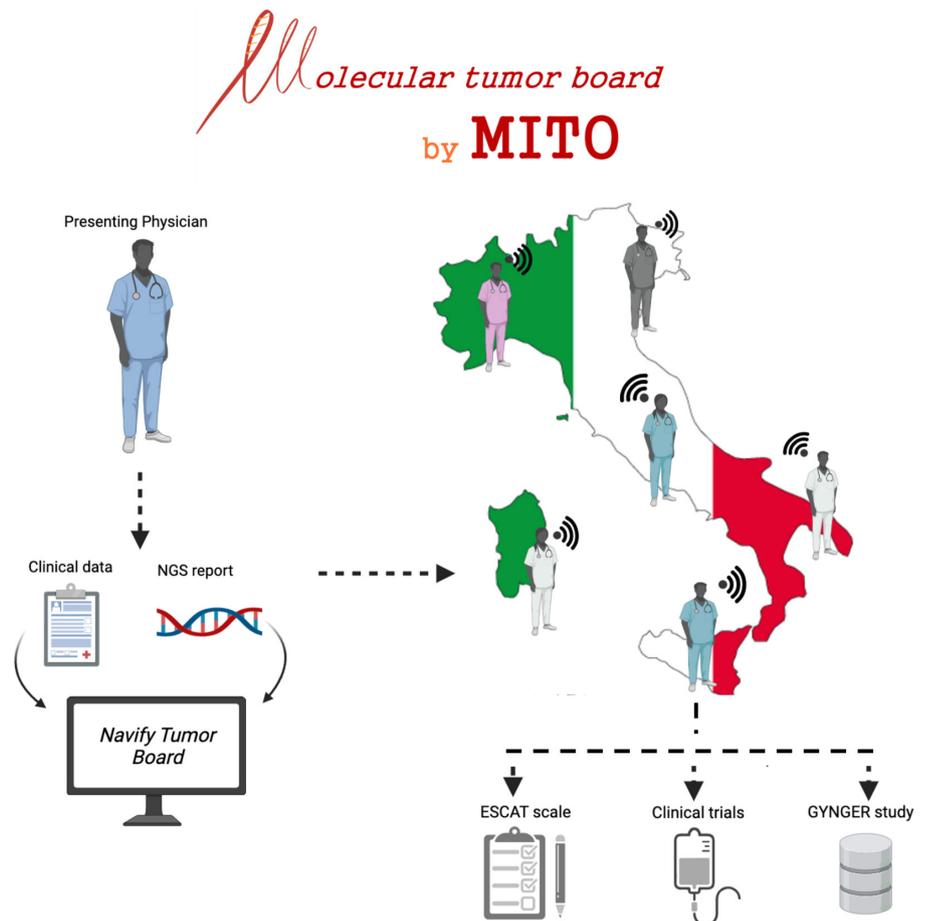


# A fully virtual and nationwide molecular tumor board for gynecologic cancer patients: the virtual experience of the MITO cooperative group

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Even if molecular biomarkers that are impacting clinical practice in gynecologic oncology are limited, our community is living in the precision medicine era where the number of patients undergoing tumor genomic profiling is increasing, as is the number of new drug approval for cancers with specific genetic alterations. In this complex scenario, molecular data must be interpreted on a case-by-case basis, and the presence of molecular tumor boards in leading the decision-making process are crucial.

In fact, molecular tumor boards can identify possible therapeutic strategies based on tumor genomic alteration in patients for which the effectiveness of standard therapies is suboptimal or a standard approach does not exist. On the other hand, molecular tumor boards can avoid the use of anticancer drugs with an insufficient level of evidence, limiting unnecessary adverse effects and unjustified costs for the public healthcare system. Moreover, molecular tumor boards can play a pivotal role in the spreading of new concepts of cancer genomics, flattening the learning curve of precision medicine, making clinicians more comfortable with molecular concepts, like allelic fraction, tumor molecular drivers, and pathogenic versus non-pathogenic genetic variants. Notwithstanding the importance of molecular tumor boards is recognized and many efforts have been made to implement this tool in high volume cancer centers, limitations due to the absence of molecular tumor boards in general rural hospitals and geographical barriers are undermining the access of clinicians to these facilities. Furthermore, routine molecular tumor boards need to consider



**Figure 1** Data flow and organization of the virtual molecular tumor board by MITO. ESCAT, ESMO scale for clinical actionability of molecular targets; GYNGER, GYNecological cancers GEnetic profile Registry; NGS, next generation sequencing.

sub-specializations in oncology; thus, sub-specialists should attend the selective board, a factor that makes molecular tumor board organization more elaborate for a single institution.

To overcome the limits of conventional molecular tumor boards taking advantage of the yet established network between the gynecologic oncology community in Italy, the MITO group has recently inaugurated the virtual

