

Personalized Medicine: An Emerging Standard of Treatment “à la carte”

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Medical Oncology is one of the continuously evolving fields in medicine. Diagnostic procedures, laboratory and radiological investigations, as well as the molecular and pathological analyses are making this specialty more challenging:

1. Discovery of new histological subtypes.
2. Newer versions of Tumor-Node-Metastasis (TNM) staging.
3. Newer histological classification based on molecular analysis.
4. A mutational or molecular based treatment targeting more specific tumor related pathways, instead of broadly expressed receptors or targets..
5. Concept of tumor heterogeneity and tumor antigenicity.
6. Concept of the adaptive resistance and the model of oligometastatic disease.

As a result, we are facing the era of newer treatments consisting of targeted and immune-based therapies shifting the anti-neoplastic treatment to a personalized medicine based therapy. It is a way to modify all the previous concepts of Medical Oncology: the cytotoxic agent which was prescribed for different histological subtypes is being replaced by a more targeted therapy with the aim to treat certain defects, pathways or surface expressed receptors. Thus, two patients with a same histological diagnosis may benefit from two different treatments and in the same perspective, one molecular targeted therapy may be prescribed to treat two different diseases. So, all mutations are not equal in oncology, and it is mandatory to provide clinicians and pathologists with higher sensitivity tests and more efficient techniques: next generation sequencing (NGS), tumor molecular profiling and other genomic and transcriptomic analyses. Every tumor has its clinical and molecular biomarkers that will serve as drivers to be targeted in the context of a personalized oncology. This is briefly the goal of the cancer genome atlas (TCGA) and the pan-cancer atlas including the cell-of-origin patterns, the oncogenic processes and most importantly, the signaling pathways that can be hit by the available targeted therapies (for example, a tyrosine kinase used in other malignancies or that failed to demonstrate a response in other trials can be prescribed to target the tumor specific pathway). Moreover, this new paradigm of treatment is defining a newer response evaluation not only depending on the known RECIST criteria, but also on pathological response and disappearance of a previously detectable aberration. Consequently, in order to handle all these modifications and make adequate decisions, Medical Oncologists must share the different

results and opinions with other colleagues based on a good multidisciplinary discussion. The molecular tumor board (TB), controversially to other TB, will require the integrated action of a large number of competences and specialists.

In conclusion, personalized medicine can be resumed as a precision medicine or a higher selective mode of treatment. Clinicians shouldn't confuse this new emerging modality with a *person or individual-based* treatment. It is a rapidly evolving landscape that may lead to a practice changing in the future. Beside discovering the tumor growth pathway and the mechanism of resistance to the standard of care, its main goals is to provide an exact tumor-based treatment, more specific and less toxic than the previous targeted therapies with a possible more durable response. There is a major shift of the paradigm from a previous simplified model of <one> gene/mutation/histology treated with <one> therapy, to a model of system biology where all alterations are taken into account for the therapeutic decision. Knowing that personalized medicine is quite promising, and many targeted therapies exist in the market, we are waiting for the results of the ongoing trials: when and at which line of treatment is it possible to adopt this strategy? Do we try it in all tumor types, leaving the known and proven standard of care, or we keep it for orphan and rare tumors?

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