Journal of Translational Medicine

RESEARCH

Open Access

Comparison of baseline patient characteristics in phase 1 and phase 2/3 clinical trials for anticancer treatments

Maria Lucia Iacovino[1], Simone Talucci[2], Laura Arenare[1], Andrea Caglio[3], Andrea Canciello[1], Flavio Salerno[3], Sergio Facchini[1], Adriano Gravina[1], Clorinda Schettino[1], Maria Carmela Piccirillo[1], Pier Paolo Olimpieri[4], Massimo Di Maio[5] and Francesco Perrone[1*]

Abstract

Background Characteristics of patients significantly differ between registrational clinical trials (CTs) and Italian real-world practice, with older median age, higher elderly (≥ 65) rate and worse performance status (PS) in the latter, without imbalance in female rate. We compared the same characteristics between registrational phase 2/3 and phase 1 CTs.

Methods Data on age, sex and PS were extracted from European Public Assessment Reports of European Medicines Agency. Weighted means and standard deviations were calculated in both groups and differences were described overall, by cancer type and drug class.

Results We collected 103 phase 2/3 and 111 phase 1 CTs, supporting 97 therapeutic indications. Age and sex were compared in 59 indications. Mean median age (SD) was 60.7 (5.1) years in phase 2/3 and 59.7 (5.6) years in phase 1 (p = 0.051). Age difference was greater for skin and breast cancer; no heterogeneity emerged among drug classes. Mean female rate was not statistically significantly lower in phase 2/3 than phase 1 CTs overall, (mean difference −4.9%, p = 0.999); difference was greater for skin and upper-gastrointestinal cancers and for cytotoxic agents. Mean PS > 1 rate, compared in 47 indications, was similar in phase 2/3 [2.3% (4.7)] and phase 1 [1.8% (3.5)] (p = 0.374); difference was greater for colorectal cancer and cytotoxic agents.

Conclusions We found no statistically significant difference in age, sex and PS between patients in phase 2/3 and corresponding phase 1 CTs for anticancer treatments. Therefore, patient selection in phase 1 trials appears crucial, considering its potential impact in later development phases.

Keywords Clinical trials, Phase 1, Age, Sex, Performance status

*Correspondence:
Francesco Perrone
f.perrone@istitutotumori.na.it
Full list of author information is available at the end of the article

© The Author(s) 2025. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

Introduction

Patient population for clinical trials (CTs) is defined by eligibility criteria, considering characteristics such as age, performance status (PS), disease stage and molecular characteristics, organ function, prior and concomitant treatments, and comorbidities. Such criteria are crucial in order to discover potential treatment benefit but also to protect the safety of enrolled patients. However, eligibility restrictions might significantly impair generalizability of trial results into the broader real-world population that will ultimately receive those interventions [1–3]. Particularly, some patient groups (pediatric, geriatric, women, racial minorities, those with impaired performance status or poor prognosis, etc.) are underrepresented in clinical trials [4–7].

We recently compared baseline characteristics of cancer patients enrolled in registrational clinical trials and real-world Italian clinical practice, accessible through web monitoring registries developed by Italian Medicines Agency (AIFA) [8]. Our analysis included data on age, sex and PS, available both in registries and trials considered by European Medicines Agency (EMA) for registration, regarding 129 treatments, and significant disparities were observed. Older median age and higher rate of elderly (> 65 years old) patients were found in clinical practice than in clinical trials. Also, patients treated in clinical practice had worse PS than those enrolled in clinical trials, while no significant imbalance was found regarding sex representativeness [9].

Few studies have investigated whether patient characteristics do actually diverge across subsequent phases of clinical development, e.g. from phase 1 to later phase 2/3 trials [10]. Phase 1 clinical trials, indeed, represent the first step in clinical research to evaluate the role of a new drug by defining the right dose and schedule, depicting a preliminary safety profile, and providing insights on anticancer activity; ultimately, informing later trials that in time will lead to regulatory agencies' approval [11]. Recently, thanks to the uprising of targeted agents, detection of anticancer activity signals in phase 1 trials is becoming more important and new agents could eventually get approval without later phases' evaluation [12]. In this evolving setting, the importance of patients' selection with its value and limitations is growing as well.

