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Short Communications

Pharmacogenomics and cancer treatment: evaluation of the efficacy of targeted therapies versus chemotherapy through a meta-analytic study of randomized clinical trials

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Abstract

Cancer is a major public health challenge in low- and middle-income countries, with particularly high mortality rate in sub-Saharan Africa and limited access to innovative care in Senegal. The aim of this study was to evaluate, through a meta-analysis of randomized clinical trials, the efficacy of targeted therapies compared with chemotherapy on the complete response rate. We conducted a systematic review (PRISMA recommendations) in both French and English using multiple databases/platforms (Google Scholar, PubMed, Cochrane Library, Journal of Clinical Oncology, NEJM, JAMA Oncology, AACR, etc.). Randomized controlled trials (RCTs) reporting complete response were included, while non-randomized studies and publications without usable clinical data were excluded. Analyses were performed using RevMan 5 with Odds Ratios (ORs) and 95% confidence intervals (95% CI), and heterogeneity was assessed using I^2. Of the 2,430 records identified, 13 trials were included in the quantitative synthesis. Targeted treatments showed overall superiority compared with chemotherapy in terms of complete response (overall OR = 0.27; 95% CI [0.17–0.44]; $p < 0.00001$), with low heterogeneity ($I^2 = 17\%$). These findings support the integration of targeted therapies/immunotherapies into therapeutic standards, while highlighting the importance of predictive biomarkers and accessibility challenges in sub-Saharan Africa.

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1. Introduction

Cancer is a major public health problem in low and middle-income countries. In sub-Saharan Africa, patients often present with advanced disease. In Africa, the lack of adequate infrastructure for patient care and reliance on traditional therapies contribute to increased overall mortality, the mortality to incidence ratio is estimated at 75%, compared with 46% in high-income countries [1]. Chemotherapy was considered as the main treatment for cancer, for a long time. However, it has major limitations, such as high

toxicity and variable efficacy depending on the cancer type. In parallel, the emergence of targeted therapies that act more specifically on defined molecular alterations offers an innovative therapeutic perspective that may reduce side effects and improve response rates [2, 3].

In Senegal, the cancer burden is increasing, and the health system faces specific challenges, particularly regarding access to innovative treatments. Medical infrastructure and available resources are often limited, making it difficult to integrate targeted therapies into standard care. Moreover, genetic and environmental characteristics specific to the Senegalese population could influence the treatment response. It is therefore crucial, in this particular context, to assess whether results obtained internationally translate into tangible clinical benefits for Senegalese patients. However, despite the abundance of randomized controlled trials (RCTs) comparing these two approaches, the findings remain inconsistent. Some RCTs report a significant advantage of targeted therapies in terms of overall survival and quality of life, while others show no statistically significant benefit compared with conventional chemotherapy

2. Materials and methods

2.1. Literature search strategy

A systematic literature search was conducted in French and English using the following databases and platforms: Google Scholar, PubMed, Cochrane Library, Journal of Clinical Oncology, Revue Française des Laboratoires, The New England Journal of Medicine, JAMA Oncology, the American Association for Cancer Research (AACR) and Lippincott Williams & Wilkins.

The search was guided by a strategy based on specific keywords related to pharmacogenomics, oncology, and randomized clinical trials. The terms used included: “pharmacogenomics”, “targeted therapies”, “randomized clinical trials”, “cancer”, “oncology”, and “meta-analysis”.

2.2. Inclusion and exclusion criteria for selected studies

Inclusion criteria

- ✓ Study design: Randomized controlled trials (RCTs) that meet international methodological standards.
- ✓ Source quality: Publications in high–impact scientific journals indexed in recognized databases such as the National Library of Medicine and ScienceDirect.
- ✓ Clinical relevance: Studies reporting the complete response rate to treatment, whether targeted therapies or chemotherapy.

Exclusion criteria:

- ✓ Non-randomized or observational studies.
- ✓ Articles that did not report clinical data on the complete response rate.
- ✓ Literature reviews, editorials, letters to the editor, and conference abstracts without complete data.
- ✓ Studies published in non-indexed or low-impact journals.

