Clinical Cancer Research (CCR):
Instructions for Authors

Scope

Clinical Cancer Research publishes innovative clinical and translational cancer research studies that bridge the laboratory and the clinic. The Journal is especially interested in clinical trials evaluating new treatments, accompanied by research on pharmacology, and molecular alterations or biomarkers that predict response or resistance to treatment. The Journal also prioritizes laboratory and animal studies of new drugs and molecule-targeted agents with the potential to lead to clinical trials, and studies of targetable mechanisms of oncogenesis, progression of the malignant phenotype, and metastatic disease.

Specific areas of interest include clinical and translational research in targeted therapies; mechanisms of drug sensitivity and resistance; pharmacogenetics and pharmacogenomics; personalized medicine; novel applications of bioinformatics and biostatistics; immunotherapy and clinical immunology; gene therapy; radiobiology and radiation oncology; large-scale molecular characterization of human tumors; diagnostic biomarkers; innovative imaging and other novel methods with potential applicability to clinical investigation; clinical genetics; and detection of minimal disease.

Categories of Publication

The following types of articles will be considered for publication. Note that word counts are exclusive of references, tables, and figure legends. Authors are advised that submissions not adhering to the guidelines provided below may be returned. NOTE: Special features in the Journal are invited by one of the Deputy Editors. If you are interested in contributing a special feature, please contact the Journal office (ccr@aacr.org).

Research Articles

Highest priority is given to manuscripts with clearest relevance to clinical medicine. In addition, studies must be original, not confirmatory; must demonstrate a clear application to the current or future practice of medicine; must describe hypothesis testing, not hypothesis generation; must possess robust statistics; must be biologically based, not empiric; and must be important and interesting to our readership. Research articles can be submitted to one of the following four categories:

- Cancer Therapy: Clinical
- Personalized Medicine and Imaging
- Cancer Therapy: Preclinical
- Biology of Human Tumors

Detailed guidelines are provided for each manuscript category and should be reviewed prior to submission.

All Clinical Cancer Research articles should adhere to the following parameters:

- 120–150-word statement of translational relevance (required)
- 250-word structured abstract
- 5,000 words of text
- 6 tables and/or figures
- 50 references

Clinical Trial Brief Reports

Submission to the Clinical Trial Brief Reports section is recommended for trials of novel agents, combinations, or indications that contain limited correlative science but report initial findings with an extraordinary degree of clinical activity, such as a high rate of complete radiographic responses. At this time only clinical trials may be submitted in a Brief Report format; all other types of research should be submitted as a standard research article. Clinical Trial Brief Reports are eligible for expedited review based on the discretion of the Editors.

Clinical Trial Brief Reports should adhere to the following parameters:

- 250-word structured abstract
- 2,500 words of text
- 4 tables and/or figures
- 20 references

Information for Specific Types of Research Articles:

Cancer Therapy: Clinical
Clinical Cancer Research is interested in reports of clinical trials that involve both early and late stages of drug development. Clinical trial manuscripts should include a clear statement of the primary objective of the study, patient eligibility criteria, the measured endpoints, and the statistical approach and analysis (particularly for any biomarker hypotheses). Early (phase 0 or phase I) studies being considered for publication in Clinical Cancer Research should report on new compounds or new drug combinations. Studies that include pharmacokinetic assays, pharmacodynamic assays as a means to understand whether the target is modulated as expected, or investigation of individual differences in drug metabolism, toxicity, or responses (i.e., pharmacologic or predictive biomarkers) are of particular interest. For clinical trials pertaining to immunotherapies, immune tests addressing the mechanism of action and potential biomarkers should be included. Clinical Cancer Research is also interested in first-in-man phase I trials of novel single agents or combinations of investigational or re-purposed agents that report initial observations resulting from perturbation of novel mechanisms of pathogenesis. In general the agent(s) studied and the mechanism(s) targeted should be justified by compelling pre-clinical data.

