Limited progress in clinical trials for rare urologic cancers: Testicular and penile cancer

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ABSTRACT

Introduction: We aimed to characterize the contemporary landscape, completion rates, and predictors of completion of clinical trials in testicular and penile cancers.
Methods: We performed a registry-based cohort analysis of *ClinicalTrials.gov* to identify interventional and observational trials in testicular or penile cancer initiated between January 1, 2000, and October 1, 2025. Trials withdrawn before enrollment, supportive-care or non-oncologic studies, epidemiologic investigations, and basket trials without predefined disease-specific enrollment targets were excluded. Extracted variables included trial design, enrollment targets, funding source, geographic region, and completion status. Firth's penalized logistic regression was used to assess predictors of trial completion. Kaplan-Meier and Cox proportional hazards models evaluated time to trial completion.
Results: Eighty-three eligible trials were identified, including 34 penile and 49 testicular cancer studies. Most trials were early-phase, non-randomized, and small. Overall completion rates were low (38% for penile cancer and 41% for testicular cancer), with no significant difference by disease site. Trials conducted outside North America were significantly more likely to complete than North American studies (adjusted odds ratio 10.21; 95% confidence interval [CI] 2.11–68.27). Time-to-event analyses similarly demonstrated faster completion among non-North American trials (multivariable hazard ratio 5.02, 95% CI 1.84–13.66).
Conclusions: Clinical trials in rare urologic cancers demonstrate persistently low completion rates and substantial geographic disparities, highlighting the need for improved international collaboration and alternative trial frameworks to enhance trial feasibility and completion.

INTRODUCTION

Conducting clinical trials in rare cancers is inherently challenging. Limited patient populations lead to slow and geographically fragmented accrual, and randomized trials are often underpowered to detect meaningful treatment differences.[1] As a result, progress has been constrained, and for many rare cancers the standard of care has remained unchanged.[2] In the United States, rare cancers are defined by the National Cancer Institute (NCI) as an incidence of fewer than 15 per 100,000 people per year,[3] while in Europe, a cancer is considered rare when it occurs in fewer than 6 per 100,000 persons per year.[4] These definitions place testicular and penile cancers within the category of rare urologic cancers, with global age-standardized rate (ASR) of 1.8 per 100,000 for testicular cancer and 0.8 per 100,000 for penile cancer.[5] Despite advances in systemic therapy and surgical techniques for many malignancies, the management of these tumors has lagged.[6,7] The need for innovation is clear: while testicular cancer is associated with excellent overall survival, many survivors experience long-term treatment-related toxicities, and a subset of young men with poor-risk metastatic disease continues to have poor survival outcomes.[6] In penile cancer, patients often undergo mutilating surgery and receive poorly tolerated systemic chemotherapy regimens, yet survival rates have shown little improvement over time.[8] The scarcity of advanced-stage clinical trials and minimal industry investment has resulted in limited clinical guidelines and an absence of new FDA-approved therapies for both penile and testicular cancers.[9] Against this backdrop, we aimed to analyse the contemporary landscape of clinical trials in rare urologic cancers, focusing on testicular and penile cancers, outlining prevailing trends, identifying unmet needs, and discussing challenges in trial design as well as opportunities for future progress in these rare genitourinary malignancies.

METHODS

Data sources and search strategy

ClinicalTrials.gov is a publicly accessible registry of clinical research studies maintained by the U.S. National Library of Medicine. It provides up-to-date information on ongoing and completed clinical trials submitted and updated by trial sponsors and investigators, including studies conducted in more than 200 countries. We applied a predefined keyword-based search strategy using Boolean operators (OR) to capture synonymous terminology for testicular and penile cancer within ClinicalTrials.gov. Because registry searches do not rely on PubMed MeSH indexing, relevant synonyms were incorporated directly into the query string. ClinicalTrials.gov was queried on October 15, 2025 for studies started between January 1, 2000, and October 1, 2025, using the following terms: ‘testicular neoplasms OR testicular cancer OR testicular germ cell tumor OR testis cancer’ OR ‘penile cancer OR penile carcinoma OR penile neoplasms OR penile squamous cell carcinoma.’

Study eligibility and data extraction

Eligible studies included interventional or observational trials enrolling patients with either testicular or penile cancer. We excluded studies that were withdrawn before recruitment, supportive-care trials, and those with non-oncologic primary endpoints (e.g., psychosocial or

fertility outcomes). Etiologic and epidemiologic investigations, such as environmental or occupational exposure case–control studies, were also excluded. In addition, basket trials (e.g., HPV-associated cancers or rare solid tumor cohorts) were excluded unless they specified a predefined enrollment target for patients with testicular or penile cancer and reported disease-specific recruitment targets.

Diagnostic studies were eligible if they (i) enrolled patients with pathologically confirmed testicular or penile cancer, or (ii) were performed to establish a diagnosis in patients with clinical or radiologic suspicion of these malignancies and evaluated oncologic diagnostic performance or clinically actionable diagnostic endpoints. Studies focused on survivorship, psychosocial outcomes, or other non-oncologic assessments were excluded. For each eligible trial, we collected information on study location (single-centre vs. multicentre), start date, primary completion date, overall completion date, date of results publication, enrollment, intervention type, funding source (institutional, industry, government, or foundation), randomization status, masking, study phase, disease stage, line of therapy, trial completion status, and primary outcome. In cases of trial discontinuation or termination, the reported reason was recorded as listed on ClinicalTrials.gov. Interventions were categorized as medical, procedural (including radiation-based), diagnostic, or other. Medical interventions were further sub-classified according to therapeutic class (e.g., chemotherapy, immunotherapy, antibody–drug conjugates).

