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(REVIEW ARTICLE)

Innovation and strategy in clinical research with the SCIO℠ method

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Abstract

Innovation in clinical research is a long-term need due to several factors, including the high failure rate and skyrocketing costs. Healthcare has been changing rapidly for many years. The COVID-19 pandemic has accelerated by helping drive the shift to value-based healthcare. Instead, the productivity of pharmaceutical development has been declining due to high failure rates in clinical research. The SCIO method is an innovative and strategic method implementing a tailored approach to drug development. The SCIO method customizes strategy and roadmap for pharmaceutical and biological candidates allowing robust clinical data generation and informed decision-making during the early clinical development stages.

The complexity of diseases contributes to the high failure rate and increases the cost of research. Clinical research in developing new drugs and treatments is associated with a high late failure rate. Late-stage trial failures can delay patients' access to potentially lifesaving or disease-modifying treatments.

Strategy is valuable in reducing late clinical trial failure. A well-developed and carefully executed strategy helps mitigate risks, optimize trial design and execution, and increase the chances of successful outcomes. A failed trial can harm the credibility by raising concerns about the research methods, the quality of the data, or the reliability of the therapy under investigation.

The SCIO is an innovative drug development method, including a strategic approach before initiating clinical trials that ensure a solid scientific basis and a reasonable likelihood of success in human trials.

Keywords: Early Clinical Studies; Drug Development Strategy; Regulatory Strategy; Translational Medicine; Clinical Plan Innovation; Clinical Trial; Clinical Research Organization; Strategy Clinical Plan; Clinical Research

1. Introduction

This article examines the pharmaceutical and biotechnology industry's challenges, including the high failure rate and skyrocketing costs. The complexity of diseases contributes to the high failure rate and increases the cost of research. New drug and treatment development is associated with a high late failure rate. Late-stage trial failures can delay patients' access to potentially lifesaving or disease-modifying treatments. Many technologies have been adopted in recent years, focusing on data collection and other aspects of clinical trial tactics. These technologies promise to reduce costs and improve the failure rate. Unfortunately, that goal was not reached. We can find the cause of it due to the common mistake of using yesterday's assumptions for tomorrow's drug development. Based on the belief that there is no goal without a strategy and that any drug development needs a strategy to generate quality data, this article presents the value of a clinical strategy and the high impact of an Early Clinical Strategy.

The innovative method proposed helps unravel the complexity of diseases, integrates clinical and regulatory finding with non-clinical evidence, and use AI and data analytics to enhance trial efficiency, and optimize trial design and execution.

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2. Innovation is a long-time need

Innovation in clinical research is a long-term need 1 due to several factors, including the high failure rate and skyrocketing costs. Many diseases, especially chronic and complex conditions, have multifactorial causes and heterogeneity among patients. Understanding the underlying mechanisms and identifying effective treatments for such diseases remains challenging. The complexity of diseases contributes to the high failure rate and increases the cost of research. New drugs and treatments development is associated with a high late failure rate. Late-stage trial failures can delay patients' access to potentially lifesaving or disease-modifying treatments. Patients eagerly anticipating the availability of a new therapy may face prolonged waiting periods or must explore alternative treatment options, which can be particularly challenging for patients with severe or life-threatening conditions who require effective treatments. In addition, clinical trial failures can harm the reputation and credibility of the organizations involved. Failed trials may raise concerns about the research methods, the quality of the data, or the reliability of the therapy under investigation. Rebuilding trust and regaining credibility after a high-profile trial failure can be challenging and time-consuming. The high failure rate underscores the need for continuous innovation to improve the success rate and increase the chances of identifying effective treatments.

Several factors contribute to the skyrocketing cost of clinical trials. A) The integration of advanced technologies and techniques, such as genetic sequencing, biomarker analysis, imaging technologies, and electronic data capture, has become more prevalent in clinical trials. While these technologies offer valuable insights, they incur additional equipment, training, data analysis, and interpretation costs. B) The complexity of study designs, such as adaptive trial designs or combination therapy trials, has risen in recent years. These designs require more sophisticated statistical analyses, monitoring, and regulatory oversight, contributing to increased costs. C) Regulatory bodies have implemented more stringent requirements for clinical trials to ensure patient safety and data integrity. Compliance with these regulations adds complexity and increases the costs of trial design, documentation, monitoring, and reporting. In addition, we should remember that the cost of developing and manufacturing investigational products, including drugs, biologics, and medical devices, has risen significantly.