2.3. Statistical analysis

Meta-analysis data were analyzed using Review Manager (RevMan), version 5. The Odds Ratio (OR), with a 95% confidence interval (95% CI), was used to assess intervention efficacy as well as the frequency of adverse events, comparing targeted therapies (TT) with conventional chemotherapy (CC).

Between-study heterogeneity was quantified using the I^2 statistic, which was expressed as a percentage. This measure reflects the proportion of the total variance attributable to variability between studies rather than chance. The interpretation thresholds were as follows:

- ✓ $I^2 < 25\%$: Low heterogeneity, indicating satisfactory consistency of results.
- ✓ $25\% \leq I^2 \leq 50\%$: Moderate heterogeneity, indicating moderate variability between studies.
- ✓ $50\% < I^2 \leq 75\%$: High heterogeneity, suggesting substantial heterogeneity.
- ✓ $I^2 > 75\%$: Very high heterogeneity, questioning the consistency of pooled estimates.

3. Results

The study selection process followed the PRISMA recommendations, from the initial identification of studies to the final inclusion. The flow diagram (Fig. 1) shows each step of this process.

We identified 2,430 studies from electronic databases. Of these, 2,362 were excluded for various reasons, including the lack of a comparison between targeted

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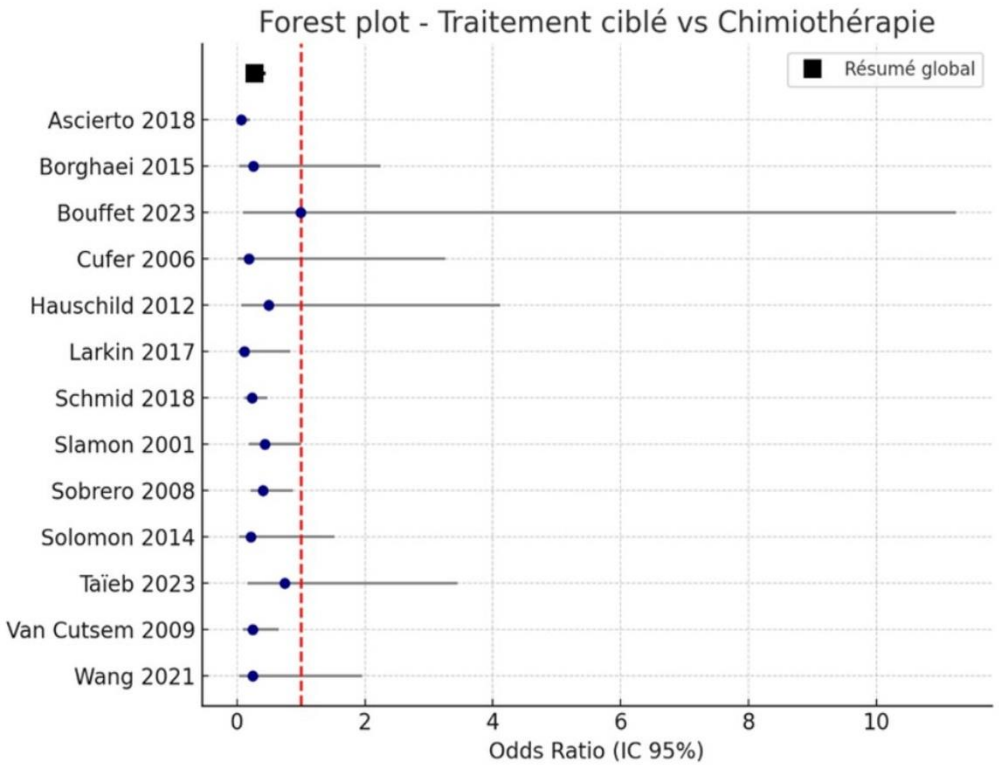

Figure 1. Flowchart of studies research.

therapy and chemotherapy. After the initial screening, 68 studies were examined in detail for relevance. At this stage, 49 studies were excluded because they did not meet the selection criteria, particularly regarding randomization. We then assessed 19 additional studies for eligibility, however, 6 were excluded due to missing essential data, notably on the number of complete responses.

