Cardiovascular

Our Expertise Is Your Advantage.

Worldwide Clinical Trials (WCT) is a global leader in cardiovascular (CV) clinical research. We have provided exemplary operational, data management, and biostatistical services for Phase II–IV trials in a host of CV indications for over 25 years. Our established relationships with key investigators, regulatory bodies, and academic research organizations in the CV field assure delivery of impeccable and statistically relevant data.

Worldwide Clinical Trials has executed 120 CV trials, delivering clinical monitoring, project management, or full clinical research services for 61.

You Need Results-Oriented Client Service.

You can rely on our CV experts' broad experience in the clinical practice of cardiology as well as their extensive knowledge of the operational challenges of advanced CV clinical research studies. WCT is committed to the success of your study. Our global team includes a network of:

- 100+ Clinical Research Associates/Trial Coordinators
- 19 Project Managers with 5 to 15 years of CV experience
- 12 Medical Monitors with CV experience[a]

Partners in Excellence

WCT is not just any contract research organization (CRO). We frequently conduct CV outcome studies in collaboration with renowned academic research organizations (AROs) such as the Thrombolysis in Myocardial Infarction (TIMI) Study Group (Brigham & Women's Hospital); Duke Clinical Research Institute (DCRI); the Antithrombotic Trials Leadership and Steering (ATLAS) Group[b]; and the Cleveland Clinic Coordinating Center for Clinical Research (C5Research). In the absence of strong ARO/CRO integration, studies are at considerable risk of operational failure. The success of our collaborations is demonstrated by the publication of high-impact scientific papers in which our professionals are recognized alongside ARO members.

Examples of WCT/ARO collaboration include:

Pravastatin or Atorvastatin Evaluation and Infection Therapy—Thrombolysis in Myocardial Infarction 22 (PROVE IT–TIMI 22) study

Cannon CP, Braunwald E, McCabe CH, Rader DJ, Rouleau JL, Belder R, Joyal SV, Hill KA, Pfeffer MA, Skene AM. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. *N Engl J Med.* 2004; 350: 1495-1504

Clopidogrel as Adjunctive Reperfusion Therapy—Thrombolysis in Myocardial Infarction 26 (CLARITY-TIMI 26) study

Sabatine MS, Cannon CP, Gibson CM, Lopez-Sendon JL, Montalescot G, Theroux P, Claeys MJ, Cools F, Hill KA, Skene AM, McCabe CH, Braunwald E. Addition of clopidogrel to aspirin and fibrinolytic therapy for myocardial infarction with ST-segment elevation. *N Engl J Med.* 2005; 352: 1179-1189

Trial to Assess the Effects of Vorapaxar in Reducing Atherothrombotic Events in Patients With Atherosclerosis—Thrombolysis in Myocardial Infarction 50 (TRA 2°P–TIMI 50)

Morrow DA, et al. Vorapaxar in the secondary prevention of atherothrombotic events. *N Engl J Med.* 2012; 366: 1404-1413. WCT personnel A Skene, K Hill, and L Bennett are included under Trial Leadership in the supplementary appendix (K Hill as head of clinical operations). *See Case Study next page.*

[a] Including one board-certified cardiologist.

[b] The ATLAS Group comprises an international panel of renowned hematological and antithrombotic experts, CPC Clinical Research, and Worldwide Clinical Trials.

CARDIOVASCULAR PORTFOLIO

HEART DISEASE

- Atrial fibrillation
- Coronary artery disease (CAD)
- Ischemic heart disease
- Heart failure
- High-risk CVD

VASCULAR DISORDERS

- Acute coronary syndrome
- Aortic aneurysm
- Arterial hypertension
- Atherosclerotic disease
- Peripheral artery disease (PAD)
- Stroke
- Venous thromboembolism

INTEGRATED TECHNOLOGY

- Clinical Trial Management System (CTMS)
- 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.

