

Clinical Trials on Colorectal Cancer in South Africa

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Abstract

Background: Colorectal cancer (CRC) is amongst the most important cancers in resource-constrained South Africa. It is crucial that setting-specific research be conducted which seeks to answer questions around the feasibility of emerging treatment modalities for CRC in South Africa, as well as the subsequent clinical outcomes in patients receiving these treatments.

Aim: To determine the status of CRC clinical trials in South Africa and identify areas in which CRC clinical trials need strengthening in this setting.

Methods: A search of ClinTrials.gov, the Pan-African Clinical Trials Registry, and PubMed was performed to identify clinical trials of CRC in South Africa. Information on each clinical trial was collected and analyzed with descriptive statistics.

Results: There were very few registered clinical trials on CRC in South Africa ($n=20$). Most studies were already completed at the time of this analysis ($n=16$, 80%), and were international multicenter studies on which South African research sites contributed data ($n=19$, 95%). Phase III trials were common ($n=19$, 95%), particularly those investigating pharmaceutical drugs ($n=15$, 75%). Most studies were funded by medical or pharmaceutical companies ($n=12$, 60%).

Conclusion: The dearth of CRC clinical trials in South Africa must be addressed. This could primarily be achieved through local capacity development in clinical oncology and research methods.

Keywords: Clinical trials, Colorectal neoplasms, Research, South Africa

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Introduction

Rapid urbanization of the South African population since the fall of Apartheid during the mid-1990's has had unintended consequences for the burden of non-communicable disease in the country¹. Colorectal cancer (CRC) is one of the fastest growing public health problems in South Africa. It is ranked amongst the most common cancers in the South Africa and represents one of the leading causes of cancer-related mortality in this setting². A recent epidemiological study involving data from the South African National Cancer Registry and Statistics South Africa reported a 2.5% annual average increase in the age-standardized incidence of CRC and a 1.3% increase in CRC age-standardized mortality rates between 2002 and 2014³. There are

no community-based screening programs for CRC in South Africa and many patients will present for diagnostic colonoscopy with locally advanced or metastatic disease, requiring treatment with surgery and/or adjuvant therapies^{2, 4}. Considering the complex treatment needs of CRC patients in resource-constrained South Africa, it is important that setting-specific research be conducted which seeks to answer questions around the feasibility of emerging treatment modalities and the subsequent clinical outcomes in patients receiving these treatments.

The aim of this study was to determine the status of CRC clinical trials in South Africa and identify areas in which CRC clinical trials need strengthening in this setting.

Methods

This research analyzed data from three sources: ClinTrials.gov, the Pan-African Clinical Trials Registry (PACTR), and the PubMed medical literature database.

Briefly, the ClinTrials.gov database is an online resource maintained by the National Library of Medicine at the US National Institutes of Health which allows the public to access information around clinical studies (both interventional and observational) being conducted in various countries⁵. This information, which is required to be regularly updated by the research sponsors or principal investigators, includes (but is not limited to) the hypotheses driving these clinical studies, study design and status, study outcomes investigated, and the funding source⁵. The PACTR is based on a similar principle to ClinTrials.gov and was launched in 2009 as a regional platform for African researchers to register their clinical research⁶. The PACTR is funded by the European and Developing Countries Clinical Trial Partnership and is endorsed by the World Health Organization⁶.

A search of the ClinTrials.gov database was performed from 1 January 1994 until 1 May 2023 using the condition/disease term “Colorectal cancer” (alternative search terms: “Bowel cancer”, “Colon cancer”, “Colonic neoplasms”, “Colorectal neoplasms”, “Rectal cancer”) and selecting the geographic region of the research as “South Africa”. Eligible clinical trials on CRC were identified for this analysis after applying pre-defined inclusion and exclusion criteria. Clinical studies which were interventional in design were included in this analysis. Duplicate records and clinical trials with a status listed as “withdrawn” or “unknown” on ClinTrials.gov were excluded. The ClinTrials.gov record for each eligible clinical trial was reviewed and the following data was collected using a Microsoft Excel spreadsheet: status of the trial, whether the trial was a multicenter study, study details (including the nature of the intervention and clinical trial phase), primary study outcome investigated, and funding source for the research. A similar search and data collection process to that performed for ClinTrials.gov was also performed for the PACTR, with the only exception being that the search dates were set from 1 January 2009 (the year that the PACTR was established) to 1 May 2023.

