UCSF UC San Francisco Previously Published Works

Title

Reporting of Physicians' or Investigators' Choice of Treatment in Oncology Randomized Clinical Trials.

Permalink https://escholarship.org/uc/item/9746t3b2

Journal JAMA network open, 5(1)

ISSN 2574-3805

Authors

Olivier, Timothée Haslam, Alyson Prasad, Vinay

Publication Date

2022

DOI

10.1001/jamanetworkopen.2021.44770

Copyright Information

This work is made available under the terms of a Creative Commons Attribution License, available at https://creativecommons.org/licenses/by/4.0/

Peer reviewed



Research Letter | Oncology Reporting of Physicians' or Investigators' Choice of Treatment in Oncology Randomized Clinical Trials

Timothée Olivier, MD; Alyson Haslam, PhD; Vinay Prasad, MD, MPH

Introduction

Randomized clinical trials (RCTs) aim to rigorously evaluate the benefits and risks of any intervention. However, RCTs may be limited if the control group does not reflect the ongoing standard of care, and especially if the control group is inferior to standard care. A cross-sectional analysis of 95 consecutive Food and Drug Administration approvals of anticancer agents between 2013 and 2018 showed that 16 (17%) were based on RCTs with suboptimal control groups.¹

Theoretically, this limitation can be overcome if the physician is allowed to choose the controlgroup treatment with access and freedom. Increasingly, trials refer to a control group of physician's choice or investigator's choice, which may be perceived as a real (unrestricted) choice among all treatment options. However, this choice can be restricted and ambiguously reported with 2 consequences. First, when the choice is restricted to a limited number of options, the wording is misleading for physicians considering it was unfettered and unlimited. Second, the restriction may penalize the control group, making it substandard by not allowing all treatment options in a specific setting.

Methods

This cross-sectional study adhered to Strengthening the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline. Because we used publicly available data, and this was not human subjects research, in accordance with 45 CFR §46.102(f), we did not submit this study to an institutional review board or require informed consent procedures.

We sought to determine the total number of published oncology RCTs reporting a physician's (or investigator's) choice, their evolution over time, whether the choice was real (unrestricted) or restricted. We systematically reviewed all reports on RCTs mentioning physician's or investigator's choice (eMethods and eFigure in the Supplement). To be included, articles had to report on RCTs studying anticancer intervention, mentioning "physician's choice" or "investigator's choice" within the title or the abstract. We excluded nononcology reports, phase 1 studies, commentaries, perspectives, and subsequent publication of the same trial. We did not restrict the period of inclusion. The analysis was descriptive, and frequencies were calculated for categorical variables throughout. Statistical analysis was performed using R software version 4.0.4 (R Project for Statistical Computing) on November 1, 2021.

Results

Out of the 284 initially identified studies, 92 studies met our inclusion criteria, published between 2007 and 2021 (**Table**). Of these 92 oncology RCTs, the most common tumor type studied was breast cancer (22 of 92 RCTs; 23.9%). Over time, there was an increase in the number of published studies mentioning a physician's or investigator's choice in the control group of oncology RCTs (eg, 2 studies in 2007, 3 studies in 2014, and 12 studies in 2021). There were 82 industry-sponsored trials (89.1%) and 10 nonprofit sponsored trials (10.9%). Among the 82 industry-sponsored trials, there

Den Access. This is an open access article distributed under the terms of the CC-BY License.

JAMA Network Open. 2022;5(1):e2144770. doi:10.1001/jamanetworkopen.2021.44770

Author affiliations and article information are listed at the end of this article.

Supplemental content

JAMA Network Open | Oncology

were 71 RCTs (77.2%) with a restricted choice and 11 (12%) offering an unrestricted choice. Among the 10 nonprofit-sponsored trials, the choice was restricted in 7 RCTs (7.6%) and unrestricted in 3 (3.3%) (**Figure**).

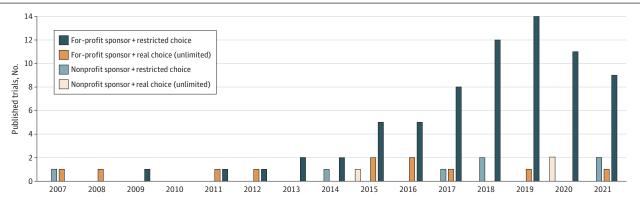
Table. Characteristics of Published Oncology RCTs Mentioning Physician's Choice or Investigator's Choice in the Control Group (N = 92)

