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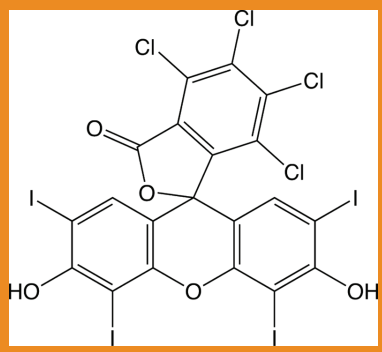
The mission of this magazine is to transform the expanding information on cancer research into understandable language to the curious and the informed.



Adenine Press, 2066 Central Avenue, Schenectady, New York 12304 USA

PV-10 in Advanced Melanoma: High Response Rates, Evidence of Systemic Response

Confirmation of high clinical response rates and further evidence of systemic effects for intralesional PV-10 (Rose Bengal 10% disodium) emerged from an updated analysis of an international, multicenter phase 2 study among 80 patients with advanced melanoma. In addition, the side effect of blistering appears to correlate with better responses and suggests immune activation, according to Sanjiv S. Agarwala, MD, professor

*of medicine at Temple University, Philadelphia, PA.**

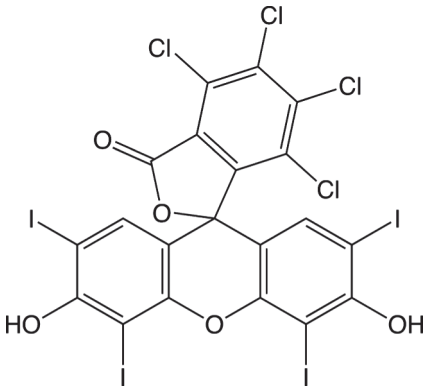
Up to 10 cutaneous or subcutaneous target lesions were injected with intralesional PV-10 in patients with stage IIIB-IV melanoma, Dr. Agarwala said in a 2013 European Cancer Congress poster presentation. The lesions were reinjected if necessary at weeks 8, 12, and 16. Up to 2 additional cutaneous or subcutaneous lesions were left untreated to assess bystander response. The primary endpoint was best overall response rate in up to 10 target lesions.

Dr. Agarwala reported that in this population of patients who were refractory to a median of 6 prior interventions, best overall response was 51% (26% complete, 25% partial). The amount of tumor burden accessible to PV-10 injection was prognostic for outcome, with both magnitude and duration of response inversely related to untreated tumor burden. For patients in whom all lesions (except for up to two untreated bystander lesions) could be treated, the best overall response rate was 63%. In subjects where all disease was treated, the complete (50%) plus partial (21%) rate further increased to 71%. The clinical response rate (complete response plus partial response plus stable disease [locoregional disease control]) was 82% in this subgroup.

In patients who experienced blistering of target lesions, the rate for complete plus partial responses (91%) was significantly higher than among those without blistering (54%, P = 0.001). "Patients get very concerned when blistering develops because they feel it may be indicating an infection, but now I can tell them that it's actually a good thing, maybe correlating with a benefit and secondly signaling that their immune system is activating." He added, "The principle is that this agent has a local chemoablative effect, one where we believe it enters into lysosomes causing local necrosis and sometimes blistering of the lesion, indicative of the observed systemic effect in 'bystander' lesions which we think is immunologically mediated," Dr. Agarwala said. The 54% complete plus partial response rate in uninjected "bystander" lesions supports that notion.

Dr. Agarwala speculated on potential uses of PV-10, should its benefits in phase 3 testing currently being planned persist and lead to ultimate approval. His surgical colleagues, he said, are interested in the possibility of presurgical PV-10 injections turning unresectable lesions into resectable ones and/or stimulating the immune system to lower the odds of recurrence.

Two groups of patients would be prime candidates, Dr. Agarwala continued: patients who are refractory to all other therapies and who have injectable disease, and patients who have injectable lesions but who are not eligible for systemic therapy (e.g., the elderly or those with comorbidities). Combining PV-10 with other therapies such as ipilimumab or nivolumab would be an attractive option. He added, "Of course, all of these need to be tested in clinical trials." ❑



Rose Bengal. PV-10 is formulated from this compound.

Postscript: *Sanjiv Agarwala, MD, is also Chief of Medical Oncology and Hematology at St. Luke's University Health Network in Bethlehem, PA.