Observational Study Report synopsis

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OVArian cancer Non-Interventional Study. Treatment hAbits and epidemiology of BRCA in Russian Federation - OVATAR

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LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation or special term	Explanation
BRCA	Breast cancer (BRCA) gene
FTC	Fallopian Tube Cancer
NIS	Non-Interventional Study
OC	Ovarian Cancer
PARP	Poly (ADP-ribose) polymerase
PC	Peritoneal Cancer

Background:

Ovarian (OC), peritoneal (PC) and fallopian tube cancer (FTC) is one of the most serious neoplasms among women. Ovarian cancer is frequently diagnosed malignancy worldwide: it is the seventh most common cancer diagnosis among women in the world (overall), and fifth – in the majority of developed countries. Annually more than 225 000 new cases of ovarian cancer (about 3.7% of all cancer cases) were registered worldwide during recent years.

In Russia, ovarian cancer incidence in 2012 has reached 11956 new cases and prevalence – 66 cases per 100000 populations. During recent ten years clear tendency for increase of ovarian cancer prevalence in RF has been observed (approximately by 36% in comparison with 2002 year). It is noteworthy, that in many cases ovarian cancer is diagnosed only at advanced stages: in majority of Russian women ovarian cancer was diagnosed at stage III (in 40, 8% of cases) or at stage IV (in 20.3% of cases).

Despite the significant reduction in mortality registered for many other cancers (mainly – due to the availability of early diagnosis methods and targeted modern treatments), ovarian cancer is still the most unfavorable of all gynecological cancers both in Russia and worldwide. Ovarian cancer survival rates are much lower than other cancers affecting women (5-year survival – 30-46%). Ovarian cancer is the 5-th most common cause of all cancer-related deaths and the first cause of gynecological cancer deaths among women. It is important, that approximately one fourth of the affected Russian women (24.3%) died during first year after OC diagnosis. In Russia and worldwide, ovarian cancer is responsible for more deaths than all other gynecologic malignancies combined (47-57% of all Russian patients with oncogynecological pathology died due to OC). It is caused by late diagnosis (due to lack of effective methods for early detection of ovarian cancer, inaccessible anatomic location of the ovaries, asymptomatic course of the disease or presence of subtle nonspecific symptoms), frequent disease recurrence with subsequent drug resistance development.

Ovarian cancers are classified into three main histological types: epithelial tumors (up to 92%), sex cord-stromal tumors (approximately 1.2%), and germ cell tumors (about 1.9%). There are four main subtypes of carcinomas: serous (68-71 %), clear cell (12-13%), endometrioid (9-11 %) and mixed (6%). Mucinous and transitional carcinomas frequency is 3% and 1%, respectively.

Fallopian tube and primary peritoneal cancers are uncommon malignancies similar to epithelial ovarian carcinoma, including histological, clinical, and etiological factors; thereby these types of cancer are considered together with ovarian carcinoma. In the large scale USA epidemiological study it was demonstrated that the age-adjusted incidence rates for ovarian carcinoma (119.9 per million) was substantially higher than for peritoneal (6.78 per million) or fallopian tube (3.72 per million) carcinomas.

Generally, the incidence of ovarian cancer is growing with increasing age: the median age of diagnosis is 60-64 years. It has been suggested that several factors, including genetic,

reproductive (e.g. infertility), hormonal (oral contraceptives) and other factors, can increase risk for ovarian cancer. According to available data, genetic factors have the strongest association with increased risk for ovarian cancer. At least 10-15% of all epithelial ovarian cancers are due to hereditary susceptibility. Mutations in the *BRCA*1 and *BRCA*2 genes account for the majority (about 90%) of hereditary ovarian cancers. In accordance with the published data the incidence of *BRCA* mutations among Russian patients with ovarian cancer varies from 4.1% to 16.8%.

Both *BRCA* proteins participate in the recognition and repair of DNA damage, therefore disturbances of *BRCA* functions result in the accumulations of genetic alterations and finally influence on the cancer development, especially ovarian and breast cancer. The cumulative lifetime risk of ovarian cancer for *BRCA*1 mutation carriers is up to 40-50% and up to 20% for women with *BRCA*2 mutation.