Based on the above considerations, we hypothesized that differences in baseline characteristics of patient population could also be revealed in early phase 1 trials and subsequent phase 2/3 trials leading to registration.

Material and methods

Study design and data sources

The present study started from a former database of 140 phase 2/3 trials of anticancer drugs selected matching 129 AIFA web monitoring registries released between January 16 th, 2013 and May 19 th, 2022 and related to 129 distinctive therapeutic indications. Phase 2/3 trials were collected from the European Public Assessment Reports (EPAR) published at EMA website; data on age (median/mean), sex (female, male) and Eastern Cooperative Oncology Group (ECOG) PS of patients enrolled were extracted. For the purpose of this study, we searched and collected from the EPARs the same data from phase 1 trials corresponding to phase 2/3 of the former database. Treatments were classified into the following categories: cytotoxic, hormonal, immunotherapy, target-based, immunotherapy + cytotoxic and target-based + cytotoxic. Solid tumours were grouped as follows: breast, lung, colorectal, prostate, other genito-urinary, gynaecological, head and neck, melanoma, neuroendocrine (NET), skin, upper-gastrointestinal cancers and sarcomas. The final database is available at https://doi.org/10.5281/zenodo.14260553.

Statistical analysis

Age, sex and PS distribution were described in phase 1 and phase 2/3 trials. Reasons for missing data were detailed; mean age was used, if available, when median age was missing; conversion from Karnofsky to ECOG scale was done if technically possible, when ECOG PS was not available. Each variable of interest (median age, rate of females and rate of patients with PS > 1) was graphically described in bivariate scatter plots reporting values for phase 1 and 2/3 clinical trials couples, size of symbols being proportional to the number of patients enrolled in phase 1 trials and color of symbols representing breast, lung, colorectal, prostate and other cancers. For each variable of interest, weighted means with standard deviations (SD), where the number of patients enrolled in phase 1 was used as weight, were calculated in both groups. The difference between weighted means in phase 2/3 and phase 1 trials was calculated and described, in the whole dataset and according to cancer type and class of drug. For the overall comparison of median age, rate of female and PS > 1 patients, Wilcoxon matched-pairs signed-rank test was applied to test the null hypothesis of no difference. No further statistical tests were applied to subgroup descriptions in order to avoid multiple testing biases.

Results

Out of 129 therapeutic indications (related to 59 anticancer drugs) for which 140 phase 2/3 trials were available in the former database, 32 were excluded, as phase 1 trials were unavailable or shared with other indications; therefore, 97 indications with corresponding phase 1 trials extracted from EPARs, were eligible for analysis. For such indications, 103 phase 2/3 and 111 phase 1 trials were available; the overall number of patients enrolled in trials was 60284 for phase 2/3 and 7369 for phase 1. Lung and breast were the most represented cancer types, being involved in 25.8% and 16.5% of all the indications, respectively. For the analysis, we excluded phase 1 trials enrolling different cancer types without providing baseline characteristics for each. In age comparison, one phase 3 trial was excluded because of missing data, as was one trial for sex comparison. For PS comparison, 21 trials were excluded because of missing data in phase 1 (n = 15), phase 2/3 (n = 3) or both (n = 3). The flowchart is reported in Fig. 1.

Distribution of median age in both groups was evaluated for 59 therapeutic indications (Fig. 2a and Table 1). Overall, weighted mean of median age (SD) was 60.7 (5.1) years in phase 2/3 and 59.7 (5.6) years in phase 1 trials, with a mean difference of 1 year (p = 0.051). Distributions by cancer type and class of drug showed mostly higher median age in phase 2/3 CTs (10 cases out of 16 subgroups). Larger differences were seen for skin and breast cancers (4.2 years and 3.1 years, respectively), while negative differences were found in colorectal (− 1.9 years), upper-gastrointestinal (− 1.4 years), head and neck (− 0.4 years) cancers and trials including cytotoxic drugs (− 0.3 years) or the combination of immunotherapy + cytotoxic (− 0.4 years).