Clinical trial sites and investigators play a crucial role in the successful execution of trials. Costs associated with site selection, training, monitoring, and compensation for investigators and study staff contribute to the overall trial expenses. Large sample sizes to demonstrate the statistical significance and adequately represent diverse patient populations, recruiting and retaining many participants, and longitudinal follow-up to assess long-term safety and efficacy outcomes in chronic conditions contribute to the overall cost of clinical trials. Addressing these factors requires innovation and strategy, which integrates optimization of trial design, streamlining regulatory processes, enhancing patient recruitment strategies, leveraging real-world evidence, and using advanced technologies. By understanding these cost drivers, it may be possible to mitigate the skyrocketing costs of clinical trials and make the process more efficient and accessible.

Many diseases, especially chronic and complex conditions, require a deep understanding of their molecular and genetic characteristics and their interaction with environmental factors. Innovation in clinical research helps unravel the complexity of diseases, leading to the development of targeted therapies and precision treatment approaches. Healthcare has been changing rapidly for many years. The COVID-19 pandemic has accelerated by helping drive the shift to value-based healthcare, the rate of change like never before. Instead, the productivity of pharmaceutical development has been declining due to high failure rates in clinical research. Clinical research represents a fulcrum for developing safe and effective drugs on time. Clinical trials are expensive and often burdensome on patients. The resources, time, and funding investments grow with the clinical development moving to successive stages, from pre-clinical to phase 3. Thus, the cost of a failed phase 3 trial is not just the cost associated with the trial itself but the cost of all prior research and trials and the cost of lost time pursuing a potentially viable alternative.

3. The SCIO℠ method

SCIO in Latin means to know, to understand, and the knowledge of "How-to." SCIO is the acronym for "Strategic Clinical Innovation Organization." It has been developed to address cost efficiency and risk management from pre-clinical to market drug development. It involves an innovative method to establish specific clinical and regulatory strategies and roadmap as part of a pre-IND and IND submission before starting tactical clinical activities by Clinical Research Organization (i.e., CRO).

The SCIO method finds its innovative and strategic development method in the rare disease drug development knowledge and experience. Clinical trials for rare diseases require a tailored approach, collaboration, flexibility, and

patient engagement. These elements have proven to be critical for the success of trials and drug market approval. The Rare Diseases drug development approach anticipated and paved the precision medicine revolution. Thus, the SCIO method is an innovative and strategic method implementing a tailored approach to the drug development for chronic diseases. As shown in Figure 1, the SCIO method includes early clinical research and regulatory strategy, innovative trial design, adoption of biomarkers, patient centricity, technologies' adoption. Early clinical research and translational medicine are the foundation of drug development. They provide valuable insights into safety, efficacy, optimal dosing, and biomarker utilization, ultimately improving patient care and facilitating the development of new and effective treatments 2.

To develop a new drug takes over 10–15 years for drug discovery and development, with an average cost of over $1–2 billion 3 It is also true that more than 90% of the drug candidates that enter Phase I trials fail adding cost to the overall drug development 4 Unfortunately, the advancement of modern technology didn't help bring the development years, its price, and the failure rate down meaningfully. That is why the clinical research development method requires innovation, which would be a long-term need if the need for medicine exists. The clinical trial process has stayed the same for decades. Although we are witnessing the adoption of multiple tools and technologies, they cannot solve the core problems of high expense or failure. Current challenges such as patient enrolment, lower patient retention rate, complexities around CRO selection and management, and protocol complexities severely delay or restrict small and medium biotech companies from introducing a product to market at the right time. The SCIO method devises an innovative translation and early development approach, which integrates nonclinical evidence into clinical research, thus supporting the regulatory strategy and building the efficacy and safety evidence since the first man to reduce risk in late clinical trials while preparing the product for market positioning.