Hereditary ovarian cancers, including *BRCA*-associated OC, are often characterized by younger age of onset, presence of cancer-affected relatives, more advanced stages at the time of diagnosis while better clinical outcomes than sporadic ovarian cancers. Women with *BRCA* mutations respond better than patients without these mutations to chemotherapies (usually – platinum-based treatment) and have improved survival despite the fact that the disease is generally diagnosed at later stage and higher grade. According to some authors, there is the distinct clinical syndrome of BRCAness in patients with *BRCA*-positive OC that includes: high response rates to first-line treatment with subsequent recurrences, long treatment-free intervals between relapses; improved overall survival and tumors of serous histology.

Currently, surgical tumor removal followed by chemotherapy with platinum-containing agents and taxanes is the standard treatment for advanced ovarian cancer. However, despite high overall response rates (up to 60–75%) with initial therapy, the majority of women with ovarian cancer relapses and requires retreatment with platinum agents. For patients who become resistant to platinum-based chemotherapy, response to other cytotoxic chemotherapeutic regimens is low (only 6–30%).

In recent years, new approaches to ovarian, peritoneal and fallopian tube cancer treatment have been developed. These methods are based on recent advances in understanding of OC genetic mechanisms, primarily on investigation of *BRCA* mutations. Development of new therapy for *BRCA*-associated ovarian, peritoneal and fallopian tube cancer is based on inhibition of the poly (ADP-ribose) polymerase DNA repair pathway. The use of these medications (PARP inhibitors) that target DNA repair disturbances in *BRCA*-associated ovarian cancer, can improve the treatment efficacy of recurrent OC and decrease the mortality from this cancer.

Rationale:

Unfortunately, the precise data concerning incidence of *BRCA* mutations among Russian patients with ovarian cancer, peritoneal and fallopian tube cancer and features of BRCA carriers are not available. The accurate information on methods of OC patients'

management and effectiveness of different treatment options in BRCAm+ Russian patients is also not available. In this connection the need in a large-scale prospective study of ovarian, peritoneal and fallopian tube cancer, especially *BRCA*-associated OC, in Russia is evident.

This study was planned to receive the information necessary for better understanding of BRCA associated OC features (epidemiology, clinical course, outcomes). Such project realisation was also aimed to clarify the treatment options used for Russian OC patients, as well as evaluate results of the treatment.

Evaluation of the proportion and characteristics of women with *BRCA*-associated ovarian cancer is important, because it enables the appropriate genetic counseling to these women and their families for improvement of medical management. In addition, this information was anticipated to make it possible to assign a targeted modern treatment of *BRCA*-associated OC in order to improve the prognosis of this disease.

Objectives and Hypotheses:

The primary objective of this NIS is to provide accurate and reliable information regarding the 1st line treatment of newly diagnosed patients with serous and/or endometrioid ovarian, peritoneal and fallopian tube cancer in the Russian routine clinical practice by evaluation of treatment approaches in the 1st line treatment.

Secondary objectives of the NIS were:

1. To describe the demographic and clinical characteristics of Russian newly diagnosed patients with ovarian, peritoneal and fallopian tube cancer;

2. To evaluate the diagnostics approaches to ovarian, peritoneal and fallopian tube cancer patients in Russian clinical centers;

3. To assess the proportion of BRCAm+ patients;

4. To determine the incidence of specific *BRCA*-mutations among Russian patients with serous and/or endometrioid ovarian, peritoneal and fallopian tube cancer;

5. To assess the outcomes of 1st line therapy of *BRCA*-associated ovarian, peritoneal and fallopian tube cancer (BRCAm+) in the population of Russian patients.

6. To describe 2d line treatment options for BRCAm+ patients with ovarian, peritoneal and fallopian tube cancer;

7. To assess the proportion of BRCAm+ patients with platinum–sensitive, platinum-resistant, platinum-refractory relapse.

Methods:

This was a multicentre, non-interventional, prospective study to be carried out in representative hospitals in order to assess ovarian, fallopian tube and peritoneal cancer management in Russia. No additional procedures besides those already used in the routine clinical practice were to be applied to the patients. Treatment assignment was to be done according to the current practice.

It was planned to enrol approximately 500 subjects in up to 30 sites in Russian Federation. The average number of patients per site was planned as 15-25; there were no restrictions on minimum and maximum number of subjects per site in this study.

The disease treatments approaches in 1st line treatment of serous and/or endometrioid ovarian, peritoneal and fallopian tube cancer (both chemotherapy and surgery) were considered as the primary outcome variable in this study.