The rate of female patients was distributed for 59 therapeutic indications as reported in Fig. 2b and Table 2. Weighted mean (SD) rate of female patients was 40.8% (27.3) in phase 2/3 and 45.7% (23.0) in phase 1 trials, mean difference being −4.9% (p = 0.999). Differences according to cancer type and class of drug were noted in both directions, the larger being for skin (mean difference 6.0%), upper-gastrointestinal (− 8.0%) cancers and trials including cytotoxic agents (− 10.5%).

Distribution of the rate of PS > 1 patients in both groups was described for 47 therapeutic indications (Fig. 2c and Table 3). Weighted mean (SD) rate of PS > 1 patients was 2.3% (4.7) in phase 2/3 and 1.8% (3.5) in phase 1 trials, with a mean difference of 0.5% (p = 0.374). Larger differences were found in colorectal cancer trials (mean difference −6.1%) and trials including cytotoxic agents (2.5%).

Discussion

Concerns over inclusiveness of patient population in clinical trials are a main issue in modern oncology. In fact, it is known that patients enrolled in trials are often highly selected, potentially resulting in different outcomes of safety and survival when compared with the real-world

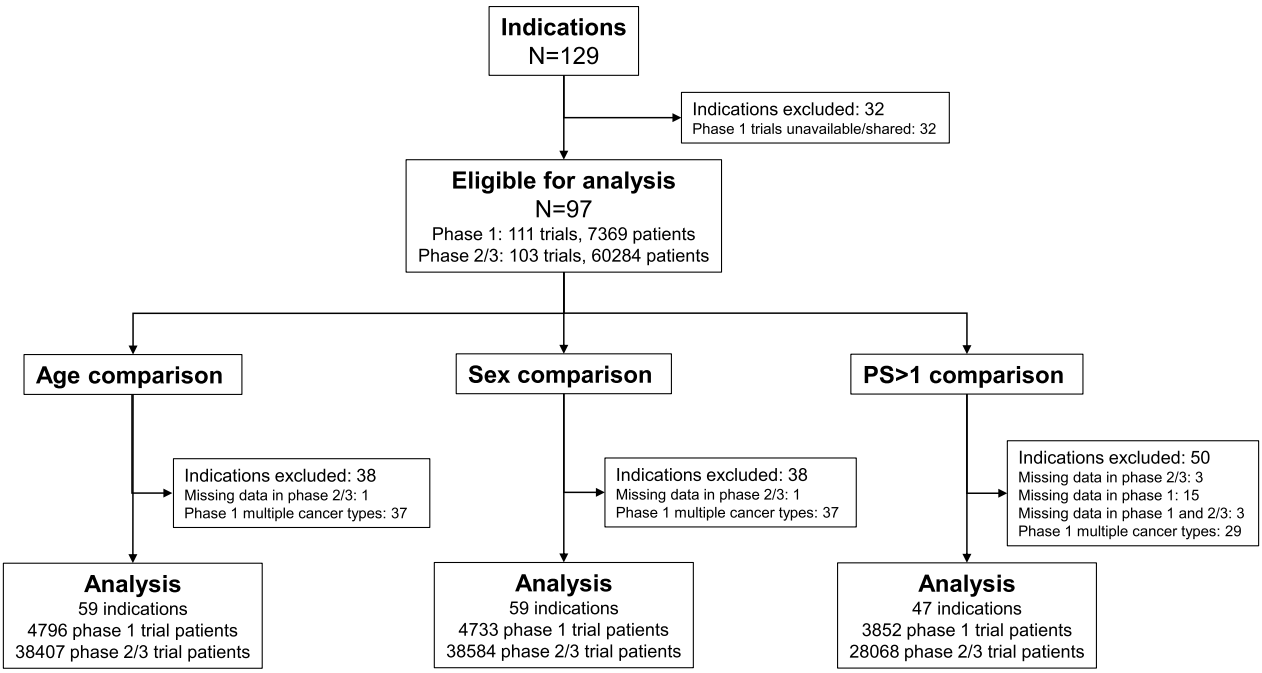

