The BeLIVE study

Measure of outcomes in patients with advanced ovarian cancer according to Homologous Recombination status and matched therapies in a real-world scenario.

A retrospective and prospective, multicenter, two cohort study.

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Principal Investigators:	Michele Bartoletti, MD
Responsibles for Study Coordination:	Mara Mantiero, MD OncoTech, Consorzio per la ricerca, la formazione e le tecnologie avanzate in oncologia
Statisticians	Marcella Montico

CONFIDENTIAL

PROTOCOL AUTHORIZATION

The BeLIVE study.

Measure of outcomes in patients with advanced ovarian cancer according to Homologous Recombination status and matched therapies in a real-world scenario.

A retrospective and prospective, multicenter, two cohort study

I have read this study protocol and agree that it contains all the information required to conduct the study. I agree to conduct the study as set out in this protocol. In particular, I Agree to adhere to the moral, ethical and scientific principles governing clinical research as Set out in the declaration of Helsinki, the guidelines on good clinical practice and the Appropriate national laws.

Principal Investigators

[redacted]

Dr. Michele Bartoletti

16 - FEB - 2024

Date

[redacted]

Dr. Mara Mantiero

16 Feb 2024

Date

Local Investigator

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ABBREVIATIONS

DFS	Disease-Free Survival
NGS	Next Generation sequencing
ORR	Overall Response Rate
OC	Ovarian Cancer
OS	Overall Survival
PARPi	Poli-ADP RIbose Polymerase inhibitors
PFS	Progression-Free Survival
VUS	Variants of uncertain significance

PROTOCOL SYNOPSIS

Study title	**BeLIVE** Measure of outcomes in patients with advanced ovarian cancer according to Homologous Recombination status and matched therapies in a real-world scenario. A retrospective and prospective, multicenter, two cohorts study.
Sponsor	OncoTech, Consorzio per la ricerca, la formazione e le tecnologie avanzate in oncologia
Principals Investigators	Michele Bartoletti, MD Mara Mantiero, MD
Steering commitee	Michele Bartoletti, MD Mara Mantiero, MD Fabio Puglisi MD, PhD Francesco Raspagliesi, MD
Consortium/network	MITO Group, Others
Study design and methods	This is a retrospective and prospective, multicenter, observational, two-cohorts study aimed to evaluate clinical outcomes and safety of patients diagnosed with advanced high grade ovarian cancer whose tumor was tested for the homologous recombination (HR) status using a validated HR deficiency test between January 2021 and January 2026. - **Cohort A**: Homologous Recombination Deficient (HRD) ovarian cancer patients treated with Olaparib plus Bevacizumab as maintenance therapies after partial or complete response to first line platinum-based chemotherapy. - **Cohort B**: Homologous Recombination Proficient (HRP) ovarian cancer patients treated as for standard clinical practice at clinician's choice.

Study population	All patients diagnosed with advanced high grade ovarian cancer who have received a homologous recombination analysis using validated HRD test between January 2021 and January 2026 are eligible. Patients resulted HRD and treated with Olaparib plus Bevacizumab will be included in Cohort A while patient with HRP tumors will be included in the Cohort B. Patients enrolled in the "compassionate use" of Olaparib (CNN program) can be included as well as patients who have received therapies according to clinical practice.
Inclusion criteria	• Female, age ≥ 18 years at the time of diagnosis • Patients diagnosed with high-grade serous or endometroid ovarian, fallopian tube, or primary peritoneal cancer undergone to Homologous Recombination test with the MyChoice HRD assay, FoundationOne DX assay or another validated HRD test, between January 2021 and January 2026: o Patients with HRD score > 42 or Loss of Heterozygosity (LOH) score high or defined as HR deficient with other tests and treated with Bevacizumab and Olaparib after first line platinum-based chemotherapy will be retrospectively or prospectively enrolled in Cohort A o Patients with HRD score < 42 or Loss of Heterozygosity (LOH) score low or defined as HR proficient with other tests and treated with first line platinum-based chemotherapy with or without bevacizumab or others targeted agents will be retrospectively or prospectively enrolled in Cohort B • Patients must be able to understand the study procedures and agree to participate in the study by providing written informed consent.
Exclusion criteria	• Patients who have not performed a validated Homologous Recombination test on tumor sample. • Patients with germline or somatic *BRCA* 1 or 2 mutations • Patients death at the time of inclusion in the current study
Primary objective	• Evaluate the clinical outcomes as measured by progression-free survival (PSF) and overall survival (OS) in patients in each study Cohorts. • Evaluate the safety of targeted agents (olaparib, niraparib, bevacizumab) used alone or in combination measured by incidence of adverse events according to the CTCAE, discontinuation rate from therapies and relative/absolute dose intensity in each study Cohorts.

