Gynaecological cancer

Oral presentations (Thu, 24 Sep, 09:00−11:00)
Gynaecological cancer

8000 ORAL

Efficacy and safety of farletuzumab, a humanized monoclonal antibody to folate receptor alpha, in platinum-sensitive relapsed ovarian cancer subjects: preliminary data from a phase-2 study

D.K. Armstrong[1], R. Coleman[2], A.J. White[3], A. Bicher[4], D.G. Gibbon[5], L. Old[6], R. Verheijen[7], S. Weil[8], M. Phillips[8], D. Chakrabarti[8]. *[1]Johns Hopkins University, Oncology, Baltimore, USA; [2]University of Texas M. D. Anderson Cancer Center, Gynecologic Oncology, Houston, USA; [3]South Texas Oncology and Hematology, Oncology, San Antonio, USA; [4]Northern Virginia Pelvic Associates, Gynecologic Oncology, Fairfax, USA; [5]Cancer Institute of New Jersey, Gynecologic Oncology, New Brunswick, USA; [6]Ludwig Institute of Cancer Research, Immunology, New York, USA; [7]VU/UMC, Gynaecologic Oncology, Amsterdam, The Netherlands; [8]Morphotek, Oncology, Exton, USA*

Background: Farletuzumab (MORAb-003) is a humanized monoclonal antibody to folate receptor alpha (FRα). FRα is over-expressed in most epithelial ovarian cancers (EOC), but largely absent on normal tissue. Farletuzumab is effective in preclinical xenograft models of ovarian cancer, active in ADCC assays, and inhibits phosphorylation of proteins by Lyn kinase. A Phase 1 study conducted with single agent farletuzumab in platinum resistant or refractory EOC subjects demonstrated signals of efficacy, and no dose-limiting toxicities or drug-related serious or severe AEs were observed.
Materials and Methods: The current study is an open-label, phase 2 study of farletuzumab in platinum-sensitive first relapsed subjects to determine the efficacy of farletuzumab as a single agent (SA), or in combination with platinum and taxane (P/T). A total of 54 subjects were eligible. Twenty eight (28) subjects who had asymptomatic CA-125 relapse received SA farletuzumab. A total of 46 subjects received P/T plus farletuzumab; 26 subjects experienced symptomatic relapse, 20 progressed on SA farletuzumab. Subjects who attained a complete or partial response (37) received SA farletuzumab maintenance therapy.
Results: Preliminary data show that of the 41 evaluable subjects receiving farletuzumab with P/T, 37 subjects (90.2%) normalized CA-125. In 10 (27%) of these 37 subjects who normalized, the second remission has been equal or as long as the first remission. Historically less than 5% patients achieve second remission longer than the first remission. By RECIST criteria (best response), 73.5% subjects achieved objective response (CR+PR), and the median PFS was 10.3 months. Subjects on SA farletuzumab had frequent SD or improvement, but no objective response or remissions were observed. No grade 3 or 4 farletuzumab-related AEs were observed and farletuzumab did not increase the toxicities of concomitant chemotherapy. The most common drug-related AEs were pyrexia, headache, and flushing.
Conclusions: Preliminary data for this study indicates that Farletuzumab with P/T significantly increases objective response rate compared to historic data for P/T alone in relapsed platinum-sensitive first-relapsed ovarian cancer subjects and increases the duration of second remission compared to first remission. A randomized global phase-3 study to test farletuzumab in combination with P/T in platinum-sensitive EOC, and a phase 2 in combination with weekly taxane in platinum-resistant EOC are currently ongoing.

8001 ORAL

Randomized multicenter phase II trial of cisplatin and ifosfamide with or without paclitaxel in recurrent or metastatic carcinoma of the uterine cervix: a Hellenic Co-operative Oncology Group (HeCOG) study

G. Mountzios[1], M.A. Dimopoulos[1], A. Bamias[1], G. Vourli[2], H. Kalofonos[3], G. Aravantinos[4], G. Fountzilas[5], C. Papadimitriou[6]. *[1]University Hospital " Alexandra" University of Athens School of Medicine, Medical Oncology, Athens, Greece; [2]Hellenic Co-operative Oncology Group (HeCOG) Data Office, Statistics, Athens, Greece; [3]University Hospital University of Patras Medical School, Department of Medicine-Division of Oncology, Patra, Greece; [4]"Agii Anargiri" Cancer Hospital, Third Department of Medical Oncology, Athens, Greece; [5]"Papageorgiou" Hospital Aristotle University of Thessaloniki School of Medicine, Medical Oncology, Thessaloniki, Greece; [6]University Hospital "Alexandra" University of Athens School of Medicine, Medical Oncology, Thessaloniki, Greece*

