Emerging insights on the biology and treatment of cutaneous T-cell lymphoma

This special issue of *Chinese Clinical Oncology* compiles a series of excellent articles covering multiple aspects of the current clinical research and treatment landscape of cutaneous T-cell lymphoma (CTCL), providing an up to date and comprehensive overview of this rapidly changing field.

Over the past 3 years, a number of major advances in basic research, outcome analysis, and drug development, including two large randomized Phase III clinical trials that led to the recent FDA approval of brentuximab vedotin (1) (ADCETRIS™, Seattle Genetics) and mogamulizumab (2) (POTELIGEO™, Kyowa Hakko Kirin), have begun to shed significant light on the molecular profile and natural history of CTCL and validated the clinical benefit of targeting the surface markers CD30 and CCR4 on neoplastic T-cells. In addition, retrospective data from the cutaneous lymphoma international consortium (CLIC), an international registry that includes centers from more than 60 countries, have begun to provide a more granular view of the knowledge gaps, unmet needs, and opportunities for improvement in the global patterns of care for CTCL, with a specific focus on patients with mycosis fungoides and Sézary syndrome (MF/SS) (3,4). The CLIC is now collecting data on a very large prospective cohort of patients with MF/SS, a critically important effort which is designed to support the development of a prognostic index for early stage MF (stage IA-IIA), called PROCLIPI (5). This initiative, led by Dr. Kim (Stanford University) and Dr. Scarisbrick (University of Birmingham, UK) begins to address the important issue of risk stratification of patients with early stage MF, which is essential to identify subsets of patients with early stage disease that should be treated more aggressively, or require systemic therapy earlier in the course of their disease.

The articles published in this special issue cover a broad spectrum of diagnostic and treatment issues that are highly relevant for physicians treating patients with CTCL. Kartan and colleagues provide a comprehensive overview of primary cutaneous CD30+ lymphoproliferative disorders (LPD), including the most recent subtypes of lymphomatoid papulosis (LyP), and describe the morphologic and immunophenotypical overlap, and the distinguishing features, between primary cutaneous CD30+ LPD and a number of systemic CD30+ LPDs that the treating physician needs to be familiar with. The article by Barta and colleagues complements nicely the one by Kartan *et al.*, by further reviewing the spectrum of CD30+ LPD with an angle at targeted therapies, and new entities. The article by Russo and colleagues describes the rapidly evolving field of Sézary syndrome, from its genetics and molecular biology, which Dr. Russo's group has contributed to characterize in major ways, to diagnosis and treatment, both of which continue to present significant challenges. Finally, the article by Moschowitz and colleagues describes very rare subtypes of CTCL and provide a practical framework to their correct diagnosis, work up, and treatment. These ultra-rare T-cell lymphoma entities are often aggressive and difficult to treat, and much remains to be done to improve patients' outcomes.

Several other articles in this special issue provide a broad overview of the treatment modalities currently available for CTCL, from skin directed therapies (Scarisbrick *et al.*), to local, involved field radiation (IFRT) (Shikama *et al.*), to total skin electron beam radiation treatment (TSEBT) (Shi *et al.*), including the increasing use of low dose TSEBT, which is well tolerated and effective, and can be repeated. Alpdogan *et al.* survey the systemic therapy landscape, but also provide some evidence-based guidance on the selection of the optimal systemic therapy for the patients who require combine modality approaches, whereas Nikbakht *et al.* review the immunological defects that underlie the development and progression of CTCL, and describe the spectrum of immunomodulatory interventions available to correct or reverse them. This is a rapidly expanding area, with a number of novel agents in development, such as checkpoint inhibitors, CD47 targeting drugs, and novel monoclonal antibodies, all of which are well-described and aptly summarized in the article by Dr. Nikbakht and colleagues. Finally, Dr. Johnson and colleagues, provide a succinct but complete overview of the use of allogeneic hematopoietic stem cell transplantation (HSCT) in the therapy of CTCL. This remains a controversial treatment modality, only applicable to a minority of cases due to its high toxicity and risk of relapse, but one that unquestionably has helped a selected group of patients with advanced stage CTCL. The last three articles in this series, by Sahu and colleagues, provide some guidance on optimal skin care in patients with CTCL, review the spectrum and clinical impact of histopathological MF variants (folliculotropic and syringotropic), and reports original data from the Jefferson multimodality CTCL program on the

use of maintenance mechlorethamine gel (VALCHLOR™, Actelion) following low dose TESBT.