A search of PubMed for published reports of CRC clinical trials in South Africa was also conducted using the following search strategy:

(“colorectal cancer”[Title/Abstract] OR “colon cancer”[Title/Abstract] OR “rectal cancer”[Title/Abstract] OR “bowel cancer”[Title/Abstract] OR “colorectal neoplasm*”[Title/Abstract] OR “colonic neoplasm*”[Title/Abstract] OR “sigmoid neoplasm*”[Title/Abstract]) AND “South Africa”[All Fields] AND (“clinical trial*”[Title/Abstract] OR “randomized controlled trial*”[Title/Abstract] OR “RCT”[Title/Abstract] OR “controlled trial*”[Title/Abstract])

An additional date limit for the PubMed search was that the studies must have been published between 1 January 1994 and 1 May 2023. The abstracts of all studies returned from the PubMed search were screened for relevance. Only studies reporting CRC clinical trials conducted in South Africa (or studies on which South African research sites contributed data) and published in English Language were eligible for inclusion in our analysis. Studies from the PubMed search which were also identified in the search of ClinTrials.gov or the PACTR were considered duplicates and excluded from our analysis.

Descriptive statistics were used to analyze the data that was entered onto the Microsoft Excel spreadsheet. The descriptive statistical analysis was performed using Microsoft Excel. The key results are presented as frequencies and percentages.

ClinTrials.gov and the PACTR do not provide any individual study participant data. Furthermore, PubMed provides medical literature in the public domain. Therefore, ethical approval to conduct this research was not required since it did not pose any threat to human subjects.

Results

A summary of results from the ClinTrials.gov database, the PACTR, and PubMed searches is shown in Figure 1.

The ClinTrials.gov search yielded 106 results, of which 87 were excluded from this analysis and 19 were included. The reasons for the exclusion of the 87 results were: duplicates = 86 and trial terminated = 1. The PACTR search yielded 2 results, of which only 1 was included. The excluded result from the PACTR was a duplicate study. Lastly, the PubMed search yielded 17 results. Of these 17 results, none were eligible for inclusion in the analysis. The reasons for excluding all 17 PubMed results were as follows: Not clinical trial = 8, not study of CRC = 3, study not conducted in South Africa = 5, and