Ultimately, 13 studies were included in our systematic review and meta-analysis, meeting all the predefined methodological criteria. The characteristics of these studies are presented in Table 1.

This table highlights the diversity of oncology clinical trials, in terms of tumor sites and participant characteristics. The median follow-up duration ranged from less than one year to more than three years, reflecting the heterogeneity in protocols and prognosis across the cancers studied. The mean age is generally between 50 and 66 years, with a notable exception for pediatric gliomas. The proportion of women is logically very high in breast cancer studies but varies across other conditions, ranging from 8.3% to 61.5%. These data reflect population diversity and help to contextualize the study results from a comparative perspective.

Information on the number of participants in each clinical trial and the success rates were collected, as shown in Table 2.

The table provides a comparison of major clinical trials assessing targeted treatments versus standard chemotherapy. Overall, targeted therapies showed higher complete response rates than chemotherapy alone, with particularly marked differences in studies such as ASCIERTO 2018 (19.05% vs 1.44%) and SLAMON 2002 (7.66% vs 3.42%). In most cases, targeted treatments demonstrated an advantage, although some studies reported more modest differences (e.g., BOUFFET 2023, 2.74% vs 2.70%).

The forest plot (Fig 2) was generated using Review Manager 5 by incorporating data from the 13 trials included in this meta-analysis. To ensure rigor and consistency, the following information was systematically extracted and entered for each study:

- Methodology: Only randomized clinical trials were considered, in line with the selection criteria.
- Population: The participants were patients with

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Table 1. Baseline characteristics of participants in the trials.

Studies	Country	Mean follow-up (years)	Cancer type	Mean age (years)	Women (%)
LARKIN 2017 [4]	14 countries	2	Advanced melanoma	59	35
SCHMID 2018 [5]	41 countries	1.1	Triple-negative breast cancer	55.5	99.65
TAIEB 2023 [6]	France	2.8	Metastatic colorectal cancer	66	53.3
SLAMON 2002 [7]	N/A	2.5	Metastatic breast cancer	52.8	100
ASCIERTO 2018 [8]	N/A	3.2	Advanced melanoma	65	41.15
SOLOMON 2014 [9]	N/A	1.4	Advanced non–small-cell lung cancer	53	61.5
SOBRERO 2008 [10]	221 sites	1.3	Metastatic colorectal cancer	62	37.13
HAUSCHILD 2012 [11]	12 countries	0.75	Metastatic melanoma	51.5	40.5
BOUFFET 2023 [12]	20 countries	1.6	Pediatric glioma	9	59.5
VAN CUTSEM 2009 [13]	N/A	2.5	Metastatic colorectal cancer	61	39.5
BORGHAEI 2015 [14]	N/A	1.4	Non–small-cell lung cancer	62	45
CUFER 2006 [15]	12 countries	0.75	Non–small-cell lung cancer	61	30.5
WANG 2021 [16]	China	0.9	Non–small-cell lung cancer	62	8.3

Table 2. Comparison of studies evaluating targeted therapy versus chemotherapy: number of participants and success rate.

Studies	Targeted therapy (TT)	Chemotherapy (CC)	Number of participants (TT/CC)	Success rate (%) (TT/CC)
LARKIN 2017 [4]	Nivolumab	Carboplatin, Paclitaxel, Dacarbazine	272 / 133	6.25 / 0.75
SCHMID 2018 [5]	Atezolizumab + Nab-Paclitaxel	Placebo + Nab-Paclitaxel	450 / 449	7.11 / 1.56
TAIEB 2023 [6]	Avelumab	FOLFOX	61 / 61	6.56 / 4.92
SLAMON 2002 [7]	Trastuzumab	Cyclophosphamide/ Paclitaxel	235 / 234	7.66 / 3.42
ASCIERTO 2018 [8]	Nivolumab	Dacarbazine	210 / 208	19.05 / 1.44
SOLOMON 2014 [9]	Crizotinib	Pemetrexed	172 / 171	1.74 / 1.17
SOBRERO 2008 [10]	Cetuximab + Irinotecan	Irinotecan	648 / 650	1.39 / 0.15
HAUSCHILD 2012 [11]	Dabrafenib	Dacarbazine	187 / 63	3.21 / 1.59
BOUFFET 2023 [12]	Dabrafenib + Trametinib	Carboplatin + Vincristine	73 / 37	2.74 / 2.70
VAN CUTSEM 2009 [13]	Cetuximab + FOLFIRI	FOLFIRI	599 / 599	0.50 / 0.33
BORGHAEI 2015 [14]	Nivolumab	Docetaxel	292 / 290	1.37 / 0.34
CUFER 2006 [15]	Gefitinib	Docetaxel	68 / 73	2.94 / 0
WANG 2021 [16]	Tislelizumab + chemotherapy	Paclitaxel + Carboplatin	239 / 121	3.35 / 0.83