Statistical analysis

Data was analyzed using descriptive and inferential statistics. Continuous variables were summarized as medians with interquartile ranges (IQRs) and compared using the Mann–Whitney U test, as appropriate. Categorical variables were reported as frequencies and percentages and compared using the Chi-square test or Fisher's exact test when cell counts were small.

Primary Analysis: The primary analysis assessed factors associated with clinical trial completion versus termination, as well as time to trial completion.

Univariate analyses were first performed to evaluate associations between individual trial characteristics and trial completion status. For the binary outcome (completion vs termination), Firth's penalized logistic regression was used to account for small sample sizes and rare outcome categories. Covariates included disease site (penile vs testicular), trial phase (early [I/II] vs late [III/IV] or not applicable), funding source (industry vs non-industry), geographic region (North America vs Europe/other), randomization (yes/no), intervention type (medical vs procedural/radiation/diagnostic/device/other), single- versus multicentre design, and planned enrollment.

Variables with clinical relevance and adequate data distribution were included in a multivariable Firth logistic regression model to identify independent predictors of trial completion. Results are reported as odds ratios (OR) with 95% confidence intervals (CI).

In parallel, time-to-event analyses evaluated factors associated with time from trial registration to completion. Trial completion was the event of interest. Trial status was determined using the ClinicalTrials.gov "Overall Status" field. Time to completion was measured from trial initiation to the registry-reported study completion date. Trials terminated

prior to completion were treated as censored at the time of termination. All remaining trials were considered ongoing and administratively censored at the date of data extraction. Kaplan–Meier curves were generated, with group comparisons performed using the log-rank test. Multivariable Cox proportional hazards models incorporated the same covariates as the logistic regression analyses.

Secondary Analysis: The secondary analyses examined temporal trends in clinical trial activity and trial design characteristics over the study period. Annual counts of registered and completed trials were summarized descriptively, and monotonic trends were assessed using Kendall's rank correlation coefficient (τ) between calendar year and trial counts. Changes over time in the annual proportions of completed trials, randomized designs, and industry-funded studies were similarly evaluated using Kendall's τ.

Exploratory Analysis: Lastly, exploratory subgroup analyses stratified temporal trends by disease site (penile vs testicular) and funding source (industry vs non-industry). All statistical tests were two-sided, with $p < 0.05$ considered statistically significant. Analyses were performed using R version 4.3.2 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Overview of included trials

The database query returned 132 penile cancer and 335 testicular cancer trials registered between January 2000 and October 2025.
After applying the study inclusion and exclusion criteria, 34 penile and 49 testicular cancer trials remained for analysis (Figure 1).

Trial characteristics

Penile and testicular cancer trials showed similar profiles (Table 1). Most were early-phase (I/II: 26/34 [76.5%] vs 25/49 [51.0%]), interventional (32/34 [94.1%] vs 38/49 [77.6%]), and non-randomized open-label in design (31/34 [91.2%] vs 41/49 [83.7%]). Drug-based therapies predominated (27/34 [79.4%] vs 28/49 [57.1%]), although testicular cancer studies more often included device or diagnostic interventions (12/49 [24.5%] vs 4/34 [11.8%]). Most trials were conducted in Europe (20/34 [58.8%] vs 31/49 [63.3%]), and nearly half in each group were single-centre. Studies largely enrolled patients with advanced disease and planned small cohorts: median 32 participants [IQR 24–42] for penile and 50 [IQR 30–210] for testicular cancer. Completion rates were comparable at data cutoff (13/34 [38.2%] vs 20/49 [40.8%]).

Primary analysis: Trial Completion and Determinants

Trial completion varied substantially across study characteristics. Disease site (penile vs testicular) was not independently associated with trial completion on univariate or multivariable analysis. Geographic region was the strongest determinant of trial completion, with European studies completed more frequently than those conducted in North America (49.0% vs 24.0%). This association was significant on univariate analysis (OR 6.54; 95% CI 1.72–27.67) and remained robust after multivariable adjustment (aOR 10.21; 95% CI 2.11–

68.27; Table 2 and Figure 2). Notably, no North America-based penile cancer trial reached completion during the study period.

Industry-funded trials demonstrated higher crude completion rates than non-industry studies (50.0% vs 36.1%); however, funding source was not independently associated with completion after adjustment (aOR 0.35; 95% CI 0.05–1.86). Interventional trials were more likely to be completed than observational studies (44.3% vs 15.4%), with drug-based interventions exhibiting the highest completion rates (49.1%); However, neither study type nor intervention type was significantly associated with trial completion in univariate analyses (univariate OR 0.66; 95% CI 0.08–7.75 for observational vs interventional studies, and univariate OR 0.51; 95% CI 0.05–2.81 for drug vs non-drug interventions). Trial phase, randomization status, and multicentre design were likewise not significantly associated with trial completion and were therefore not retained as independent predictors in adjusted models (all $p > 0.05$).