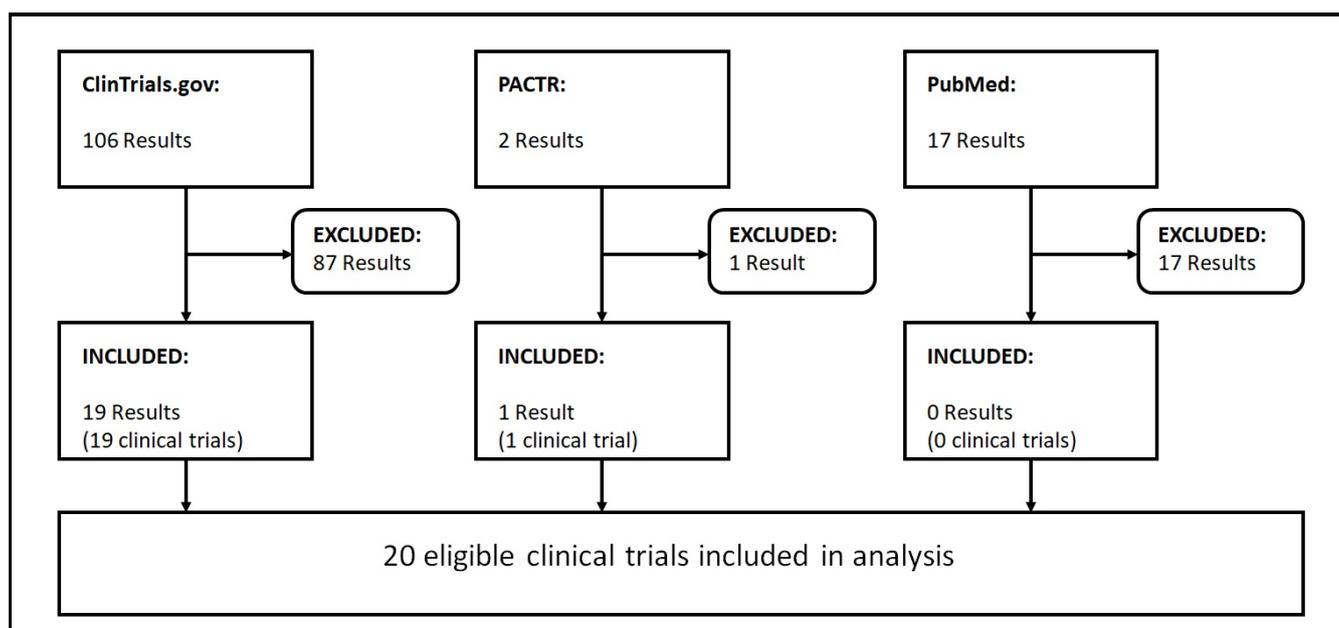


Figure 1. Study selection process for this analysis

duplicate study from a record already identified in the ClinTrials.gov search = 1. Therefore, the final number of clinical trials included in this analysis was 20.

A description of the 20 clinical trials included in this analysis is provided in Table 1.

A timeline of the clinical trials is also provided as Figure 2.

Sixteen of the 20 clinical trials (80%) were already listed as completed at the time that this analysis was performed. A total of 19 clinical trials (95%) were registered as multicenter studies, on which South African research sites contributed data. There was only one single center South African study (5%). The majority of trials (15 studies, 75%) involved administration of pharmaceutical drugs without radiation or biological treatments. Nineteen of the 20 studies (95%) were Phase III clinical trials.

The most frequently researched primary study outcomes were progression-free survival (7 studies, 35%), overall survival (4 studies, 20%), and disease-free survival (4 studies, 20%). Lastly, more than half of clinical trials were funded solely by the medical or pharmaceutical industry (12 studies, 60%).

Table 1. Summary of the 20 clinical trials included in this analysis

Study characteristic	n (%)
Status	
Completed	16 (80)
Recruiting	1 (5)
Active, not recruiting	3 (15)
Multicenter study	
Yes, but only South African study sites	0 (0)
Yes, international study	19 (95)
Not multicenter study	1(5)
Intervention description	
Drug only	15 (75)
Drug and biological	2 (10)
Drug and radiation	2 (10)
Preoperative patient educational intervention	1 (5)
Clinical trial phase	
Phase II/III	1 (5)
Phase III	19 (95)
Most investigated primary study outcome	
Progression-free survival	7 (35)
Overall survival	4 (20)
Disease-free survival	4 (20)
Other	3 (15)
Not mentioned	2 (10)
Funding source	
Medical or pharmaceutical industry only	12 (60)
Other funders (not-for-profit)	7 (35)
Jointly funded by medical/ pharmaceutical industry and other funders	1 (5)

generation of South African clinician researchers be encouraged to seek alternative streams of funding for their setting-specific clinical trials, other than funding being offered by overseas-based medical or pharmaceutical companies.

This study was not without limitations, the two most important of which were 1). Potential selection bias introduced in this analysis because there might have been a small number of South African CRC clinical trials that were not registered on the ClinTrials.gov or PACTR databases, or studies not published in PubMed journals; and 2). Information on a registered clinical trial may have changed over time and might not have been updated on the ClinTrials.gov or PACTR database by the principal investigator or sponsor. These limitations can be addressed by encouraging South African clinician researchers to publicly share information around their clinical research on a continuous basis.

Conclusion

This analysis highlights the need for capacity development in clinical oncology and research methodology in South Africa, the importance of bringing cutting-edge research around new treatments to the country, and the potential caveats of clinical trials sponsored by overseas-based medical or pharmaceutical companies. South African clinician researchers should also be encouraged to share information around the CRC studies they are conducting.

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Authors' contribution

Conception or design: Both authors; Acquisition, analysis or interpretation of data: Both authors; Drafting or revising the manuscript: Both authors; Approval of the manuscript version to be published: Both authors; Agreement to be accountable for all aspects of the work: Both authors.

Conflict of interest

The authors declare that they have no conflict of interest to disclose.

Data availability

The data used in this research is publicly available on the ClinTrials.gov and the Pan-African Clinical Trials Registry databases, as well as PubMed.

Ethical considerations

Not applicable.

Funding

Not applicable.

Study registration

Not applicable.

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