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Study defines clinical trials likely to exclude patients with brain metastases

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Non-small cell lung cancer frequently spreads to the central nervous system (CNS), but patients with CNS metastases may be excluded from clinical trials of new drugs. A University of Colorado Cancer Center study being presented at the 16th World Conference on Lung Cancer reveals the full extent to which the CNS may be under-explored in clinical research.

The study combed the website ClinicalTrials.gov to identify 413 open lung cancer clinical trials. Overall, 41 percent of trials only included patients if their CNS disease was previously treated. Twenty-six percent allowed in patients with CNS involvement and no previous treatment. Fourteen percent excluded all patients with a history of brain spread and nineteen percent of trials did not comment on any criteria related to CNS disease at all.

When multiple different subcategories of clinical trial were considered, only the sponsor of the trial was significantly associated with strict CNS exclusion, with university-sponsored trials being significantly less likely to exclude such patients than industry-sponsored trials (Hazard Ratio 0.442, p=0.0342).

"On one hand, if a new drug works great in the rest of the body but somehow doesn't get into the brain, including patients with untreated brain metastases could put the patients at increased risk as well as lower the initial estimates of the drug's activity," says Caroline McCoach, MD, PhD, investigator at the CU Cancer Center and the presenting author of

the study. "But on the other hand, if we fail to include patients on the trial of a drug that does work in the brain, we may not discover the drug's activity for a long time and patients who may benefit would be inappropriately excluded."

"The fact that the only dominant factor affecting strict exclusion was the sponsor of the trial suggests that some of our current practice may be based more on habit, than perhaps universally agreed upon scientific rationale," says D. Ross Camidge, MD, PhD, Joyce Zeff Chair in Lung Cancer Research at the CU Cancer Center and senior author of the study.

Indeed, in the last two years, the Response Assessment in Neuro-Oncology (RANO) group, an assembly of international experts, have been driving a series of publications that have started to build a more rational approach to addressing brain metastases in clinical trials.

"Dr. McCoach's presentation really defines the status quo for how lung cancer patients with CNS disease are being treated in clinical trials and has already started a lot of debate within the RANO group," Camidge says.

"What we really want to see are sensible clinical trial designs, with CNS inclusion and exclusion criteria that are logical and appropriate given both what is or isn't known about the drug's activity in the brain and how far advanced an experimental drug is in development at the time," says Camidge. "In an ideal world that might well involve dedicated clinical trial sub-studies looking at patients with untreated CNS disease very early in drug development, trying to see if there is a CNS signal to explore further, or modify later trials to more appropriately manage risks if the drug is unlikely to work in the CNS."

"Sometimes, we may have to learn by mistakes," says McCoach

explaining that many trials of the new class of immunotherapy drugs completely excluded patients with brain metastases yet newer data seems to show that CNS responses can safely occur and this early caution and denial of trial access to such patients may not have been warranted.

"The brain is an important battleground for treatment right now, and you can't really force the issue of wanting better trial designs until you show people the lack of consensus in how we are currently doing things. The goal of this study was to highlight the full extent of current practice and open up the field for more informed debate," she says.

Provided by University of Colorado Denver