Editorial

Sharing data: a requirement for expanding precision oncology

Olivier Trédan

Department of Medical Oncology, Leon Berard Cancer Center, Lyon, France

Correspondence to: Olivier Tredan, MD, PhD. Department of Medical Oncology, Leon Berard Cancer Center, 28 Rue Laennec, 69008 Lyon, France. Email: olivier.tredan@lyon.unicancer.fr.

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Identification of somatic genomic variants in tumor DNA to identify matched targeted agents (MTAs—drugs that are supposed to target the abnormal encoded proteins) is nowadays accessible to patients from several companies and may be funded by Health Insurances. A lot of cancer centers have developed institutional precision profiling programs. Beyond the fact that using molecular profiling is feasible in the clinic, what is the optimal goal of this genomic medicine? The level of outcome improvement in studies investigating the impact of MTAs on a broad variety of advanced cancers (pathology-agnostic therapies) have proven to be limited. Reports of precision medicine clinical trials [including the prospective randomized SHIVA trial (1)] demonstrated minimal impact of MTAs on large population of patients with advanced cancers (even though the molecular profile of each patient's tumor was established with a specific mandatory biopsy) (2).

Nevertheless, genomic characterization of known biomarkers (e.g., *HER2*, *EGFR*, *BRAF*, *ALK*- or *NTRK*-fusions, or DNA repair genes) lead to unseen tumor responses for a sub-group of patients, albeit the molecular aberration is not a tumor-specific somatic mutation (3). Most patients' tumors carry numerous tumor molecular alterations, suggesting that customized MTAs combination is definitively forthcoming treatment strategies (4). Single tumor biopsy appeared not to be sufficient enough to give an exhaustive representation of the tumor genomic heterogeneity, suggesting that new innovative approaches are needed, such as sequential liquid biopsies (5). The interaction between the tumor and its immune microenvironment is a dynamic process, playing a significant role in treatment efficacy, suggesting that integrative approach to capture the evolution and function of geographically distinct cell populations has to be implemented (6). Drug selection and dosage should also be individualized as obvious physiological and pharmacogenomics discrepancies exist between cancer patients (7). To address all these numerous issues, it appeared crucial to develop new tools or methods to enable researchers to increase the number of available data (patient phenotypes, RNA/DNA variants, treatment response/resistance). Precision medicine continue to move to a data-driven discipline, including currently novel approaches in immunology, cancer cell plasticity, or protein expression regulation (epigenetic, alternative splicing etc.).

In their article, Le Texier and coll. used a scientometric approach to emphasize the increased number of scientific publications on data sharing in the era of precision medicine. Articles on data sharing underline the power of multiple data sources to identify trends allowing faster and meaningful progress in cancer patient management. In pediatric oncology for example, clinicians face rare diseases with heterogeneous genomic alterations and frequent epigenetic aberrations (8). Having access to different databases (including clinical parameters, genetic variants and relative gene expression profiles) enables to analyze and combine thousands of relevant clinical and molecular information. Le Texier and coll. observed during the last 15 years a rapid growth of publications and citations on data sharing, however the quantitative production across countries and institutions is unequal. Since sequencing programs were mostly funded by American and European agencies, publications in this topic arise from a limited number of institutions (mostly US, UK and Canada).

Likewise, in recognition of the clinical value of data sharing, these funding agencies continue to strongly encourage researchers to contribute to public databases.

In which way this assessment of the number of publications in the era of data sharing could be useful for us to understand the current evolution of precision medicine? The number of publications in this field increases as some databases are free open-source softwares. Their use is widespread so that it becomes rapid and easy to generate new scientific results to publish. In the daily practice of precision medicine programs, bio-pathologists and geneticists need to access the frequencies of somatic variants described in open-source databases such as cBioPortal (http://cbioportal.mskcc.org/) or Catalogue of Somatic Mutations in Cancer (COSMIC). Molecular-based treatment decision requires available data based on previous studies integrating mutations and therapy response, such as in the Personalized Cancer Therapy Knowledge for Precision Oncology (https://pct.mdanderson.org). For example, in our ProfiLER program (9), we have used those open-source databases and we were enthused by the published experience of the Personalized Medicine Clinical Service at Moffitt Cancer Center in Tampa, Florida (10). We quoted their work in our own publication (9), both work referring to cBioPortal, COSMIC or published experiences from others. The increase in citations reflects a shared desire to learn and grow from the knowledge of multidisciplinary researchers. The scientometric analysis described by Le Texier and coll. has the advantage of giving a snapshot of the situation regarding data-sharing in 2019 and its evolution towards cross-disciplinarity. However, the authors' conclusions may be biased due to the limited number of publications analyzed and the search stringency.

Molecular data available in the US and European metabases (metadata) are expected to be standard and reliable (with respect to sequencing protocols, quality controls and data annotations). Other genomic data produced by other institutions could be challenging to incorporate and assess. However, an international effort has to be made, since non-US and non-European genomic profiles should be implemented in order to increase the number of samples and allele frequency information. Furthermore, genomic data generated from prospective clinical trials, especially those collected by industrial companies, are not systematically implemented in these databases. As low as 15% of samples from clinical trials were accessible 2 years after publication of primary results, as a result of lack of data sharing policy/process (11). Giving assess to genomic database to large broader researchers remains a sensitive matter because sharing the primary DNA sequence may result in potential patient identification. North-American and European clinicians along with data scientists are still limited (with restrictive agreements) for the large dissemination of these genomic databases. The recent general data protection regulation (GDPR), applicable as of May 25th 2018, to harmonize data privacy laws across Europe, is currently mandatory for any given project involving data. Albeit constraining, this new regulation gives a legal frame to address data sharing at the level of a country or Europe, in order to prevent any abuses.

Overall, the article from Le Texier and coll. illustrates that data sharing is an emerging field of expertise, requiring multidisciplinary collaborations. It gives us an optimistic outlook for the motivation in the oncology community to pursue data sharing around the world, so that patients worldwide benefit from past experiences to improve their own care.

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