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Incidence and risk of developing photosensitivity with targeted anticancer therapies

To the Editor: Photosensitivity has been reported anecdotally and inconsistently with targeted cancer therapies, such that the incidence and risk are unknown.[1] We conducted a PubMed search for studies published during January 1966-February 28, 2016, combining 2 concepts using the operator and generic name of the drug and the study phase. Further, we performed an independent search with the Web of Science database for studies published during 1945-February 28, 2016, using the same aforementioned PubMed search terms.

We selected all trials that met the following criteria for systematic review and meta-analysis: study was a prospective phase 2 or 3 clinical trial conducted in human cancer patients available in the English language, participants were assigned treatment with targeted agents at their approved doses, data regarding the occurrence of photosensitivity was reported, and the targeted therapy was a single agent.

We found 47,750 eligible published reports regarding targeted anticancer therapies (Fig 1). A total of 10 clinical trials met our inclusion criteria: 6 phase 2 and 4 phase 3 trials totaling 2938 enrolled patients. Among these trials, 8 involved the treatment of solid tumors, 1 hematologic malignancies, and 1 both tumor types (Table I).

Photosensitivity was only reported with vandetanib, vemurafenib, and nivolumab agents. The calculated overall incidence of all-grade photosensitivity when using the random-effects model (heterogeneity Q 95.355, $I^2 = 91.61$, $P < .001$) was 21.5% (95% confidence interval [CI] 14.2%-31.2%). The incidence was lowest for nivolumab (1.5%, 95% CI 0.5%-4.4%) in a phase 3 melanoma trial.[2] Incidence was highest with vemurafenib (53.1%, 95% CI 44.5%-61.5%) in a phase 2 trial in melanoma.[3] Data for all-grade photosensitivity was available for 9 studies of nivolumab, vemurafenib, and vandetanib.

Based on a fixed-effects model (heterogeneity test, Q = 5.801, I^2 = 48.285, P = .122), vemurafenib has an increased risk for all-grade photosensitivity with a relative risk of 2.14 (95% CI 0.52-8.91, Fig 2). The calculated overall incidence of high-grade photosensitivity with the random-effects model (heterogeneity, Q = 5.801, $I^2 = 48.285$, $P = .122$) was 2.1% (95% CI 0.8%-5.4%). Trials involving vemurafenib (n = 3) and vandetanib (n = 1) were included, and the incidence was highest (4.1%, 95% CI 1.3%-12.0%) in a phase 2 double-blind placebo-controlled trial of vandetanib in thyroid cancer.[4] Seven other trials reported no high-grade events of photosensitivity. High-grade photosensitivity was not reported in 1 vemurafenib trial in which all-grade events were reported.[5]

This is the first systematic review to report the incidence and risk for photosensitivity with targeted cancer drugs. We found that vemurafenib, vandetanib, and nivolumab were associated with an increased incidence and risk of developing photosensitivity. A limitation of the study is that only published data from trials was included, as raw data from trials was not available. Although most cases are not high grade, photosensitivity might cause morbidity, affecting quality of life and consistent dosing of cancer agents. Education on photoprotection and management of established photosensitivity are therefore key in the optimization of agents associated with this adverse event.

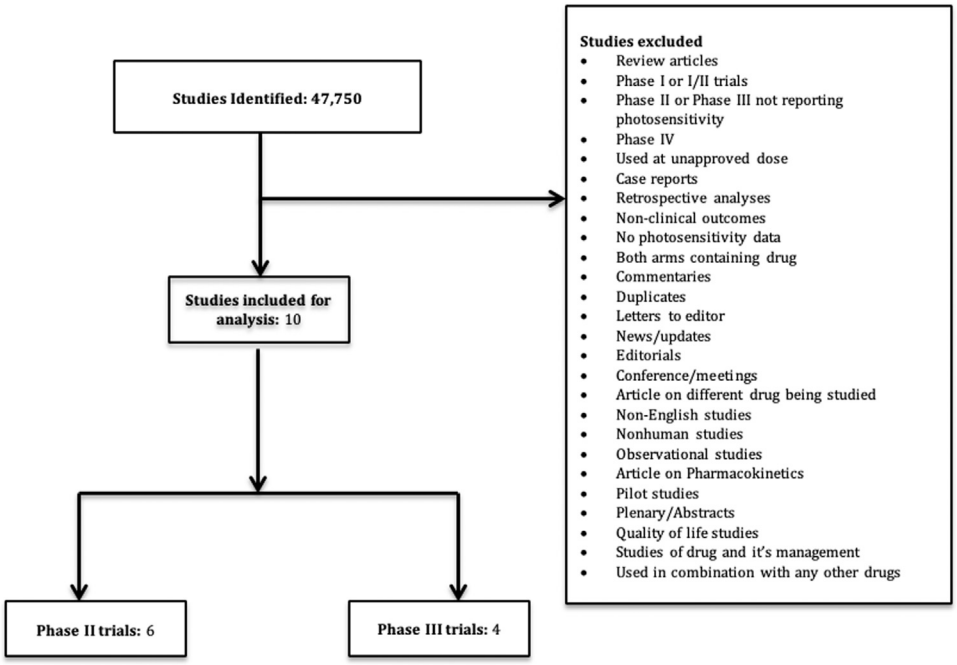

Fig 1. Summary of literature search and reasons for trial exclusion.

