

Worldwide Clinical Trials

Preparing CRAs for Success in Oncology: Targeted Training in an Era of Advanced Therapeutics

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Abstract

Clinical Research Associates (CRAs) play a crucial role in the success of clinical trials, particularly in oncology. They provide key functions of monitoring and managing clinical trials and are also the sponsor's eyes and ears at the site level. The rapid developments in advanced therapeutics, particularly within oncology, require robust and targeted training programs to ensure CRAs are well-prepared to meet the challenges of clinical research associated with investigational products with unique mechanisms of action and highly nuanced patient populations. This white paper explores the importance of comprehensive CRA training, identifies challenges in current training paradigms, and outlines strategies to improve the overall efficiency and effectiveness of CRAs.

Behind the Scenes of Clinical Trials: The Unseen Expert

CRAs play an integral role in managing, monitoring, and facilitating clinical trials, ensuring smooth and ethical trial conduct while adhering to strict regulatory guidelines, overseeing the well-being of subjects, and maintaining data integrity. Thus, a CRA's role is critical in ensuring that clinical trials collect reliable data and facilitate unencumbered biostatistical analyses to successfully advance the development of new treatments.

CRAs, for example, provide the first signal of potential protocol deviations for consideration by the extended project team to ensure site staff take action to resolve or prevent recurrence. They act as protocol subject matter experts (SMEs) in study operations, thus bridging the gap between medical and scientific experts and the operational requirements of the trial. Given the complexity of clinical trials, with the need to effectively integrate sources across study staff, precisely defining CRA's responsibilities avoids regulatory issues that could potentially impugn data integrity. Additionally, CRAs preemptively address logistical impediments that could delay study initiation with predictable timelines for initiation and conclusion.

A Strong Foundation Begins with Bespoke CRA Training

Training and clearly defining the CRA role is paramount to ensure clinical trial integrity, compliance, and success. Specifically, regular, up-to-date training is essential as regulatory guidelines continually evolve. Proper training must include well-defined roles and relevant information crucial for CRAs to perform their duties effectively. Untrained CRAs lead to inadequately trained clinical sites about the specifics of a given study and inefficiencies in study monitoring, which become a significant hurdle for efficient clinical trial execution.

Comprehensive therapeutic-specific training ensures that CRAs are knowledgeable across multiple domains relevant to Successful study prosecution. These include regulatory requirements, ethical standards associated with patient care, the ability to ensure data quality and integrity across efficacy and safety measures, and protocol adherence. Moreover, consistent, in-depth CRA training improves individual performance and makes the role more uniformly structured and transparent across institutions or sites involved in the study, aligning study expectations (**Figure 1**).