Secondary objectives	• To describe the clinical outcomes according to disease stage, surgical timing, residual disease after surgery in each cohort • To describe the clinical characteristics of patients for which the combination therapy was offered (Cohort A); • To describe the treatment approach to HRP patients in a real word scenario in Italy (Cohort B).
Duration of participation	Patients with available HRD test result at the time of study entry will be retrospectively or prospectively enrolled. Patients will be followed up prospectively up to 3 years from enrollment for primary and secondary objectives.
Approximate Number of Patients	Give the retrospective and prospective nature of the trial, no pre-specified sample size has been planned. The estimated sample size is about 300 patients.
Number of Study Centers	21 centers will be involved in the study
Withdrawal criteria	During the study a patient must be discontinued if any of the following apply: • Consent withdrawal at the patient's own request or at the request of their legally authorized representative; • Termination of the study.

INTRODUCTION

Ovarian cancer is the second most frequent gynecological tumor but is the first in order of mortality[1]. Its relative low incidence and the absence of screening programs, represent major limitations to early disease detection[2]. The high mortality rate depends also on the lack of early symptoms, which means that most patients are diagnosed at advanced stage of disease, and on the limited results obtained from treatments. In fact, although ovarian cancer is considered a chemo-sensitive cancer, long-term control of the tumor is un unmet need since nearly 70% of patients will develop resistance to cytotoxic agents, in particular to platinum salts[3]. The median progression-free survival (PFS) for patients with advanced disease ranges between 16 and 23 months while the median overall survival (OS) lies between 31 and 65 months and strategy to improve outcome are urgently needed.

1. Background

For patients with ovarian cancer, cytoreductive surgery, aimed to remove all the macroscopic implants from the abdomen and the pelvis, represents the only curative treatment option and is the therapeutic mainstay in early and advanced disease. Platinum salts, instead, used in combination with taxanes, are the standard first line chemotherapeutic agents employed. However, even when an optimal cytoreductive surgery is performed and 6 to 8 cycles of a platinum-based chemotherapy are administered, prognosis for patients with advanced ovarian cancer remains poor, with approximately 70–80% of patients experiencing a disease recurrence within 3 years. Consequently, the 5-year survival rate is still below 50%.

Thus, it is necessary to develop additional therapeutic strategy, that can prolong the benefit of platinum-based chemotherapy, in order to avoid recurrence and to improve overall survival. Improving the effectiveness of systemic treatment has been the major challenge of gynecologic oncology research. In the past 30 years most of changes have included using different treatments schedule (e.g. dose dense regimens), different modalities of treatment' administration (e.g. intraperitoneal chemotherapy and HIPEC) and different platinum-based combinations. (e.g. pegylated liposomal doxorubicin along with platinum salts). The first targeted agent approved by the Food and Drugs Administration (FDA) for the treatment of advanced OC was the humanized anti- VEGF antibody bevacizumab, back in 2017[4]. A further turning point in the first line setting was the publication of results from the biomarker-driven phase 3, SOLO1 study, following which, olaparib maintenance was established as the new standard of care in advanced ovarian cancer patients harboring a BRCA 1 or 2 deleterious mutation[5]. Moreover, the SOLO1 trial paved the way for two other milestone trials, the PRIMA and PAOLA1 studies, whose results have broadened the spectrum of patients who can benefit from a PARPi maintenance also to those with tumors presents Homologous Recombination deficiency (HRD)[6,7]. Although these results are encouraging and will probably modify the ovarian cancer's course, especially in the disease presenting a BRCA 1-2 mutation, the occurrence of PARPi resistance, which seems to overlap partially with platinum-resistance, is becoming an unmet clinical need and a major challenge for the

near future[8]. Moreover, not all ovarian cancers will benefit from treatment with PARPi and, non-serous OC patients are poorly represented in pivotal clinical trials and thus have limited therapeutic options both in the up-front setting or in case of disease recurrence. In the latter case, systemic chemotherapy has been historically guided by the time span from the last platinum therapy and disease recurrence, the so-called platinum-free interval. In this setting, targeted agents include bevacizumab for platinum resistant or sensitive disease and PARPi as maintenance or active therapy, even if the current early use of these agents, alone or in combination, limits their availability for recurrent ovarian cancer.