| Uncell Oncloay RCT characteristicsUnsertited choiceFumor typeFurner typeAcute myeloid leukemia\$(3.8)1(7.1)4(4.3)Alt types01(7.1)1(1.1)Anyeloid leukemia1(1.3)01(1.1)Breast cancer19(24.4)3(21.4)22 (23.9)Chronic tymphorytic leukemia1(1.3)01(1.1)Endometrial cancer5(6.4)01(1.1)Esophageal cancer3(3.8)03(3.3)Follicular tymphoma1(1.3)01(1.1)Esophageal cancer4(5.1)04(4.3)Giblabdare cancer4(5.1)04(4.3)Giblabdare cancer2(2.6)02(2.2)Giblobardon02(1.3)2(2.2)Giblobardon02(1.1)1(1.1)Gastric cancer4(5.1)01(1.1)Head and neck squamous cell carcinoma2(2.6)02(2.2)Muther-ell lymphoma1(1.3)01(1.1)Nasopharyngeal cancer7(9.0)1(7.1)8(8.7)Non-small cell lung cancer7(9.0)1(7.1)8(8.7)Protesta cancer2(2.6)02(2.2)Protesta cancer2(2.6)02(2.2)Protesta cancer7(9.0)1(7.1)8(8.7)Non-small cell lung cancer7(9.0)1(7.1)8(8.7)Protesta cancer2(2.6)02(2.2)Protesta cancer1(3.3)01(3.3)Protesta ca | | Published oncology RCTs, No. (%) (N = 92) | | |
|--|---------------------------------------|---|--------------|----------------------|
| Tumor type Acute myeloid leukemia 3 (3.8) 1 (7.1) 4 (4.3) All types 0 1 (7.1) 1 (1.1) Amyloidosis 1 (1.3) 0 1 (1.1) Breast carcer 19 (24.4) 3 (21.4) 22 (23.9) Chronic lymphocytic leukemia 1 (1.3) 1 (7.1) 2 (2.2) Colorectal cancer 5 (6.4) 0 5 (5.4) Diffuse large 8-cell lymphoma 1 (1.3) 0 1 (1.1) Esophageal cancer 3 (3.8) 0 3 (3.3) Follicular lymphoma 1 (1.3) 0 1 (1.1) Gastric cancer 0 1 (7.1) 1 (1.1) Gastric cancer 4 (5.1) 0 4 (4.3) Glioblastoma 0 2 (2.2) 1 (1.1) Head and neck squamous cell carcinoma 2 (2.6) 0 2 (2.2) Glioblastoma 1 (1.3) 0 1 (1.1) Mantle-cell lymphoma 1 (1.3) 0 1 (1.1) Mantle-cell lymphoma 1 (1.3) 0 1 (1.1) | | Unrestricted choice | | |
| Acute myeloid leukemia 3 (3.8) 1 (7.1) 4 (4.3) All types 0 1 (7.1) 1 (1.1) Anyloidoisis 1 (1.3) 0 1 (1.1) Breast cancer 19 (24.4) 3 (21.4) 22 (2.3) Chronic (tymphocytic leukemia 1 (1.3) 1 (7.1) 2 (2.2) Colorectal cancer 5 (6.4) 0 5 (5.4) Diffuse large B-cell lymphoma 1 (1.3) 0 1 (1.1) Esophageal cancer 3 (3.8) 0 3 (3.3) Follicular lymphoma 1 (1.3) 0 1 (1.1) Gastric cancer 0 1 (7.1) 1 (1.1) Gastric cancer 0 2 (1.4) 2 (2.2) Gliobastoma 0 2 (1.4) 2 (2.2) Lymphoma 1 (1.3) 0 1 (1.1) Mantle-cell lymphoma 1 (1.3) 0 1 (1.1) Mantle-cell lymphoma 1 (1.3) 0 1 (1.1) Mantle-cell lymphoma 1 (1.3) 0 1 (1.1) Nasopharyngeal cancer | Oncology RCT characteristics | No (n = 78) | Yes (n = 14) | Overall (n = 92) |
| All types 0 1 (7.1) 1 (1.1) Amyloidosis 1 (1.3) 0 1 (1.1) Breast cancer 19 (24.4) 3 (21.4) 22 (23.9) Chronic lymphocytic leukemia 1 (1.3) 1 (7.1) 2 (2.2) Colorectal cancer 5 (6.4) 0 5 (6.4) Diffuse large B-cell lymphoma 1 (1.3) 0 1 (1.1) Edometrial cancer 3 (3.8) 0 3 (3.3) Follicular lymphoma 1 (1.3) 0 1 (1.1) Gasthic cancer 0 1 (7.1) 1 (1.1) Gasthic cancer 4 (5.1) 0 4 (4.3) Glioblastoma 0 2 (1.4.3) 2 (2.2) Glioblastoma 1 (1.3) 0 1 (1.1) Mantle-cell lymphoma 1 (1.3) 0 1 (1.1) Non-small cell ung cancer | Tumor type | | | |
| Amyloidolsis 1 (1.3) 0 1 (1.1) Breast cancer 19 (24.4) 3 (21.4) 22 (23.9) Chronic lymphocytic leukemia 1 (1.3) 1 (7.1) 2 (2.2) Colorectal cancer 5 (6.4) 0 5 (5.4) Diffuse large B-cell lymphoma 1 (1.3) 0 1 (1.1) Esophageal cancer 3 (3.8) 0 3 (3.3) Follicular lymphoma 1 (1.3) 0 1 (1.1) Gastric cancer 0 1 (7.1) 1 (1.1) Gastric cancer 4 (5.1) 0 4 (4.3) Glioblastoma 0 2 (2.2) 2 (2.2) Gioma 1 (1.3) 0 1 (1.1) Head and neck squamous cell carcinoma 2 (2.6) 0 2 (2.2) Lymphoma 1 (1.3) 0 1 (1.1) Mastrie-cell lymphoma 1 (1.3) 0 1 (1.1) Mastrie-cell lymphoma 1 (1.3) 0 1 (1.1) Mastrie-cell lymphoma 1 (1.3) 0 1 (1.1) Nor-small cell lung ca | Acute myeloid leukemia | 3 (3.8) | 1 (7.1) | 4 (4.3) |
