



Our Knowledge Is Your Gain.

Recent understandings have both enlightened and complicated oncology clinical research. Key among them is the heterogeneity of tumors at the same primary site. The ensuing necessity for companion diagnostics to identify which patients will benefit from a targeted therapy and for rapid identification of molecules that can sidestep acquired resistance, plus progress in immunologic- and vaccine-based treatments, have increased the complexity of drug development. At Worldwide Clinical Trials (WCT), our core oncology expertise means your trial starts from a favorable, advanced position. Our commitment to your study objectives and our ability to proactively identify and overcome operational challenges mitigate your risk.

WCT Is Your Translational Research Partner.

How does WCT differ from other contract research organizations (CROs) you may be considering? You want to bridge the gap between basic research and the production of agents that benefit patients. WCT offers experience in:

- Implementing traditional and accelerated dose escalation designs and sequential trial designs that deliver innovation and efficiencies in phase I and phase I/II studies
- Facilitating gene-expression profiling in exploratory studies designed to identify patients for whom molecularly targeted therapies may be efficacious
- Producing adaptive study designs that permit modification of a trial's course based on accumulating results, potentially allowing much smaller and more focused oncology trials^a
- Working with targeted therapies featuring innovative biological properties
- Executing complex, multi-part designs in later-phase trials.

Additionally, we can collaborate on “basket studies,” which enroll patients with a particular mutation regardless of their cancer type.^b

ONCOLOGY PORTFOLIO

SOLID TUMOR MALIGNANCIES

- Brain
- Breast
- Colorectal
- Head and neck
- Renal cell
- Liver
- Lung
- Melanoma
- Ovarian
- Pancreatic
- Prostate
- Stomach/ GI cancer
- Thyroid
- Mixed solid tumors

HEMATOLOGIC MALIGNANCIES

- Leukemia
- Multiple myeloma
- Myelodysplastic syndrome
- Non-Hodgkin's lymphoma

SUPPORTIVE CARE

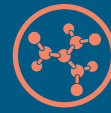
- Chemotherapy-induced nausea and vomiting
- Chemotherapy-associated fatigue
- Chemotherapy-induced neutropenia
- Pain

 DISCOVER MORE ONLINE
WORLDWIDE.COM

^a For example, see Ivanova A, Murphy M. An adaptive first-in-man dose escalation study of NGX267: Statistical, clinical, and operational considerations. *J Biopharm Stat.* 2009; 19: 247-255.

^b Various studies are underway to test the efficacy of this approach, including the National Cancer Institute's Molecular Analysis for Therapy Choice (MATCH) Program, in which approximately 1000 patients will be assigned to phase II trials (each N=30) and treated with 1 of 20–25 drugs that target the genetic abnormalities being tested for in this study. Patients whose cancers progress during the first assigned treatment may be able to join another MATCH trial arm if they have a second actionable molecular target in their tumors. The success of the basket trial design depends on collaboration among pharmaceutical companies. In preliminary comments, the FDA has indicated it could approve drugs with basket-study data alone.





WCT STAFF EXPERIENCE

28 project managers

161 clinical research assoc

19 clinical trial assoc



A solid staff with oncology experience is available to help you.



DISCOVER MORE ONLINE
WORLDWIDE.COM

Partnership Example: Biosimilar Development

WCT and a mid-sized pharmaceutical company collaborated on a phase-III development plan, and WCT oncology professionals advised and supported:

- Protocol design
- Regulatory strategy
- Scientific methods
- Site identification and activation
- Statistical plan design
- Trial execution

WCT assisted in the choice of combination chemotherapy, with a focus on ensuring global acceptance and facilitating input from key opinion leaders to expedite full protocol development. We also performed a comprehensive feasibility assessment and a comparability analysis of biosimilar data for the Investigational Medicinal Product Dossier. Robust start-up metrics have assured strong implementation of this clinical trial.

Client Feedback

“WCT has accomplished work within the agreed timelines and budgetary constraints and has already surpassed several goals. Deliverable quality has been excellent. My company will definitely consider WCT for future studies.”