Background: We undertook a randomized phase II trial to test whether the addition of paclitaxel to the cisplatin and ifosfamide (IP) combination could improve objective-response (OR) rate, progression-free (PFS) and overall survival (OS) in patients with recurrent or metastatic cancer of the uterine cervix.
Methods: Eligible patients were randomly allocated to receive either the IP regimen (ifosfamide 1.5 g/m^2, intravenously, daily, on days 1 through 3 with Mesna uroprotection and cisplatin 70 mg/m^2 on day 2) or the same drug combination with the addition of paclitaxel 175 mg/m^2, given on day 1 as a 3-hour infusion (ITP regimen). Cycles were administered every 4 weeks on an outpatient basis for a target of six cycles using G-CSF support. The primary endpoint of the study was objective response, while PFS, OS and toxicity were secondary endpoints.
Results: One-hundred fifty-three patients were randomly assigned to either IP (74 patients) or ITP (79 patients) regimen. Median follow-up was 57.3 months. Toxicity was similar in both arms with the exception of a modest increase in neurotoxicity in the ITP arm. OR rate was significantly higher in the ITP group (59% versus 33%, p = 0.002, Fisher's exact test). Median PFS was 7.9 months (95% CI, 6.1−9.8) for patients in the ITP arm and 6.3 months (95% CI, 4.3−8.2) in the IP arm (p = 0.023). Median OS was 15.4 months (95% CI, 8.6−22.3) for patients in the ITP arm and 13.2 months (95% CI, 10.9−15.5) in the IP arm, respectively (p = 0.048). In multivariate analysis, patients in the ITP arm had a Hazard Ratio (HR) of 0.70 (95% CI, 0.49−0.99; p = 0.046) for relapse or progression and a HR of 0.75 (95% CI, 0.53−1.08; p = 0.124) for death compared to patients in the IP arm. Only performance status (PS), age at diagnosis and treatment arm were predictive for relapse/progression and survival in the multivariate setting.
Conclusions: The addition of paclitaxel to the IP combination leads to a significant improvement in OR rate and PFS in women with recurrent or metastatic cancer of the uterine cervix at the cost of a modest increase in neurotoxicity. The ITP regimen merits further investigation in randomized phase III studies.

8002 ORAL

What is the best schedule of Topotecan? – weekly versus routine 5-day schedule in patients with platinum-resistant ovarian cancer – a randomized, multicenter trial of the North-Eastern German Society of Gynaecological Oncology (TOWER)

J. Sehouli[1], G. Oskay-Özcelik[1], D. Stengel[2], P. Harter[3], C. Kurzeder[4], A. Belau[5], S. Markmann[6], R. Lorenz[7], L. Mueller[8], W. Lichtenegger[1]. *[1]Charite-Universitätsmedizin Berlin, Department of Gynecology and Obstetrics, Berlin, Germany; [2]Unfallkrankenhaus Marzahn, Department of Reconstructive Surgery, Berlin, Germany; [3]Frauenklinik Wiesbaden, Department of Gynecologic Oncology, Wiesbaden, Germany; [4]Universitäts-Frauenklinik Ulm, Department of Gynecologic Oncology, Ulm, Germany; [5]NOGGO, Department of Gynecologic Oncology, Greifswald, Germany; [6]NOGGO, Department of Gynecologic Oncology, Rostock, Germany; [7]NOGGO, Department of Gynecologic Oncology, Braunschweig, Germany; [8]NOGGO, Department of Gynecologic Oncology, Berlin, Germany*

Background: A 5-day regimen (Tc) of Topotecan is approved and effective in women with platinum-resistant recurrent ovarian cancer. Newer phase-two trials show a more favourable toxicity profile of weekly administration of Topotecan (Tw) without compromising its anti-tumor activity. Therefore we conducted the first randomized multicenter trial to validate this assumption.
Materials and Methods: The trial was pre-registered at clinicaltrials.gov (NCT00170677). Women with platinum-resistant ovarian and fallopian tube cancers or primary peritoneal carcinoma, and measurable or assessable disease (GCIG criteria) were randomized to receive either Tw (d1,8,15/q28d, 4 mg/m^2) or Tc (d1−5/q21d, 1.25 mg/m^2). The pre-defined stopping rule, based on the primary endpoint of best CA-125 or tumor response, was not reached (presented at ASCO 2007, Abstract 5526). This permitted the accrual of 194 patients, 154 of whom could be assessed for CA-125 or tumor response (SD + CR + PR). We also compared progression-free (PFS) and overall survival (OS), as well as toxicity between trial groups.
Results: Mean age was 61.8 (SD 9.8) years, and 59 women were on third-line treatment. Patients received a total of 809 cycles of chemotherapy. Demographic baseline characteristics, tumor stages and grades, and previous lines of chemotherapy were well balanced between treatment groups. There were 35 / 75 (47%) and 45 / 79 (57%) responses in the Tw and Tc groups, respectively (Risk Ratio [RR] 1.22, 95% CI 0.89−1.66). Median PFS and OS did not differ markedly between both regimens (3.2 versus 4.4 months, hazard ratio [HR] 1.30, 95% CI 0.96−1.77 and 9.8 versus 10.0 months, HR 1.08, 95% CI 0.77−1.52). The risk of grade III/IV hematological toxicity was significantly lower in the Tw group (anemia: RR 0.35, p = 0.007, neutropenia: RR 0.38, p = 0.0001, thrombopenia: RR 0.23, p = 0.0004). QoL data were similar in both arms.