The Impact of Modifying Eligibility Criteria on Accrual to Cancer Clinical Trials

Jeffrey Thompson[1], David Streeter[1], Dinesh Pal Mudaranthakam[1], Joseph M Unger[2], Mark Fleury[3]

1. The University of Kansas Cancer Center, Kansas City, KS, USA, 2. Fred Hutchinson Cancer Research Center 3.American Cancer Society Cancer Action Network, Inc.

Introduction

Recently ASCO, the Friends of Cancer Research, and the USFDA proposed modifications to "default" eligibility criteria often used in oncology clinical trials. These recommendations are meant to ensure criteria are scientifically justified, and if implemented would make trials more representative of the population with cancer. We hypothesized that these changes would also increase the pool of potential trial participants, but the impact of these recommendations on patient enrollment to trials has not been evaluated using comprehensive patient-level eligibility data.

Goals We utilized the Curated Cancer Clinical Outcomes Database (C3OD) database of The University of Kansas Cancer Center as a resource for evaluating the potential magnitude of the ASCO recommendations on trial participation for patients with any solid tumor. The goal was to examine both the marginal (i.e. individual) and joint (i.e. combined) impact of modifying the following selected eligibility criteria: brain metastases, HIV status, renal function, hepatic function, and prior malignancies. An examination modifying the joint impact is of interest given the fact that criteria are likely correlated. Together these evaluations will provide a benchmark for the impact of adopting these recommendations.

Future Directions

Retrospectively apply the ASCO recommended criteria to a set of actual, completed clinical treatment protocols, to identify the impact of trial criteria modification on the speed with which these trials would have been completed.

Methods

The C3OD database provides an opportunity to quantify the potential effect of adopting the recommendations. One major advantage of this unique resource is its capacity to identify modifications to specified eligibility criteria, rather than simply their exclusions or removal. The large size of the data resource enables detailed examination of the influence of modifying selected eligibility criteria across different cancer types and treatments, including immunotherapies and targeted agents.

With this approach we identified a population based upon certain criteria, then layered each additional criterion on top of this population to simulate a cohort. We could then “toggle” these criteria as needed (and in specific combinations) to determine increased or decreased pool-size.

We then calculated an overall participation increase by using the US overall trial participation rate of 8%.

C3OD was used exclusively to determine these data which sits on-top of KUMC’s EMR as a data source. Each criterion was entered individually and in combinations to determine the subpopulation. Criteria combinations were determined to be erroneous in the calculation of Total Possible Gain in Eligibility due to the fact that if a subject had >1 criteria, then the sum of patients per criterion (Total Possible Gain in Eligibility) would begin to decrease, leading us to skewed results. Due to this we designed the methods to only consider each criterion individually vs. total N of the population.

Results

In total, data on n=62,572 adult (age >18 years) of a total patients with any solid tumor malignancy were available. The inclusion of patients with brain metastases was estimated to increase available patients by 68 (0.1%); of patients >12 years by 120 (0.2%); of patients positive for HIV by 159 (0.3%); of patients with renal dysfunction as measured by measured by creatinine clearance from 30-60 mL/min by 138 (0.2%); of patients with hepatic dysfunction (ascites) by 587 (0.9%); and of patients with prior malignancy between 2 to 5 years before most recent cancer diagnosis by 2979 (4.8%) (see Table). The inclusion of patients with any one of these conditions could increase the pool of available patients by up to 6.7%, which would allow up and additional to 5695 (5%) additional patients to participate in this analysis. Additionally, if the overall trial participation rate in the U.S. is 8%, then that would raise the additional participants to 9112 if the national overall percentage was applied against this cohort.

Criterion	Difference in patients by modifying criterion (n=62572)	Percent increase in eligible pool
Age down to 12 years	120	0.2%
Brain metastases	68	0.1%
HIV/AIDS positive	159	0.3%
Renal dysfunction (creatinine clearance)	138	0.2%
Hepatic dysfunction (ascites)	587	0.9%
Prior malignancies	2979	4.8%

The recently recommended expansion of eligibility criteria would have varying impacts on patient eligibility depending on the disease condition. Our estimate of the cumulative impact of expanding all comorbidities combined indicates that several thousand patients would be available for trial participation each year, with accompanying benefits on the speed with which trials are conducted and the accessibility of trial participation as a choice for care for patients with cancer.