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http://abstract.asco.org/AbstView_74_51434.html**P2 Study of NKTR-102 in Women with Platinum Resistant/Refractory Ovarian Cancer**

Author(s): I. B. Vergote, J. P. Michal, C. H. Pippitt Jr., G. G. Rao, D. L. Spitz, N. Reed, G. G. Dark, A. Garcia, D. J. Maslyar, G. J. Rustin; University Hospital Leuven, Leuven, Belgium; Gynecologic Oncology Associates, Newport Beach, CA; Piedmont Hematology-Oncology Associates, PLLC, Winston-Salem, NC; Tennessee Oncology, Nashville, TN; Palm Beach Cancer Institute, West Palm Beach, FL; EORTC, Glasgow, United Kingdom; Northern Centre for Cancer Treatment, Newcastle upon Tyne, United Kingdom; University of Southern California, Los Angeles, CA; Nektar Therapeutics, San Carlos, CA; Mount Vernon Cancer Centre, Middlesex, United Kingdom

Abstract:

Background: NKTR-102, a topoisomerase I inhibitor-polymer conjugate with reduced peak concentrations and a continuous concentration profile, demonstrated broad antitumor activity based on RECIST criteria in a phase I study, including ovarian cancer. The GCIG criteria integrate RECIST with CA-125. This study evaluated the GCIG, RECIST, and CA-125 responses (50% decline in CA-125) in patients (pts) with platinum-resistant or -refractory ovarian cancer following treatment with NKTR-102. **Methods:** This open-label, phase II randomized study enrolled pts to receive NKTR-102 IV at a target dose of 145 mg/m² q14d or q21d; each schedule followed a two-stage Simon design. Eligible patients had resistant/refractory ovarian cancer ("refractory" defined as progression within 3 weeks of last platinum), ECOG PS 0-1, adequate renal, hepatic, and marrow function. The primary endpoint was GCIG response rate; secondary endpoints were safety, PFS, and OS. **Results:** 71 pts were randomized and treated (36 on the q14d and 35 on the q21d schedule). Median age was 61; ECOG PS 0/1 equaled 52%/48%; median number of prior platinum-based and total regimens was 2 and 3, respectively. Of the 71 pts, 42 were platinum-resistant and 27 were platinum-refractory (2 pts were entered with platinum-sensitive disease). In pts with resistant/refractory disease, GCIG response rates (confirmed and unconfirmed) based on composite RECIST/CA-125 data was 47% for the q14d and 41% for the q21d schedules. RECIST responses (confirmed and unconfirmed) were 27% and 22% for the q14d and q21d schedules, respectively. CA-125 responses were 61% (q14d) and 52% (q21d); median time to first 50% decline of CA-125 was 31 days. Common related grade 3/4 toxicities (q14d/q21d schedules) were diarrhea (22%/11%), dehydration (14%/6%), hypokalemia (14%/6%), fatigue (6%/11%), nausea (14%/3%), and neutropenia (8%/9%). One pt each died due to neutropenic sepsis and pre-renal azotemia. **Conclusions:** Single-agent NKTR-102 demonstrates significant anti-tumor activity in heavily pretreated pts with platinum-resistant/refractory disease based upon GCIG and RECIST criteria with a tolerable toxicity profile. CA-125 responses were rapid, generally occurring within one month.