Dear colleagues, first of all on behalf of the Hellenic Cooperative Oncology Group, I would like to thank the organizing committee for its kind invitation and for giving me the opportunity to talk about our Group, to outline its internal structure and to help you get a glimpse of our activities.

The Hellenic Cooperative Oncology Group (herein mentioned with its abbreviated name, HeCOG), is a non-profit organization founded back in 1992, by the Directors of 4 Medical Departments in Greece. Currently, it has become a network comprised of 23 Departments or Clinics of Medical Oncology across Greece and Cyprus.

The aims that were initially set and are still in effect, namely

- Promotion of clinical and translational research in Oncology
- Continuing medical education of young oncologists and other researchers on new technologies, innovative treatments and recent advances in patient management
- Increase of public awareness with regard to current prevention strategies and cancer treatments through scientific meetings, conferences etc.

The internal structure of our Group is depicted in the diagram. Obviously, above all, is the Board of Directors of the 13 major Medical Oncology Departments. There is also a Scientific Committee, in which each Dept has appointed 1-2 representatives depending on the size of the Dept. and last but not least is the HeCOG Central Data Office.

The brain and the heart of HeCOG is its headquarters located in Athens, the Central Data Office.

Its highly educated and experienced employees are operating different sections, as you can see in the slide. Additionally, we have hired data managers and research nurses in all major affiliated Oncology Departments. Internal monitors are responsible for monitoring all clinical studies conducted by our Group, which are often sponsored by pharmaceutical companies and filed in international registries.

Over the years and in order to stimulate research interest, we have established working groups, supervised by the Scientific Committee, composed by physicians with different specialties, such as medical oncologists, radiation oncologists, surgeons, pathologists, radiologists and basic scientists. Some of these groups, depicted on the slide, are currently inactivated but most of them remain active and very productive, such as the breast cancer, GI, lung cancer and OBGYN groups.

Over the last two decades, we have created a relatively large biological material repository, comprising of approximately 14,000 formalin-fixed paraffin-embedded tumor tissue samples and 13,000 germline DNA samples, mainly from patients participating in clinical trials. All tissue samples are accompanied by electronically annotated clinicopathological data.

The vast majority of these patients had early breast cancer or CRC.

Translational research is performed in several HeCOG-affiliated laboratories across Greece. However, research regarding tumor tissue is mainly done at the Laboratory of Molecular Oncology, which is operating, in commodate, at the AUTH. The Molecular Diagnostics Laboratory of the National Centre for Scientific Research at Demokritos, located in Athens, is responsible mainly for genetic studies and the CARING Laboratory, at the University of Ioannina, for liquid biopsy studies.

At the Laboratory of Molecular Oncology, we developed 3 areas of research, IHC, FISH and lately NGS. All tumors are centrally characterized by experienced pathologists for parameters, such as tumor cell content, tumor microenvironment, protein receptors etc. Tumor DNA and RNA accompanied in most cases with genomic DNA, are also extracted from all patients with adequate tissue.

A signed informed consent for the use of biological material for future research purposes has been collected from each patient before the acquisition of such tissue samples. This procedure has been our standard practice since 1997, when we first started collecting tumor tissue samples for translational research.

We apply the Ion Torrent semiconductor technology with 2 different machines, 1 Personal Genome Machine (PGM) and 1 Ion Proton.

We have previously published the clinical significance of molecular alterations in breast, colorectal, NPC and biliary tumors. Analysis in other tumor types are in preparation. In our Precision Medicine Initiative, we integrated tumor molecular profiling data from our research database to investigate the clinical relevance of pathogenic mutations across tumor types. The majority were breast and colorectal tumors, but our analyses also included pancreatic, ovarian, endometrial and other tumors.

From 5,000 patients, 3,084 informative tumors were available for analysis. Among those, 57% had pathogenic mutations (mutation annotation was performed at MD Anderson). We explored co-mutations and mutual **exclusivity** between commonly mutated genes, along with their prognostic significance.

We have identified approximately 14,000 mutations, 6,000 of which were pathogenic in 57% of the tumors.

Some tumors had 1 or more pathogenic mutations. In purple we see the proportion of patients with 2 or more pathogenic mutations. And the proportion was different depending on the tumor type, as you can see in the bars.

More commonly mutated genes were TP53, PIK3CA, KRAS and BRCA1.

Horizontal bars indicate proportion of patients whose tumors had a pathogenic mutation.

Pathogenic mutations in different genes appeared to be associated with overall survival, as did combinations of mutated genes. For example co-mutation of BRCA1 and TP53 conferred poorer risk to such patients compared to BRCA1 and TP53 mutations alone.

This difficult to read slide depicts forest plots. The prognostic significance of these genes and combinations of genes was maintained in multivariate analyses.

Part of this analysis will be presented at the next ESMO 2018, in Munich.

Regarding productivity, our Group is characterized by a sustained and internationally recognized presence, as well as by rich scientific accomplishments. Up to December

of 2017, we have published over 600 manuscripts in high impact factor International Journals.

The cumulative impact factor of these papers is 2,418 while the total number of citations exceeds 18,000.

In addition, we are very keen on pursuing international collaborations with other Groups or Institutions.

You can see a few examples of such collaborations, all resulting in papers published in high-level Journals. Financing our activities is obviously a big problem these days of economic crisis in our country, but we don't give up. On the contrary, we strive to find grants or sign new contracts with Pharma. At any rate, financial resources are mostly contracts with International Pharma, grants from the European Union and donations from grateful individuals, in this order.

Dear colleagues,

When we initially started this endeavour, to establish for the first time a Cooperative Group in Greece, we had a vision for bridging the gap between cancer patients and modern, at the time, clinical research and putting our small country in the global map of Cancer Research.

27 years later, I believe that we have largely achieved this goal. Nowadays however, we are facing new challenges. Firstly, to apply the principles of Precision Oncology in an era of limited health resources and secondly to maintain the oncologic services offered to our cancer patients at the highest level. I strongly believe that by staying united, as we used to be, and by being committed to our primary goals, set 27 years ago, we can accomplish our mission.

Before closing my talk, I would like to express my gratitude to the thousands of patients and their loved ones for having trusted us by participating in the clinical trials conducted by our Group and for generously donating biological material for research purposes. I would like to thank all HeCOG personnel and colleagues for their strong commitment. Finally, I thank all colleagues of the Laboratory of Molecular Oncology

and especially Prof. Vasiliki Kotoula for their hard work and dedication and commitment for achieving our goals.

Thank you for your attention.