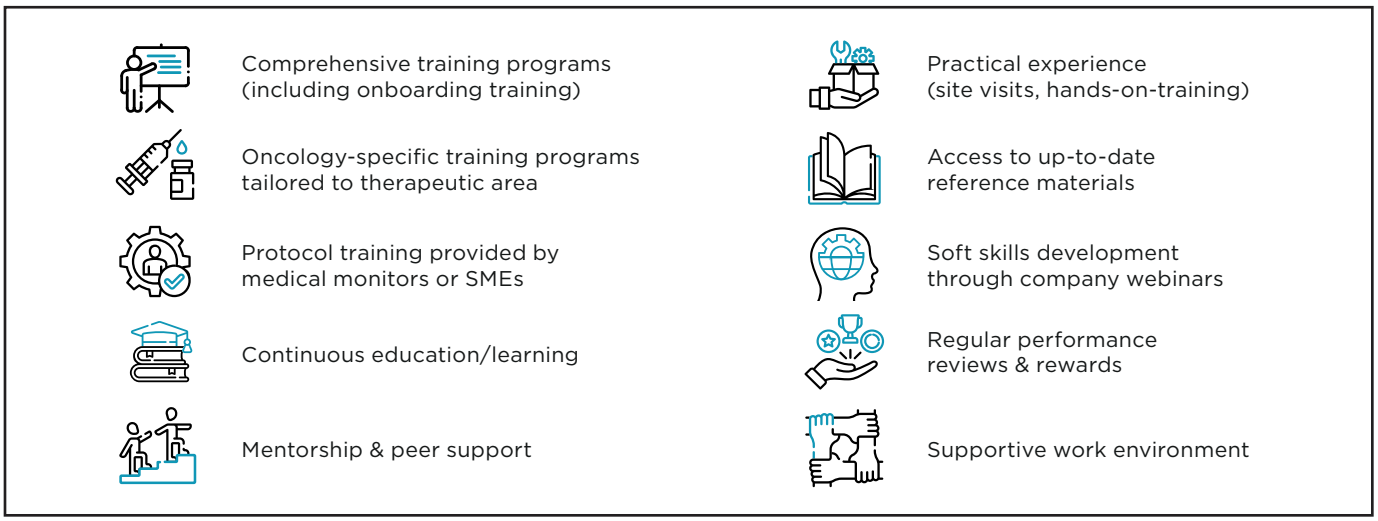


Figure 1. *How to prepare CRAs for success.*

The Unique Challenge of Oncology Studies

Some specific considerations for CRAs working in oncology accentuate the importance of dedicated training in this therapeutic area. Challenges revolve around the complexity of the design of Phase I oncology programs, the unique requirements of site selection and staff credentialing, and issues regarding patient recruitment and retention.

For example, unique challenges associated with increasingly complex oncology designs include widespread use of adaptive trial methodology, highly detailed eligibility criteria, personalized treatment plans, and multiple study endpoints, which are emblematic of this therapeutic area, requiring comprehensive CRA training.[1] At the site level, CRA activity may inform the modification of key design elements for an ongoing study, particularly in Phase I clinical research characterized more by learning rather than confirming. For example, given the significant morbidity associated with cancer and the potential risks related to investigational products, ensuring patient safety is critical. For Phase I research, limited numbers of patients commonly inform this at a given dosage level and duration of exposure.

Site selection can significantly impact study start-up timelines and overall study metrics, so choosing an appropriate site with the ability to conduct oncology trials within the framework of internationally accepted good clinical practice (GCP) guidance is critical. CRAs must assess site qualifications regarding facilities and staffing, initiate sites, including contracting and ethics committee requirements, and ensure adequate preparation of each center to handle the unique demands of an oncology trial, with the specific pharmacological attributes of the test agent.

Patient recruitment and retention can be difficult in oncology studies due to the disease burden, demanding treatment schedules, and adverse events. Comparable challenges exist across therapeutic areas where there is a significant unmet need.[2] As a result, CRAs must ensure that they adequately support sites to enhance patient recruitment and retention and that sites are well-equipped to handle the complexities of an oncology clinical trial.

A Mosaic of Measures and Endpoints

Oncology studies collect biomarker and genetic data to create a more comprehensive assessment of treatment outcomes. As a result, CRAs must also ensure these samples are collected, processed, and

stored appropriately during the trial.[3,4] Given that oncology trials require collaboration with a diverse range of specialists (e.g., oncologists, radiologists, and pathologists), CRAs must be able to coordinate activities across a multidisciplinary team to ensure smooth study execution.[5]

As in other therapeutic areas of industry-sponsored research, oncology studies are subject to stringent regulatory oversight. CRAs must ensure that all regulatory documents are current, and that the study complies with local and international regulations, such as those set by the FDA, EMA, or other regulatory bodies. Thorough CRA training fosters confidence, saves time, facilitates asking more critical questions throughout the study, and permits CRAs to be a study asset. Understandably, oncology trials generate a large amount of data, including laboratory and imaging results and clinical assessments (e.g., clinician-based, observer-based, performance-based, and patient-derived). In aggregate, these data requirements accentuate the need for scrutiny in a heavily regulated environment. Finally, CRAs must ensure accurate and timely data collection, verification, and entry into electronic data capture `systems to fully enable the determination of fundamental quality metrics across a multicenter study on an ad hoc
level if required.

From Theory to Practice: Real-World Challenges in Oncology CRA Training

Multimodality training programs are characteristic of the challenges clinical trials must address in successful CRA training. For example, a practical training approach uses “lunch and learns” with the CRA team, allowing for a casual, open forum once a month where CRAs can discuss their roles or any issues that have arisen since the previous meeting. These topics are often suggested by the CRAs themselves, either through their requests for additional information or by sharing lessons learned from recent, relevant, and real-life experiences.