- Oncology Clinical Program Lead

“Very impressed with WCT team performance and professionalism. We appreciate your efforts!”

- Director, Clinical Development Biologics

Directing the Approach

Whether your new targeted therapy or immunotherapy is first tested in volunteers or in cancer patients, WCT can lead from the start of your program through preparation and submission of core documentation to regulators. For example, we strongly advocate scheduling pre-Investigational New Drug (IND) meetings with the FDA (or obtaining scientific advice from the European Medicines Agency) to test the response to your drug-development strategy. Early interaction is particularly desirable when the proposed clinical development program incorporates innovative trial methodology or evaluates a compound considered first-in-class for a given tumor. Additionally, WCT is establishing master confidential disclosure agreements with premier oncology phase-I units in the US, Europe, and Singapore that offer access to virtually all types of cancer patients. The US unit enrolls approximately 1000 oncology patients in phase I trials every year. Tumor tissue at this location is minimally screened against a panel of 50 mutations/markers, with the capability of testing >400, depending on drug target. All of the units offer assessment of your inclusion and exclusion criteria, for alignment with the available patient population and likelihood of efficient enrollment (performed only with your approval, of course).



WCT can advise whether a phase I/II study (ie, determination of maximum tolerated dose [MTD] or biologically effective dose [BED], followed by population expansion for safety assessment and, potentially, signals of efficacy) would be beneficial. Combined phases can minimize risks to patients and allow faster development. In our experience, use of 3-4 sites is ideal for MTD/BED determination. We then rapidly recruit to efficiently transition from phase I to phase II, and in the process shift the focus of clinical evaluation to patients with a single tumor type contingent upon emerging efficacy and safety signals.

Driving Geographic Success

As oncology drug development has gathered pace and more new molecules fill the research pipeline, competition for investigators and patients has intensified, impacting timelines and inflating trial costs. WCT clients benefit from our operational capabilities in emerging regions such as the Middle East and North Africa, where competition is lower and patient access is less encumbered. Our capabilities also fully extend to regions such as the Russian Federation and Central/Eastern Europe where the centralized healthcare system promotes efficiencies in study execution by establishing large referral networks for recognized centers of excellence, and to Asia-Pacific.

We understand that in-depth knowledge of local standards of care and regional variations in oncology practice can materially impact a site's ability to actively enroll in a proposed program. Our extensive experience with local cultural, medical, and regulatory environments translates into reliable intelligence about territories to access as well as those to avoid, which results in the delivery of impeccable data vital to successful oncology clinical research.

Delivering Experience

Since 2008, WCT has conducted more than 80 oncology trials under WCT project management and monitoring and contributed other services as well.

WCT has orchestrated phase I-IV and non-interventional studies in solid tumors, hematologic malignancies, and supportive care. Our oncology team is supported by a global network of experienced sites, about which we can offer detailed knowledge. Partner with us for strategic therapy development (see figure next page).

WCT's portfolio of oncology experience

Kinase inhibitors	Biologic agents: Anti-CD20/CD22, EGFR, HER2, VEGF
Cytotoxics	
Gene silencing (siRNA)	Novel molecular targets: HDAC inhibitors, Hsp 90, Apoptosis pathway agents
Vaccines	
Immunotherapy	

EGFR=epidermal growth factor receptors, HDAC=histone deacetylase, HER2= human epidermal growth factor receptor 2, HSP=heat shock protein, VEGF=vascular endothelial growth factor



Oncology

INTEGRATED TECHNOLOGY

- Clinical Trial Management System
- Electronic Data Capture
- Interactive Voice Response System (IVRS)
- Interactive Web Response System (IWRS)
- IxRS technology



Our Supply Management and Randomization Technology (SMaRT) offers a cost-effective solution for centralized randomization, drug inventory management, and controlled code-break capabilities. WCT also is a leader in developing bespoke IxRS solutions for sponsors. With the capability to integrate complex IxRS needs into sponsor data systems, we can reduce costs while enhancing both quality and efficiency.