Clinical Cancer Research will consider phase II trials that represent a possible advance in the treatment of cancer. Priority will be given to studies that include pharmacokinetic, pharmacodynamic, or pharmacogenetic endpoints. Reports of phase II trials should include a discussion of sample size calculations. Phase II trials that identify new active agents or regimens or that utilize novel biostatistical methods are also of interest. Clinical Cancer Research does not usually accept phase II trials that include few patients or are unlikely to be studied in phase III trials. Reports of randomized, controlled trials should follow CONSORT guidelines. In addition, PL 110-85, Title VIII, mandates the submission of "basic results" data for certain clinical trials of drugs, biologics, and devices. The law applies to trials that are not phase I or small device feasibility studies and that have at least one site in the United States. Basic results include summary data tables of baseline characteristics, participant flow, outcomes, and adverse events. There are no patient level data. See additional information on clinical trial registry in the General Instructions for Authors.

**Personalized Medicine and Imaging**

1. They are definitive in size and statistical power. Prospective studies or prospective-retrospective studies will receive priority. Retrospective studies will be considered, but they should include verification using an independent cohort.
2. They describe a unique cohort with results that directly impact clinical practice. (For rare cancer types, it is recognized that small cohorts will be analyzed.)
3. They adhere to the REMARK criteria as listed in their guidelines (http://jnci.oxfordjournals.org/content/97/16/1180/T1.expansion.html).
4. They contain thorough specimen collection data, assay validation, and statistical rigor.
5. They are based on (or include) mechanistic data.

**Imaging**

Clinical Cancer Research is interested in imaging studies that have a clearly stated hypothesis and include either clinical data or pre-clinical data that strongly points toward clinical translation. Namely, there should be a clear clinical application that will have a significant impact on patient diagnosis or management. Studies focusing primarily on imaging methodology, in the absence of addressing a clinically relevant biological issue (e.g., imaging or measuring the activity of a relevant signaling pathway that is correlated to disease progression or treatment response) are discouraged. Imaging studies should have the following characteristics:

1. For new (or novel applications of established) imaging paradigms, confirmation using independent assays of efficacy is required.
2. For new imaging paradigms addressing significant clinical issues (or preclinical studies that have the potential to address significant clinical issues) for which an established imaging paradigm exists, it is encouraged that the "new" imaging paradigm be directly compared with the "established" imaging paradigm (unless there is a good reason not to perform the comparison).
3. Appropriate statistics should be applied to the "hypothesis-testing" experiments presented in the Results section.
4. For preclinical imaging studies, authors should include more than one relevant tumor cell line or animal-bearing tumor model.
5. For clinical imaging studies, authors should include the elements of the associated therapeutic study, including a clear description of the clinical study design, inclusion/exclusion criteria, a description of study procedures (imaging and non-imaging), a statistical plan, and when appropriate a sample size/power calculation.
6. Images must include a quantitative (or semi-quantitative) intensity/pseudo-color scale bar (except MRI or CT for anatomic imaging); the maximum and minimum numeric values with appropriate units need to be presented.

**Cancer Therapy: Preclinical**
Clinical Cancer Research prioritizes the preclinical evaluation of novel compounds and rational combinations for cancer therapy. Due to the overwhelming number of submissions in this Section of the Journal, guidelines are listed below to assist authors in their preparation of the manuscript. Flexibility will be maintained in the review process in regard to the availability of cell lines, model systems, tissues, and other resources for particular cancer types.