Moreover, protocols can be amended multiple times during the study, requiring ongoing training and updates to keep CRAs informed of the latest changes, with an ability to inform study site staff of those changes in a timely and meaningful fashion. Beyond role training, it is also an excellent space for CRAs to gain practical experience with public speaking, training techniques that are potentially useful to site staff and presentations. Furthermore, CRAs should participate in study-specific continued learning and eLearn activities for protocol training to assess comprehension throughout the course. This also promotes mentorship between the medical team and clinical trial managers. Incorporating training based on lessons learned at predefined milestones is also a good idea.

Specialized Training

- Specialized assessments and measures based on therapeutic area
- Indication and protocol-specific training
- Clearly delineated roles with focus on unique components of each role

Depth vs. Breadth

- Balance between comprehensive overview and critical areas
- Theoretical knowledge and practical, hands-on experience
- Critically assess data completion, accuracy, and that it makes sense

Variable Background Experience

- Accommodate different levels of prior knowledge and experience
- Ongoing professional development to keep up with changes

Adequate Resources for Training

- Time, cost, and access to training
- High-quality training agnostic of region, education, background, or employer

Specialized Training:
Different therapeutic areas require specialized assessments and measurements. In oncology, CRAs need to understand general oncology-relevant training while balancing indication- and protocol-specific training, including tumor and safety assessments. Cell and gene therapy with CRISPR, for example, requires specialized training. Clearly delineating roles and focusing on the unique components of each role ensures successful and adequately run trials.

Depth vs. Breadth:
It can be a challenge to define training requirements while balancing depth and breadth, which means that training programs must strike a balance between providing a comprehensive overview of essential topics and delving into specific areas critical to a CRA's role. In addition, finding the right balance of theoretical knowledge and practical, hands-on experience is essential but complex. Further, as more and more data become available in real-time during study conduct, CRAs are expected to understand the relationship between them and be able to critically assess if the data are complete, accurate, and if they make sense when considered overall.

Variable Background Experience:
CRAs come from a range of educational and professional backgrounds, so training programs must accommodate different levels of prior knowledge and experience. Beyond the initial training, CRAs require ongoing professional development to keep up with changes in oncology, necessitating continuing educational opportunities.

Adequate Resources for Training:
Time, cost, and access to training are also issues. Creating and delivering comprehensive training programs can be time-consuming and costly, posing challenges for organizations with limited resources. Furthermore, ensuring that all CRAs have access to high-quality training, regardless of their geographic region, educational or professional background, individual learning styles, or employer, is another hurdle.

Regulatory Compliance:
Another challenge faced is the ongoing regulatory changes for clinical trials, which include new guidelines and requirements introduced regularly by regulatory bodies, such as the FDA and EMA. Keeping training materials current can be a constant challenge. Furthermore, regulatory requirements can differ significantly across regions, necessitating the knowledge of multiple regulatory environments for CRAs who are working on global studies.