Fig. 1 Flowchart of the study

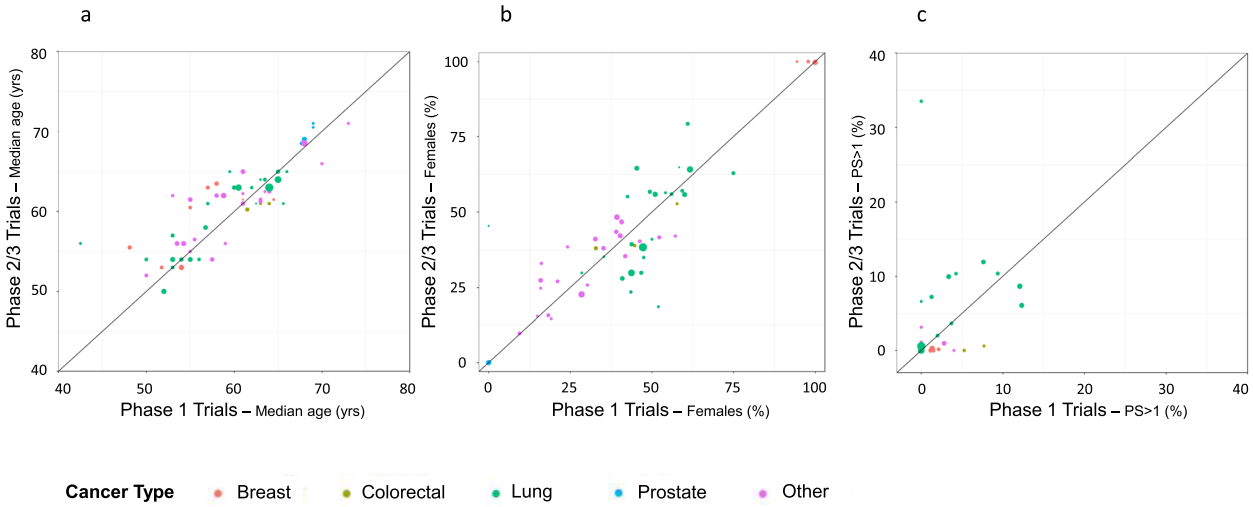

Fig. 2 Distribution by type of cancer of patients' characteristics in phase 1 and 2/3 clinical trials (**a** median age, **b** female rate; **c** PS > 1 rate)

Table 1 Weighted mean (SD) of patients' median age in phase 1 and 2/3 clinical trials by cancer type and drug class

	N° indications	Phase 2/3 trial wMean Median age (SD), years	Phase 1 trial wMean Median age (SD), years	Delta	p value
Overall	59	60.7 (5.1)	59.7 (5.6)	1.0	0.051
By cancer type					
Breast	8	57.7 (4.5)	54.6 (3.8)	3.1	
Colorectal	3	60.6 (0.4)	62.5 (1.1)	− 1.9	
Lung	23	60.0 (4.8)	59.6 (5.2)	0.4	
Prostate	4	69.2 (0.8)	68.1 (0.4)	1.1	
Genito-urinary	5	65.7 (3.3)	64.4 (5.4)	1.3	
Gynaecological	–	–	–	–	
Head and neck	3	58.0 (2.7)	58.4 (3.8)	− 0.4	
Melanoma	9	59.0 (4.0)	57.2 (3.2)	1.8	
NET	–	–	–	–	
Skin	2	66.0 (4.5)	61.8 (10.0)	4.2	
Sarcoma	–	–	–	–	
Upper-gastrointestinal	2	62.5 (0)	63.9 (0.2)	− 1.4	
By drug class					
Cytotoxic	3	59.9 (2.1)	60.2 (3.8)	− 0.3	
Hormonal	3	69.0 (0.5)	68.0 (0.3)	1.0	
Immunotherapy	12	63.8 (2.5)	62.7 (4.0)	1.1	
Immunotherapy plus cytotoxic	6	59.2 (5.5)	59.6 (5.0)	− 0.4	
Target therapy	32	58.3 (4.9)	57.2 (5.0)	1.1	
Target therapy plus cytotoxic	3	57.5 (2.1)	54.9 (5.8)	2.6	