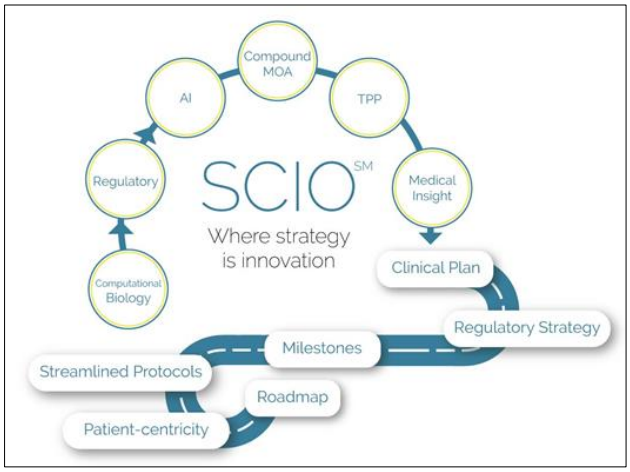

Figure 1 The SCIO[SM] Strategy and Innovation method

The SCIO overcomes the silos and, at a time, approaches, promoting a perfect match between the product mechanism of action (MOA) to the target indication.

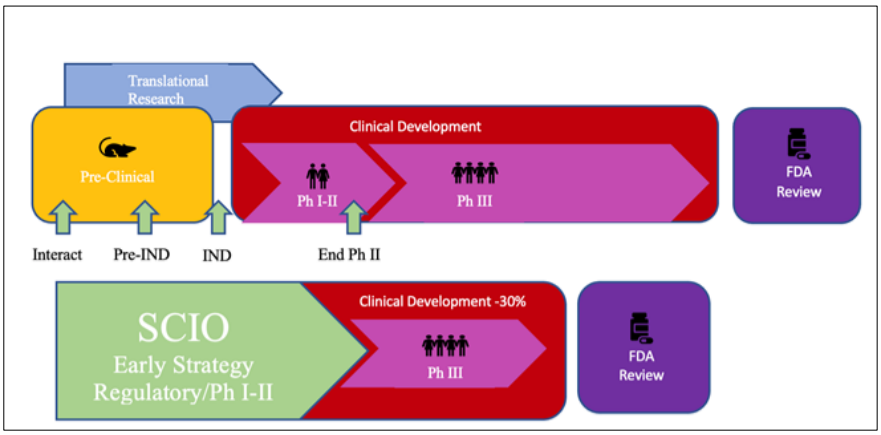

Figure 2 The SCIO[SM] method

The SCIO's objective is to innovate and advance the clinical development process, improving clinical trials' efficiency, effectiveness, and outcomes. The SCIO employs strategic approaches and adopts innovative practices to overcome the challenges associated with traditional clinical development. Leveraging artificial intelligence (AI), data analytics, and a deep understanding of regulatory affairs and medical knowledge to streamline processes, enhance patient recruitment and engagement, and optimize trial design and execution. The ultimate goal of the SCIO method is to innovate the clinical research process. Thus, SCIO has been evolving alongside advancement with new technologies and cutting-edge scientific concepts. That is why SCIO tackles the challenges coming with traditional clinical development and transforms itself to meet products' specific needs. As shown in Figure 2, SCIO bridges the non-clinical research and translational medicine with first-in-human phase 1/2A studies to reduce risk over the so-called Death Valley as well as late-stage failures. Integrating regulatory requirements with clinical needs in the early product's development strategy sets a roadmap that streamlines the clinical plan and study designs. The SCIO generates a clear roadmap from the first in human to the market approval before the start of tactics activities and study implementation, resulting in a time and cost saving of up to 30% in trials expense.

Based on the belief that there is no goal without a strategy, any drug development needs a strategy to generate quality data. SCIO is designed to help pharmaceutical innovators to address their concerns, maneuver around evolving challenges, identify time and cost efficiencies, and relieve risk management on their journey to market approval. The SCIO method allows for better decisions leveraging the potential of each asset generating strategic options.

Drug development and clinical research require deep experience. However, we often must correct a common mistake using yesterday's assumptions for tomorrow's drug development. Today's technological molecules require innovation in the development process. Evidence from marketed products proves that identical molecules developed by different sponsors generated variable drug opportunities. Drug development involves a high level of complexity, and factors contributing to the success or failure of a drug which can be multifaceted, including clinical trial outcomes, safety concerns, efficacy, market demand, competition, and regulatory decisions. Data also shows that an early strategy, from indication selection and validation into phase I-II trial, leads to a competitive advantage that a late development redirection of optionality and decisions cannot replace. It indicates that with different strategies, one product may have different destinies. That is why weighing options before starting regulatory activities and ensuing clinical execution is essential, which means bringing together the right population with meaningful endpoints, clinical and surrogate, and negotiating with the regulators.

