinal-femoral lymph node up to 18 mm. (sum. 83 mm).



The tumor shrinkage was: pelvic tumor up to 42 mm and lymph nodes up to 16 mm. (sum. 56 mm). A partial response was registered.



Complete cytoreductive surgery was performed on 05.07.2021. The response is still ongoing.



The treatment is ongoing.

Conclusions

The interim results of our study showed that adding p62/SQSTM1-encoding plasmid to standard Gemcitabine chemotherapy for advanced platinum-resistant ovarian cancer appears to be a safe, well-tolerated and effective. The study is ongoing.

Acknowledgements

- The patients and their families
- Investigators and clinic staff
- Dr. Robert Devlin and Mr. Aaron Shneider for editorial assistance

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