Time-to-event analysis

Kaplan–Meier analysis of the overall cohort demonstrated a median time to trial completion of 11.75 years (95% CI 5.33–not estimable; Figure 3). When analyzed by geographic region, trials conducted in Europe or other regions exhibited a significantly faster time to completion compared with those conducted in North America, as assessed by the log-rank test ($p = 0.013$). Consistent with this finding, univariate Cox regression indicated a higher hazard of completion among Europe/Other trials (HR 2.98, 95% CI 1.21–7.30).

In multivariable Firth-penalized Cox proportional hazards analysis, geographic region remained independently associated with time to trial completion, with Europe/Other trials demonstrating a significantly higher hazard of completion compared with North American trials (HR 5.02, 95% CI 1.84–13.66; $p < 0.001$). Industry funding was also independently associated with a higher hazard of completion (HR 2.45, 95% CI 1.09–5.49; $p = 0.029$). In contrast, multicentre design was not independently associated with time to completion (HR 1.33, 95% CI 0.64–2.75; $p = 0.441$), while trials with a planned enrollment of ≥20 participants exhibited a markedly lower hazard of completion compared with smaller trials (HR 0.06, 95% CI 0.02–0.17; $p < 0.001$; Table 3).

Temporal trends in trial activity and design

Between 2000 and 2025, annual registration of penile and testicular cancer trials remained low, with a median of 4 trials per year (range 1–7), and no clear monotonic change over time (Figure 4; Supplementary Table 1). In contrast, the proportion of trials reaching completion declined significantly across the study period (Kendall's $\tau = -0.39$, $p = 0.013$), decreasing from near-complete completion rates in the early 2000s to fewer than 25% in more recent years (Figure 4; Supplementary Table 2).

No consistent temporal trends were observed in randomization rates or industry funding proportions overall. When stratified by disease site, testicular cancer trials demonstrated a significant decline in the proportion of randomized studies over time ($\tau = -0.35$, $p = 0.039$), whereas no corresponding trend was observed among penile cancer trials (Supplementary

Table 2). Across all years, the majority of trials remained non-randomized and non–industry funded.

DISCUSSION

A clinical trial's feasibility, reflected by its ability to complete as intended, is predicated on meticulous planning. Rare cancers are uniquely difficult, as small, heterogeneous, and geographically dispersed patient populations amplify operational risk. Testicular and penile cancers represent rare urologic malignancies at the population level, despite the relative clinical familiarity of testicular cancer within younger patient populations. Completion determines whether assumptions about sample size, timelines, randomization, and endpoint selection translate into interpretable evidence and inform regulatory review and clinical guideline development. We evaluated testicular and penile cancer trials registered over 25 years.

Our primary analysis demonstrated that geographic location was strongly associated with trial completion. Overall, 33 of 83 eligible trials (39.8%) reached completion, but this outcome varied markedly by region. Trials conducted in Europe/Other regions were more than seven times more likely to be completed than those based in North America, and this effect remained consistent across disease site, study phase, and funding source. Notably, within our study cohort, no North America–based penile cancer trial achieved completion during the study period. The impact of geographic region persisted after adjustment for clinically relevant covariates and supported by time-to-event analyses, with European/Other trials completed earlier than North American studies.

Stensland et al. similarly observed reduced completion rates among U.S.-only urologic oncology trials.[10] Because the association persisted after adjustment for funding source, trial design, and enrollment size, it likely reflects broader system-level factors not captured in registry variables. Europe has well-established rare-cancer research ecosystems and cross-border referral infrastructures that facilitate centralized coordination, multicentre accrual, and harmonized trial conduct,[11] advantages that are particularly critical when eligible patients are scarce. Patient-level financial barriers, including travel and treatment-related costs, are generally lower and more predictable in many European health systems, whereas out-of-pocket expenses remain a frequent obstacle to trial participation in the United States.[12] In addition, as of 2022, the European regulatory environment benefits from the Clinical Trials Regulation and its centralized submission system, which streamlines approvals and reduces start-up delays across multiple countries.[13] Together, these differences create a more favorable landscape for trial completion in rare cancers across Europe.

Another factor that may contribute to the relative feasibility of clinical trials for penile and testicular cancer in Europe is simple epidemiology, with more patients available for enrollment. Incidence rates of testicular cancer are higher in Western, Northern, and Southern Europe compared with the United States,[14] and, given the markedly higher prevalence of circumcision in the United States[15], among other contributing factors, penile cancer incidence is higher in most European countries.[16]

The finding that nearly one in three trials failed to complete highlights a significant feasibility gap compared with other genitourinary malignancies, where prior work estimates

failure rates closer to one in six.[10] This difference likely reflects the extreme rarity of testicular and penile cancers, which magnifies the logistical and accrual challenges intrinsic to clinical research in small populations.