WORLDWIDE CLINICAL TRIALS
SCIENTIFICALLY MINDED • MEDICALLY DRIVEN

Proficiency in CV Outcome Trials

You likely plan to enroll thousands of patients across hundreds of centers around the world using inclusion/exclusion criteria that are highly specific and outcome measures that are relatively discrete. Therefore it is critical that the infrastructure be scalable and fully adaptable from country to country and site to site. Our operational acumen is impeccable, with well-considered team composition, communication strategies (with study sites as well as multiple vendors), and collaborative support. We offer proven patient recruitment and retention plans. WCT's fluid control ensures that we meet objectives and adhere to timelines while remaining flexible in the face of any challenges.

WCT services and infrastructure spanning >7,900 sites and >158,000 patients

Acute coronary syndrome		
OPUS–TIMI 16	10,300 patients	800 sites
PROVE IT–TIMI 22	4,000 patients	300 sites
MERLIN–TIMI 36	6,560 patients	500 sites
PLATO	18,624 patients	862 sites
EMIP-FR	6,270 patients	79 sites
MAGIC	5,600 patients	94 sites
VISTA-16	5,189 patients	362 sites
Heart failure		
PRIME II	1,800 patients	140 sites
COMET	3,000 patients	200 sites
CIBIS III	1,000 patients	120 sites
Thrombolysis		
TRA 2°P–TIMI 50	26,449 patients	1032 sites
InTIME II–TIMI 17	15,000 patients	850 sites
CLARITY–TIMI 28	3,500 patients	319 sites
LATE	5,700 patients	250 sites
INJECT	6,000 patients	210 sites
GUSTO III (Europe)	6,000 patients	250 sites
HERO–2	8,000 patients	90 sites
Venous thromboembolism		
Ongoing	8,000 patients	500 sites
High cardiovascular risk—diabetes, obesity		
PROactive	5,238 patients	321 sites
Ongoing	12,000 patients	700 sites

Case Studies Provide the Evidence.

A phase III, randomized, double-blind, placebo-controlled study of a platelet PAR-1 receptor inhibitor in atherosclerosis, 2007–2012

Patients: Adults with history of MI, ischemic stroke, or PAD.

Recruitment: 1,032 sites in 32 countries including Asia-Pacific, South Africa, Western and Eastern European Union, and North and South America.

Enrollment: 26,449 randomized to 2 treatment arms.

Main objective: Evaluate efficacy and safety of study drug added to standard therapy (ST) in reducing incidence of atherothrombotic events relative to ST alone.

WCT collaborated with the TIMI Study Group to provide project and site management[a], global CTMS, IVRS, statistical programming, drug supply, and investigator payment services. Challenges included numerous cultures and time zones and retaining subjects over 4–5 years. WCT solutions were ready from the start, due to a Project Operating Procedure (POP) Manual compiled from our extensive experience. WCT now uses this POP Manual as a template for large studies. Integration of WCT services, efficient coordination of vendors, and immediate contact and tracking of patients after only 1 missed visit were some of the many WCT solutions that allowed identification of 4,074 endpoints and produced a 99.9% follow-up rate (2% of patients withdrew consent for follow-up).

Trial was cited as a "model of rigor" for execution and data integrity by FDA CV Advisory Panel.

[a] Except in North America (316 sites). WCT conducted clinical monitoring for UK (48 sites).

[b] 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 temperature-controlled pharmacokinetic samples, etc.

V.1 - May 15 - USL

Cardiovascular Disease

KEY SERVICES

- Biostatistical service
- Clinical monitoring
- Data and Safety Monitoring Board charters and management
- Data management
- Endpoint adjudication process
- Global project management
- Investigator meetings
- Medical monitoring/ pharmacovigilance
- Medical writing
- Protocol design
- Protocol feasibility assessment
- Regulatory affairs (includes consultancy)
- Safety monitoring
- Scientific consultancy
- Site identification
- Third-party collaborations[b]

INTERNATIONAL: +44 (0) 20 7121 6161

AMERICAS: +1 610 964 2000

wwctrials.com

WORLDWIDE CLINICAL TRIALS

SCIENTIFICALLY MINDED • MEDICALLY DRIVEN