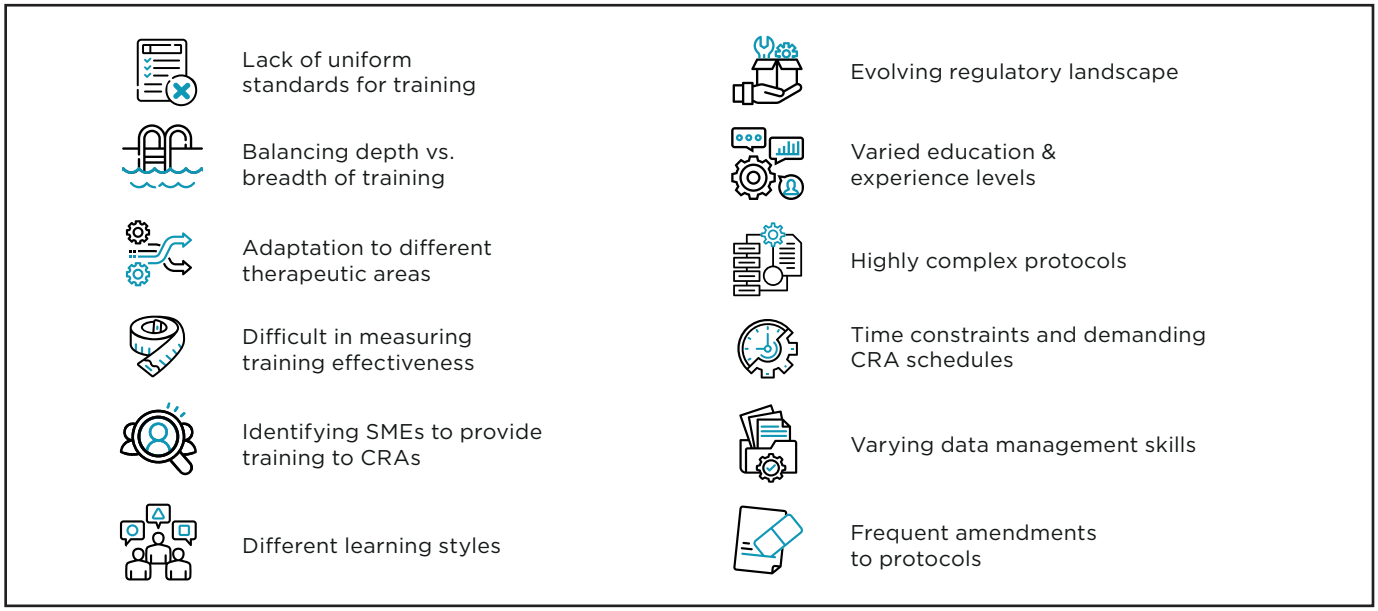


Figure 2. *Challenges in defining training requirements.*

Unifying Training Programs: Bridging the Gaps in Standards

In addition to the unique oncology-related challenges, the need for harmonization in CRA training programs can pose obstacles to clinical research across sponsors, therapeutic areas, treatment modalities, and geographical regions. Commonly encountered challenges include inconsistent training quality and variations in skills and knowledge, even within project teams experienced in oncology research. Such challenges collectively impact data quality and integrity, operational deficiencies, regulatory noncompliance, and collaboration with others in the field due to varying expectations regarding monitoring competencies.

Therefore, consistency in training programs is critical for reliable data and participant experiences across sites. However, different training programs may emphasize different concepts and training modules, which becomes even more challenging in multi-regional studies with various regulatory bodies. Balancing the consistency and amount of information to avoid overload while keeping training materials relevant is vital. Current GCP training guidelines stipulate that CRAs should have the necessary scientific, clinical, and regulatory knowledge to monitor a study adequately. Still, detailed scientific or medical information may be extraneous. Regardless, clinical research training programs offered by organizations such as Certified Clinical Research Professionals Society, Society of Clinical Research Associates, or Association of Clinical Research Professionals still lack clear guidelines or requirements for minimum training/education requirements for CRAs.

Oncology trials specifically require additional specialized training in managing serious adverse events, as these trials often follow patients until their death. Therefore, CRAs should have a thorough understanding of safety reporting requirements and the range of potential toxicities that might be encountered based on the specific indication and the nature of the pharmacological properties of the investigational product. However, defining the SMEs for the training content can present added complexity when developing training materials. Trainers need not always be the SME for the content in development, making it challenging to identify the best SME stakeholder to help build the material. Moreover, additional unique oncology trial challenges include role variability depending on the clinical trial phase or therapeutic area.

There is a need to develop uniform standards for training programs incorporating a common curriculum. Worldwide's CRA Academy aims to bring together the necessary components to ensure uniform, consistent, and reliable training for individuals transitioning to the CRA role. The CRA Academy provides the foundational knowledge of their roles and responsibilities.

Beyond Traditional Methods: Revolutionizing CRA Training for Optimal Performance

Mentors

It has been axiomatic across various disciplines within medicine that "one-on-one" mentoring in the direct application of any given task can be extraordinarily effective. On-the-job training, pairing new CRAs with experienced mentors within their intended therapeutic area, and open communication with medical monitors are crucial for effective learning. Trialists should encourage CRAs to participate in mentorship programs, matching less experienced CRAs with seasoned peers who can provide guidance, support, and progress evaluations.