Implementing clinical trials is challenging, but barriers are amplified in rare tumors, making careful planning essential, particularly around endpoint selection and realistic accrual targets. The lower completion hazard observed in trials with larger planned enrollment likely reflects prolonged accrual timelines inherent to rare cancers, where higher recruitment targets may substantially delay completion. Endpoints must be both clinically meaningful and operationally achievable within small, slow-accruing populations. As Steidle et al. demonstrated,[17] selecting an appropriate primary endpoint has downstream regulatory implications; trials showing patient-centred efficacy signals, such as OS (when feasible) or validated surrogates like independently assessed ORR with durability or PFS with blinded review, are more likely to inform approvals and guidelines. In parallel, accrual planning is critical. Prior analyses show that poor accrual is the leading cause of trial failure,[18] and even some trials that technically reach completion do so with insufficient sample size,[19] limiting statistical power and interpretability.

Beyond operational factors, disease-specific characteristics also constrain trial activity. In metastatic testicular cancer, cisplatin-based regimens already cure approximately 85 percent of patients,[20] making it extremely difficult to demonstrate meaningful improvement without prohibitively large sample sizes. Non-inferiority designs aimed at reducing toxicity encounter similar challenges because very high baseline cure rates leave little acceptable margin. These limitations can reduce enthusiasm among both investigators and industry, since small patient populations combined with limited potential for new approvals offer minimal commercial incentive.[21]

Nevertheless, several developments over the last decades offer reasons for optimism. Historically, drug development for rare cancers was considered financially impractical due to limited commercial potential. In response, the U.S. FDA enacted the Orphan Drug Act in 1983, providing incentives such as market exclusivity, tax credits, and regulatory support to stimulate investment in rare-disease therapeutics.[22] In our cohort, 66% of trials evaluated medical therapies, including agents developed through orphan designation. For example, brentuximab vedotin, originally designed for CD30-positive lymphomas, was studied in testicular cancer in phase II trials such as NCT02689219 and NCT01851200.

Recent advances in next-generation sequencing and precision oncology have enabled tumor-agnostic therapeutic strategies.[23] By selecting treatment based on molecular alterations rather than tumor origin, these approaches broaden eligibility and facilitate accrual across otherwise rare subgroups.[24]

Innovative trial designs have also emerged to address many of the structural barriers highlighted by our findings. Basket trials enroll patients based on shared molecular or biological features rather than tumor site, allowing accrual across multiple rare histologies.[25] For instance, some studies have grouped penile cancer with HPV-related malignancies under a unified protocol. However, we elected not to include most basket trials in our analysis because many do not prespecify a minimum enrollment for penile or testicular cancer, and in

many cases, it is unclear whether any such patients actually participated. Platform and other master-protocol designs provide an additional solution by studying multiple therapies or molecularly defined cohorts under a single framework, pooling patients across institutions and simplifying activation to overcome the fragmentation and slow accrual that limit traditional stand-alone studies.[26]

Despite initiatives that should, in principle, concentrate more research on these rare malignancies, our temporal analysis did not show an increase in the number of registered trials over time. This absence of growth does not necessarily imply that fewer patients with penile or testicular cancer are accessing research therapies, as some may be enrolled in excluded study designs. For example, Puljak et al. identified 50 interventional GCT trials enrolling both ovarian and testicular cancer.[27]

This study has several limitations. First, ClinicalTrials.gov was our sole registry, and not all European or international studies are consistently registered there. Many European trials are registered in EudraCT or other regional platforms, and some academic studies may not be listed on ClinicalTrials.gov. Our dataset may underrepresent non–North American activity, potentially exaggerating geographic differences. Second, registry entries rely on investigator-submitted information and are subject to delays, incomplete fields, or inaccurate reporting. Key variables such as accrual targets, reasons for termination, or publication of results may be missing or updated after completion. Finally, "completion" does not guarantee scientific success; some trials finish with inadequate accrual or without published outcomes, limiting their clinical impact. Because termination precludes completion, competing-risk methods could be considered; however, given the exploratory design and limited sample size, we used a standard Cox framework and interpret hazard estimates cautiously.

Future efforts should prioritize designs that enhance feasibility in small populations, including centralized referral networks and multinational master-protocol trials. Harmonized registry reporting and prespecified penile or testicular cohorts within broader multi-tumor studies would improve transparency and relevance. Strategies such as remote participation and patient-support mechanisms may broaden access and increase enrollment of eligible patients.

CONCLUSIONS

This study demonstrates that clinical research in penile and testicular cancer is faltering. Trials remain scarce, underpowered, and frequently terminate before completion, particularly in North America. These failures prevent meaningful advances for patients with rare GU tumors. European rare-cancer networks and streamlined regulatory pathways appear to offer a workable blueprint. Unless the U.S. adopts comparable infrastructure, multinational accrual pathways, centralized approvals, realistic enrollment targets, and patient financial protections, the field will continue to stagnate. Immediate investment in efficient, collaborative trial models is needed for innovation to reach this underserved population.