1.1 Bevacizumab

Bevacizumab is a recombinant, humanized anti-VEGF monoclonal IgG1; its mechanism of action is represented by selective binding to circulating VEGF; in this way, Bevacizumab can block the biologic activity of human VEGF, provoking a reduction in the vascularization of tumors, thereby inhibiting tumor growth[9].

In the GOG-0218 study, a double-blind, placebo-controlled, phase 3 trial, women diagnosed with stage III or stage IV epithelial ovarian cancer, who had previously undergone debulking surgery, were randomly assigned to receive one of the three following treatments: chemotherapy with carboplatin plus paclitaxel versus chemotherapy with carboplatin plus paclitaxel in association with bevacizumab versus chemotherapy with carboplatin plus paclitaxel in association with bevacizumab, followed by bevacizumab as maintenance monotherapy. The results of this study have shown that the use of bevacizumab, during and up to 10 months after carboplatin and paclitaxel chemotherapy, prolonged the median PFS[10].

In the ICON7 study, a randomized, phase III trial, that has involved 1528 patients with high-risk early-stage disease or advanced stage ovarian carcinoma, women were randomized to receive conventional carboplatin plus paclitaxel for 6 cycles in the first arm, or the same treatment plus bevacizumab during chemotherapy, with bevacizumab monotherapy continuing for an additional 36 weeks in the second arm. The results of this trial have shown an improvement of PFS and of OS in the second arm. Moreover, women who had the bigger benefit from adding bevacizumab to chemotherapy, were those with the higher risk of recurrence[11].

As a result of these evidence, the addition of the antiangiogenic agent bevacizumab to carboplatin plus paclitaxel, followed by bevacizumab alone, is actually a standard option in patients with newly diagnosed advanced ovarian cancer[12].

1.2 Homologous recombination deficiency (HRD) and synthetic lethality

Tumors often have DNA repair defects, suggesting additional inhibition of other DNA repair pathways in tumors may lead to synthetic lethality. Accumulating data demonstrate that DNA repair-defective tumors, in particular homologous recombination (HR), are highly sensitive to DNA-damaging agents. Thus, HR-defective tumors exhibit potential vulnerability to the synthetic lethality approach, which may lead to new therapeutic strategies. It is well known that poly (adenosine diphosphate (ADP)-ribose) polymerase (PARP) inhibitors show the

synthetically lethal effect in tumors defective in BRCA1 or BRCA2 genes encoded proteins that are required for efficient HR[13].

1.3 PARP inhibitors

Recently, in the SOLO1 trial, the PARP inhibitor Olaparib provided a substantial PFS benefit as maintenance monotherapy in patients with newly diagnosed advanced ovarian cancer, whose tumors had a BRCA1 o BRCA2 mutation and who had a complete or partial clinical response after platinum-based chemotherapy 5. However, HRD is not limited to tumors with BRCA mutations and is present in approximately 50% of high-grade serous ovarian tumors. Moreover, the addition of an antiangiogenic agent to a PARP inhibitor in phase 2 studies involving patients with relapsed platinum-sensitive ovarian cancer resulted in longer progression-free survival than the use of a PARP inhibitor alone.

PAOLA 1 is a randomized, double-blind phase 3 trial, in which eligible patients with newly diagnosed, advanced, high-grade ovarian cancer, who had a complete or partial response after first-line platinum-taxane chemotherapy plus bevacizumab**,** were randomized to receive olaparib or placebo in association with bevacizumab in maintenance therapy up to 24 months**,** regardless the BRCA mutation status. After a median follow-up of 22.9 months, the median progression-free survival was 22.1 months with olaparib plus bevacizumab and 16.6 months with placebo plus bevacizumab. The hazard ratio (olaparib group vs. placebo group) for disease progression or death was 0.33 (95% CI, 0.25 to 0.45) in patients with tumors positive for homologous-recombination deficiency (HRD), including tumors that had BRCA mutations (median progression-free survival, 37.2 vs. 17.7 months), 0.43 (95% CI, 0.28 to 0.66) in patients with HRD-positive tumors that did not have BRCA mutations (median progression-free survival, 28.1 vs. 16.6 months) and 0.92 (median PFS 16.9 vs 16.0 months) in HRD negative patients suggesting no additional benefit of olaparib in the last group[12].