Along with other diagnosis examinations the analysis of frequent mutations in the genes *BRCA1* and *BRCA2* (5382insC, 4153delA, 185delAG, C61G (c.300T>G) and 6174delT, as well as additional mutations in the genes *BRCA* tested in routine in laboratories) was to be performed in samples of biological material (blood) by local or regional laboratories. All patients were planned to undergo the broadened genetic testing panel in the central laboratories (sequencing of all coding areas of genes *BRCA*1 and *BRCA*2, exons deletion analysis in blood and tumor tissue).

Those patients with BRCAm+ OC were to be observed prospectively during 2 years after the baseline visit or till progression at the 1st line treatment with regards to OC treatment details and outcomes. The patients for whom *BRCA* mutations not found were planned to participate in the baseline assessments only and were not to be followed up. Accordingly, 1 study visit (screening/baseline) was planned for all patients and 1 additional visit after 24 months /or at the time of BRCAm+ determination if it was later than 24 months, besides screening/baseline visit were planned for BRCAm+ patients.

Results:

This observational study was planned to receive the information necessary for better understanding of BRCA associated ovarian cancer features (epidemiology, clinical course, outcomes). The primary objective of the study was to provide accurate and reliable information regarding the 1st line treatment of newly diagnosed patients with serous and/or endometrioid ovarian, peritoneal and fallopian tube cancer in the Russian routine clinical practice by evaluation of treatment approaches in the 1st line treatment.

This was non-interventional multicentre study conducted in 29 sites in Russia. A total of 500 patients with newly diagnosed ovarian, peritoneal and fallopian tube cancer were enrolled, 141 (28.2%) patients were identified as having BRCA mutation gene and included in Full

Analysis Set. Median age of enrolled females was 54.0 years (mean age was 53.9 ± 11.2 years), majority of patients were White (95.6%). There were no notable differences in terms of demographics between patients with and without BRCA gene mutations, however percentage of women younger than 50 years was a bit higher in BRCA+ group (40.4% (57/141) and 30.4% (108/355) respectively).

At baseline visit majority of enrolled females had ECOG performance score 0 or 1 (93.2%), there was no meaningful differences found between BRCA+ and BRCA- subgroups.

ECOG performance status evaluated in patients with BRCA gene mutations at baseline and at 2-years follow-up visit did not show substantial changes during this period.

Majority of women enrolled in the study were newly diagnosed with ovarian cancer (480 patients or 96.0%), 19 (3.8%) patients had fallopian tube cancer and 1 (0.2%) patient - peritoneal cancer. Median duration of disease at the time of enrolment was 3.93 weeks and ranged from 0 to 26.3 weeks. In most cases diagnosis was established based on histology results examination (in 89.6% (448/500) of patients) or after surgery (in 80.0% (400/500) of patients). Cytological results were used for diagnosis in 36.2% (181/500) of patients. The most frequently used clinical diagnostic methods were ultrasound examination of pelvic / abdominal organs (in 69.8% (349/500) of patients) and gynecological examination (in 63.6% (318/500) of patients).

Serous adenocarcinoma as histological type of tumor was observed in 87.6% (438/500) of enrolled women. Percentage of patients with this type among females with and without BRCA alterations was 94.3% (133/141) and 84.8% (301/355), correspondingly. More than half of population had IIIC or IV stage of disease according to FIGO classification. In BRCA+ patients percentage of women with IIIC or IV stage of ovarian cancer was higher than in BRCA- patients (66.0% (93/141) and 54.1% (192/355), respectively).

26.6% of study population had a family history of cancer diseases. In BRCA+ patients percentage of women having relatives with oncological diseases was higher than in BRCA- patients (44.0% (62/141) and 19.7% (70/355), respectively). These data are in line with those obtained in available reference literature, according to that approximately 20% of ovarian cancer cases, particularly high-grade serous tumors, are estimated to be caused by inherited mutations that confer elevated risk, the majority from BRCA1 and BRCA2. The risk of developing ovarian cancer by age 80 is estimated to be 44% and 17% in BRCA1 and BRCA2 mutation carriers, respectively. Mutations in BRCA1 and BRCA2 account for almost 40% of ovarian cancer cases in women with a family history of the disease.

More than half of the patients participated in this study (64.8%, 324/500) had concomitant diseases in medical history at the time of enrolment. The most frequent diagnosis was essential hypertension or hypertension (19.0% (95/500) and 10.0% (50/500), respectively), cardiac diseases were reported for 16.2% of patients, 14.2% of women had chronic gastritis, 11.4% of patients had hepatobiliary disorders.