REFERENCES

1. Tan SB. Strategy for randomised clinical trials in rare cancers. *BMJ* 2003;327:47-9. https://doi.org/10.1136/bmj.327.7405.47
2. Sandler A, Reilly K, Widemann B. Editorial: Special issue on rare cancers. *Curr Probl Cancer* 2021;45:100774. https://doi.org/10.1016/j.currproblcancer.2021.100774
3. National Cancer Institute. NCI dictionary of cancer terms: Rare disease. Available at: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/rare-disorder (accessed May 31, 2026)
4. Gatta G, Capocaccia R, Botta L, et al. Rare cancers are not so rare: The rare cancer burden in Europe. *Eur J Cancer* 2011;47:2493-511. https://doi.org/10.1016/j.ejca.2011.08.008
5. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2021;71:209-49. https://doi.org/10.3322/caac.21660
6. McHugh DJ, Gleeson JP, Feldman DR. Testicular cancer in 2023: Current status and recent progress. *CA Cancer J Clin* 2024;74:167-86. https://doi.org/10.3322/caac.21819
7. Masterson TA, Tagawa ST. A 25-year perspective on advances in an understanding of the biology, evaluation, treatment and future directions/challenges of penile cancer. *Urol Oncol* 2021;39:569-76. https://doi.org/10.1016/j.urolonc.2021.05.021
8. Deng X, Li Z, Gao X, et al. Trends in incidence, mortality, and survival of penile cancer in the United States: A population-based study. *Front Oncol* 2022;12:891623. https://doi.org/10.3389/fonc.2022.891623
9. Malshy K, Steidle M, Taussky D, et al. Impact of industry collaboration on US Food and Drug Administration approval success in genitourinary malignancy phase III clinical trials. *JCO Oncol Pract* 2025. https://doi.org/10.1200/OP-25-00194
10. Stensland KD, Galsky MD, Messing EM, et al. Estimating the rate and reasons of clinical trial failure in urologic oncology. *Urol Oncol* 2021;39:154-60. https://doi.org/10.1016/j.urolonc.2020.10.070
11. Blay JY, Coindre JM, Ducimetiere F, et al. European Reference Network for rare adult solid cancers, statement and integration to health care systems of member states: A position paper of the ERN EURACAN. *ESMO Open* 2021;6:100174. https://doi.org/10.1016/j.esmoop.2021.100174
12. Klamerus JF, Bruinooge SS, Bhatt A, et al. The impact of insurance on access to cancer clinical trials at a comprehensive cancer center. *Clin Cancer Res* 2010;16:5997-6003. https://doi.org/10.1158/1078-0432.CCR-10-1451
13. Patrick-Brown TDJ, Hemkens LG, Speich B, et al. Experiences and challenges with the new European Clinical Trials Regulation. *Trials* 2024;25:3. https://doi.org/10.1186/s13063-023-07869-x
14. Znaor A, Skakkebæk NE, Rajpert-De Meyts E, et al. Global patterns in testicular cancer incidence and mortality in 2020. *Int J Cancer* 2022;151:692-8. https://doi.org/10.1002/ijc.33999
15. Morris BJ, Wamai RG, Henebeng EB, et al. Estimation of country-specific and global prevalence of male circumcision. *Popul Health Metr* 2016;14:4. https://doi.org/10.1186/s12963-016-0073-5
16. Fu L, Wang S, Zhang Y, et al. Global pattern and trends in penile cancer incidence: Population-based study. *JMIR Public Health Surveill* 2022;8:e34874. https://doi.org/10.2196/34874

17. Steidle M, Malshy K, Taussky D, et al. Study endpoint fulfillment and FDA approval success in phase III clinical trials of genitourinary malignancies. *Clin Genitourin Cancer* 2025;23:102436. https://doi.org/10.1016/j.clgc.2025.102436
18. Stensland KD, McBride RB, Mao J, et al. Adult cancer clinical trials that fail to complete: An epidemic? *J Natl Cancer Inst* 2014;106. https://doi.org/10.1093/jnci/dju229
19. Stensland K, Mao J, Master VA, et al. Assessing genitourinary cancer clinical trial accrual sufficiency using archived trial data. *JCO Clin Cancer Inform* 2020:614-22. https://doi.org/10.1200/CCI.20.00031
20. Singla N, Bagrodia A, Baraban E, et al. Testicular germ cell tumors. *JAMA* 2025;333:793. https://doi.org/10.1001/jama.2024.27122
21. Oing C, Kollmannsberger C, Oechsle K, Bokemeyer C. Investigational targeted therapies for the treatment of testicular germ cell tumors. *Expert Opin Investig Drugs* 2016;25:1033-43. https://doi.org/10.1080/13543784.2016.1195808
22. Seoane-Vazquez E, Rodriguez-Monguio R, Szeinbach SL, Visaria J. Incentives for orphan drug research and development in the United States. *Orphanet J Rare Dis* 2008;3:33. https://doi.org/10.1186/1750-1172-3-33
23. Subbiah V, Gouda MA, Ryll B, et al. The evolving landscape of tissue-agnostic therapies in precision oncology. *CA Cancer J Clin* 2024;74:433-52. https://doi.org/10.3322/caac.21844
24. Subbiah V, Othus M, Palma J, et al. Designing clinical trials for patients with rare cancers: Connecting the zebras. *Am Soc Clin Oncol Educ Book* 2025;45. https://doi.org/10.1200/EDBK-25-100051
25. Hyman DM, Puzanov I, Subbiah V, et al. Vemurafenib in multiple nonmelanoma cancers with BRAF V600 mutations. *N Engl J Med* 2015;373:726-36. https://doi.org/10.1056/NEJMoa1502309
26. Woodcock J, LaVange LM. Master protocols to study multiple therapies, multiple diseases, or both. *N Engl J Med* 2017;377:62-70. https://doi.org/10.1056/NEJMra1510062
27. Puljak L, Poklepovic Pericic T, Vrdoljak E, et al. Trials of interventions for ovarian and testicular germ cell tumors registered in ClinicalTrials.gov: A cross-sectional study. *Eur J Surg Oncol* 2025;51:108545. https://doi.org/10.1016/j.ejso.2024.108545

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FIGURES AND TABLES

Figure 1. Trial selection flow diagram.