In the same setting, PRIMA trial, is a randomized, double-blind, phase 3 trial in which patients with newly diagnosed, advanced, high grade serous and endometrioid ovarian cancer responding to first line platinum-paclitaxel chemotherapy were randomized to receive niraparib, which is another PARP inhibitor, or placebo, as maintenance treatment. Of the 733 patients who underwent randomization, 373 (50.9%) had tumors with homologous-recombination deficiency. Among the patients in this category, the median progression-free survival was significantly longer in the niraparib group than in the placebo group[6].

1.4 Open questions and aims of the current study

According to results presented above, is possible to conclude that the magnitude of benefit from targeted therapies in newly diagnosed ovarian cancer is deeply affected by the biomarkers' status (BRCA and HR status). While it appears clear that BRCA mutated patients benefit the most from PARPi and the addition of bevacizumab seems not providing further advantages, the best strategy for HRD and HRP patients is far from be defined. For HRP patients, current strategies include the incorporation of bevacizumab with chemotherapy and then as maintenance or the use of niraparib as maintenance after

chemotherapy in case of partial of complete response. Despite this, the best approach is debated, and chemotherapy alone is also a reasonable option for these patients. Moreover, for HRD patients, the use of olaparib plus bevacizumab raises concerns about toxicities since 20% of patients in the PAOLA 1 trial discontinued treatments for adverse events. Starting from this scenario, the aims of the current study are to describe the clinical outcomes and safety of patients with advanced ovarian cancer receiving targeted therapies according to tumor biomarker's status in a real word setting. Secondary objective is to describe the approach to HRP patients in real practice in Italy.

2. Study design and methods

2.1 Study design

This is a retrospective and prospective, multicenter, observational, two-cohorts study aimed to evaluate clinical outcomes and safety of patients diagnosed with advanced high grade ovarian cancer whose tumor was tested for the homologous recombination status using a validated HRD test between January 2021 and January 2026:

- **Cohort A**: Homologous Recombination Deficient (HRD) ovarian cancer patients treated with Olaparib plus Bevacizumab as maintenance therapies after partial or complete response to first line platinum-based chemotherapy.
- **Cohort B**: Homologous Recombination Proficient (HRP) ovarian cancer patients treated as for standard clinical practice at clinician's choice.

Alive patients who have finished the first line treatment (including maintenance) with or without disease progression while signing the informed consent form will be enrolled retrospectively.

Alive patients candidate to receive a first line therapy will be enrolled prospectively as soon as molecular data (BRCA status and HRD) are available.

2.2 Study population

All patients diagnosed with advanced high grade ovarian cancer who have received an homologous recombination analysis using a validated HRD test, between January 2021 and January 2026, are eligible. Patients resulted HRD and treated with Olaparib plus Bevacizumab will be retrospectively or prospectively included in Cohort A, while patient with HRP tumors will be retrospectively or prospectively included in the Cohort B. Patients enrolled in the "compassionate use" of Olaparib (CNN program) can be included as well as patients who have received therapies according to clinical practice.

2.3 Inclusion criteria

- Female, age ≥ 18 years at the time of diagnosis
- Patients diagnosed with high-grade serous or endometroid ovarian, fallopian tube,

or primary peritoneal cancer undergone to Homologous Recombination test between January 2021 and January 2026:

- Patients with HRD score > 42 or Loss of Heterozygosity (LOH) score high or defined as HR deficient with other tests and treated with Bevacizumab and Olaparib after first line platinum-based chemotherapy will be retrospectively or prospectively enrolled in Cohort A
- Patients with HRD score < 42 or Loss of Heterozygosity (LOH) score low or defined as HR proficient with other tests and treated with first line platinum-based chemotherapy with or without bevacizumab or others targeted agents will be retrospectively or prospectively enrolled in Cohort B

- Patients must be able to understand the study procedures and agree to participate in the study by providing written informed consent (see details in informed consent section).

2.4 Exclusion criteria

- Patients who have not performed a validated Homologous Recombination tests are not eligible for this study.
- Patients with germline or somatic *BRCA* 1 or 2 mutations
- Patients death at the time of inclusion in the current study

3. Objectives and endpoints

3.1 Primary objective

The primary objective of the study is to evaluate the clinical outcomes and the safety in patients treated with targeted anticancer therapies in each study cohort.