**Table 1** Main tumor agnostic/biomarker driven clinical trials based on NGS analysis active in Italy (December 2021)

Trial name	Molecular driver	Targeted agent	Study design	Population
Tumor-Agnostic Precision Immuno-Oncology and Somatic Targeting Rational for You (TAPISTRY) Platform Study (NCT04589845)	<ul style="list-style-type: none"> <li>▶ ROS1 fusions</li> <li>▶ NTRK1/2/3 fusion</li> <li>▶ ALK fusion</li> <li>▶ TMB high</li> <li>▶ AKT1/2/3 mutation</li> <li>▶ HER2 mutation</li> <li>▶ MDM2-amplified, TP53 wild-type</li> <li>▶ PIK3CA mutation</li> <li>▶ BRAF class II–III mutations</li> <li>▶ RET fusion</li> </ul>	<ul style="list-style-type: none"> <li>▶ Entrectinib</li> <li>▶ Alecetinib</li> <li>▶ Atezolizumab</li> <li>▶ Ipatasertib</li> <li>▶ Trastuzumab emtansine</li> <li>▶ Idasanutlin</li> <li>▶ Inavolisib</li> <li>▶ Belvarafenib</li> <li>▶ Pralsetinib</li> </ul>	Phase II, multicohort	Advanced solid tumors
A Study Evaluating the Efficacy and Safety of Biomarker-Driven Therapies in Patients With Persistent or Recurrent Rare Epithelial Ovarian Tumors (NCT04931342)	<ul style="list-style-type: none"> <li>▶ PTEN loss of function mutations</li> <li>▶ AKT1/2/3 mutation</li> <li>▶ PIK3CA mutation</li> <li>▶ ERBB2 mutation or amplification</li> </ul>	<ul style="list-style-type: none"> <li>▶ Ipatasertib</li> <li>▶ Cobimetinib</li> <li>▶ Trastuzumab emtansine</li> <li>▶ Atezolizumab</li> <li>▶ Bevacizumab</li> <li>▶ Paclitaxel</li> </ul>	Phase II, multicohort	Persistent or recurrent rare epithelial ovarian cancers
Safety and Efficacy of Retifanlimab alone or in Combination With Other Therapies in Participants With Advanced or Metastatic Endometrial Cancer Who Have Progressed on or After Platinum-based Chemotherapy. (POD1UM-204) (NCT04463771)	<ul style="list-style-type: none"> <li>▶ MSI high</li> <li>▶ TMB high</li> <li>▶ POLE mutations</li> <li>▶ FGFR 1,2,3 mutation or alteration</li> </ul>	<ul style="list-style-type: none"> <li>▶ Retifanlimab</li> <li>▶ Epacadostat</li> <li>▶ Pemigatinib</li> </ul>	Phase II, multicohort	Advanced or metastatic endometrial cancer
A Study of Erdafitinib in Participants With Advanced Solid Tumors and Fibroblast Growth Factor Receptor (FGFR) Gene Alterations (NCT04083976)	<ul style="list-style-type: none"> <li>▶ FGFR gene alterations</li> </ul>	<ul style="list-style-type: none"> <li>▶ Erdafitinib</li> </ul>	Phase II, single cohort	Advanced solid tumor
The Rome Trial From Histology to Target: the Road to Personalize Target Therapy and Immunotherapy (ROME) (NCT04591431)	<ul style="list-style-type: none"> <li>▶ EGFR mutation</li> <li>▶ ERBB2 amplification or mutation</li> <li>▶ mTOR mutation</li> <li>▶ AKT mutation</li> <li>▶ BRAF V600E mutation</li> <li>▶ CDK 4/6 mutation</li> <li>▶ CDKN2A mutation</li> <li>▶ BCR-ABL gene fusion</li> <li>▶ SMO/PTCH1 mutation</li> <li>▶ JAK mutation</li> <li>▶ FGFR 1-2-3 gene alterations</li> <li>▶ PI3KCA, AKT, PTEN mutations</li> <li>▶ NTRK 1-2-3 fusion</li> <li>▶ ROS1 fusion</li> <li>▶ MSI high</li> <li>▶ TMB high</li> </ul>	<ul style="list-style-type: none"> <li>▶ Erlotinib</li> <li>▶ Trastuzumab</li> <li>▶ Trastuzumab emtansine</li> <li>▶ Pertuzumab</li> <li>▶ Lapatinib</li> <li>▶ Everolimus</li> <li>▶ Vemurafenib</li> <li>▶ Cobimetinib</li> <li>▶ Alecetinib</li> <li>▶ Brigatinib</li> <li>▶ Palbociclib</li> <li>▶ Ponatinib</li> <li>▶ Vismogedib</li> <li>▶ Itacitinib</li> <li>▶ Ipatasertib</li> <li>▶ Entrectinib</li> <li>▶ Atezolizumab</li> <li>▶ Nivolumab</li> <li>▶ Ipilimumab</li> <li>▶ Pemigatinib</li> </ul>	Randomized, phase II	Advanced solid tumor

NGS, next generation sequencing .

molecular tumor boards by MITO, a fully virtual and nationwide molecular tumor board focused on gynecologic cancers. The project has been matched with the GYNecological cancers GEnetic profile Registry (GYNGER), an observational, retrospective–prospective clinical study aimed at collecting clinical and molecular data from patients, with a focus on those suffering from rare gynecological cancers.

The molecular tumor board by MITO is reserved for the MITO group's members. Launched in June 2021, to date the project totals approximately 50 fellows, including medical oncologists, gynecologists, pathologists, molecular biologists, geneticists, and clinical study coordinators. Virtual meetings are scheduled every 2 weeks on the

videoconferencing platform Zoom, which the invited-only members can access via computer or mobile device. Until 72 hours before the planned meeting, members can submit anonymized clinical cases using the platform Navify Tumor Board (NTB, Roche Molecular Systems, Santa Clara, CA). All members are allowed to enter the Navify Tumor Board to study and prepare clinical case(s) days before the scheduled meeting. When a case is discussed for molecular data interpretation, the board's final decision can be the ranking of a molecular alteration and its matched drug using the ESMO Scale for Clinical Actionability of molecular Targets (ESCAT), the patient's referral to a biomarker-driven trial or expanded access program active in Italy (Table 1), and finally,

the patient's enrollment in the GYNGER study (Figure 1).

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