OncoImmunology 1:9, 1457–1459; December 2012; © 2012 Landes Bioscience

Advancing the field of cancer immunotherapy

MIATA consensus guidelines become available to improve data reporting and interpretation for T-cell immune monitoring

Axel Hoos,[1,3,*] Sylvia Janetzki[2,3] and Cedrik M. Britten[4,5]

[1]Glaxo Smith Kline; Collegeville, PA USA; [2]Zellnet Consulting; Fort Lee, NJ USA; [3]Cancer Immunotherapy Consortium; Cancer Research Institute; New York, NY USA; [4]Translational Oncology; University Medical Center of the Johannes Gutenberg-University Mainz GmbH; Mainz, Germany; [5]Association for Cancer Immunotherapy (CIMT); Mainz, Germany

It has been two years since clinical development of cancer immunotherapy has started to turn from decades of failures to its first successes in randomized Phase 3 trials with Sipuleucel-T, a dendritic cell-based vaccine, and ipilimumab, a monoclonal antibody targeting CTLA-4. Both are increasing patient survival in their target diseases.[1,2] The path to these successes was, in part, paved by the methodological improvements regarding clinical endpoints for immunotherapy development that enabled the understanding of the clinical observations made for these agents and the differentiation of immunotherapy kinetics from chemotherapy kinetics.[3] Such methodological improvements do not come easy and require broad consensus across the community that uses these methods for them to be widely applicable. The adaptation of immunotherapy clinical endpoints took about five years, and has shown that consensus work facilitated by community organizations like the Cancer Immunotherapy Consortium (CIC) or the Association for Cancer Immunotherapy (CIMT) can be impactful and systematically fill gaps that prevent advances in our field.[4]

Similarly, other methodological improvements are needed in this space and have been worked on by several community organizations for years. The first that comes to mind is the effort of harmonizing the use of immune monitoring assays in multi-center clinical trials through a data-driven, SOP-based process that enables individual centers to use their own assay protocols and still achieve a low level of data variability across centers.[5] This program has been running since 2005 and has delivered practical recommendations for the community based on the recognition of critical experimental variables that impact assay performance and should be reported to assess the results. By design, this assay harmonization project, which focused on frequently-used assays such as ELISPOT, intracellular cytokine staining or HLA-peptide multimer staining, has focused on assay conduct and did not address data reporting.[5,6] However, it has not escaped the attention of many immunotherapy experts that the methods and results published for immune monitoring experiments are still inconsistently reported, often leading to missing information and difficulties in data interpretation across publications.[7] Ultimately, the full utility of measuring immune response to immunotherapeutic interventions as a biomarker or surrogate for clinical outcomes will strongly depend on the interpretability and reproducibility of such data across trials. As before, the solution to this methodological problem seems to lie in a community-wide consensus process that would establish minimum reporting criteria for immune monitoring data.[6,7]

Indeed, after about three years of an intense vetting process across the immunotherapy communities in cancer, infectious diseases and autoimmunity, the Minimal Information about T cell assays (MIATA) guidelines were published recently in *Immunity*.[8] MIATA's aim was to improve interpretation and data comparison across immune monitoring experiments reported in different publications by creating a minimum reporting framework for consistent and community-wide use. The components included in the MIATA guidelines were oriented on the variables identified to bear most impact on performance of a given T-cell assay experiment in clinical trials. Information to be reported falls in the following categories:

- Sample
- Assay
- Data Acquisition
- Results
- Laboratory Environment

The concept of Minimal Information (MI) projects is not new and has been successfully applied in other areas of biomedical sciences such as the reporting of high-throughput genomic experiments (Minimum Information About Microarray Experiments, MIAME) and a variety of other assays (www.mibbi.org),[9,10] which has greatly improved reporting of such experiments.

A hallmark of MIATA was its intense vetting process, including two public consultation periods and two open workshops over a three-year period with frequent reach-out to the community[11] and a project website (www.miataproject.org) to transparently show progress of the initiative and feedback received from participants. Overall, MIATA includes active contributions from more than 120 peers from academic and industry scientists.[8] The guidelines are published as open

*Correspondence to: Axel Hoos; Email: axel.x.hoos@gsk.com
Submitted: 09/05/12; Accepted: 09/06/12
http://dx.doi.org/10.4161/onci.22308

access in the July issue of *Immunity* (www.cell.com/immunity/retrieve/pii/S1074761312002919) and are accessible through the MIATA website. MIATA aims to be come part of instructions for authors of immunology-based science journals.

Great efforts were made to ensure MIATA would ask only for "minimum information" needed to achieve its goal, which simplifies practical implementation and limits the burden on the reporting scientists. To assist investigators to achieve a rather straightforward use of MIATA, various supporting documents are provided on the MIATA website, which include (1) a checklist for MIATA compliance, (2) example reports, (3) guidance for donor information and (4) terms related to the laboratory environment. Nevertheless, the use of MIATA will take some effort from authors to adapt the *Materials and Method* section of new manuscripts to MIATA style. MIATA adherence can easily be checked via the online checklist (www.miataproject.org/checklist.pdf).

Implementation of MIATA Across the Field

The success of MIATA will strongly depend on its implementation. Several immunology-based journals, including *OncoImmunology*, have pledged to participate in a test phase of MIATA during which a voluntary reporting of minimum information on T-cell experiments from clinical trials published in the respective journals would be offered to authors submitting manuscripts to those journals. After the test period, the use of MIATA may become a mandatory component of instructions for authors in the respective journals.