| Breast cancer 19 (24.4) 3 (21.4) 2 (2.3.9) Chronic lymphocytic leukemia 1 (1.3) 1 (7.1) 2 (2.2) Colorectal cancer 5 (6.4) 0 5 (5.4) Diffuse large B-cell lymphoma 1 (1.3) 0 1 (1.1) Esophageal cancer 3 (3.8) 0 3 (3.3) Follicular lymphoma 1 (1.3) 0 1 (1.1) Galtic cancer 0 1 (7.1) 1 (1.1) Galtic cancer 0 1 (1.3) 0 1 (1.1) Galtic cancer 1 (1.3) 0 1 (1.1) Galtic cancer 1 (1.3) 0 1 (1.1) Mathe-cell lymphoma 1 (1.3) 0 1 (1.1) Mathe-cell lymphoma 1 (1.3) 0 1 (1.1) Non-spall cell lumg cancer 7 (9.0) 1 (7.1) 8 (8.7) Ovarian | All types | 0 | 1 (7.1) | 1 (1.1) |
| Chronic lymphocytic leukemia 1 (1.3) 1 (7.1) 2 (2.2) Colorectal cancer 5 (6.4) 0 5 (5.4) Diffuse large B-cell lymphoma 1 (1.3) 0 1 (1.1) Endometrial cancer 1 (1.3) 0 1 (1.1) Esophageal cancer 3 (3.8) 0 3 (3.3) Follicular lymphoma 1 (1.3) 0 1 (1.1) Galbladder cancer 0 1 (7.1) 1 (1.1) Gastric cancer 4 (5.1) 0 4 (4.3) Glioblastoma 0 2 (2.2) 1 (1.1) Head and neck squamous cell carcinoma 2 (2.6) 0 2 (2.2) Melanoma 1 (1.3) 0 1 (1.1) Mantle-cell lymphoma 1 (1.3) 0 1 (1.1) Nasopharyngeal cancer 0 1 (7.1) 8 (8.7) Ovarian cancer 7 (9.0) 1 (7.1) 8 (8.7) Ovarian cancer 7 (9.0) 1 (7.1) 8 (8.7) Ovarian cancer 7 (9.0) 1 (7.1) 8 (8.7) Ovar | Amyloidosis | 1 (1.3) | 0 | 1 (1.1) |
| Colorectal cancer 5 (6.4) 0 5 (5.4) Diffuse large B-cell lymphoma 1 (1.3) 0 1 (1.1) Endometrial cancer 1 (1.3) 0 1 (1.1) Esophageal cancer 3 (3.8) 0 3 (3.3) Follicular lymphoma 1 (1.3) 0 1 (1.1) Galtbladder cancer 0 1 (7.1) 1 (1.1) Galtbladder cancer 0 2 (14.3) 2 (2.2) Glioblastoma 0 2 (2.4) 2 (2.2) Glioma 1 (1.3) 0 1 (1.1) Head and neck squamous cell carcinoma 2 (2.6) 0 2 (2.2) Meanoma 1 (1.3) 0 1 (1.1) Mantle-cell lymphoma 1 (1.3) 0 1 (1.1) Masopharyngeal cancer 0 1 (7.1) 8 (8.7) Non-small cell lung cancer 7 (9.0) 1 (7.1) 8 (8.7) Ovarian cancer 2 (2.6) 0 2 (2.2) Prostate cancer 2 (2.6) 0 2 (2.2) Prostate cancer | Breast cancer | 19 (24.4) | 3 (21.4) | 22 (23.9) |
| Diffuse large B-cell lymphoma 1 (1.3) 0 1 (1.1) Endometrial cancer 1 (1.3) 0 1 (1.1) Esophageal cancer 3 (3.8) 0 3 (3.3) Follicular lymphoma 1 (1.3) 0 1 (1.1) Galbbadder cancer 0 1 (7.1) 1 (1.1) Gastric cancer 0 2 (14.3) 2 (2.2) Glioblastoma 0 2 (14.3) 2 (2.2) Lymphoma 1 (1.3) 0 1 (1.1) Head and neck squamous cell carcinoma 2 (2.6) 0 2 (2.2) Lymphoma 1 (1.3) 0 1 (1.1) Mathe-cell lymphoma 1 (1.3) 0 1 (1.1) Meanoma 4 (5.1) 1 (7.1) 5 (5.4) Mesothelioma 1 (7.1) 1 (1.1) Nasopharyngeal cancer 0 1 (7.1) 1 (1.1) Nasopharyngeal cancer 7 (9.0) 1 (7.1) 8 (8.7) Parceas cancer 2 (2.6) 0 2 (2.2) Prostate cancer 2 (2.6) 0 2 (2.2) | Chronic lymphocytic leukemia | 1 (1.3) | 1 (7.1) | 2 (2.2) |
| Endometrial cancer 1 (1.3) 0 1 (1.1) Esophageal cancer 3 (3.8) 0 3 (3.3) Follicular lymphoma 1 (1.3) 0 1 (1.1) Gallbladder cancer 0 1 (7.1) 1 (1.1) Gattric cancer 4 (5.1) 0 4 (4.3) Glioblastoma 0 2 (14.3) 2 (2.2) Glioma 1 (1.3) 0 1 (1.1) Head and neck squamous cell carcinoma 2 (2.6) 0 2 (2.2) Lymphoma 2 (2.6) 0 2 (2.2) Melanoma 4 (5.1) 1 (7.1) 5 (5.4) Mesothelioma 1 (1.3) 0 1 (1.1) Non-small cell lung cancer 0 1 (7.1) 1 (1.1) Non-small cell lung cancer 7 (9.0) 1 (7.1) 8 (8.7) Pancreas cancer 2 (2.6) 0 2 (2.2) Renal cancer 1 (1.3) 1 (7.1) 8 (8.7) Pancreas cancer 2 (2.6) 0 2 (2.2) Small-cell lung cancer 2 (2. | Colorectal cancer | 5 (6.4) | 0 | 5 (5.4) |