The SCIO method customizes strategy and roadmap for each pharmaceutical and biological candidate. It allows for robust clinical data generation and informed decision-making during the clinical development stages. The SCIO assesses the potential of the preclinical asset, evaluates the level of certainty for strategic options, analyzes various data sources for patient enrollment and recruitment, optimizes trial design including predictive modeling, implements risk assessment/mitigation with real-time monitoring, supports decisions making with safety and efficacy data analysis. A successful clinical development for drug and medical device companies requires an early strategy with a flexible roadmap that makes it actionable and sustainable. A customized strategy and roadmap allow for robust clinical data generation and informed decision-making. Setting clear goals is essential to managing risk and pre-empting challenges.

4. Early strategy, between nonclinical and first in human, improves productivity and reduces risk of failure

Early clinical research and translational medicine are critical in advancing medical knowledge, improving patient care, and accelerating the development of new therapies. Translational medicine focuses on moving scientific discoveries from bench into bedside for patient care. It facilitates moving basic research findings into clinical practice and therapeutic interventions. Early clinical research is crucial in evaluating the safety, efficacy, and feasibility of novel treatments. Early clinical research enables identifying and validating biomarkers, genetic markers, patient stratification strategies, and other predictive factors that can guide clinical research accelerating the development of targeted new therapies. By identifying promising compounds early on and efficiently evaluating their safety and efficacy, researchers can streamline the development pathway and quickly bring new treatments to patients. Through phase I and II clinical trials, sponsors can assess the safety, dosage, and potential efficacy of novel drugs, or medical devices. Phase 1/2 trials provide the foundation for subsequent larger-scale trials and regulatory approval processes. Early clinical research can identify ineffective or unsafe interventions, thus, saving resources, and preventing potential harm. Translational medicine investigations, by studying patient populations and clinical data, can unveil valuable insights into the underlying mechanisms of diseases, and understand diseases' pathophysiology, progression, and heterogeneity. Early clinical research allows for the assessment of treatment safety and the monitoring of adverse effects. Phase I clinical trials, specifically designed to evaluate safety and dosage, provide crucial information on potential risks and side effects

associated with new treatments, which knowledge can refine interventions, optimize dosages, and ensure patient safety in subsequent clinical trials and clinical practice.

Avoiding late-stage clinical trial failures requires careful planning, diligent execution, and ongoing evaluation throughout the entire trial process. Before initiating clinical trials, extensive preclinical research is conducted to gather comprehensive data on the investigational therapy's safety, efficacy, and mechanism of action. It ensures the treatment has a solid scientific basis and a reasonable likelihood of success in human trials. The clinical trial design should be carefully considered to maximize the chances of success, which includes defining clear objectives, selecting appropriate endpoints, determining sample size, and establishing inclusion/exclusion criteria. Proper patient selection is critical to the success of a clinical trial. Eligibility criteria must be well-defined and designed to include patients most likely to benefit from the therapy being tested, including disease stage, biomarker status, and relevant patient characteristics. Conducting pilot studies and phase I/II trials before large-scale phase III trials gather important preliminary data, assesses safety and efficacy, and informs decision-making for the subsequent trial stage. An iterative method allows for the early identification of potential issues and course correction when needed. Conducting a thorough risk assessment before and during the trial is crucial. Identifying and mitigating potential risks early on can help prevent or minimize late-stage failures. Risk assessment includes the evaluation of scientific, operational, regulatory, and patient safety risks. Implementing robust data monitoring and analysis processes is essential for evaluating trial progress. Regular data reviews help identify trends, assess safety signals, and make informed decisions about trial continuation or modification. Engaging multidisciplinary teams and seeking input from key opinion leaders and experts in the therapeutic area provides valuable insights and perspectives. Collaboration with experienced investigators, biostatisticians, and regulatory and clinical research experts helps optimize trial design, reduce biases, and ensure compliance with regulatory requirements. Clear and transparent communication among stakeholders is crucial throughout the trial. Communication includes open and frequent communication with regulatory agencies, ethics committees, investigators, and patients. In addition, transparent reporting of trial results, regardless of the outcome, contributes to the scientific community's collective knowledge. Clinical trials must be viewed as iterative processes that allow for continuous learning and adaptation. Regular trial data analysis, emerging scientific knowledge incorporation, and flexibility in adjusting trial protocols based on new information help mitigate risks and improve trial outcomes. Implementing appropriate strategies minimizes the risk of late-stage trial failures and increases the chances of successful outcomes.