Table I. Clinical trials

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Robert C et al. *New Engl J Med*. 2015;372:30-9.
Robert C et al. *New Engl J Med*. 2015;372(4):320-330.
Sosman JA et al. *New Engl J Med*. 2012;366(8):707-714.
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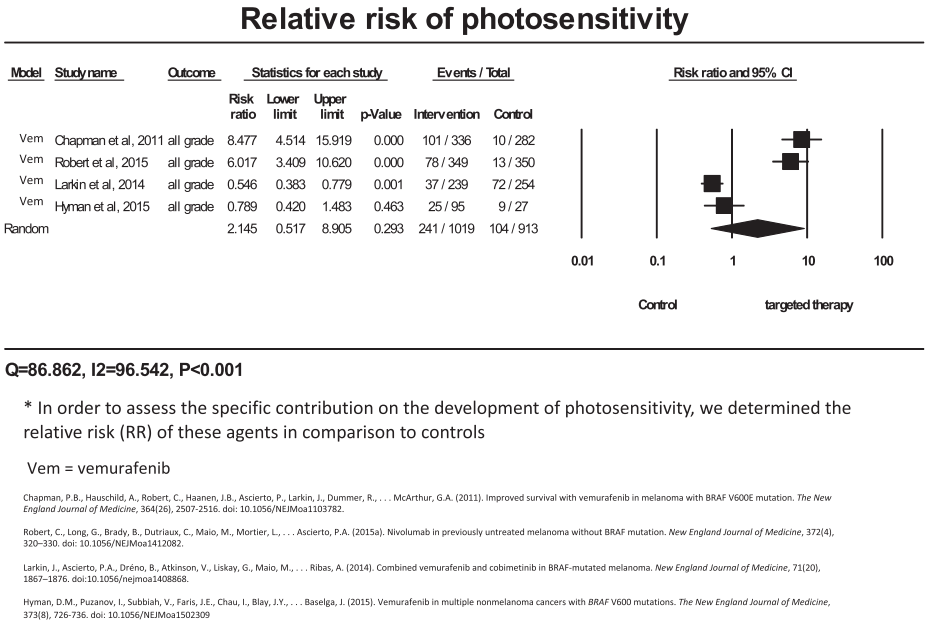

Fig 2. Relative risk for all-grade photosensitivity. To assess the specific contribution on the development of photosensitivity, we determined relative risk of these agents in comparison to controls. *CI*, Confidence interval; *N*, nivolumab; *Va*, vandetanib; *Vem*, vemurafenib.

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Determining patient preferences and willingness to pay related to scar length and appearance after skin cancer treatment on the face and trunk: A multicenter discrete choice experiment

To the Editor: Discrete choice experiments (DCEs) identify patient preferences while reducing the opportunity for bias. DCEs have been increasingly used in health care research to ascertain patient preferences.[1-3] In this study, we provide DCE data from a large multicenter cohort that illustrates how patients value cosmetic outcomes after skin cancer surgery and how patient values vary with tumor location and risk.

The study was approved by the University of Pennsylvania Institutional Review Board and was performed at 4 clinical sites: the University of Pennsylvania, the University of Missouri, the University of Mississippi, and Good Dermatology. A DCE was designed using Conjoint.ly online software[4] to assess patient preferences and willingness to pay (WTP) with respect to several attributes of skin cancer treatment. Levels used for the scar length attribute were 1 inch, 2 inches, 5 inches, and 8 inches. Levels for the scar appearance attribute were a barely visible scar or an obvious scar. Cost measures were attached to each DCE scenario to allow for a WTP analysis. These values began at $50 and increased in $200 increments.

Patients who predominately, but not exclusively, had undergone Mohs micrographic surgery and their accompanying friends and family were asked to participate in exchange for a $10 Amazon.com gift card. The experiment began with an introductory stated-choice survey to educate respondents on the included attributes of treatment: anesthesia type, risk of repeat excision, risk of recurrence, margin status, wound closure timing, scar length,