NET neuroendocrine tumors

population [13]. We previously found significant disparities in age and PS status between patients enrolled in registrational trials and real-world practice. Patients in clinical practice, indeed, were on average more than 5 years older, with a higher rate of elderly and worse performance status. Rate of female patients was balanced overall, with some differences when considering specific cancer types [9]. Given these results, we searched for a

Table 2 Weighted mean (SD) of female rate in phase 1 and 2/3 clinical trials by cancer type and drug class

	N° indications	Phase 2/3 trial	Phase 1 trial	Delta	p value
		wMean Female rate (SD), %	wMean Female rate (SD), %		
Overall	59	40.8 (27.3)	45.7 (23.0)	− 4.9	0.999
By cancer type					
Breast	7	99.8 (0.2)	99.5 (1.3)	0.3	
Colorectal	3	41.1 (5.7)	40.9 (9.6)	0.2	
Lung	24	46.2 (14.6)	50.0 (8.8)	− 3.8	
Prostate	4	0	0	0	
Genito-urinary	5	24.6 (2.1)	24.4 (5.7)	0.2	
Gynaecological	–	–	–	–	
Head and neck	3	17.9 (9.1)	14.7 (4.0)	3.2	
Melanoma	9	42.8 (4.1)	39.8 (4.9)	3.0	
NET	–	–	–	–	
Skin	2	28.0 (12.0)	22.0 (2.5)	6.0	
Sarcoma	–	–	–	–	
Upper-gastrointestinal	2	35.7 (11.1)	43.7 (15.8)	− 8.0	
By drug class					
Cytotoxic	3	33.0 (6.4)	43.5 (7.4)	− 10.5	
Hormonal	3	0	0	0	
Immunotherapy	12	34.9 (8.4)	37.3 (9.8)	− 2.4	
Immunotherapy plus cytotoxic	6	57.3 (37.0)	64.5 (32.2)	− 7.2	
Target therapy	32	55.4 (21.6)	54.7 (20.6)	0.7	
Target therapy plus cytotoxic	3	27.8 (14.5)	21.0 (12.9)	6.8	

NET neuroendocrine tumors

similar trend in earlier phases, as a potential cause of over-selection. Indeed, it is well known that criteria for phase 1 enrolment are even more stringent, due to strict molecular and clinical selection for new potentially toxic target agents, several prohibited concomitant conditions and medications that could possibly interfere with the novel drugs tested [14]. Also, there might be a clinician bias leading to consider early-phase trials as more unsafe for patients, consequently reducing the number of candidates for clinical protocols. Phase 1 trials might also be more demanding for patients because of a greater number of planned visits and procedures. This could lead to exclusion of patients considered unable to adhere to trial rules or lacking social support.

Previous works have investigated disparities in phase 1 trials' enrolment [15, 16]. Although upper age limits are mostly absent in trial protocols, older patients might be excluded from phase 1 clinical trials due to concerns about potential comorbidities, altered pharmacokinetics, and presumed frailty, thus limiting insights into treatment effects for older adults, despite the high prevalence of cancer in this population [17–19]. However, our analysis did not find statistically significant differences in age between phase 1 and phase 2/3 trial populations, revealing disparities in both directions when considering different cancer types, with no clear evidence of elderly underrepresentation in early phase research. Consistently with our findings, a recently published cross-sectional study conducted at an Academic Center in Massachusetts reported disparities in phase 1 versus 2/3 enrolment based on ethnicity, while no differences emerged by age, and also by insurance status, marital status and income [10]. This evidence could possibly suggest a similar role of age in patient selection for clinical trials, regardless of the phase.

