Abstracts

observed among BRCA2 heterozygous patients (p.Q3299X: n = 2; c.5345dupA: n = 1; c.7408_7409delTT: n = 1). Given the high frequency of mutations in BRCA1 gene, we added to the study 44 consecutive patients with triple-negative breast cancer. This effort relied on the fact, that BRCA1 is specifically associated with the triple-negative phenotype of breast cancer disease; 3 (7%) additional BRCA1 mutation carriers (c.3627_3628delAG: n = 2; c.1338_1339delAG: n = 1) were revealed. All patients with the BRCA1 c.3627_3628delAG pathogenic variant also carried linked c.1067G>A (p.Q356R) polymorphic substitution; therefore, BRCA1 c.3627_3628delAG is indeed a founder allele, but not a mutational hot spot. In addition to BRCA1/2, one HGSOc patient carried ATM truncating variant (p.Q1171X). There were no instances of PALB2 or TP53 germline alterations.

Conclusion* This is a small-scale study, which resulted in convincing demonstration of a strong founder effect in Chechen women with hereditary breast-ovarian cancer. Genetic testing of non-selected HGSOc patients allows highly efficient analysis of ethnicity-specific spectrum of BRCA1/2 mutations.

319 GYNECOLOGIC MALIGNANCIES IN THE ERA OF PRECISION MEDICINE

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Introduction/Background* Personalized medicine is replacing the classical one-size-fits-all traditional oncology approaches tailoring the most appropriate therapy for each patient. Molecular and genomic profiling diagnostic tools are implementing patients' journey.

Methodology This is a single centre prospective study performed from January 2020 and April 2021 at Fondazione IRCCS Istituto Nazionale dei Tumori di Milano (Italy). All consecutive, heavily pretreated patients, for whom effective conventional treatments were not available, were enrolled in this study and underwent molecular and genomic profiling via Foundation One CDx test.

Result(s)* Overall, 63 heavily pretreated patients had Foundation One CDx test. We identified 10 patients (16%) with mutation or genetic signatures candidate to use personalized therapy (table 1). Out of 10 patients, 4 are patients affected by cervical, 4 by endometrial and the remnant are affected by ovarian carcinoma. Actually 1 patient is receiving immunotherapy with atezolizumab plus anti-ICOS and 1 is undergoing evaluation in order to start same drugs; 2 patients with ovarian cancer had BRAF/V600E mutations and are ongoing on treatment with trametinib +/- dabrafenib; 2 patients with cervical cancer had PI3KCA mutations and are treating with alpelisib. Furthermore, in 4 patients an actionable mutation was found but standard chemotherapeutic treatment is still ongoing (Table 2).

Immunotherapy and target therapy are administered into the clinical trial or thank to compassionate use.

Conclusion* Molecular and genomic profiling of gynecological malignancies is not clinical practice. We demonstrated that in

Abstract 319 Table 1 Global patients

Patients total N (%)	63 (100)
Age median (range)	59 (29-78)
Primary tumor	17 (27)
Ovarian carcinoma	5 (8)
Endometrial carcinoma	33 (52)
Cervical carcinoma	4 (6)
Uterine sarcoma	1 (2) 2 (3)
Vaginal carcinoma	
Bartholin's gland adenocarcinoma	
Target therapy	10 (16)

Abstract 319 Table 2 Molecular characteristics & target therapy

Patient	Age	Pathology	Mutation	Target therapy
1	77	Clear cell endometrial carcinoma	mut. L755S ERBB2	Evaluable for Afatinib
2	67	High grade serous ovarian carcinoma	Mut. V600E BRAF	Ongoing Dabrafenib + trametinib
3	54	Squamous cervical carcinoma	HPV at ISH	Ongoing Atezolizumab + anti ICOS
4	52	Endometrial carcinosarcoma	MSI	Evaluable for Atezolizumab
5	71	Endometrial carcinoma	Mut R88Q PI3KCA	Evaluable for Everolimus + exemestane
6	30	Mucinous cervical adenocarcinoma	splice site (134 +1G>T) PTEN	Evaluable for Everolimus
7	60	Low grade serous ovarian carcinoma	Mut. V600E BRAF	Ongoing Trametinib
8	41	Squamous cervical carcinoma	Mut p.E545K PI3KCA	Ongoing Alpelisib
9	71	Endometrioid Endometrial carcinoma	Mut. Q546P PI3KCA	Evaluable for Alpelisib
10	39	Neuroendocrine cervical cancer	Mut p.E545K PI3KCA	Ongoing Alpelisib

this population identified alterations, by genetic driver, could help to find a new therapeutically opportunity. This allows to identify predictive biomarkers for target therapies in order to offer new therapeutic prospective for our gynecologic patients.

323 CHARACTERISATION OF INTRA-TUMOURAL HETEROGENEITY IN HIGH GRADE SEROUS OVARIAN CANCER

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Introduction/Background* High-grade serous ovarian cancer (HGSOc) is typified by extensive genomic instability and intra-tumoural heterogeneity (ITH). The majority of patients relapse and eventually acquire resistance to platinum-based chemotherapy. Diverse mechanisms leading to platinum