Continuous-Infusion Topotecan and Erlotinib: A Study in Topotecan-Pretreated Ovarian Cancer Assessing Shed Collagen Epitopes as a Marker of Invasiveness

EIRAN WARNER,^a LEONARD LIEBES,^b BENJAMIN LEVINSON,^b ANDREA DOWNEY,^b AMY TIERSTEN,^b FRANCO MUGGIA^b

^aBeth Israel Medical Center, New York, New York, USA; ^bNew York University Cancer Institute, New York, New York, USA

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AUTHOR SUMMARY

ABSTRACT

Background. Continuous-infusion topotecan with erlotinib has the potential to reverse topotecan resistance due to drug efflux mechanisms. We assessed the activity of such a regimen in ovarian cancer patients previously failing bolus topotecan. Assay for shed collagen epitopes recognized by antibody HU177 during treatment explored its ability to reflect tumor invasion.

Methods. Topotecan 0.4 mg/m² per day was administered by continuous infusion for 9–10 days every 3 weeks. Erlotinib, 150 mg orally, was administered on days 1–10 of each cycle. Cycles were repeated until progression or toxicity. Serum for shed HU177 collagen epitopes was collected weekly. This was a two-stage design to detect a CA-125 response rate of at least 20% in 30 patients after completing two treatment cycles. The trial would be terminated early if there were less than two CA-125 responses in 16 patients. Four or more CA-125 responses in 30 patients would justify further study of this regimen in prior topotecan treatment failures.

Results. Six patients were enrolled, with four receiving three or more cycles and one achieving a partial response by cancer antigen 125 (CA-125) criteria. Shed epitope levels became undetectable on at least one measurement in all patients who received three or more cycles (Fig. 1A) and reappeared concomitantly with rises in CA-125 and clinical progression (Fig. 1B). After logistical delays, the trial was closed by the sponsor's decision to stop developing erlotinib in ovarian cancer.

Conclusion. Continuous-infusion topotecan with erlotinib was found safe in six pretreated ovarian cancer patients; one met CA-125 criteria for partial response. Serial shed epitope levels to reflect invasiveness deserve further study. *The Oncologist* 2014;19:250

DISCUSSION

The combination of erlotinib and infusional topotecan in patients with epithelial ovarian cancer previously failing topotecan was

Figure 1. Monitoring of combination treatment. A, B, C, D, and F refer to patients. (A): Topotecan and erlotinib. (B): CA-125 in units/mL.

assessed in only six patients, providing little additional information on possible reversal of topotecan resistance by using infusion and/or contributions by concomitant erlotinib that had prompted our original communications [11]. Erlotinib used in the intermittent schedule had no appreciable skin toxicity. In contrast, marrow suppression and gastrointestinal intolerance from topotecan were common; however, three to seven cycles were tolerated by four of the six patients in the current study.

HU177-shed epitope levels mostly decreased with each cycle, eventually becoming undetectable in the two patients who showed declines in CA-125 (qualifying as partial response in one). Shed epitope levels were again detected on clinical progression, suggesting a possible relationship between shed appearance of serum epitope levels and tumor invasion. We cannot exclude that these changes reflect unknown biological effects of erlotinib, a drug that has not shown useful activity in ovarian cancer studies to date [8].

Author disclosures and references available online.

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Correspondence: Franco Muggia, M.D., New York University Cancer Institute, Room BCD556, 550 First Avenue, New York, New York, 10016, USA. Telephone: 212-263-6485; E-Mail: Franco.Muggia@nyumc.org Received October 9, 2013; accepted for publication December 31, 2013; first published online in *The Oncologist Express* on February 21, 2014. ©AlphaMed Press; the data published online to support this summary is the property of the authors. <http://dx.doi.org/10.1634/theoncologist.2013-0398>