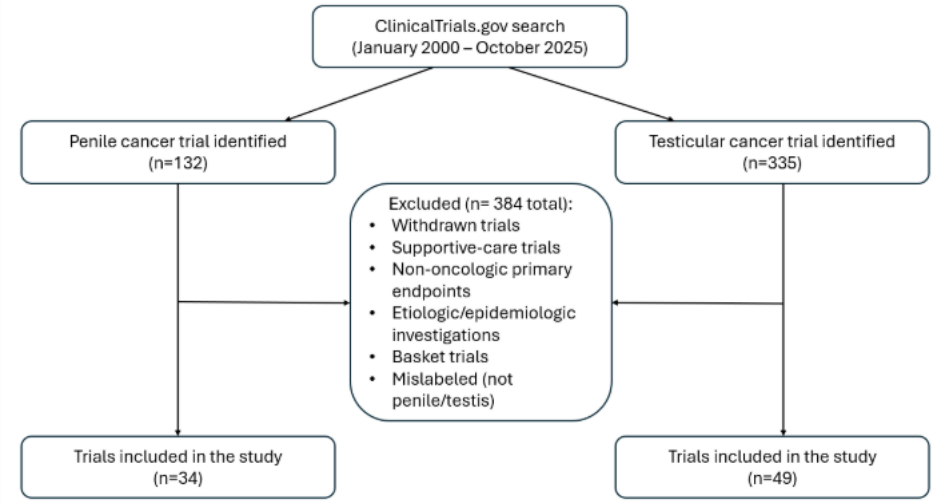

Figure 2. Forest plot of multivariable predictors of trial completion.

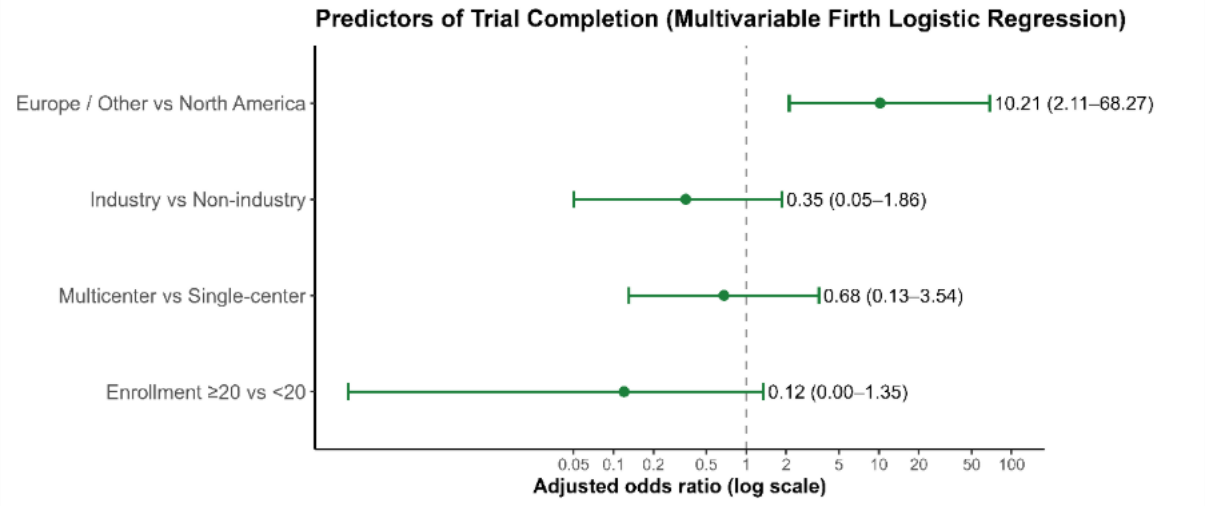

Figure 3. Kaplan-Meier curves for time to trial completion (A) overall; and (B) by region. Kaplan-Meier survival analysis shows the unadjusted hazard ratio with statistical significance assesed using the log-rank test. In (A), the overall cohort is shown, with a median time to trial completion of 11.75 years (95% CI 5.33–not estimable). In (B), time to trial completion is shown by geographic region, demonstrating a higher rate of completion among Europe or other region trials compared with trials conducted in North America (unadjusted hazard ratio 2.98, 95% confidence interval [CI] 1.21–7.30, log-rank p=0.013).