The clinical outcomes that will be measured in both study cohorts are:

- progression-free survival (PSF) as the time from treatment's start to disease progression or death for any cause
- overall survival (OS) as the time from treatment's start to death for any cause

Relatively to safety, in detail the following parameters will be recorded:

- Toxicity evaluated according to CTCAE vers 5.0
- Percentage of patients with dose reductions
- Percentage of patients with dose interruptions due to toxicity
- Percentage of patients with treatment discontinuations due to toxicity
- Toxicity according to initial dose of targeted agents
- Incidence of myelodysplastic syndrome and acute myeloid leukaemia in patients receiving PARPi

3.2 Secondary objectives

The secondary objectives are to collect the clinical outcomes, according to disease stage, surgical timing, residual disease after surgery in each cohort; therefore, to describe the clinical characteristics of patients for which the combination therapy was offered (Cohort A) and to describe the treatment approach to HRP patients in a real word scenario in Italy (Cohort B).

3.3 Data collected

Baseline data: Patient demographics and disease/treatment history will be collected from clinical records

1) Demographic: age, weight, height, pre-existing hypertension and comorbidities, and ECOG at time of enrollment
2) Medical/family history of cancer: history of other cancers, family history of cancers
3) Ovarian cancer diagnosis history: age of patient at cancer diagnosis, tumor histology, FIGO stage, primary tumor location, CT Scan (Thoracic, Abdominal, Pelvic)
4) Biomarker data collected per clinical routine and reported as available from medical charts: BRCA/HRD status. Type of HRD test performed;
5) Ovarian cancer treatment history:
    - Time of debulking surgery (primary or interval)
    - Outcome post debulking surgery (primary or interval): Visible Residual Disease or No visible residual disease
    - Description of prior chemo/platinum lines (including drugs/regimens, start and end dates, and frequency)
    - Response to last chemo/platinum line
    - Weeks after last platinum administration
6) In case of disease relapse/progression, date of disease relapse or progression, site of relapse/progression, CA125 at disease relapse/progression;
7) Date of second surgery if performed;
8) Description of second line chemotherapy (including drugs/regimens, start and end dates, and frequency) and its outcome in term of recist or CGIG criteria f tumor response (CA125 based);
9) Status (death or alive) and respective date.

Patient's characteristics and disease profile:

10) Platelet, neutrophiles and hemoglobin count at targeted treatment initiation

11) CA125 levels as collected per standard of care at the time of treatment's start and at the time of recurrence
12) Starting PARPi dose
13) Time and reason for dose reduction(s), including new dose prescribed
14) Time and reason for treatment termination
15) Duration of treatment
16) Post targeted therapy progression treatments: type and outcome of subsequent chemotherapy lines

4. Study duration and follow up

Patients with available HRD test result at the time of study entry will be retrospectively or prospectively enrolled. Patients will be retrospectively or prospectively enrolled from January 2021 to January 2026. The study will close in January 2029, this means that the last patients enrolled will be followed up prospectively for up to 3 years for primary and secondary objectives, independently of whether they are taking therapies or not.

5. Number of centers

This multicenter observational study involves approximately 21 Italian sites.

6. Withdrawal criteria

Specific reasons for discontinuing from the current study include the following reasons:

- Withdrawal of consent;
- Termination of the study.

7. Statistical plan and data analysis

7.1 Sample size and power considerations

Given the retrospective and prospective nature of the trial, the sample size is estimated according to the number of patients available.

At least 300 patients are to be selected considering both cohorts together. As HRD patients are about 50% of ovarian cancer patients, the two cohorts will consist of approximately 150 patients each.

With this number it is judged that the progression-free survival after first line treatments (independently from targeted agents used) will be estimated with sufficient accuracy.

With the available sample size, the width of 95% confidence intervals for frequency of toxicity in the two cohorts will be as follows:

N	Observed Frequency	Width of 95% CI	Lower Limit	Upper limit
150	10%	10%	5%	15%
150	20%	13%	14%	26%
150	30%	15%	23%	37%
150	40%	16%	32%	48%
150	50%	16%	42%	58%

7.2 Interim analysis

An interim analysis after 50% (i.e. about 150 patients) of the recruitment will be performed in order to obtain a first insight of the results

7.3 Analysis

PFS will be measured from the date of treatment's start to the date of first observed disease progression (relapse) or death. Standard statistics will be used to evaluate data (Kaplan Mayer; median and 95 % CI). In order to estimate the impact of therapy among our cohort of patients, all covariates (main prognostic factor for advanced ovarian cancer as residual disease, stage, Histotype) will be entered in a univariate and multivariate model (if the number of events will suffice) in order to identify predictors of survival outcomes. Survival outcomes will be assessed using Cox proportional hazard model. 95% confidence intervals (95%CI) will be estimated for each comparison when appropriate.

