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# Personalized cancer medicine

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Worldwide Innovative Networking in personalized cancer medicine

FOCUS ON PERSONALIZED MEDICINE

# WIN Consortium—challenges and advances

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**The importance of appropriate patient selection necessitates novel clinical trial design and biomarker-driven trials to allow delivery of the right drug to the right patient at the right time—personalized cancer medicine. The WIN Consortium promotes collaboration between critical stakeholders and offers diverse populations of cancer patients the opportunity to participate in clinical trials with new drugs and biologics that target their tumor.**

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The worldwide annual cancer incidence is 14 million people, and recent advances in cancer research are helping to create new possibilities for the treatment and management of therapy for this disease. It is well known that cancer is caused by the abnormal function of genes that control cell proliferation and function, and we have extensive information on the intricate cellular pathways and networks in which the molecular products of these genes participate. The genes in a genome can now be sequenced in days rather than years, and at costs that are approaching the practical limits for clinical utility. Normal and abnormal gene products can be detected with immunohistochemistry and proteomic techniques that are steadily improving. Biotechnology and drug companies and academic institutions have the capability of being far more efficient in designing new anticancer drugs and biological agents and testing their preclinical efficacy. By combining these advances, it has become possible to design clinical trials in which a patient is assigned a drug based on the presence of biomarkers in that patient's tumor. This approach often results in high response rates for the effective drugs and biologics that target these biomarkers.

The past two decades have witnessed the successful introduction of targeted agents such as imatinib, bevacizumab, trastuzumab, cetuximab, gefitinib and erlotinib for the treatment of hematologic and solid tumors. Recent presentations at the 2010 meetings of the American Association for Cancer Research and ASCO have highlighted the acceleration of accomplishments in personalized cancer therapy for the treatment of lung cancer. For instance, the BATTLE clinical trial showed that adaptive randomization of new drugs in the phase II setting, based on biomarkers in a patient's tumor biopsy that identify abnormal genes or gene products, can enhance clinical outcomes.[1] The BATTLE lung cancer trial is discussed in this issue[2] as a new approach to early diagnosis and treatment of cancer. Another advance in lung cancer was demonstrated by preselecting for the presence of a translocation in *ALK* that is present in less than 5% of patients with non-small-cell lung cancer. Administration of the anti-ALK drug PF-02341066 produced response rates of more than 50%.[3]

These trials are among a number of studies that have provided important lessons for clinical research. By preselecting for patients with abnormalities in the specific targets for which new drugs have been designed, it is likely that efficacy can be demonstrated (or will not be demonstrated) far more quickly and efficiently than in an unselected patient population. This means that diagnostic tests for biomarkers must be developed in parallel with new drugs. It also means that for trials with drugs targeting the products of genes that are not commonly mutated or functioning abnormally in human cancers, it will be necessary to screen cancers from large numbers of patients derived from diverse populations to identify appropriate candidates for treatment.

While these research observations are promising, too few patients are being placed on such clinical trials today—in fact, less than 5% even in the most developed countries. Cancer patients urgently need increased access to biomarker-driven trials with new targeted therapies.

With these considerations in mind, the Worldwide Innovative Networking (WIN) Consortium was initiated by the Institut Gustave Roussy (France) and The University of Texas MD Anderson Cancer Center (USA), as a non-profit non-governmental organization bringing together cancer centers from five continents to address this challenge. WIN aims to foster and facilitate collaboration between clinical cancer centers, pharmaceutical and technology companies, patient advocacy groups, governmental institutions and other stakeholders in the field of diagnosis and personalized treatment of cancer. It will coordinate and promote clinical trials for diverse populations of patients from North and South America, Europe, Asia, Africa and the Middle East. The goal of WIN is to apply recent knowledge and discoveries in research and technology to achieve more rapid and efficient translation of groundbreaking personalized cancer medicine discoveries into the standard for clinical care for those patients who are likely to receive meaningful benefits.

As a first step, the WIN Consortium will focus on the discovery and clinical application of new biomarkers and technologies in the field of early diagnostics and personalization of cancer therapeutic strategies, and the use of these biomarkers in early phase clinical trials. Principal investigators from WIN Consortium member organizations will submit innovative clinical studies for review by an independent Scientific Advisory Board (SAB). Trials approved by the Consortium leadership, with the advice of the SAB, will be managed by the principal investigator and his/her institution, with the full support of the WIN Consortium, and

they will be made available for participation of patients from all member institutions that choose to join the trial. In this way, patients representing many different nationalities and ethnic groups can be efficiently screened for eligibility.

A second step for the WIN Consortium will be to utilize innovative statistical designs to select more efficiently and effectively from among a number of new drugs against a particular target. Examples include Bayesian adaptive designs in phase I trials, randomized phase II trials, retrospective-prospective studies for biomarker development, and the use of novel surrogate end points such as imaging. We also plan to move more rapidly into exploration of combinations of new drugs against a single target or multiple targets. This effort will require collaborations and strategic partnerships between WIN and two or more companies, because more than one diagnostic test and drug will be involved in these trials. Potential gains for a company include identification of biomarker tests that are useful for its drug, improved early phase I indication of efficacy upon which to base decisions on further drug development, and, through early studies with combinations, an increased chance for demonstrating efficacy in the case of a drug whose target is beneficial but not critical for the survival of a cancer cell.

The WIN Consortium brings together the critical stakeholders in new cancer drug development—including skilled clinical investigators, companies producing new biomarker tests and technologies, pharmaceutical and biotechnology companies, and cancer patients—and gives them access to diverse populations of cancer patients for participation in clinical trials. This type of mechanism for collaborative clinical investigation is essential if we are to speed up the process of developing personalized cancer treatment based on the prescription of targeted treatments that are most likely to be effective for appropriately selected patients. Knowledge gained from WIN clinical trials will be disseminated widely in the medical research community. The use of operating processes and data management systems, which harmonize as closely as possible with current best practice standards, will aid in transmission of knowledge and may serve in turn to increase the standardization of clinical trials information, worldwide.

> **“The WIN Consortium brings together the critical stakeholders in new cancer drug development”**

The authors are honored to have been elected as leaders of the WIN Consortium at the July 2010 gathering of cancer centers for the second WIN Symposium on personalized cancer therapy, in Paris. We are pleased to have this opportunity to present the rationale and goals for forming WIN, and we invite interested cancer centers with strong experience in the clinical investigation of new cancer drugs and biological agents and biomarker development, as well as others in the commercial and scientific community, to contact us if there is interest in participation and membership.

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**Competing interests**

R. L. Schilsky declares he has associations with the following company: Foundation Medicine. See the article online for full details of the relationship. The other authors declare no competing interests.

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