Early strategy can facilitate the adoption of alternative paths in several ways. Developing an early strategy allows organizations to align sponsor’s objectives and priorities with potential benefits and capabilities. By clearly defining the goals and desired outcomes, organizations can identify areas where AI can be most beneficial and focus their efforts accordingly. Various algorithms and computational methods are employed to aid in discovering, designing, and optimizing new drugs. Examples are the machine learning algorithms that help predict outcomes such as disease progression, treatment response, adverse events, or patient stratification based on various clinical and molecular data; analysis of large-scale genomics, proteomics, and metabolomics data which can uncover patterns, correlations, and molecular signatures that may be indicative of specific clinical outcomes or treatment efficacy; help identify potential safety concerns, drug-drug interactions, and signal detection from real-world data sources; and optimizing clinical trial design like adaptive trial design algorithms which dynamically adjust trial parameters based on accumulating data, optimizing the patient allocation and treatment regimens. The algorithms depend on the research question, available data, and the desired outcome.

Early strategy can involve conducting proof-of-concept studies to evaluate AI adoption's feasibility and potential benefits in specific areas of interest. Proof-of-concept studies provide valuable insights and inform the decision-making process for AI adoption. An early strategy helps organizations assess resource needs and allocate them effectively to support studies implementation. Organizations can proactively address critical considerations and lay the foundation for successful clinical research by developing an early strategy.

5. Strategies and Innovation in Early Clinical Research

Strategy is of great value in healthcare and medicine. Clinical trials are vital for evaluating the safety and efficacy of new therapeutics and interventions. However, they are complex, time-consuming, and costly. A well-designed early strategy streamlines clinical trials by identifying patient populations, defining endpoints, optimizing study designs, and leveraging innovative technologies, expediting new therapies' development and regulatory approval. A well-defined early clinical development strategy provides a clear roadmap and direction for decision-making in healthcare and medicine. It helps stakeholders align their efforts and prioritize resources. A strategic approach ensures that actions are purposeful and focused on achieving desired outcomes. Healthcare resources, including funding, personnel, and infrastructure, are often limited. A strategy optimizes resource allocation by identifying priorities, setting goals, and

allocating resources to maximize their impact. It is essential in high technology product trials, where efficient use of resources can accelerate development and improve patient outcomes. Clinical research in modern healthcare is increasingly complex. Precision medicine and targeted therapies require a deep understanding of diseases underlying mechanisms and heterogeneity. A strategic approach enables researchers and clinicians to navigate this complexity, identify alternative therapeutic approaches and develop innovative treatment that target specific disease characteristics.

Strategy is valuable in reducing late clinical trial failure. A well-developed and carefully executed strategy helps mitigate risks, optimize trial design and execution, and increase the chances of successful outcomes. A strategic approach involves conducting a comprehensive risk assessment to identify potential risks and challenges that may arise during the trial. By proactively identifying these risks, strategies can be developed to mitigate them and minimize their impact on the trial's success including addressing scientific, operational, regulatory, and patient safety risks. Strategy is crucial in optimizing the trial design to increase the likelihood of success including carefully considering patient selection criteria, endpoints, sample size, statistical power, and control group selection. A well-designed trial that aligns with the strategic objectives of the study increases the chances of generating meaningful and reliable results. Precision medicine approaches and the use of biomarkers helps identify patient subgroups that are more likely to respond to investigational therapy. Developing a strategy incorporating patient stratification based on biomarkers or other relevant factors increases the chances of demonstrating efficacy and reducing the likelihood of late-stage trial failures.