Two thirds of enrolled patients (77.6%, 388/500) underwent tumor markers blood testing prior to treatment. CA-125 was detected in all women except 1, 88.9% (344/387) of these patients had elevated level of CA-125 (>35 U/ml). 15.2% (59/388) of patient had CA-19-9 in the blood. CA-72-4 was detected in 2.3% (9/388) of patient tested. CEA was presented in 15.2% (59/388) of enrolled patients for whom testing was performed. This marker was detected more frequently in BRCA2m+ patients than in BRCA1m+ patients: 28.0% (7/25) vs. 9.0% (8/89), correspondingly.

Among 496 patients underwent genetic testing on BRCA, 28.4% (141 of 496 women) had at least 1 alteration in BRCA gene. Blood testing for frequent BRCA1/2 mutations, as well as broadened blood and tissue testing was carried out for 79.2% (396/500), 94.0% (470/500) and 82.4% (412/500) of all enrolled patients, respectively. For blood testing for frequent BRCA1/2 mutations the most frequent methods were high-resolution melting analysis, allele-specific PCR and Sanger sequencing. Among methods for broadened testing next generation sequencing was the most widely used.

Initial blood testing for frequent BRCA1/2 mutations allowed to observe mutations in BRCA gene in 12.9% (51/396) of patients tested. Broadened blood and tissue genetic testing detected BRCA1 alterations in 15.1% (71/470) and 20.6% (85/412) of patients underwent blood and tissue testing, correspondingly. BRCA2 alterations were observed in 4.7% (22/470) of patients underwent broadened blood testing and in 6.8% (28/412) of patients underwent tissue testing.

The most frequent BRCA1 mutation was 5382insC, it was observed in 60.8% (31/51) of patients with mutations detected with blood test for frequent mutations. Broadened blood testing revealed to find out this alteration in 26.8% (19/71) of patients. 5382insC in tissue was detected in 20.6% (30/85) of patients. 4154delA was observed with blood testing for frequent BRCA1 mutations in 11.8% (6/51) of patients. Broadened blood and tissue genetic testing allowed to detect this alteration in 5.6% (4/71) and in 7.1% (6/85) of patients. Blood genetic testing for frequent BRCA1 mutations detected 185delAG in 3.9% (2/71) of women. 5.6% (4/71) of cases of 185delAG were detected with broadened blood testing and the same number of cases with tissue testing (4.7%, 4/85). C61G (c.300T>G) was detected with blood genetic testing for frequent BRCA1 mutations in 3.9% (2/71) of women. Broadened blood testing revealed to find this mutation in 8.5% (6/71) of patients and tissue tests – in 5.9% (5/85) of patients. Other mutations were observed in 19.6% (10/51) of women using screening blood testing, in 53.5% (38/71) of women using broadened blood testing and in 47.1% (40/85) of patients by tissue testing.

BRCA2 alterations were detected by broadened testing in 22 cases of 470 (4.7%) in blood samples and in 28 cases of 412 (6.8%) in tissue samples. 6174delT was observed only in one blood sample.

Totally 422 patients (84.4% of 500 women) received surgical treatment at the moment of enrolment to the study, for 74 patients surgery was planned and 4 women were unable to underwent surgical treatment, among the reasons there were serious somatic condition, multiple metastases, massive tumor lesion of peritoneum and the greater omentum with signs of invasion into anterior abdominal wall, invasive growth of ovarian tumor.

78.2% (391/500) of patients underwent surgical cytoreduction. Diagnostic laparotomy was conducted in 7.6% (38/500) of patients.

Prior to surgery 24.0% (120/500) of enrolled patients received chemotherapy, for majority of them combined regimen was used. All patients except one (this patient received pyrimidine analogue capecitabine and tamoxifen) used platinum compounds (carboplatin, cisplatin, paract). 100 patients received taxanes (paclitaxel, taxacad, paclikal, sindaxel, taxotere, docetaxel). Other drugs (anthracyclines and related substances, nitrogen mustard analogues, pyrimidine analogues) were used for chemotherapy prior to surgery by less than 2% of patients.

Almost all patients (95.8%, 479/500) received 1st line chemotherapy / adjuvant therapy. Platinum compounds were included in therapy for all women except three. Carboplatin and cisplatin were most frequently used drugs, they were administered to 62.8% (314/500) and to 28.8% (144/500) patients, correspondingly. Taxanes were used for 1st line chemotherapy / adjuvant therapy by 66.0% of patients (330/500). In this group paclitaxel was the most frequent drug, it was administered to more than half of patients (56.4%, 282/500). 15.4% (77/500) of patients received anthracyclines and related substances and 10.6% (53/500) of patients received nitrogen mustard analogues. In first drug group doxorubicin was administered predominantly (13.0%, 65/500), in second drug group cyclophosphan was mainly used (8.0%, 40/500).