| Esophageal cancer 3 (3.8) 0 3 (3.3) Follicular lymphoma 1 (1.3) 0 1 (1.1) Galtbladder cancer 0 1 (7.1) 1 (1.1) Gastric cancer 4 (5.1) 0 4 (4.3) Glioblastoma 0 2 (14.3) 2 (2.2) Glioma 1 (1.3) 0 1 (1.1) Head and neck squamous cell carcinoma 2 (2.6) 0 2 (2.2) Melanoma 1 (1.3) 0 1 (1.1) Mantle-cell lymphoma 1 (1.3) 0 1 (1.1) Nasopharyngeal cancer 0 1 (7.1) 5 (5.4) Mesothelioma 1 (1.3) 0 1 (1.1) Non-small cell lung cancer 7 (9.0) 1 (7.1) 8 (8.7) Pancreas cancer 2 (2.6) 0 2 (2.2) Renal cancer 7 (9.0) 1 (7.1) 8 (8.7) Pancreas cancer 2 (2.6) 0 2 (2.2) Renal cancer 1 (1.3) 1 (7.1) 2 (2.2) T-cell lymphoma 3 (3.8) <td>Diffuse large B-cell lymphoma</td> <td>1 (1.3)</td> <td>0</td> <td>1 (1.1)</td> | Diffuse large B-cell lymphoma | 1 (1.3) | 0 | 1 (1.1) |
| Follicular lymphoma 1 (1.3) 0 1 (1.1) Galtibladder cancer 0 1 (7.1) 1 (1.1) Gastric cancer 4 (5.1) 0 4 (4.3) Glioblastoma 0 2 (14.3) 2 (2.2) Glioma 1 (1.3) 0 1 (1.1) Head and neck squamous cell carcinoma 2 (2.6) 0 2 (2.2) Lymphoma 1 (1.3) 0 1 (1.1) Matte-cell lymphoma 1 (1.3) 0 1 (1.1) Melanoma 4 (5.1) 1 (7.1) 5 (5.4) Melanoma 4 (5.1) 1 (7.1) 5 (5.4) Mesothelioma 1 (1.3) 0 1 (1.1) Nasopharyngeal cancer 0 1 (7.1) 8 (8.7) Ovarian cancer 7 (9.0) 1 (7.1) 8 (8.7) Pancreas cancer 2 (2.6) 0 2 (2.2) Renal cancer 1 (1.3) 1 (7.1) 8 (8.7) Pancreas cancer 2 (2.6) 0 2 (2.2) Renal cancer 1 (1.3) 1 (7.1)< | Endometrial cancer | 1 (1.3) | 0 | 1 (1.1) |
| Gallbladder cancer 0 1 (7.1) 1 (1.1) Gastric cancer 4 (5.1) 0 4 (4.3) Glioblastoma 0 2 (14.3) 2 (2.2) Glioma 1 (1.3) 0 1 (1.1) Head and neck squamous cell carcinoma 2 (2.6) 0 2 (2.2) Lymphoma 1 (1.3) 0 1 (1.1) Mathe-cell lymphoma 2 (2.6) 0 2 (2.2) Melanoma 4 (5.1) 1 (7.1) 5 (5.4) Mesothelioma 1 (1.3) 0 1 (1.1) Nasopharyngeal cancer 0 1 (7.1) 1 (1.1) Non-small cell lung cancer 7 (9.0) 1 (7.1) 8 (8.7) Ovarian cancer 7 (9.0) 1 (7.1) 8 (8.7) Pancreas cancer 2 (2.6) 0 2 (2.2) Renal cancer 1 (1.3) 1 (7.1) 2 (2.2) Small-cell lung cancer 2 (2.6) 0 2 (2.2) T-cell lymphoma/leukemia 3 (3.8) 0 3 (3.3) T-cell lymphoma/leukemia | Esophageal cancer | 3 (3.8) | 0 | 3 (3.3) |
| Gastric cancer 4 (5.1) 0 4 (4.3) Glioblastoma 0 2 (14.3) 2 (2.2) Glioma 1 (1.3) 0 1 (1.1) Head and neck squamous cell carcinoma 2 (2.6) 0 2 (2.2) Lymphoma 1 (1.3) 0 1 (1.1) Mantle-cell lymphoma 2 (2.6) 0 2 (2.2) Melanoma 4 (5.1) 1 (7.1) 5 (5.4) Mesothelioma 1 (1.3) 0 1 (1.1) Nasopharyngeal cancer 0 1 (7.1) 1 (1.1) Nasopharyngeal cancer 7 (9.0) 1 (7.1) 8 (8.7) Ovarian cancer 7 (9.0) 1 (7.1) 8 (8.7) Pancreas cancer 2 (2.6) 0 2 (2.2) Renal cancer 1 (1.3) 1 (7.1) 8 (8.7) Prostate cancer 2 (2.6) 0 2 (2.2) Small-cell lung cancer 2 (2.6) 0 2 (2.2) T-cell lymphoma 3 (3.8) 0 3 (3.3) T-cell lymphoma/leukemia 1 (1.3)< | Follicular lymphoma | 1 (1.3) | 0 | 1 (1.1) |
| Glioblastoma 0 2 (14.3) 2 (2.2) Glioma 1 (1.3) 0 1 (1.1) Head and neck squamous cell carcinoma 2 (2.6) 0 2 (2.2) Lymphoma 1 (1.3) 0 1 (1.1) Mantle-cell lymphoma 2 (2.6) 0 2 (2.2) Melanoma 4 (5.1) 1 (7.1) 5 (5.4) Mesothelioma 1 (1.3) 0 1 (1.1) Nasopharyngeal cancer 0 1 (7.1) 1 (1.1) Non-small cell lung cancer 7 (9.0) 1 (7.1) 8 (8.7) Ovarian cancer 7 (9.0) 1 (7.1) 8 (8.7) Pancreas cancer 2 (2.6) 0 2 (2.2) Renal cancer 1 (1.3) 1 (7.1) 8 (8.7) Pancreas cancer 2 (2.6) 0 2 (2.2) T-cell lymphoma 3 (3.8) 0 3 (3.3) T-cell lymphoma/leukemia 1 (1.3) 0 1 (1.1) Urothelial carcinoma 3 (3.8) 0 3 (3.3) Setting | Gallbladder cancer | 0 | 1 (7.1) | 1 (1.1) |