different types of cancer.

- Interventions: Targeted therapies were compared with standard chemotherapy.
- Outcomes: The reported parameters included tumor reduction, overall survival, and therapeutic response.

The main endpoint analyzed in this meta-analysis was the complete response rate, which was chosen as the central indicator to evaluate the comparative efficacy of the therapeutic strategies.

The forest plot (Fig 2) shows the overall superiority of targeted treatments compared with chemotherapy, with an overall odds ratio of 0.27 (95% CI: 0.17–0.44), indicating a significant reduction in the risk of unfavorable events ($p < 0.00001$). Between-study heterogeneity remained low ($I^2 = 17\%$), which strengthened the robustness of the results.

4. Discussion

The results of this meta-analysis, incorporating 13 randomized clinical trials, demonstrate the overall

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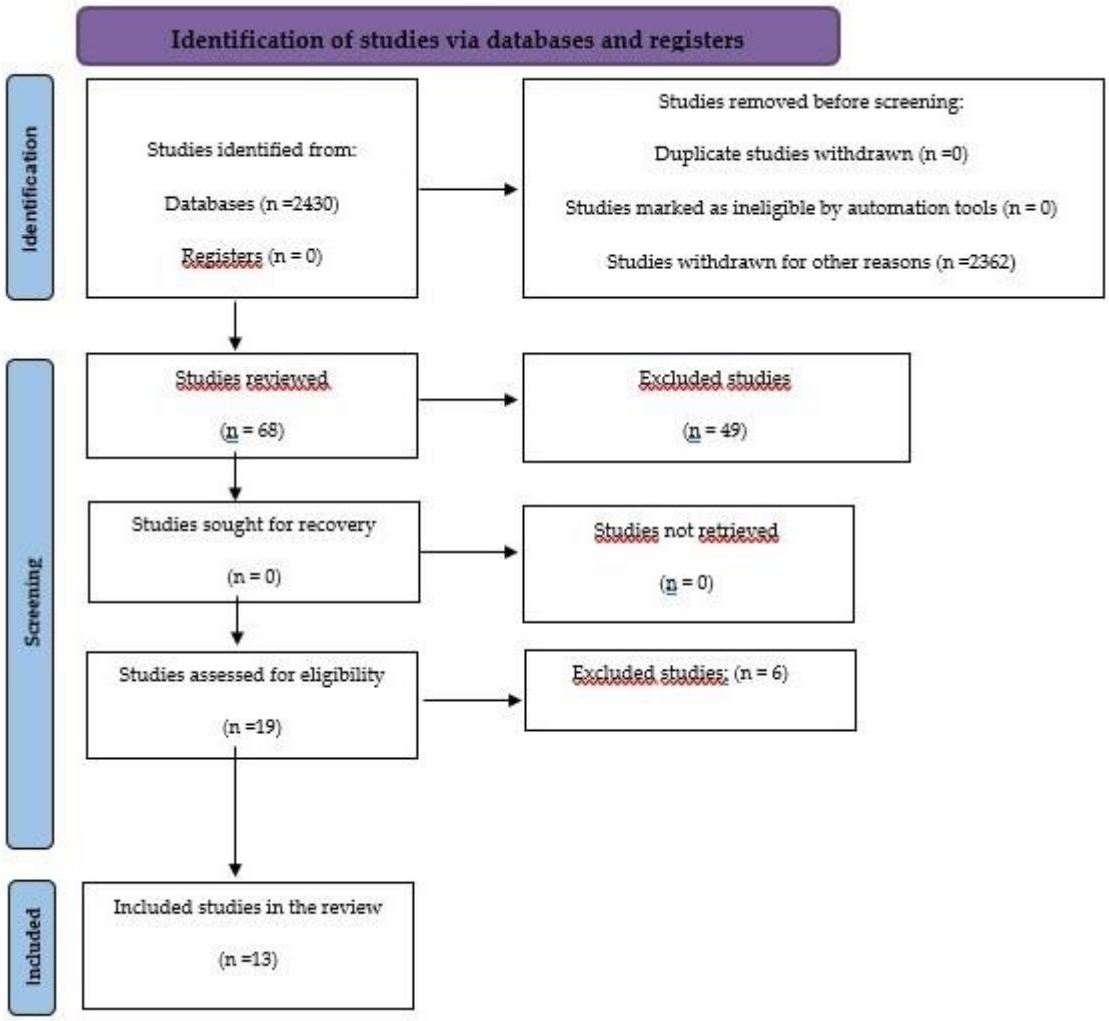