Among 141 BRCA+ patients preoperative therapy was conducted for 25.5% (36/141), number of treatment courses varied from 1 to 6. 98.6% (139/141) of BRCA+ patients received 1st line / adjuvant therapy. 2nd line chemotherapy was used by 44.7% (63/141) of BRCA+ patients. Combined regimen of therapy was used for majority of patients (82.5%, 52/63). For 2nd line chemotherapy platinum compounds (carboplatin, cisplatin, eloxatin), taxanes (paclitaxel, docetaxel) and pyrimidine analogues (gemcitabine) were mainly used.

Maintenance therapy was conducted only in 5.6% (28/500) of enrolled patients, most of them -17 (3.4%) patients – received letrozole. The only PARP inhibitor Lynparza (olaparib) approved as maintenance treatment for patients with BRCAm advanced ovarian cancer was prescribed only to 5 patients with BRCA1 gene alteration, i.e. 3.5% of all BRCAm+ patients.

Complete response, partial response or stabilization on 1st line / adjuvant therapy was registered for 111 of 139 patients (55.4%, 12.9% and 11.5% correspondingly). Progression was observed for 12.2% (17/139) of patients. Among BRCA2+ patients progression was noticed only for 1 woman (3.4% of 29 patients), percentage of such patients in BRCA1+ subgroup was 14.5% (16/110). Because of organizational reasons results for response were recorded for patients at different time of observational period. Therefore, progression as best response was recorded for 6 women that revealed signs of progression during the therapy or within first month after its completion, for 4 patients that showed progression during 6 month and for 7 patients that showed progression after 6 month or more after last dose of therapy. By the time of study completion approximately half of BRCA+ patients (52.5%, 73/139) had disease progression. Percentage of such patients in BRCA1+ and BRCA2+ subgroups was comparable: 53.6% (59/110) vs. 48.3% (14/29), correspondingly. Early progression was

observed more frequently in BRCA1+ subgroup than in BRCA2+. During therapy or less than 1 month after the last administration of platinum compounds 11.9% (7/110) of BRCA1+ patients showed progression (platinum-refractory relapse), while in BRCA2+ subgroup nobody had platinum-refractory relapse. Progression during 6 month after last dose of platinum compounds (platinum-resistant relapse) was observed in 23.7% (14/110) of BRCA1+ subgroup and in 15.4% (2/29) of BRCA2+ subgroup.

The median time to progression was 25.5 months without notable difference between patients with mutation in BRCA1 and BRCA2 genes. In patients with late stages of disease the median time to progression was shorter: 15.6 months (95% CI 11.9; 25.5 months) for IIIC stage and 14.3 months (95% CI 7.9; 22.3 months) for IV stage. Among BRCA+ patients underwent cytoreduction, median time to progression was longer in subgroup without visible residual tumor than in subgroup with size of residual tumor <1 cm (36.4 months vs. 15.3 months, correspondingly).

12.1% (17/141) of patients with mutation in BRCA gene died during the study, almost all of them (except one) - due to progression of the disease.

Conclusion:

This large-scale prospective non-interventional study was conducted to receive information about percentage and characteristics of women with BRCA-associated ovarian cancer, to evaluate diagnostic approaches and treatment methods applied to newly diagnosed ovarian, peritoneal and fallopian tube cancer patients in the Russian routine clinical practice. All these objectives were met.

A total of 500 patients with newly diagnosed ovarian, peritoneal and fallopian tube cancer were enrolled in 29 clinical sites, 28.2% (141/500) of these patients were identified as having BRCA mutation gene (BRCA+ patients).

The vast majority of women enrolled in the study were diagnosed with ovarian cancer (96.0%, 480/500), only 3.8% (19/500) of patients had fallopian tube cancer and one patient (0.2%) - peritoneal cancer. Serous adenocarcinoma as histological type of tumour was observed in 87.6% (438/500) of enrolled women (94.3%, 133/141, in BRCA+ and 84.8%, 301/355, in BRCA- patients). In BRCA+ patients, percentage of women with stage of ovarian cancer was higher than in BRCA- patients (66.0% (93/141) and 54.1% (192/355), respectively), as well as percentage of women with a family history of oncological diseases (44.0% and 19.7% respectively).