Also when considering the rate of female patients enrolled, no statistically significant difference emerged overall. As women and men may respond differently to treatments, given women's unique biology, including hormonal differences and varied responses to medications, these results reassure about the generalizability of clinical trials findings into female population. When women are equitably represented, early-phase trials can more accurately capture sex-specific responses to investigational therapies, leading to better-informed dosing, fewer adverse events, and eventually improved outcomes. Interestingly, lower female rate was found in phase 1 trials evaluating

Table 3 Weighted mean (SD) of PS > 1 rate in phase 1 and 2/3 clinical trials by cancer type and drug class

	N° indications	Phase 2/3 trial wMean PS > 1 rate (SD), %	Phase 1 trial wMean PS > 1 rate (SD), %	Delta	p value
Overall	47	2.3 (4.7)	1.8 (3.5)	0.5	0.374
By cancer type					
Breast	6	0.1 (0.2)	1.2 (0.6)	− 1.1	
Colorectal	2	0.2 (0.3)	6.3 (1.2)	− 6.1	
Lung	22	4.1 (5.9)	2.9 (4.3)	1.2	
Prostate	–	–	–	–	
Genito-urinary	4	0.5 (0.3)	0.3 (1.0)	0.2	
Gynaecological	–	–	–	–	
Head and neck	1	0	0	0	
Melanoma	8	0.2 (0.3)	0.4 (1.0)	− 0.2	
NET	–	–	–	–	
Skin	2	1.7 (1.6)	0	1.7	
Sarcoma	–	–	–	–	
Upper-gastrointestinal	2	0.2 (0.1)	0	0.2	
By drug class					
Cytotoxic	3	6.6 (5.9)	4.1 (3.8)	2.5	
Hormonal	–	–	–	–	
Immunotherapy	10	0.4 (0.3)	0.2 (0.8)	0.2	
Immunotherapy plus cytotoxic	6	0.1 (0.1)	0.6 (0.7)	− 0.5	
Target therapy	28	3.5 (5.8)	3.0 (4.3)	0.5	
Target therapy plus cytotoxic	–	–	–	–	

NET neuroendocrine tumors, *PS* performance status

treatments for skin cancer, confirming a trend that was already seen for registrational trials when compared to clinical practice in our previous study. These results could eventually advocate the need for a focus on this specific cancer type.

As to performance status, differences in both directions were found when comparing the rate of patients with PS > 1 in phase 1 and 2/3 clinical trials, but without statistical significance. Indeed, many clinical trials restrict enrolment to patients with ECOG PS 0–1 regardless of phases, prioritizing individuals who are healthier and potentially more resilient to drug toxicities, possibly explaining why poor PS rate was low on average in both populations.

Despite our findings appear encouraging in terms of phase 1 clinical trials' inclusiveness and accessibility, some limitations must be advised. Firstly, the low number of indications (ranging from 47 to 59) for which we were able to compare the two populations. The initial denominator was actually higher (129) but yet not fully representative of all the indications available for cancer treatment, because it was selected based on the presence within AIFA administrative registries. In addition, the number of indications was further reduced by the need to exclude basket trials not providing patients' characteristics by each cancer type. By including those trials, in fact, the overall comparison would have been biased by the inherent epidemiological characteristics of distinct cancers (e.g. endometrial and ovarian cancer cohorts would necessarily have a 100% rate of female patients, as prostate cancer cohort would have none; also, the incidence of various cancer types differs significantly across age groups, partially reflecting distinct biological and environmental risk factors). Moreover, a descriptive analysis of distributions by cancer type could not be performed for such trials, thus generating confusion and potentially leading to inaccurate insights.