Critical components of a mentorship program include identifying experienced medical professionals with extensive clinical research experience and a strong background in the relevant therapeutic areas for the conducted trials. Mentorship activities should consist of regularly scheduled meetings to discuss any trial-related issues, challenges, and learning opportunities, discussions of case studies and real-world examples to improve problem-solving and decision-making skills, provide constructive feedback and regular evaluations of the mentorship program's effectiveness using surveys and participant feedback.

When pairing CRAs with medical monitors, it is vital to consider the therapeutic area and acknowledge the career goals and eagerness to mentor others in the field to ensure the success of the mentor-mentee relationship. Doing so will ensure that CRAs better understand medical and clinical research concepts and can identify and confidently address issues that arise during study conduct. For organizations, this will increase CRA retention and job satisfaction, create a skilled and knowledgeable workforce, and ensure high quality and compliance in clinical research.

Additionally, providing CRAs with a medical mentor can significantly improve their professional development and the quality of clinical trials. It is helpful to emphasize the importance of mentoring experiences and point CRAs to other publications addressing training within formal GCP guidelines. Experience, the ability to observe colleagues and mentors is essential to supplement formal training with variables related to experience, working across different types of studies, participation in pharmaceutical-sponsored clinical trials, and the total amount of hours spent in training ranked in that order of importance.[6] This mentorship program should help CRAs better understand medical and clinical research concepts, strengthen their decision-making during monitoring activities and site management, promote continuous learning, and address questions about the therapeutic area or the investigational product.

Universal Training Requirements

Furthermore, potential mitigation strategies include developing universal training requirements and competencies for CRAs to ensure consistent knowledge and skills across the board. Creating and fostering certification programs ensures CRAs have met the specific training and competency required for clinical research. Implementing mandatory continuing education for CRAs can help keep their knowledge and skills up to date with the rapidly evolving landscape and current guidelines. Studies should prioritize collaboration among stakeholders to develop and implement standardized training programs (**Figure 3**).

