long-term treatment-related neurotoxicity occurred in only 1.6% and 1.0% of patients in the docetaxel- and non-docetaxel-based regimens, respectively.

Although the addition of docetaxel to anthracycline-based adjuvant chemotherapy did not improve DFS or OS, the data suggested a benefit of sequential docetaxel in patients with highly proliferative ER-positive breast cancer, concluded Prof Sonnenblick.

Trial Will Evaluate Niraparib vs Placebo in Platinum-Sensitive Patients With Ovarian Cancer

Written by Maria Vinall

Niraparib is a potent oral PARP1 and PARP2 (poly [ADP-ribose] polymerase) inhibitor with antitumor activity in germline BRCA mutation (gBRCAmut) ovarian cancer and BRCA-negative (non-gBRCAmut) high-grade serous ovarian cancer (HGSOC).

Niraparib demonstrated antitumor activity in a recent phase 1 (dose-finding) trial of patients with advanced solid tumors (half the population enriched for *BRCA1* and *BRCA2* mutations) [Sandhu SK et al. *Lancet Oncol.* 2013]. Niraparib was well tolerated in this study, with a relatively low rate of grade 3 and 4 toxicities. The most common grade 3 or 4 treatment-related adverse events were anemia and thrombocytopenia (9% and 8% for grade 3 and 1% and 7% for grade 4, respectively) and 4% each for fatigue and neutropenia grade 3. Among study participants with sporadic HGSOC, 3 of 4 platinum-sensitive patients achieved RECIST responses (Response Evaluation Criteria in Solid Tumors). Based on these results, further trials were recommended.

Mansoor R. Mirza, MD, Oncology, Nordic Society of Gynaecologic Oncology and Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark, presented the study design of an ongoing niraparib maintenance study examining platinum-sensitive patients with ovarian cancer and deleterious gBRCA^{mut} or high-grade serous histology non-gBRCA^{mut} (NOVA; NCT01847274).

The repeating 28-day maintenance cycle begins with screening and is followed by evaluation of gBRCA mutation status. From there, randomization occurs in 2 groups: gBRCA^{mut} (n = 180) and non- gBRCA^{mut} (n = 180). Each group is further divided into 2 groups: those receiving 300 mg of niraparib and those receiving placebo. After this, end points are assessed.

Women are eligible to participate in this phase 3 trial who are aged ≥ 18 years with histologically confirmed ovarian cancer, including either a tumor with HGSOC histology or known gBRCA^{mut}, and who have completed ≥ 2 courses of platinum-containing therapy with documented platinum sensitivity (complete or partial remission; no measurable lesion > 2 cm and normal CA125 or > 90% decrease during the last platinum regimen). Patients must also have an Eastern Cooperative Oncology Group score of 0 to 1 and normal organ function.

The primary study objective is to evaluate the effect of niraparib (300 mg, QD) on progression-free survival (PFS). Secondary objectives include additional measures of clinical benefit: patient-reported outcomes; PFS2, defined as the time from treatment randomization to the assessment of progression on a subsequent anticancer therapy or death by any cause; chemotherapy-free interval; and overall survival. Corrected QT intervals will be evaluated in a subset of patients. Other secondary objectives are to evaluate the safety and tolerability of niraparib versus placebo, the concordance of the centralized *BRCA* mutation test and a candidate companion diagnostic test with respect to gBCRA^{mut} patients, and the effects of food on the pharmacokinetics of niraparib.

The efficacy of oral niraparib will be determined by PFS as assessed by RECIST 1.1 via computed tomography or magnetic resonance imaging every 2 cycles through cycle 14, then every 3 cycles. Other end points are assessed by various targeted questionnaires. Analysis of 2 independent patient cohorts (deleterious gBRCA^{mut} and high-grade serous or high-grade predominantly serous histology non-gBRCA^{mut}) is being conducted under the hypothesis that patients with gBRCA mutations are enriched for responsiveness to niraparib. Pharmacokinetics will be assessed in all patients, and food effects will be assessed in a subset of patients who ingest a high-fat meal. This trial is being conducted in Europe, the United States, and Canada.

Niraparib is also being investigated in a phase 3 trial in patients with Her2-negative, germline *BRCA* mutation–positive breast cancer [BRAVO; NCT01905592].

Everolimus Safe and Effective for Advanced pNET: Final Results of RADIANT-3

Written by Brian Hoyle

Final overall survival (OS) and safety results of the phase 3 Everolimus and Octreotide in Patients With Advanced Carcinoid Tumor trial [RADIANT-3; NCT00412061] have bolstered previous findings that everolimus is effective and safe in the treatment of advanced pancreatic neuroendocrine tumors (pNET).