Other analysis will include summary statistics, including number and percentage for categorical variables and number of patients, mean, standard deviation, median, minimum, and maximum for continuous variables. 95% CI will be estimated when appropriate.

Adverse event intensity/severity will be coded using the current version of CTCAE and will be summarized for all treated participants. Incidence of AEs occurring during the study will be summarized by system organ class and preferred term. Adverse events will also be summarized by causality and grade. Serious adverse events will be listed separately.

8. Ethical and regulatory requirements

The procedures set out in this study protocol are designed to ensure that the promoter and the Investigators abide by the principles of the Good Clinical Practice guidelines of the International Conference on Harmonization (ICH) and the Declaration of Helsinki in the conduct, evaluation and documentation of this study. The study will be carried out adhering to local legal requirements and the applicable national law, whichever represents the greater protection for the individual.

8.1 Informed consent

Informed consent will be collected during routine visits. The process of obtaining informed consent should be documented in the patient source documents. The date when a subject's Informed Consent was actually obtained will be captured in database form.

The Local Principal Investigator or his/her representative will explain the nature of the study to participant and answer all questions regarding the study and will:

- Ensure that each subject is given full and adequate oral and written information about the nature, purpose, possible risk and benefit of the study
- Inform each patients that their participation is voluntary and that may withdraw their consent at any time and for any reason.
- Ensure that each subject is given the opportunity to ask questions and allowed time to consider the information provided
- Ensure that the original, signed Informed Consent Forms are stored in the Investigator's Study File
- Ensure that a copy of the signed Informed Consent Forms is given to the subject

It is understood that the subjects will be considered unavailable only after having made all reasonable efforts to contact them, such as by:

- checking whether they are still alive;
- browsing through their clinical records;
- contacting such telephone numbers as may be available;
- obtaining contact information from population and/or health care registers.

9. Administrative aspect

This study is a non-profit investigator-initiated trial. The promoter OncoTech, Consorzio per la ricerca, la formazione e le tecnologie avanzate in oncologia. An agreement between the Promoter and each participating centre will be stipulated.

Study protocol, patient information and informed consent will be submitted to the appropriate Ethical Committees for approval. At each centre, the study will only be started after being approved by the institutional Ethical Committee. The promoter will inform the Ethical Committees about any changes in the study protocol which could interfere with the patient's safety. Furthermore, the institutional review board will be informed of the planned or premature end of the study.

9.1 Insurance

Being an observational study, and according to Italian guidelines for observational studies (31/03/2008 in G.U. n. 76), no additional insurance policy will be needed beyond those already required by current medical practice.

10. Data Collection Procedures

Patient registration and data collection are electronically managed through an Electronic Data Capture system.

The Sponsor will supply the above-mentioned electronic Case Report Forms (eCRFs) to participating centers.

All eCRFs are to be completed and reviewed by the Investigator/designated Staff.

It is each Investigator's responsibility to ensure that eCRFs accurately reflect data contained in subject's records (e.g., source documents). The Investigator is also responsible for assuring that data entry and updates are performed in a timely manner.

Automatic validation programs check for data discrepancies in the eCRFs allow modification or verification of the entered data by the investigator staff.

Contacts for registration will be supplied in the section 12.

10.1 Data Protection

The collection and processing of personal data from subjects enrolled in this study will be limited to those data that are necessary to investigate the clinical outcomes and the safety in patients treated with targeted anticancer therapies in each study cohort.

These data must be collected and processed with adequate precautions to ensure confidentiality and compliance with applicable data privacy protection laws and regulations.

The Investigator/Sponsor ensures that the personal data will be:

- processed fairly and lawfully
- collected for specified, explicit, and legitimate purposes and not further processed in a way incompatible with these purposes
- adequate, relevant, and not excessive in relation to said purposes
- accurate and, where necessary, kept current

Explicit consent for the processing of personal data will be obtained from the participating subject (or his/her legally acceptable representative) before collection of data. Such consent should also address the transfer of the data to other entities and to other countries.

The subject has the right to request through the Investigator access to her personal data and the right to request rectification of any data that are not correct or complete. Reasonable steps should be taken to respond to such a request, taking into consideration the nature of the request, the conditions of the study, and the applicable laws and regulations.

11. Publications of study protocol and results

The information regarding the study and all results, data, information developed, generated or derived from the same study are confidential and exclusive property of the promoting site. The final publication of trial results will be written on the basis of the analysis performed as approved by the steering committee. Publications will be decided by the Principal Investigator in agreement with the steering committee.

12. Study contacts

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