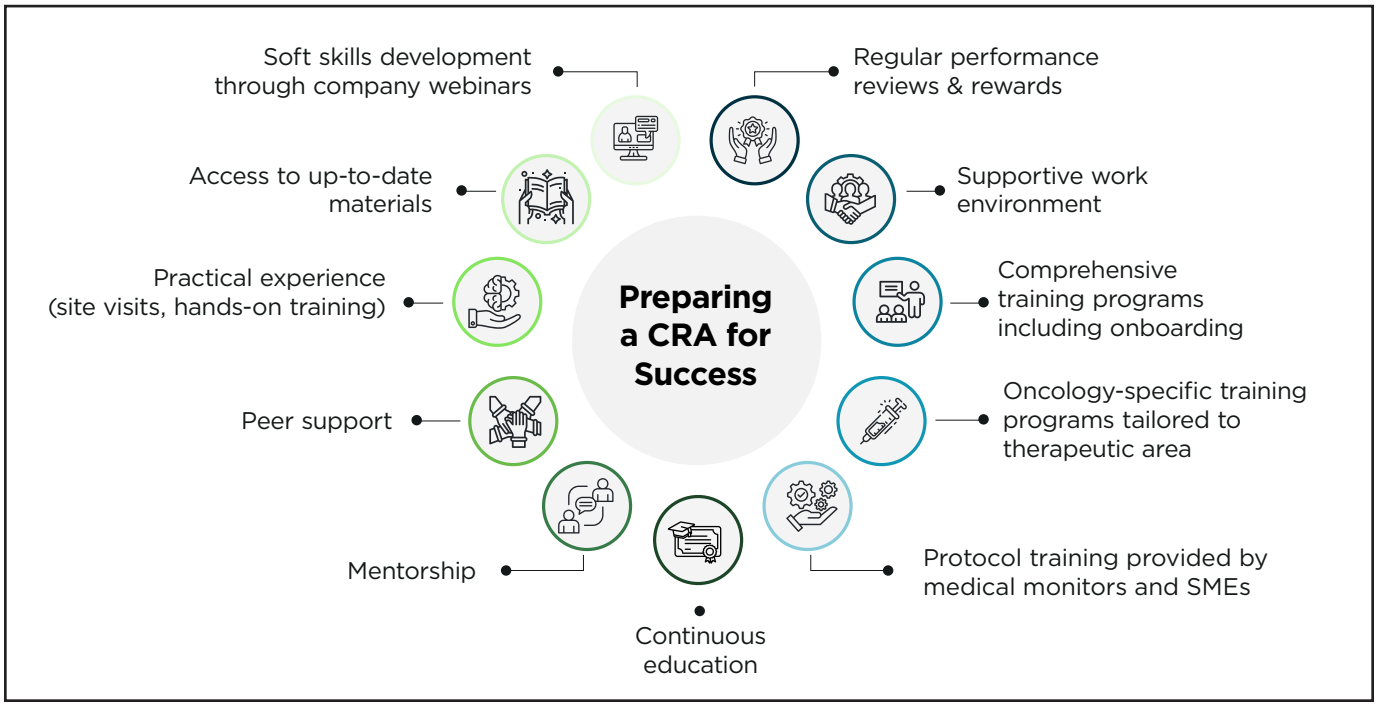


Figure 3. *Training and preparation encompass a wide array of factors for success.*

Regular Competency and Task Assessments

In most respects, the assessment of competencies will cover the domains reported by other research professionals. These include general operation and management, regulatory requirements for developing novel therapeutic entities, the ethical conundrum of balance in clinical care and clinical management for research purposes, unique data collection, and management challenges, and the overall scientific framework justifying the study.[7] These assessments help identify further training needs and ensure optimal CRA performance. These assessments can inform revised training programs and address any gaps in initial training. Integrating regular oncology summits for clinical trial managers and CRAs, focusing on core concepts ensures information is relayed accurately and keeps everyone on the same page. Regular assessments help identify areas where CRAs may need additional training or support, ensuring they are current on industry practices and regulations. In addition, these assessments provide feedback that trainers can use to improve CRA performance, promote a culture of continuous improvement and standardize practices across different sites and studies, resulting in more consistent and reliable trial outcomes while ensuring clinical trial quality and compliance.

Developing a comprehensive framework that assesses competency and outlines the essential skills and knowledge required for CRAs is critical and should be consistent with industry standards and regulatory requirements. This can be particularly challenging as perceived self-competencies across key domains often differ substantially based on the background of the individual queried.[8] Quizzes, practical tests, performance reviews, and peer evaluations are all examples of tools that educators can use to assess theoretical knowledge and practical skills. The implementation of regular assessments should follow this to ensure continuous evaluation and improvement. CRAs should also be encouraged to attend workshops, webinars, and courses to keep their skills current.

The Evolution and Future of CRA Academies

Changes in industry standards, technological advances, and a focus on professional development and continuous learning will likely impact the future of CRA training. Using e-learning platforms that provide interactive and customizable training modules allows CRAs to access training materials at their leisure. It facilitates continuous learning and monitoring of CRA competency with an increasingly dispersed workforce.

Virtual training can make continuous learning more efficient and deliver training at the right time. Implementing artificial intelligence to personalize these training programs can assist CRAs in progressing and analyzing their performance to identify knowledge gaps and additional training requirements, something that medical education programs are already exploring.[9] As is true in all therapeutic areas, training for CRAs should be tailored to their specific roles and responsibilities within clinical research. This may include specific training for different therapeutic areas, study phases, and types of clinical trials.

Currently, across the industry, CRA academies can offer an on-site CRA traveling training series in which academy participants travel to investigative sites with experienced CRA mentors who provide on-the-job training for the various monitoring visits. In addition, CRA training programs include a competency or task assessment, as well as an on-site visit assessment tool for our CRAs of all experience levels.

Current and future goals emphasize advanced therapeutic training for specific oncology indications such as cell therapies and bispecific antibodies. The collective goal is to provide solid training to CRAs, empowering them to ask more informed and informative questions. By continuously improving training programs, the pharmaceutical industry aims to enhance the quality and efficiency of clinical trials.

For more details or to discuss how the method and technique of CRA training in oncology at Worldwide can benefit a clinical trial, contact us.

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