Early stopped clinical trials in oncology: a comparison between Europe and America

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Background. Clinical Trials (CT) are the clinical-scientific tools to assess the best therapies in several medical areas. The poor prognosis of oncological diseases makes the development of new drugs of the utmost importance and, for this reason, early stopped CT (ESCT) are an important issue in the oncological setting.

Here we present updated analyses of ESCT with results.

Methods. We queried the ClinicalTrial.gov Database for CT from the foundation year up to 1st February 2022 searching for key terms such as “cancer”, “neoplasm”, “malignant”, “tumor” and “oncology” without any restriction. Afterward, the filters “Suspended”, “Withdrawn” and “Terminated” were applied. All studies were revised, checking the pertinence with cancer diagnosis, treatment, Quality of Life (QoL) or oncological pain management and divided in 36 categories, whereas Completed (C) trials were used as comparators. All comparisons were performed with Pearson’s χ² test, using Yates correction for continuity.

Results. A total of 10260 ESCT were found among these studies, but after the revision, only 9346 ESCT were found pertinent and included in the final analysis. Among the causes for ESTC, the most frequently reported cause was “Poor Accrual” (30.7%), whereas “Insufficient Funds” (6.1%) and “Sponsor Decision” were at second and third place, respectively. We compared ESCT with C trials performed in Europe and USA finding a difference strongly significant (p<0.0001) with a risk almost doubled for American trials than European ones (OR = 1.98; 95% CI 1.86 - 2.11). However, considering only interventional trials, we performed a subgroup analysis considering the different trial phases and registering a significant difference between America and Europe (p< 0.0001). The difference was confirmed by direct comparisons in all CT phases, I (OR = 2.27, 95% CI 1.87 - 2.78; p< 0.0001), II (OR = 3.99, 95% CI 3.3 - 4.8; p< 0.0001) and III (OR = 5.86, 95% CI 4.6 - 7.57; p< 0.0001).

Conclusions. CT development could be critical during the trial course and several causes can influence an early stop. Enrolment, funds and Sponsor decisions are still motivation of CT interruption but evidences suggest that Europe has lower proportions of stopped trials than USA, suggesting better performance and trial designs.