| Glioma 1 (1.3) 0 1 (1.1) Head and neck squamous cell carcinoma 2 (2.6) 0 2 (2.2) Lymphoma 1 (1.3) 0 1 (1.1) Mantle-cell lymphoma 2 (2.6) 0 2 (2.2) Melanoma 4 (5.1) 1 (7.1) 5 (5.4) Mesothelioma 1 (1.3) 0 1 (1.1) Nasopharyngeal cancer 0 1 (7.1) 1 (1.1) Non-small cell lung cancer 7 (9.0) 1 (7.1) 8 (8.7) Ovarian cancer 7 (9.0) 1 (7.1) 8 (8.7) Pancreas cancer 2 (2.6) 0 2 (2.2) Renal cancer 1 (1.3) 1 (7.1) 2 (2.2) Small-cell lung cancer 2 (2.6) 0 2 (2.2) T-cell lymphoma/leukemia 1 (1.3) 1 (7.1) 2 (2.2) T-cell lymphoma/leukemia 1 (1.3) 0 1 (1.1) Urothelial carcinoma 3 (3.8) 0 3 (3.3) Setting 4 (5.1) 1 (7.1) 5 (5.4) < | Gastric cancer | 4 (5.1) | 0 | 4 (4.3) |
| Head and neck squamous cell carcinoma 2 (2.6) 0 2 (2.2) Lymphoma 1 (1.3) 0 1 (1.1) Mantle-cell lymphoma 2 (2.6) 0 2 (2.2) Melanoma 4 (5.1) 1 (7.1) 5 (5.4) Mesothelioma 1 (1.3) 0 1 (1.1) Nasopharyngeal cancer 0 1 (7.1) 1 (1.1) Non-small cell lung cancer 7 (9.0) 1 (7.1) 8 (8.7) Ovarian cancer 7 (9.0) 1 (7.1) 8 (8.7) Pancreas cancer 2 (2.6) 0 2 (2.2) Prostate cancer 2 (2.6) 0 2 (2.2) Renal cancer 1 (1.3) 1 (7.1) 2 (2.2) Small-cell lung cancer 2 (2.6) 0 2 (2.2) T-cell lymphoma 3 (3.8) 0 3 (3.3) T-cell lymphoma/leukemia 1 (1.3) 0 1 (1.1) Urothelial carcinoma 3 (3.8) 0 3 (3.3) Setting 4 (5.1) 1 (7.1) 5 (5.4) Ope | Glioblastoma | 0 | 2 (14.3) | 2 (2.2) |
| Lymphoma 1 (1.3) 0 1 (1.1) Mantle-cell Lymphoma 2 (2.6) 0 2 (2.2) Melanoma 4 (5.1) 1 (7.1) 5 (5.4) Mesothelioma 1 (1.3) 0 1 (1.1) Nasopharyngeal cancer 0 1 (7.1) 1 (1.1) Non-small cell lung cancer 7 (9.0) 1 (7.1) 8 (8.7) Ovarian cancer 7 (9.0) 1 (7.1) 8 (8.7) Pancreas cancer 2 (2.6) 0 2 (2.2) Prostate cancer 2 (2.6) 0 2 (2.2) Renal cancer 1 (1.3) 1 (7.1) 2 (2.2) Small-cell lung cancer 2 (2.6) 0 2 (2.2) T-cell lymphoma 3 (3.8) 0 3 (3.3) T-cell lymphoma/leukemia 1 (1.3) 0 1 (1.1) Urothelia carcinoma 3 (3.8) 0 3 (3.3) Setting 4 (5.7) 2 (14.3) 8 (8.7) Design 1 (7.1) 5 (5.4) Open | Glioma | 1 (1.3) | 0 | 1 (1.1) |
| Mantle-cell lymphoma 2 (2.6) 0 2 (2.2) Melanoma 4 (5.1) 1 (7.1) 5 (5.4) Mesothelioma 1 (1.3) 0 1 (1.1) Nasopharyngeal cancer 0 1 (7.1) 8 (8.7) Non-small cell lung cancer 7 (9.0) 1 (7.1) 8 (8.7) Ovarian cancer 7 (9.0) 1 (7.1) 8 (8.7) Pancreas cancer 2 (2.6) 0 2 (2.2) Prostate cancer 2 (2.6) 0 2 (2.2) Renal cancer 1 (1.3) 1 (7.1) 2 (2.2) Small-cell lung cancer 2 (2.6) 0 2 (2.2) T-cell lymphoma 3 (3.8) 0 3 (3.3) T-cell lymphoma/leukemia 1 (1.3) 0 1 (1.1) Urothelia carcinoma 3 (3.8) 0 3 (3.3) Setting 3 (3.8) 0 3 (3.3) Early 6 (7.7) 2 (4.3) 8 (8.7) 3 (3.4) Design 74 (94.9) 13 (92.9) 87 (94.6) </td <td>Head and neck squamous cell carcinoma</td> <td>2 (2.6)</td> <td>0</td> <td>2 (2.2)</td> | Head and neck squamous cell carcinoma | 2 (2.6) | 0 | 2 (2.2) |
| Metanoma 4 (5.1) 1 (7.1) 5 (5.4) Mesothelioma 1 (1.3) 0 1 (1.1) Nasopharyngeal cancer 0 1 (7.1) 1 (1.1) Non-small cell lung cancer 7 (9.0) 1 (7.1) 8 (8.7) Ovarian cancer 7 (9.0) 1 (7.1) 8 (8.7) Pancreas cancer 2 (2.6) 0 2 (2.2) Prostate cancer 2 (2.6) 0 2 (2.2) Renal cancer 1 (1.3) 1 (7.1) 2 (2.2) Small-cell lung cancer 2 (2.6) 0 2 (2.2) T-cell lymphoma 3 (3.8) 0 3 (3.3) T-cell lymphoma/leukemia 1 (1.3) 0 1 (1.1) Urothelial carcinoma 3 (3.8) 0 3 (3.3) Setting | Lymphoma | 1 (1.3) | 0 | 1 (1.1) |
| Mesothelioma 1 (1.3) 0 1 (1.1) Nasopharyngeal cancer 0 1 (7.1) 1 (1.1) Non-small cell lung cancer 7 (9.0) 1 (7.1) 8 (8.7) Ovarian cancer 7 (9.0) 1 (7.1) 8 (8.7) Pancreas cancer 2 (2.6) 0 2 (2.2) Prostate cancer 2 (2.6) 0 2 (2.2) Renal cancer 1 (1.3) 1 (7.1) 2 (2.2) Small-cell lung cancer 2 (2.6) 0 2 (2.2) T-cell lymphoma 3 (3.8) 0 3 (3.3) T-cell lymphoma/leukemia 1 (1.3) 0 1 (1.1) Urothelial carcinoma 3 (3.8) 0 3 (3.3) Setting Advanced 72 (92.3) 12 (85.7) 84 (91.3) Early 6 (7.7) 2 (14.3) 8 (8.7) Design 2 27 (34.6) 8 (57.1) 35 (38.0) 3 51 (65.4) 6 (42.9) 57 (62.0) 3 35 (38.0) 3 35 (38.0) 35 (3 | Mantle-cell lymphoma | 2 (2.6) | 0 | 2 (2.2) |