Diagnostics approaches to ovarian, peritoneal and fallopian tube cancer patients were evaluated. In most cases diagnosis was established based on histology results (in 89.6% (448/500) of patients) or after surgery (in 80.0% (400/500) of patients). Cytological results were used for diagnosis in 36.2% (181/500) of patients. The most frequently used clinical diagnostic methods were ultrasound examination (in 69.8% (349/500) of patients) and gynaecological examination (in 63.6% (318/500) of patients).

Tumour markers blood testing was performed in 77.6% (388/500) of patients. The most frequently detected marker was CA-125, it was positive in all women except one. CEA was presented in 15.2% (59/388) of enrolled patients for whom testing was performed. This marker was detected more frequently in BRCA2m+ patients than in BRCA1m+ patients: 28.0% (7/25) vs. 9.0% (8/89), correspondingly. CA-19-9 and CA-72-4 were presented in 15.2% (59/388) and 2.3% (9/388) of patient tested respectively.

Incidence of specific BRCA-mutations among Russian patients with ovarian, peritoneal and fallopian tube cancer was determined. Blood testing for frequent BRCA1 mutations allowed to observe mutations in BRCA1 gene in 12.9% (51/396) of patients tested. Broadened blood and tissue genetic testing detected BRCA1 alterations in 15.1% (71/470) and 20.6% (85/412) of patients underwent blood and tissue testing, correspondingly. BRCA2 alterations were observed in 4.7% (22/470) of patients underwent blood testing and in 6.8% (28/412) of patients underwent tissue testing.

The most frequent BRCA1 mutation was 5382insC (detected using initial blood test in 60.8% (31/51) of patients with mutations). 4154delA was observed in 11.8% (6/51) of patients using blood testing for frequent mutations, 185delAG - in 3.9% (2/71) of women. BRCA2 alterations were detected by broadened testing in 4.7% 22/470) of cases in blood samples and in 6.8% (28/412) of cases in tissue samples. 6174delT was observed only in one blood sample.

Treatment options and outcomes of BRCA-associated ovarian, peritoneal, and fallopian tube cancer (BRCAm+) were assessed in this study. Generally management of these patients were conformed to the Practical recommendations on the medical treatment of patients with ovarian cancer used in Russian routine clinical practice. Treatment results were expected for this severe disease. By the end of the study approximately half of BRCA+ patients (52.5%, 73/139) had disease progression. Percentage of such patients in BRCA1+ and BRCA2+ subgroups was comparable: 53.6% (59/110) vs. 48.3% (14/29), correspondingly. Early progression was observed more frequently in BRCA1+ subgroup than in BRCA2+. During therapy or less than 1 month after completion of 1st line therapy 11.9% (7/110) of BRCA1+ patients showed progression (platinum-refractory relapse), while in BRCA2+ subgroup nobody had platinum-refractory relapse. Progression during 6 month after last dose of platinum compounds (platinum-resistant relapse) was observed in 23.7% (14/110) of BRCA1+ subgroup and in 15.4% (2/29) of BRCA2+ subgroup.

Analysis of available reference literature showed that BRCA1/2 genes testing began to play a very important role in diagnostics of ovarian, peritoneal, and fallopian tube cancer in connection with the development of the poly-ADP-ribose polymerase (PARP) inhibitor olaparib used to treat ovarian cancer patients with BRCA1 and BRCA2 mutations. Olaparib has also been used as maintenance therapy for patients with platinum-sensitive recurrent BRCAm+ ovarian cancer. Therefore, gene-targeted therapies provide a new possibility for the personalized treatment of ovarian cancer patients. Results of the Phase III SOLO-1 clinical trial showed that Lynparza (olaparib) reduces the risk of disease progression or death by 70% in patients with newly-diagnosed, advanced BRCA-mutated ovarian cancer.

Results of this non-interventional study showed that analysis of frequent mutations in the BRCA1/2 genes performed in routine practice can be insufficient for precise diagnostics of ovarian, peritoneal and fallopian tube cancer, as blood testing for frequent BRCA mutations allowed to observe mutations in BRCA1/2 genes only in small percentage of patients. It is necessary to discuss possible changes in practical recommendations of ovarian cancer management in Russia in order to include more accurate and modern methods of genetic analysis (i.e. PCR diagnostics or the complete sequencing of the BRCA1/2 genes) to implement personalized gene-targeted treatment of ovarian cancer patients in Russian routine clinical practice.