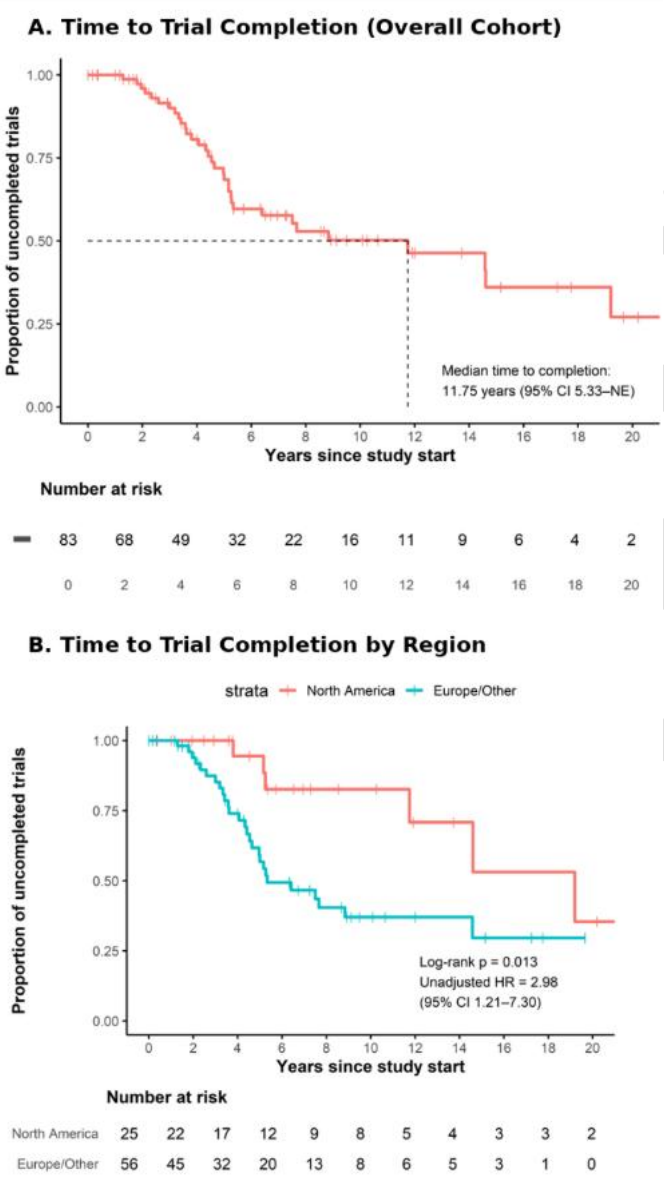

Figure 4. Temporal trends in penile and testicular cancer trials (2000−2025). (A) Annual number of registered trials stratified by recruitment status. Bars are color-coded to indicate completed, terminated, ongoing, and other/suspended trials. (B) Annual proportion of trials reaching completion; point size reflects the number of trials registered per year.

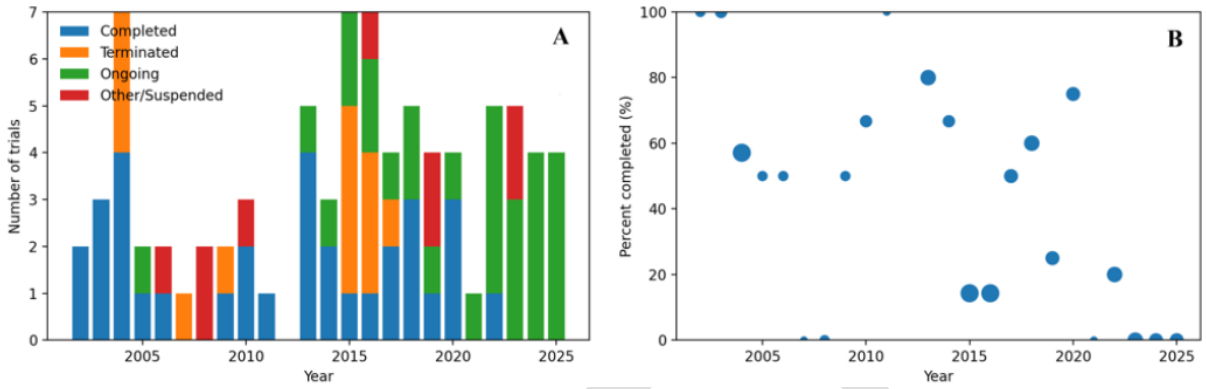

Table 1. Baseline characteristics of penile and testicular cancer trials			
Characteristic	**Overall (n=83)**	**Penile (n=34)**	**Testicular (n=49)**
Trial characteristics			
Geographic region, n (%)			
North America	25 (30.1)	8 (23.5)	17 (34.7)
Europe	51 (61.4)	20 (58.8)	31 (63.3)
Other	5 (6.0)	5 (14.7)	0 (0.0)
Not reported	2 (2.4)	1 (2.9)	1 (2.0)
Study setting, n (%)			
Single-center	41 (49.4)	17 (50.0)	24 (49.0)
Multicenter	38 (45.8)	15 (44.1)	23 (46.9)
Not reported	4 (4.8)	2 (5.9)	2 (4.1)
Primary sponsor, n (%)			
Non-industry	61 (73.5)	22 (64.7)	39 (79.6)
Industry	22 (26.5)	12 (35.3)	10 (20.4)
Study phase, n (%)			
Early (1/2)	51 (61.4)	26 (76.5)	25 (51.0)
Late (3.4)	7 (8.4)	1 (2.9)	6 (12.2)
Not reported/not applicable	25 (30.1)	7 (20.6)	18 (36.7)
Randomization, n (%)			
Non-randomized	72 (86.7)	31 (91.2)	41 (83.7)
Randomized	11 (13.3)	3 (8.8)	8 (16.3)
Masking, n (%)			
Blinded	0 (0.0)	0 (0.0)	0 (0.0)