Figure 2. Forest plot comparing the effectiveness of targeted therapies versus chemotherapy in terms of complete response.

superiority of targeted treatments compared with conventional chemotherapy in the management of the cancers studied.

4.1. Comparison of complete response rates.

The comparative table shows that targeted treatments achieved higher complete response rates than chemotherapy alone in most studies. Particularly marked differences were observed in ASCIERTO 2018 (19.05% vs 1.44%) and SLAMON 2002 (7.66% vs 3.42%), supporting the greater efficacy of immunotherapy and monoclonal antibodies in specific settings such as advanced melanoma and HER2 + breast cancer. Nevertheless, some studies have reported modest differences or no clear benefit (e.g., BOUFFET 2023, pediatric gliomas: 2.74% vs 2.70%), reflecting variability in efficacy by tumor type and patient age.

The forest plot provides a synthesized view of this trend. The overall odds ratio was estimated to be 0.27 (95% CI: 0.17–0.44) ($p < 0.00001$), indicating a significant reduction in the risk of unfavorable events with targeted treatment. Low heterogeneity ($I^2 = 17\%$) reinforces the robustness of these findings, suggesting the relative consistency of effects across the included trials. These data confirm that targeted therapies represent a major therapeutic advance in several cancer types, rather than a marginal benefit.

These results support the integration of targeted therapies and immunotherapy into international therapeutic standards, particularly for cancers, in which gains in survival and response are clinically meaningful. However, between-study variability highlights the need to better characterize predictive biomarkers of response to identify patient subgroups that are most likely to benefit. In addition, the high cost of these therapies and their limited accessibility

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in certain settings, notably sub-Saharan Africa, remain major challenges for their wider implementation.

It should be noted that some trials included a relatively limited number of patients, which may have affected the statistical power. In addition, this meta-analysis focused on the complete response rate as the primary endpoint, whereas other clinical outcomes (overall survival, progression-free survival, quality of life) are also essential for a comprehensive evaluation of therapeutic efficacy.

5. Conclusions

This meta-analysis suggests that targeted therapies offer greater efficacy than conventional chemotherapy in terms of complete response in several cancers. These results support the value of precision oncology, based on the identification of molecular alterations and therapeutic adaptation to the patient's profile. However, the variability of results and accessibility constraints require cautious interpretation. Further studies, as well as enhanced diagnostic and training capabilities, will be necessary for broader integration of these approaches into clinical practice.

Disclaimer (artificial intelligence)

Author(s) hereby state that no generative AI tools such as Large Language Models (ChatGPT, Copilot, etc.) and text-to-image generators were utilized in the preparation or editing of this manuscript.

Authors' contributions

Designed, wrote, corrected and validated the manuscript, M.F., S.A.; corrected and validated the manuscript, data interpretation and revised the manuscript, M.D., M.S., A.M.D.

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Availability of data and materials

All data will be made available on request according to the journal policy.

Conflicts of interest

The authors declare no competing interests.

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