New Anticancer Agents Have Distinctive Toxicities

BY BRUCE JANCIN

Amsterdam - The highly promising new class of investigational anticancer agents known at cytotoxic T-lymphocyte antigen 4 blockers has a characteristic group of side effects of special interest to dermatologists, gastroenterologists, and endocrinologists, Dr. Alexander M. Eggener said at the 11th World Congress on Cancers of the Skin.

Two fully human monoclonal antibodies to CTLA4 are making major waves in oncology circles because of their efficacy in early clinical trials for the treatment of advanced melanoma, a disease which has seen discouragingly little therapeutic progress in the last 3 decades.

But it is apparent that this impressive ef

fects is one of the main hallmarks which have led to the development of these drugs, and which may render them useful in a sizable minority of cases, trigger IRAEs.

"If you have subclinical autoimmune disease, you may be propelled into clinical disease manifestations because the hand brake is off your T-cell populations," Dr. Eggener explained at the congress, cosponsored by the Skin Cancer Foundation and Erasmus University.

Dermatologic IRAEs take the form of an array of rashes, vitiligo, and pruritic conditions involving specific T-cell infiltrates at the lesion sites. They are mild to moderate grade 1 or 2 side effects that resolve with corticosteroid therapy or discontinuation of the biologic agent.

Gastrointestinal IRAEs most often consist of mild to moderate enterocolitis. But occasionally, the colitis is grade 3, marked by bloody diarrhea with severe perforation, which is potentially fatal. Aggressive medical management, often including high doses of steroids, is sometimes required to control these toxicities.

Endocrinologic IRAEs are particularly puzzling, because they involve mainly the pituitary, a gland ordinarily very well protected against autoimmune disease. But a small number of patients with metastatic melanoma or renal cancer who are placed on anti-CTLA4 monoclonal antibody therapy—less than 1% thus far—develop autoimmune hypophysitis.

"You go into an Addisonian crisis. It's not at all a small thing," Dr. Eggener said as he reviewed a punch biopsy of the pituitary of a patient who died of the disease. "It's a very singular experience for the patient, as well as for their families.

"These patients have a sudden onset of weakness, darkening of the skin, and low blood pressure, which can be a medical emergency."