In conclusion, similar characteristics observed in baseline populations suggest no evident disparities in patient enrolment for early phase trials as compared to later trials supporting drug registration. A possible explanation may be that criteria (in terms of age, sex, performance status) applied in patient selection for phase 1 trials directly inform also patient selection strategies for later phase 2/3 trials. This might be the result of "study expansion" approaches or conservative strategies tending to apply the evidence available from early phases into study designs of later phases, in a way that may lead to

"a priori" homogenization of eligible patients throughout drug development. Given that patient selection remains conservative from the beginning of clinical development, improving phase 1 trials' design appears crucial for subsequent experimental development because it might notably affect further patient selection and generalizability of results. Moreover, the role of phase 1 trials in generating meaningful preliminary efficacy data that may lead to accelerated approvals from regulatory agencies, particularly for high-need cancers lacking effective treatments, is rising. Consequently, this shift emphasizes the constant need for robust, diverse phase 1 data to warrant a wider patients' selection also for later phases and to ensure that early approvals align with real-world patient outcomes.

Abbreviations

AIFA	Italian Medicines Agency
CT	Clinical trial
EMA	European Medicines Agency
EPAR	European Public Assessment Reports
NET	Neuroendocrine tumours
PS	Performance status

Acknowledgements
Not applicable.

Author contributions
MLI, ST, MDM, FP conceptualized the study. MLI, ST, ACag, ACan, FS, SF collected data on clinical trials. MLI, LA, SF performed analyses. MLI, FP wrote the first draft of manuscript; all authors contributed to the interpretation of results, and approved the final version of the manuscript and accept responsibility to submit for publication.

Funding
This work was partially supported by the Italian Ministry of Health within the Ricerca Corrente Project L4/10 of the National Cancer Institute of Naples, IRCCS Fondazione G.Pascale; however, the Italian Ministry of Health played no further role in the study.

Availability of data and materials
The datasets generated and/or analysed during the current study are available in the ZENODO repository, (https://doi.org/10.5281/zenodo.14260553).

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
ST: reports current employment at Menarini Ricerche SpA, Pomezia. AG: reports travel and accommodation expenses fees from Bayer. MCP: reports honoraria from Astellas, Pfizer, Ipsen, Astrazeneca for speaker activities; from AstraZeneca, Bayer, Roche for financial support to institutional research activities. MDM.: reports honoraria from AstraZeneca, Boehringer Ingelheim, Janssen, Merck Sharp & Dohme (MSD), Novartis, Pfizer, Roche, GlaxoSmithKline, Amgen, Merck, Takeda, Viatris, Ipsen, Astellas for consultancy or participation to advisory boards; institutional funding for work in clinical trials/contracted research from Beigene, Exelixis, MSD, Pfizer and Roche. FP: reports institutional grants or contracts from Roche, Bayer, AstraZeneca, Pfizer, Incyte, Tesaro/GSK, Merck; consulting fees from Bayer, Pierre Fabre, Astra Zeneca, Incyte, Ipsen, Clovis, Astellas, Sanofi, Roche, Pfizer; leadership in scientific society: President of AIOM 2023–2025. All remaining authors declare that they have no competing interests.

Author details
[1]National Cancer Institute IRCCS Fondazione G.Pascale, via M. Semmola 52, 80131 Naples, Italy. [2]Menarini Ricerche SpA, via T. Speri 10, 00071 Pomezia, Italy. [3]Department of Oncology, University of Turin, Ordine Mauriziano Hospital Umberto I, Largo Filippo Turati 62, 10128 Turin, Italy. [4]Italian Medicines Agency, via del Tritone 181, 00187 Rome, Italy. [5]Department of Oncology, University of Turin, AOU Città della Salute e della Scienza di Torino, C.so Bramante 88, 10126 Turin, Italy.