Strategy guides the implementation of robust data monitoring and analysis processes throughout the trial which include defining appropriate data monitoring committees, establishing clear analysis plans, and conducting regular interim analyses. By closely monitoring the trial data, early signs of efficacy or safety concerns can be detected, allowing for timely decision-making and potential course correction. A strategic approach involves:

- Proactively engaging with regulatory agencies
- Understanding their requirements
- Ensuring compliance throughout the trial
- Regular communication
- Adherence to regulatory guidelines
- Addressing any concerns or questions regulatory authorities raise.

By maintaining a strong relationship with regulatory agencies, the likelihood of regulatory obstacles leading to trial failure can be reduced. Strategy can incorporate adaptive trial designs that allow for modifications to the trial protocol based on accumulating data. This adaptive approach allows for flexibility in response to emerging information, ensuring that the trial remains aligned with the strategic goals and increases the chances of success.

The strategy encourages collaboration and partnerships among various stakeholders involved in the clinical trial process. Such partnerships foster exchanging knowledge, resources, and expertise, improving the trial design, implementation, and patient recruitment. By incorporating strategic elements into the clinical trial process, the risks of late-stage trial failures can be minimized, and the chances of successful outcomes can be increased. Strategy provides a framework for thoughtful decision-making, risk management, and optimization throughout the trial, ultimately contributing to a higher likelihood of success.

Innovation, including AI, epigenetics, genetics, metabolomics, and other emerging areas, is essential in drug development and driving the expansion of knowledge to explore new frontiers, uncover novel insights, and deepen our understanding of complex biological processes. For example, epigenetic and genetic research can provide valuable information about an individual's susceptibility to certain diseases, enabling personalized prevention and treatment plans. Metabolomics can reveal metabolic profiles and biomarkers that aid in early disease detection and personalized therapy selection. Innovation is vital for addressing unmet medical needs and tackling challenging health issues. Researchers and innovators can address diseases and conditions with limited treatment options by thinking outside the box and developing novel solutions. For example, advancements in gene therapy have brought new hope to individuals with genetic disorders by providing potential cures or disease-modifying treatments. New technologies, tools, and treatment modalities allow healthcare providers to deliver more precise, targeted, and special care. For instance, genomics and molecular profiling innovations contribute to precision medicine, enabling tailored therapies that result in improved treatment responses and reduced side effects. Innovation often leads to increased efficiency and cost savings in healthcare. New technologies and approaches can streamline processes, improve workflow, and reduce the burden on healthcare systems. Moreover, innovations that improve healthcare delivery and outcomes contribute to a sustainable healthcare system by reducing costs, optimizing resource allocation, and improving patient outcomes.

Innovation and early strategy enable sponsors to collaborate on complex problems and accelerate the pace of clinical research, leading to more impactful research and translation into clinical practice.

6. Conclusion

Pharmaceutical productivity has been declining due to the high clinical trial failure rate. Clinical research represents a fulcrum for developing safe and effective drugs on time. Clinical trials are expensive and often burdensome on patients. The resources, time, and investment grow with the successive stages, from pre-clinical to phase 3. Thus, the cost of a failed phase 3 trial is not just the cost associated with the trial itself but the cost of all prior research and trials and the cost of lost time pursuing a potentially viable alternative. Strategy fosters exchanging knowledge, improving trial design patient recruitment, minimizing risks of late-stage trial failures, and increasing chances of a successful outcome can be increased. Strategy provides a framework for thoughtful decision-making, risk management, and optimization throughout the trial, ultimately contributing to a higher likelihood of success. Early strategy can facilitate the adoption of alternative paths in several ways. Developing an early strategy allows organizations to align the sponsor's objectives and priorities with potential benefits and capabilities.

In conclusion, we described that an early strategy can significantly benefit traditional clinical research. The SCIO aims to innovate and advance the clinical development process, improving clinical trials' efficiency, effectiveness, and outcomes. The presented method employs strategic approaches and adopts innovative practices to overcome the challenges associated with traditional clinical development. The SCIO method devises an innovative translation and early development approach, which integrates nonclinical evidence into clinical research, thus supporting the regulatory strategy and building the efficacy and safety evidence since the first man to reduce risk in late clinical trials while preparing the product for market positioning.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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