| Nasopharyngeal cancer 0 1 (7.1) 1 (1.1) Non-small cell lung cancer 7 (9.0) 1 (7.1) 8 (8.7) Ovarian cancer 7 (9.0) 1 (7.1) 8 (8.7) Pancreas cancer 2 (2.6) 0 2 (2.2) Prostate cancer 2 (2.6) 0 2 (2.2) Renal cancer 1 (1.3) 1 (7.1) 2 (2.2) Small-cell lung cancer 2 (2.6) 0 2 (2.2) T-cell lymphoma 3 (3.8) 0 3 (3.3) T-cell lymphoma/leukemia 1 (1.3) 0 1 (1.1) Urothelial carcinoma 3 (3.8) 0 3 (3.3) Setting 4dvanced 72 (92.3) 12 (85.7) 84 (91.3) Early 6 (7.7) 2 (14.3) 8 (8.7) Design 1 (7.1) 5 (5.4) Open 74 (94.9) 13 (92.9) 87 (94.6) Phase 27 (34.6) 8 (57.1) 35 (38.0) </td <td>Melanoma</td> <td>4 (5.1)</td> <td>1 (7.1)</td> <td>5 (5.4)</td> | Melanoma | 4 (5.1) | 1 (7.1) | 5 (5.4) |
| Non-small cell lung cancer 7 (9.0) 1 (7.1) 8 (8.7) Ovarian cancer 7 (9.0) 1 (7.1) 8 (8.7) Pancreas cancer 2 (2.6) 0 2 (2.2) Prostate cancer 2 (2.6) 0 2 (2.2) Renal cancer 1 (1.3) 1 (7.1) 2 (2.2) Small-cell lung cancer 2 (2.6) 0 2 (2.2) T-cell lymphoma 3 (3.8) 0 3 (3.3) T-cell lymphoma/leukemia 1 (1.3) 0 1 (1.1) Urothelial carcinoma 3 (3.8) 0 3 (3.3) Setting | Mesothelioma | 1 (1.3) | 0 | 1 (1.1) |
| Ovarian cancer 7 (9.0) 1 (7.1) 8 (8.7) Pancreas cancer 2 (2.6) 0 2 (2.2) Prostate cancer 2 (2.6) 0 2 (2.2) Renal cancer 1 (1.3) 1 (7.1) 2 (2.2) Small-cell lung cancer 2 (2.6) 0 2 (2.2) T-cell lymphoma 3 (3.8) 0 2 (2.2) T-cell lymphoma/leukemia 1 (1.3) 0 1 (1.1) Urothelial carcinoma 3 (3.8) 0 3 (3.3) Setting - - - - Advanced 72 (92.3) 12 (85.7) 84 (91.3) Early 6 (7.7) 2 (14.3) 8 (8.7) Design - - - Blind 4 (5.1) 1 (7.1) 5 (5.4) Open 74 (94.9) 13 (92.9) 87 (94.6) Phase - - - - 2 27 (34.6) 8 (57.1) 35 (38.0) - 3 51 (65.4) 6 (42.9) | Nasopharyngeal cancer | 0 | 1 (7.1) | 1 (1.1) |
| Pancreas cancer 2 (2.6) 0 2 (2.2) Prostate cancer 2 (2.6) 0 2 (2.2) Renal cancer 1 (1.3) 1 (7.1) 2 (2.2) Small-cell lung cancer 2 (2.6) 0 2 (2.2) T-cell lymphoma 3 (3.8) 0 3 (3.3) T-cell lymphoma/leukemia 1 (1.3) 0 1 (1.1) Urothelial carcinoma 3 (3.8) 0 3 (3.3) Setting 4dvanced 72 (92.3) 12 (85.7) 84 (91.3) Early 6 (7.7) 2 (14.3) 8 (8.7) Design 4 (5.1) 1 (7.1) 5 (5.4) Open 74 (94.9) 13 (92.9) 87 (94.6) Phase 2 27 (34.6) 8 (57.1) 35 (38.0) 3 51 (65.4) 6 (42.9) 57 (62.0) 5ponsor Any industry involvement 71 (91.0) 11 (78.6) 82 (89.1) | Non-small cell lung cancer | 7 (9.0) | 1 (7.1) | 8 (8.7) |
| Prostate cancer 2 (2.6) 0 2 (2.2) Renal cancer 1 (1.3) 1 (7.1) 2 (2.2) Small-cell lung cancer 2 (2.6) 0 2 (2.2) T-cell lymphoma 3 (3.8) 0 3 (3.3) T-cell lymphoma/leukemia 1 (1.3) 0 1 (1.1) Urothelial carcinoma 3 (3.8) 0 3 (3.3) Setting 3 (3.8) 0 3 (3.3) Kalvanced 72 (92.3) 12 (85.7) 84 (91.3) Early 6 (7.7) 2 (14.3) 8 (8.7) Design 1 (7.1) 5 (5.4) Open 74 (94.9) 13 (92.9) 87 (94.6) Phase 2 2.7 (34.6) 8 (57.1) 35 (38.0) 3 51 (65.4) 6 (42.9) 57 (62.0) 57 (62.0) | Ovarian cancer | 7 (9.0) | 1 (7.1) | 8 (8.7) |
| Renal cancer 1 (1.3) 1 (7.1) 2 (2.2) Small-cell lung cancer 2 (2.6) 0 2 (2.2) T-cell lymphoma 3 (3.8) 0 3 (3.3) T-cell lymphoma/leukemia 1 (1.3) 0 1 (1.1) Urothelial carcinoma 3 (3.8) 0 3 (3.3) Setting 3 (3.8) 0 3 (3.3) Advanced 72 (92.3) 12 (85.7) 84 (91.3) Early 6 (7.7) 2 (14.3) 8 (8.7) Design 4 (5.1) 1 (7.1) 5 (5.4) Open 74 (94.9) 13 (92.9) 87 (94.6) Phase 2 27 (34.6) 8 (57.1) 35 (38.0) 3 31 (65.4) 6 (42.9) 57 (62.0) | Pancreas cancer | 2 (2.6) | 0 | 2 (2.2) |