1. Highest priority will be given to preclinical studies that involve new targets and/or are based on strong mechanism-based hypotheses. For compounds that constitute a new member of an already reported class (e.g., tyrosine kinase inhibitors), data to identify an advantage, or a novel indication for this compound, relative to others already published, would be considered a strength.
2. If available, multiple tumor cell lines must be presented to confirm the generality of the results. Confirmed using clinical tumor material is considered a strength.
3. The in vitro validation of in vivo data is needed, including xenografts, patient-derived xenografts, orthotopic models, genetically engineered mice, tumor explants, syngeneic mouse hosts for immunological studies, veterinary animals, or other related information. In vivo experiments should have a measurable endpoint. Explanation should be provided as to why particular models were chosen.
4. Pharmacodynamic analysis of in vivo samples to confirm target engagement following an intervention or other mechanistic hypotheses is strongly recommended. To the extent possible, analysis of an entire pathway rather than a single protein or gene is favored.
5. For in vivo studies of radiation, fractionated doses will be favored over single-dose studies.
6. For in vivo studies testing novel drugs, it is recommended to include a control arm with the standard of care in order to understand the magnitude of the benefit.
7. For drugs in clinical use, pharmacokinetic data to correlate the observed therapeutic effect with clinically achievable concentrations would constitute a strength. Pharmacokinetic data for investigational compounds are encouraged.
8. For rational combinations, statistical analysis of additive or synergistic effects is mandatory.

Biology of Human Tumors

Manuscripts published in the Biology of Human Tumors Section will report novel findings with direct translational implications. Biological studies must be mechanistic, based on novel findings, and of eventual clinical importance. Use of at least two model systems, and in vivo data with clear endpoints, are needed. Authors should justify their selection of model systems. The human relevance of biological studies should be confirmed using human tumor data. Human tumor-based studies of biomarkers for molecular diagnosis or classification of cancer, or biomarkers predictive of metastasis, are also of interest. Tumor cohort studies should be definitive in size and statistical power, and confirmed using an independent cohort. In most cases, prospective studies concerning the natural history of disease are not of interest. Manuscripts reporting data from human tumors must adhere to the REMARK criteria (http://jnci.oxfordjournals.org/content/97/16/1180/T1.expansion.html).

Novelty will be a paramount gauge of relevance to this Section of the Journal. Manuscripts examining a previously published finding in a new cancer histology should be submitted elsewhere, as should be papers that are largely confirmatory with incremental new information. Novelty can be demonstrated both in topics of widespread interest and in new, previously unrecognized fields. Clinical/Translational relevance will constitute another important gauge of interest for publication in this Section of the Journal. The ability of the findings to inform or alter clinical practice can be immediate or in the foreseeable future. In general, Clinical Cancer Research is not interested in papers presenting the general molecular biology of cancer without obvious translational relevance; descriptive studies and purely in silico studies are discouraged.

CCR Reviews

Concise treatments of timely subjects important to cancer researchers, Review Articles for Clinical Cancer Research are meant to stimulate consideration of new ideas and approaches and provide updates of new paradigms and innovative ideas for investigation. They need not present a comprehensive review of the literature. Brief reviews will receive priority. Authors of unsolicited Review Articles should first submit an outline of the proposed article for consideration by the Editors (ccr@aacr.org).

- 250-word abstract
- 3,000 words of text
- 5 tables and/or figures
- 75 references

Perspectives

Perspectives put forward the authors' point of view on a topic of current interest in translational and clinical cancer research. They are short, thoughtful, and creative presentations of a theory or theories and not intended as comprehensive reviews of the literature.

- 120–150-word statement of translational relevance (required)
- 250-word abstract
- 1,600–2,400 words of text
- 5 tables and/or figures
- 50 references

Letters to the Editor
In the spirit of open scientific dialogue, the Editor-in-Chief invites the submission of correspondence that presents considered opinions in response to articles published in the Journal. Letters to the Editor will be reviewed and, if found to meet the requisite publication criteria (scholarly commentary on a subject of import and interest to the broad readership, length appropriate to the content), the Letter may be sent to the author(s) of the originally published article and possibly to other interested parties for a response to be published in the same issue as the Letter. Correspondence concerning articles that have not been published in *Clinical Cancer Research* will not be considered. Please note that the Journal will not consider Letters to the Editor regarding *Clinical Cancer Research* articles that were published more than 12 months earlier than the date of the letter.

- 400 words of text
- Include a title: “Running title of the original article” — Letter
- 5 references; the first reference must be to the original article
- No tables or figures, unless agreed to by the Editor