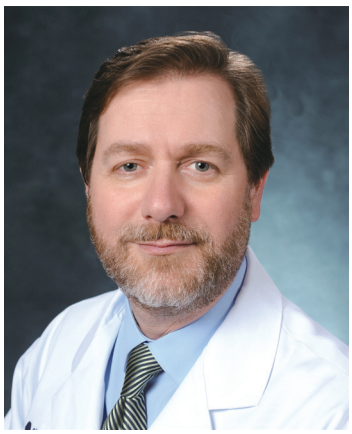
In aggregate, these contributions give the reader a very good view of the current state of the art in CTCL and offer strong evidence that the field is rapidly moving forward towards more effective and safer therapies, and better ways to classify and diagnose CTCL, in all its diverse presentations and manifestations.

Acknowledgements

None.

References

1. Prince HM, Kim YH, Horwitz SM, et al. Brentuximab vedotin or physician's choice in CD30-positive cutaneous T-cell lymphoma (ALCANZA): an international, open-label, randomised, phase 3, multicentre trial. Lancet 2017;390:555-66.
2. Kim YH, Bagot M, Pinter-Brown L, et al. Mogamulizumab versus vorinostat in previously treated cutaneous T-cell lymphoma (MAVORIC): an international, open-label, randomised, controlled phase 3 trial. Lancet Oncol 2018;19:1192-204.
3. Scarisbrick JJ, Prince HM, Vermeer MH, et al. Cutaneous Lymphoma International Consortium Study of Outcome in Advanced Stages of Mycosis Fungoides and Sézary Syndrome: Effect of Specific Prognostic Markers on Survival and Development of a Prognostic Model. J Clin Oncol 2015;33:3766-73.
4. Quaglino P, Maule M, Prince HM, et al. Global patterns of care in advanced stage mycosis fungoides/Sezary syndrome: a multicenter retrospective follow-up study from the Cutaneous Lymphoma International Consortium. Ann Oncol 2017;28:2517-25.
5. Scarisbrick JJ, Quaglino P, Prince HM, et al. The PROCLIPI international registry of early-stage mycosis fungoides identifies substantial diagnostic delay in most patients. Br J Dermatol 2018. [Epub ahead of print].



Pierluigi Porcu

Joya Sahu

Wenyin Shi

Pierluigi Porcu
Division of Hematologic Malignancies and Hematopoietic Stem Cell Transplantation, Department of Medical Oncology, Sidney Kimmel Cancer Center at Jefferson Health, Thomas Jefferson University, Philadelphia, USA.
(*Email: Pierluigi.Porcu@jefferson.edu*)
Joya Sahu
Department of Dermatology and Cutaneous Biology, Thomas Jefferson University, Philadelphia, PA, USA.
(*Email: Joyasahumd@gmail.com*)
Wenyin Shi
Radiation Oncology, Thomas Jefferson University Hospital, Philadelphia, PA, USA.
(*Email: Wenyin.Shi@jefferson.edu*)
doi: 10.21037/cco.2019.01.04
Conflicts of Interest: The authors have no conflicts of interest to declare.
View this article at: http://dx.doi.org/10.21037/cco.2019.01.04

Cite this article as: Porcu P, Sahu J, Shi W. Emerging insights on the biology and treatment of cutaneous T-cell lymphoma. Chin Clin Oncol 2019;8(1):1. doi: 10.21037/cco.2019.01.04