| Small-cell lung cancer 2 (2.6) 0 2 (2.2) T-cell lymphoma 3 (3.8) 0 3 (3.3) T-cell lymphoma/leukemia 1 (1.3) 0 1 (1.1) Urothelial carcinoma 3 (3.8) 0 3 (3.3) Setting 3 (3.8) 0 3 (3.3) Advanced 72 (92.3) 12 (85.7) 84 (91.3) Early 6 (7.7) 2 (14.3) 8 (8.7) Design 4 (5.1) 1 (7.1) 5 (5.4) Open 74 (94.9) 13 (92.9) 87 (94.6) Phase 2 27 (34.6) 8 (57.1) 35 (38.0) 3 51 (65.4) 6 (42.9) 57 (62.0) Sponsor Any industry involvement 71 (91.0) 11 (78.6) 82 (89.1) | Prostate cancer | 2 (2.6) | 0 | 2 (2.2) |
| T-cell lymphoma 3 (3.8) 0 3 (3.3) T-cell lymphoma/leukemia 1 (1.3) 0 1 (1.1) Urothelial carcinoma 3 (3.8) 0 3 (3.3) Setting 3 (3.8) 0 3 (3.3) Advanced 72 (92.3) 12 (85.7) 84 (91.3) Early 6 (7.7) 2 (14.3) 8 (8.7) Design 4 (5.1) 1 (7.1) 5 (5.4) Open 74 (94.9) 13 (92.9) 87 (94.6) Phase 2 27 (34.6) 8 (57.1) 35 (38.0) 3 51 (65.4) 6 (42.9) 57 (62.0) Sponsor Any industry involvement 71 (91.0) 11 (78.6) 82 (89.1) | Renal cancer | 1 (1.3) | 1 (7.1) | 2 (2.2) |
| T-cell lymphoma/leukemia 1 (1.3) 0 1 (1.1) Urothelial carcinoma 3 (3.8) 0 3 (3.3) Setting 4dvanced 72 (92.3) 12 (85.7) 84 (91.3) Early 6 (7.7) 2 (14.3) 8 (8.7) Design 4 (5.1) 1 (7.1) 5 (5.4) Open 74 (94.9) 13 (92.9) 87 (94.6) Phase 2 27 (34.6) 8 (57.1) 35 (38.0) 3 51 (65.4) 6 (42.9) 57 (62.0) 57 (62.0) Sponsor 71 (91.0) 11 (78.6) 82 (89.1) | Small-cell lung cancer | 2 (2.6) | 0 | 2 (2.2) |
| Urothelial carcinoma 3 (3.8) 0 3 (3.3) Setting | T-cell lymphoma | 3 (3.8) | 0 | 3 (3.3) |
| Setting Advanced 72 (92.3) 12 (85.7) 84 (91.3) Early 6 (7.7) 2 (14.3) 8 (8.7) Design 4 (5.1) 1 (7.1) 5 (5.4) Open 74 (94.9) 13 (92.9) 87 (94.6) Phase 2 27 (34.6) 8 (57.1) 35 (38.0) 3 51 (65.4) 6 (42.9) 57 (62.0) Sponsor 4ny industry involvement 71 (91.0) 11 (78.6) 82 (89.1) | T-cell lymphoma/leukemia | 1 (1.3) | 0 | 1 (1.1) |
| Advanced 72 (92.3) 12 (85.7) 84 (91.3) Early 6 (7.7) 2 (14.3) 8 (8.7) Design Blind 4 (5.1) 1 (7.1) 5 (5.4) Open 74 (94.9) 13 (92.9) 87 (94.6) Phase 2 27 (34.6) 8 (57.1) 35 (38.0) 3 51 (65.4) 6 (42.9) 57 (62.0) Sponsor | Urothelial carcinoma | 3 (3.8) | 0 | 3 (3.3) |
| Early 6 (7.7) 2 (14.3) 8 (8.7) Design 4 (5.1) 1 (7.1) 5 (5.4) Open 74 (94.9) 13 (92.9) 87 (94.6) Phase 2 27 (34.6) 8 (57.1) 35 (38.0) 3 51 (65.4) 6 (42.9) 57 (62.0) Sponsor 4ny industry involvement 71 (91.0) 11 (78.6) 82 (89.1) | Setting | | | |
| Design Blind 4 (5.1) 1 (7.1) 5 (5.4) Open 74 (94.9) 13 (92.9) 87 (94.6) Phase 2 27 (34.6) 8 (57.1) 35 (38.0) 3 51 (65.4) 6 (42.9) 57 (62.0) Sponsor | Advanced | 72 (92.3) | 12 (85.7) | 84 (91.3) |
| Bind 4 (5.1) 1 (7.1) 5 (5.4) Open 74 (94.9) 13 (92.9) 87 (94.6) Phase 2 27 (34.6) 8 (57.1) 35 (38.0) 3 51 (65.4) 6 (42.9) 57 (62.0) Sponsor X X X X Any industry involvement 71 (91.0) 11 (78.6) 82 (89.1) | Early | 6 (7.7) | 2 (14.3) | 8 (8.7) |
| Open 74 (94.9) 13 (92.9) 87 (94.6) Phase 2 27 (34.6) 8 (57.1) 35 (38.0) 3 51 (65.4) 6 (42.9) 57 (62.0) Sponsor III (78.6) 82 (89.1) | Design | | | |
| Phase 27 (34.6) 8 (57.1) 35 (38.0) 3 51 (65.4) 6 (42.9) 57 (62.0) Sponsor Any industry involvement 71 (91.0) 11 (78.6) 82 (89.1) | Blind | 4 (5.1) | 1 (7.1) | 5 (5.4) |
| 2 27 (34.6) 8 (57.1) 35 (38.0) 3 51 (65.4) 6 (42.9) 57 (62.0) Sponsor X <thx< th=""> <thx< th=""> X <</thx<></thx<> | Open | 74 (94.9) | 13 (92.9) | 87 (94.6) |
| 3 51 (65.4) 6 (42.9) 57 (62.0) Sponsor Any industry involvement 71 (91.0) 11 (78.6) 82 (89.1) | Phase | | | |
| Sponsor 71 (91.0) 11 (78.6) 82 (89.1) | 2 | 27 (34.6) | 8 (57.1) | 35 (38.0) |
| Any industry involvement 71 (91.0) 11 (78.6) 82 (89.1) | 3 | 51 (65.4) | 6 (42.9) | 57 (62.0) |
| | Sponsor | | | |
| No industry involvement 7 (9.0) 3 (21.4) 10 (10.9) | Any industry involvement | 71 (91.0) | 11 (78.6) | 82 (89.1) |
| | No industry involvement | 7 (9.0) | 3 (21.4) | 10 (10.9) |

