Erythropoiesis stimulating agents (ESAs): Conflicts of interest in the pursuit for the true association between pharmaceutical manufacturer's research and basic science research findings

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In 2007, tumor progression and mortality risks with erythropoiesis stimulating agents (ESAs) were reported by the Food and Drug Administration (FDA). Also, the National Cancer Institute convened a workshop with academic investigators and ESA manufacturers' investigators to review preclinical findings on erythropoietin receptor (EpoRs) in the cancer setting. Prior to this workshop, articles from academia identified EpoRs on cancer cells, while articles from investigators employed by ESA manufacturers did not. We updated this analysis following the workshop.

Articles identified in MEDLINE and EMBASE databases (1989–2012) investigating preclinical ESA findings were reviewed. Outcomes included Epo receptors, signaling events, cellular function, and qualitative conclusions. Outcomes were reported according to academic investigators (100 publications) and investigators employed by ESA manufacturers (5 publications).

Academic investigators differed from investigators employed by ESA-manufacturers with respect to identifying: EpoRs on cancer cell lines (97% versus 60%); EPO-induced signaling events associated with tumor promotion (88% versus 0%), and EPO-induced cellular function changes associated with tumor growth or metastases (73% versus 0%). Among studies from academic investigators, publications reported after the NCI workshop were more likely than those reported earlier to identify EpoRs on cancer cells (96% versus 60%) and Epo-induced changes in cellular function (80% versus 30%). Among academic investigators with financial conflicts of interest, preclinical findings reported after the workshop versus before were more likely to identify upregulated erythropoietin receptors, (100% versus 50%), EPO-induced signaling events (100% versus 0%), and EPO-induced cell-function changes (66% versus 0%). (p<0.05 for all comparisons)

Academic investigators have increasingly reported detrimental effects of ESAs in preclinical settings. Manufacturer-employed investigators consistently report no adverse preclinical effects, observations discordant with advisories disseminated by ESA manufacturers.

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