Results Reporting and Other Analyses of Head and Neck Cancer Clinical Trials in the United States

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Background

- Under-reporting of results in medical research is a trend that has been covered extensively in the literature going back to the 1990s, with the selective reporting of clinical trials results receiving the most press given the particularly delicate nature of research involving human subjects. A response to these reports has been increased pressure on investigators to release all results of clinical trials, regardless of outcomes. Some progress has been made in this direction, yet reporting of results of clinical trials is nowhere near 100%.

- Given that every clinical trial involves substantial financial investment and risk to participants, with the outcomes having an enormous impact potential on public health, it is felt that each trial conducted should have the opportunity to add to the scientific body, even if results seem insignificant.

- This holds especially true in the field of head and neck cancer research, where therapeutic advances have been lagging - the first new drug in 45 years to be approved for treating head and neck cancer came in 2006 - and the potential public health benefit of new treatments could be substantial.

- Open access to the methods and results from past head and neck cancer clinical trials has the potential to limit overlap and guide better research design among prospective trials, ultimately translating to more efficient exploration of treatment modalities, and decreased risk of harmful exposures among trial participants.

Methods

- **Study Sample**: For this study we used Clinicaltrials.gov as the sole data source.

- **Variables**: Most of the data points were pulled directly from Clinicaltrials.gov when the dataset was downloaded from NLM. These variables were title, phase, enrollment, sponsor, study design, status, results reporting, and all relevant dates. A few variables were included in the downloaded data, but in order to verify completeness of information we double checked them on Clinicaltrials.gov to ensure they matched the variables listed on the site.

- **Analysis**: We performed a descriptive analysis of Dataset 1 to identify general characteristics of head and neck cancer clinical trials since September 2005. We listed values and percentages for the relevant variables. We then performed a descriptive analysis of Dataset 2 to identify the most common drugs and drug combinations used in head and neck cancer clinical trials. We also performed a descriptive analysis of several variables for each drug and drug combination, both to show the values alone and to compare the values among each regimen. Finally, we performed a statistical analysis comparing NIH sponsored trials to industry sponsored trials, using Chi-squared to identify statistical differences among relevant variables.

Results

- **General Characteristics**: Several specific drug regimens have been used repeatedly in head and neck cancer clinical trials (Table 1). The variable X in the table refers to a drug used in combination with the drugs mentioned by name. The most often used drugs denoted by the X were other chemotherapy drugs. Cisplatin combined with another drug has been the most common treatment regimen studied, being used in 33 trials. Erlotinib was the most common single drug treatment studied, being used in 9 different trials. Trials of cetuximab had the longest time to completion, averaging 69.4 months, and radiation and surgery were more often included in combination treatment trials than single drug trials.

- **Single Drugs**: When drugs used in head and neck cancer clinical trials were broken down and analyzed individually we found that cisplatin has both the highest gross usage, being used in 94 separate trials, as well as the highest frequency of use, being used in almost 5 trials per year. Cetuximab, docetaxel, paclitaxel, fluorouracil, and erlotinib all show frequent and common use in head and neck cancer trials as well (Figure 1).

- **Results Reporting**: Disregarding sunitinib - due to only having one reported trial - trials using sunitinib monotherapy had the highest publication rate both per trial, with 1 paper per trial, and per year, with 1.5 papers per year (Figure 2). Publication rates per trial may correlate with efficacy of the drug regimen studied, as positive outcomes in clinical trials are more likely reported than negative ones. Annual publication rates likely correlate more with the frequency of clinical trials using a specific drug regimen. Correspondingly, we found a high annual publication rate of trials using cisplatin combined with another drug, which is consistent with cisplatin’s indication for use in head and neck cancer. The average number of publications per trial was 0.51, similar to the rate found earlier in our study. The average rate of positive publications was 65% (data not shown).

Recommendations

In head and neck cancer research, there is a significant gap between the trials conducted and reported results. The number of treatment regimens studied has significant overlap, and it cannot be discerned whether this overlap is a necessary burden or a manifestation of inefficiency in the systematic study and execution of trials designed to find the best treatment of head and neck cancer. We recommend improvements in the current reporting structure, for both NIH and industry sponsored trials, to make the following data available and easily obtained by other researchers and the public at large: positive trials, negative trials, funding allocated to a specific trial, and a clinical impact summary for the trial. This should also be encouraged in peer-reviewed journals, where negative studies should be as welcome as positive studies. Increased reporting of results will ideally reduce the risk that subjects and resources will be put to trials which may have too much overlap and hence unnecessary redundancy. Again, the exact amount of this redundancy already present is unknown, but the current study suggests that it may be greater than is currently understood.