Abbreviation: RCT, randomized clinical trial.

🖞 JAMA Network Open. 2022;5(1):e2144770. doi:10.1001/jamanetworkopen.2021.44770

Figure. Cumulative Yearly Number of Published Oncology Randomized Clinical Trials Mentioning Physician's Choice or Investigator's Choice in the Control Group (N = 92)



Discussion

This cross-sectional study, to our knowledge the first to address this research question, found that the physician's or investigator's choice may be ambiguously reported and is associated with a restricted choice in most oncology RCTs using these terms. Most of these reports are also funded at least partly by for-profit entities.

Consider the most represented tumor type of our included trials, breast cancer (23.9%): in a trial investigating sacituzumab govitecan in patients with triple negative breast cancer, the physician's choice was restricted to 4 options, not allowing platinum nor anthracyclines, 2 highly active agents, possibly leading to substandard outcomes.³

One limitation of our study is that we did not assess for the prevalence of the included reports as compared with all published oncology RCTs. As an estimation, when they were 121 published RCTs in breast cancer between 2014 and 2017, we included 6 breast cancer trials (6 of 121; 4.6%).² Also, as another potential limitation, we restricted our search to MEDLINE.

Physician's or investigator's choice have been used for decades in the literature; however, they are increasing over time. This is an important trend to be aware of in oncology RCTs. Through imprecise wording, potentially masking substandard control group, treating physicians may inaccurately think that the reported results can be generalized to their patients, whereas this may not be true. Our findings suggest that editors and regulators should demand clarification in the use of these terms within RCTs protocols and reports.

ARTICLE INFORMATION

Accepted for Publication: November 30, 2021.

Published: January 21, 2022. doi:10.1001/jamanetworkopen.2021.44770

Open Access: This is an open access article distributed under the terms of the CC-BY License. © 2022 Olivier T et al. *JAMA Network Open*.

Corresponding Author: Timothée Olivier, Department of Oncology, Geneva University Hospital, Four Gabrielle-Perret-Gentil Street, Geneva 1205, Switzerland (timothee.olivier@hcuge.ch).

Author Affiliations: Department of Oncology, Geneva University Hospital, Geneva, Switzerland (Olivier); Department of Epidemiology and Biostatistics, University of California, San Francisco (Olivier, Haslam, Prasad).

Author Contributions: Dr Olivier had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Olivier, Prasad.

Acquisition, analysis, or interpretation of data: Olivier, Haslam.

Drafting of the manuscript: Olivier.

Critical revision of the manuscript for important intellectual content: All authors.

JAMA Network Open. 2022;5(1):e2144770. doi:10.1001/jamanetworkopen.2021.44770

JAMA Network Open | Oncology

Statistical analysis: Olivier.

Supervision: Prasad.

Conflict of Interest Disclosures: Dr Prasad reported receiving press royalties from Johns Hopkins, personal fees from Medscape, royalties from MedPage, consulting fees from United Healthcare, speaking fees from Evicore, speaking fees from New Century Health, and personal fees from Patreon Plenary Session (podcast has Patreon backers) outside the submitted work. No other disclosures were reported.

Funding/Support: This project was funded by Arnold Ventures, LLC through a grant paid to the University of California, San Francisco.

Role of the Funder/Sponsor: The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

REFERENCES

1. Hilal T, Sonbol MB, Prasad V. Analysis of control arm quality in randomized clinical trials leading to anticancer drug approval by the US Food and Drug Administration. *JAMA Oncol.* 2019;5(6):887-892. doi:10.1001/jamaoncol. 2019.0167

2. Wells JC, Sharma S, Del Paggio JC, et al. An analysis of contemporary oncology randomized clinical trials from low/middle-income vs high-income countries. *JAMA Oncol*. 2021;7(3):379-385. doi:10.1001/jamaoncol.2020.7478

3. Olivier T, Prasad V. Sacituzumab govitecan in metastatic triple negative breast cancer (TNBC): four design features in the ASCENT trial potentially favored the experimental arm. *Transl Oncol*. 2021;15(1):101248. doi:10. 1016/j.tranon.2021.101248

SUPPLEMENT.

eMethods. Method for the Research and Selection of Articles eFigure. Flowchart of the Article Selection Process