Open-label/not applicable	83 (100.0)	34 (100.0)	49 (100.0)
Study type, n (%)			
Interventional	70 (84.3)	32 (94.1)	38 (77.6)
Observational	13 (15.7)	2 (5.9)	11 (22.4)
Therapeutic category, n (%)			
Drug	55 (66.3)	27 (79.4)	28 (57.1)
Procedure/radiotherapy	13 (15.7)	4 (11.8)	9 (18.4)
Device/diagnostic	16 (19.3)	4 (11.8)	12 (24.5)
Estimated enrollment, median (IQR)	40 [25–83]	32 [24–42]	50 [30–210]
Not reported, n	3	0	3
Trial initiation year, median (IQR)	2016 [2009–2020]	2019 [2015–2022]	2014 [2007–2018]
Disease characteristics			
Stage, n (%)			
Localized/early stage	–	Stage I–II: 12 (35.3)	Stage I: 12 (24.5)
Regional disease	–	–	Stage II: 7 (14.3)
Advanced disease	–	Stage III–IV: 22 (64.7)	Stage III: 24 (49.0)
Multiple stages	–	–	6 (12.2)
Line of therapy, n (%)			
First-line	–	14 (41.2)	14 (28.6)
≥ Second-line	–	15 (44.1)	21 (42.9)
Not applicable	–	5 (14.7)	14 (28.6)

Data are presented as n (%); median [Q1, Q3]. NR: not reported; NA: not applicable.

Table 2. Trial completion rates and predictors of completion by study characteristic								
Variable	**Category**	**Completed/total – all**	**Completed/total – penile**	**Completed/total – testicular**	**Univariate OR (95% CI)**	**p**	**Adjusted OR (95% CI)**	**p**
Disease site	Testicular	–	–	–	1.32 (0.37–4.67)	0.668	–	–
Funding source	Non-industry	22/61 (36.1)	7/22 (31.8)	15/39 (38.5)	Ref	–	Ref	–
	Industry	11/22 (50.0)	6/12 (50.0)	5/10 (50.0)	0.79 (0.22–2.98)	0.720	0.35 (0.05–1.86)	0.221
Geographic region	North America	6/25 (24.0)	0/8 (0.0)	6/17 (35.3)	Ref	–	Ref	–
	Europe/other	27/56 (48.2)	11/25 (44.0)	16/31 (51.6)	6.54 (1.72–27.67)	0.006	10.21 (2.11–68.27)	0.003
Trial phase	Early (1/2)	24/51 (47.1)	10/26 (38.5)	14/25 (56.0)	Ref	–	–	–
	Late (3/4)	3/7 (42.9)	0/1 (0.0)	3/6 (50.0)	1.10 (0.16–12.25)	0.930	–	–
Randomization	Non-randomized	29/72 (40.3)	12/31 (38.7)	17/41 (41.5)	Ref	–	–	–
	Randomized	4/11 (36.4)	1/3 (33.3)	3/8 (37.5)	0.70 (0.13–4.49)	0.685	–	–

Study type	Interventional	31/70 (44.3)	13/32 (40.6)	18/38 (47.4)	Ref	–	–	–
	Observational	2/13 (15.4)	0/2 (0.0)	2/11 (18.2)	0.66 (0.08–7.75)	0.708	–	–
Intervention type	Non-drug	6/28 (21.4)	4/8 (50.0)	2/20 (10.0)	Ref	–	–	–
	Drug	27/55 (49.1)	10/27 (37.0)	17/28 (60.7)	0.51 (0.05-2.81)	0.462	–	–
Centres	Single-center	17/41 (41.5)	7/17 (41.2)	10/24 (41.7)	Ref	–	Ref	–
	Multicenter	16/38 (42.1)	6/15 (40.0)	10/23 (43.5)	0.61 (0.16–2.13)	0.441	0.68 (0.13–3.54)	0.639
Enrollment size	<20	7/8 (87.5)	5/6 (83.3)	2/2 (100)	Ref	–	Ref	–
	≥20	26/75 (34.7)	8/28 (28.6)	18/47 (38.3)	0.15 (0.00–1.40)	0.108	0.12 (0.00–1.35)	0.094

Table 3. Multivariable Cox proportional hazards model for time to completion			
Variable	**Hazard ratio**	**95% confidence interval**	**p**
Region: Europe/other (vs. North America)	5.02	1.84–13.66	<0.001
Funding: Industry (vs. non-industry)	2.45	1.09–5.49	0.029
Centers: Multicenter (vs. single-center)	1.33	0.64–2.75	0.441
Planned enrollment ≥20 vs. <20	0.06	0.02–0.17	<0.001

Cox proportional hazards model; robust standard errors.