The mutational model for cancer care

- Tumors generate, develop, and spread within the organism following an accumulation of genomic driver mutations
- The molecular alterations recurring across histologically different tumors may be captured by the latest generation sequencing tools (next generation sequencing, NGS), both qualitatively ant quantitatively - mutational tumor burden -
- The mutational characteristic of tumors is the basis for new molecular targeted therapies (‘druggable’ or ‘actionable’ mutations)
- The increasing availability of effective and manageable molecular targeted drug leads to a personalized treatment in settings of patients

Defining the target: next generation sequencing (NGS)

- Different platforms, technology, NGS panels and tissues (i.e. liquid biopsy), the implementation of which depends on the clinical needing
- NGS panels with CE-IVD marking and approval by US and/or EU regulatory agencies guarantee more reliability
- Laboratories using NGS panel must undergo internal validation, verification and external quality assessment
- The decision to implement NGS tests in-house or to externalize must take into account expected activity loads, experience of the lab, and participation in research programs

Action the target: the Molecular Tumor Board (MTB)

- The complexity of mutational model requires interdisciplinary teams which take care of clinical procedures balanced with economic appropriateness and sustainability
- MTB Involves oncologists, hematologists, pathologists, surgeons, molecular biologists, geneticists, bioinformaticians, radiologists, pharmacologists, hospital pharmacists
- MTB meets regularly to the choice of active drugs (or combinations) that can already be available and reimbursed, or available but not registered for a specific indication (off-label), or in clinical trials
- Patients with locally advanced or metastatic tumors or with early tumors with poor prognosis and/or orphan of personalized treatments
- MTB must establish a clear and concise reporting system including the druggable and actionable mutations as well as the recommended therapy, and the clinical outcome should be registered

Mastering the shift from histology-based to mutational model

- The current FDA and EMA model of target oncological drugs is based on location of cancer -> histology -> biomarker -> drug use indications
- FDA approval of pembrolizumab independently of the location of the tumor ('agnostic approval'), stigmatizes urgency for national health care services to assist patients by adopting the mutational model
- To avoid geographic and economic disparities current regulations should be exploited
- To guarantee shared rules and standards, MTBs should operate through a web-based platform centrally managed by AIFA. The platform would create an institutional database of genomic-clinical-therapeutic and outcomes data and safeguard the ethical and economical principles of the health system