DISCOVER MORE ONLINE
WORLDWIDE.COM

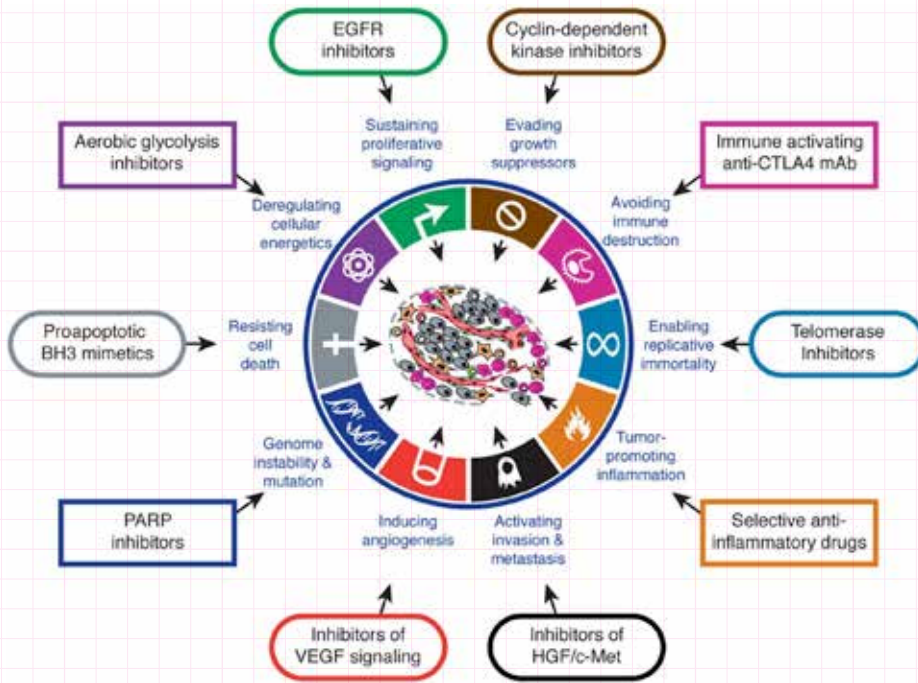


WORLDWIDE CLINICAL TRIALS
SCIENTIFICALLY MINDED • MEDICALLY DRIVEN



KEY SERVICES

- Biostatistical service
- Clinical monitoring
- Data management
- Investigator site selection
- Investigator meetings
- Global project management
- IVRS/IWRS for supply management and randomization
- Medical monitoring
- Medical writing
- Pharmacovigilance
- Protocol feasibility assessment
- Protocol design
- Regional drug depot services
- Regulatory affairs (includes regulatory consultancy)
- Safety monitoring
- Scientific consultancy
- Third-party collaborations ^a



Therapeutic Targeting of the Hallmarks of Cancer. These 8 acquired capabilities that allow cancer cells to survive, proliferate, and disseminate, plus 2 enabling characteristics (tumor-promoting inflammation and genome instability and mutation), are integral components of most forms of cancer. Note that listed agents are examples. WCT strategically partners with our oncology clients to support their targeted therapy development. (From Hanahan D, Weinberg RA. Hallmarks of cancer: The next generation. *Cell*. 2011; 144: 646-674. With permission of Elsevier.)

Client Testimonials

“This is a challenging project in a number of respects, not least of which is the timeline. We are impressed with the WCT approach to problem-solving ... we’ll continue to partner closely.”

- Senior Director, Experimental Medicine,
Gene Expression Profiling, Oncology

“I would work with WCT again in a heartbeat. The project support staff was fantastic, and my effort was significantly less for this study because WCT took ownership of the protocol responsibilities so well. A truly great outsourcing experience.”

- Director, Clinical Operations, Oncology

INTERNATIONAL: +44 (0) 20 7121 6161

AMERICAS: +1 610 964 2000

worldwide.com

IVRS=Interactive Voice Response System, IWRS= Interactive Web Response System

^a WCT partners with a range of specialized service providers, including centralized clinical and imaging laboratories, drug procurement and management specialists, and logistics support for transfer of tumor samples, temperature-controlled pharmacokinetic samples, etc.