Adoption and utility of MIATA will depend on both the reporting scientists and the editorial teams and reviewers of journals. There are clear incentives for both groups to adopt MIATA: (1) adoption increases the quality standard of published immune monitoring data in the immunotherapy space, thus also increasing the credibility of the space, the probability of scientific success and the probability for funding for new research; (2) adherence to MIATA may be seen as a "label of honor" for the scientist indicating a high level of transparency; (3) adherent manuscripts will be listed on the MIATA homepage thus increasing awareness of readers and citability of the publication.

A mechanism for reviewing MIATA adherence of new manuscripts is to be established with journals. After a MIATA adherent manuscript is published, authors can contact the MIATA core team (input@miataproject.org), which will list the paper online including a link to the publication. While implementation will take some efforts across the community, there are already first signs of interest in MIATA: The initial MIATA announcement has been cited more than 50 times, and the first MIATA-adherent publications are appearing on its website. On behalf of the community-wide effort to improve reporting of immune monitoring results, we encourage all authors who aim to publish such experimental data in *OncoImmunology* to voluntarily use MIATA to present your information. It will enhance the quality of your publication, allow you to become familiar with this new process and support the implementation across the community.

There is precedence for such implementation through MIAME for genomic microarray experiments, where the initial free-choice adoption of the MIAME guidelines[9] in a test phase allowed the community to understand its value and practical utility and ultimately led to the mandatory inclusion of MIAME in authors' instructions by medical journals. Today, microarray data cannot be published without MIAME compliance, a result that found acceptance in the community through this rather inclusive instead of forceful approach. A similar progression may be envisioned for MIATA.

The outlook for the cancer immunotherapy field is improving with any new initiative that increases available tools, creates better reproducibility of results and enables biomarker or clinical development. As was demonstrated for the adaptation of clinical endpoints for cancer immunotherapy[3] or the introduction of MIAME for genomic microarray experiments,[9] MIATA has the potential to make an important contribution to the cancer immunotherapy community. In addition, MIATA may also serve other scientific communities utilizing T-cell assays.[8] MIATA is part of an ongoing effort to introduce new or improve existing tools and methods for the development of cancer immunotherapies, known as the Immuno-Oncology framework.[4,12] With such initiatives, the community is now likely accelerating the success rate for new therapeutic developments in this space.

References

1. Kantoff PW, Higano CS, Shore ND, Berger ER, Small EJ, Penson DF, et al.; IMPACT Study Investigators. Sipuleucel-T immunotherapy for castration-resistant prostate cancer. N Engl J Med 2010; 363:411-22; PMID:20818862; http://dx.doi.org/10.1056/NEJMoa1001294.
2. Hodi FS, O'Day SJ, McDermott DF, Weber RW, Sosman JA, Haanen JB, et al. Improved survival with ipilimumab in patients with metastatic melanoma. N Engl J Med 2010; 363:711-23; PMID:20525992; http://dx.doi.org/10.1056/NEJMoa1003466.
3. Hoos A, Eggermont AMM, Janetzki S, Hodi FS, Ibrahim R, Anderson A, et al. Improved endpoints for cancer immunotherapy trials. J Natl Cancer Inst 2010; 102:1388-97; PMID:20826737; http://dx.doi.org/10.1093/jnci/djq310.
4. Hoos A, Britten CM, Huber C, O'Donnell-Tormey J. A methodological framework to enhance the clinical success of cancer immunotherapy. Nat Biotechnol 2011; 29:867-70; PMID:21997622; http://dx.doi.org/10.1038/nbt.2000.
5. van der Burg SH, Kalos M, Gouttefangeas C, Janetzki S, Ottensmeier C, Welters MJ, et al. Harmonization of immune biomarker assays for clinical studies. Sci Transl Med 2011; 3:08ps44; PMID:22072636; http://dx.doi.org/10.1126/scitranslmed.3002785.
6. Britten CM, Janetzki S, van der Burg SH, Gouttefangeas C, Hoos A. Toward the harmonization of immune monitoring in clinical trials: quo vadis? Cancer Immunol Immunother 2008; 57:285-8; PMID:17721782; http://dx.doi.org/10.1007/s00262-007-0379-z.
7. Janetzki S, Britten CM, Kalos M, Levitsky HI, Maecker HT, Melief CJM, et al. "MIATA"-minimal information about T cell assays. Immunity 2009; 31:527-8; PMID:19833080; http://dx.doi.org/10.1016/j.immuni.2009.09.007.
8. Britten CM, Janetzki S, Butterfield LH, Ferrari G, Gouttefangeas C, Huber C, et al. T Cell Assays and MIATA: The Essential Minimum for Maximum Impact. [Letter]. Immunity 2012; 37:1-2; PMID:22840835; http://dx.doi.org/10.1016/j.immuni.2012.07.010.
9. Brazma A, Hingamp P, Quackenbush J, Sherlock G, Spellman P, Stoeckert C, et al. Minimum information about a microarray experiment (MIAME)-toward standards for microarray data. Nat Genet 2001; 29:365-71; PMID:11726920; http://dx.doi.org/10.1038/ng1201-365.

10. Taylor CF, Field D, Sansone S-A, Aerts J, Apweiler R, Ashburner M, et al. Promoting coherent minimum reporting guidelines for biological and biomedical investigations: the MIBBI project. Nat Biotechnol 2008; 26:889-96; PMID:18688244; http://dx.doi.org/10.1038/nbt.1411.

11. Britten CM, Janetzki S, Van der Burg SH, Huber C, Kalos M, Levitsky HI, et al. Minimal information about T cell assays: the process of reaching the community of T cell immunologists in cancer and beyond. Cancer Immunol Immunother 2010; In press; PMID:21080166.

12. Hoos A, Britten C. The immuno-oncology framework: Enabling a new era of cancer therapy. Oncoimmunology 2012; 1:334-9; PMID:22737609; http://dx.doi.org/10.4161/onci.19268.