Received: 11 February 2025 Accepted: 16 April 2025
Published online: 16 May 2025

References

1. Jin S, Pazdur R, Sridhara R. Re-evaluating eligibility criteria for oncology clinical trials: analysis of investigational new drug applications in 2015. J Clin Oncol. 2017;35:3745–52.
2. Kim ES, Bruinooge SS, Roberts S, et al. Broadening eligibility criteria to make clinical trials more representative: American Society of Clinical Oncology and friends of cancer research joint research statement. J Clin Oncol. 2017;35:3737–44.
3. Lichtman SM, Harvey RD, Damiette Smit MA, et al. Modernizing clinical trial eligibility criteria: recommendations of the American Society of Clinical Oncology-Friends of cancer research organ dysfunction, prior or concurrent malignancy, and comorbidities working group. J Clin Oncol. 2017;35:3753–9.
4. Magnuson A, Bruinooge SS, Singh H, et al. Modernizing clinical trial eligibility criteria: recommendations of the ASCO-friends of cancer research performance status work group. Clin Cancer Res. 2021;27:2424–9.
5. Poon R, Khanijow K, Umarjee S, et al. Participation of women and sex analyses in late-phase clinical trials of new molecular entity drugs and biologics approved by the FDA in 2007–2009. J Womens Health (Larchmt). 2013;22:604–16.
6. Riner AN, Girma S, Vudatha V, et al. Eligibility criteria perpetuate disparities in enrollment and participation of black patients in pancreatic cancer clinical trials. J Clin Oncol. 2022;40:2193–202.
7. Scher KS, Hurria A. Under-representation of older adults in cancer registration trials: known problem, little progress. J Clin Oncol. 2012;30:2036–8.
8. Montilla S, Xoxi E, Russo P, et al. Monitoring registries at Italian medicines agency: fostering access, guaranteeing sustainability. Int J Technol Assess Health Care. 2015;31:210–3.
9. Iacovino ML, Celant S, Tomassini L, et al. Comparison of baseline patient characteristics in Italian oncology drug monitoring registries and clinical trials: a real-world cross-sectional study. Lancet Reg Health Eur. 2024;41:100912.
10. Perni S, Moy B, Nipp RD. Disparities in phase 1 cancer clinical trial enrollment. Cancer. 2021;127:4464–9.
11. Araujo D, Greystoke A, Bates S, et al. Oncology phase I trial design and conduct: time for a change—MDICT Guidelines 2022. Ann Oncol. 2023;34:48–60.
12. Weber JS, Levit LA, Adamson PC, et al. American Society of Clinical Oncology policy statement update: the critical role of phase I trials in cancer research and treatment. J Clin Oncol. 2015;33:278–84.
13. Murthy VH, Krumholz HM, Gross CP. Participation in cancer clinical trials: race-, sex-, and age-based disparities. JAMA. 2004;291:2720–6.
14. Flannery MA, Culakova E, Canin BE, et al. Understanding treatment tolerability in older adults with cancer. J Clin Oncol. 2021;39:2150–63.
15. Charton E, Baldini C, Fayet Y, et al. Inequality factors in access to early-phase clinical trials in oncology in France: results of the EGALICAN-2 study. ESMO Open. 2023;8:101610.
16. Ho J, Pond GR, Newman C, et al. Barriers in phase I cancer clinical trials referrals and enrollment: five-year experience at the Princess Margaret Hospital. BMC Cancer. 2006;6:263.

17. Basche M, Baron AE, Eckhardt SG, et al. Barriers to enrollment of elderly adults in early-phase cancer clinical trials. J Oncol Pract. 2008;4:162–8.
18. Ferlay J, Colombet M, Soerjomataram I, et al. Cancer statistics for the year 2020: an overview. Int J Cancer. 2021;149:778–89.
19. Lewis JH, Kilgore ML, Goldman DP, et al. Participation of patients 65 years of age or older in cancer clinical trials. J Clin Oncol. 2003;21:1383–9.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.