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Meeting Report

The American Society of Clinical Oncology 2016 annual meeting: A review and summary of selected abstracts☆

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1. Introduction

From June 2 to June 7, 2016, the American Society of Clinical Oncology (ASCO) met once again in Chicago, IL, USA. The theme of this year's meeting was "Collective Wisdom". The goal of the organizers was clearly to focus on the team format though which clinical and scientific breakthrough occur. This was highlighted in the remarks made by Vice President Biden as he addressed the conference attendees on June 6 in a speech about his Cancer Moonshot program. This year, the main plenary sessions included large randomized studies investigating the role of prolonged aromatase inhibition in women with early stage breast cancer (Abstract #LBA1); the use of temozolomide and short course radiation compared to short course radiation alone in elderly patients with glioblastoma (Abstract #LBA2); and the use of tandem myeloablative autologous stem cell transplant in children with neuroblastoma (Abstract #LBA3); and comparison of daratumumab, bortezomib and dexamethasone in combination versus bortezomib and dexamethasone alone in multiple myeloma (Abstract #LBA4). There were 9 abstracts selected for oral presentation in the gynecologic oncology oral session and 11 selected for poster discussion. Three themes emerged from these presentations: Established concepts with new data in ovarian cancer; Immunotherapy advances in gynecologic cancers; and Optimization of treatment by utilizing molecular analysis. This review will summarize selected studies with further detailed data presented in the tables for all Phase III and II study abstracts for ovarian, endometrial, and cervical cancers (Tables 1 and 2).

2. Established concepts, new data in ovarian cancer

In the wake of the presentation of Gynecologic Oncology Group Protocol 252 at the 2016 Annual Meeting of the Society of Gynecologic Oncology in March, there has been renewed interest in the role of intraperitoneal chemotherapy (IP) in the treatment of ovarian cancer given the negative findings of such a large trial [1]. OV-21/PETROC was a randomized two stage Phase II study of IP versus IV chemotherapy following neoadjuvant therapy and optimal interval cytoreduction in ovarian cancer patients (Abstract #5503). The authors hypothesized that IP therapy delivered after optimal cytoreduction in the neoadjuvant setting would receive a benefit similar to that of those patients who receive benefit from IP chemotherapy after optimal primary cytoreduction. The study randomized patients with at least stage IIB to IV (by pleural effusion only) who had received 3 or 4 cycles of platinum and taxane chemotherapy and less than one centimeter of residual disease at the time of interval cytoreduction to three arms in the initial phase. Arm 1 included IV carboplatin at AUC5/6 on day 1, paclitaxel 135 mg/m^2 on day 1 and paclitaxel 60 mg/m^2 on day 8. Arm 2 was IP cisplatin at 75 mg/m^2 and paclitaxel at the same doses as Arm 1 with the exception of IP administration of the day 8 paclitaxel. Arm 3 was IP carboplatin at AUC 5/6 and again the same paclitaxel dose and strategy as Arm 2. After reviewing the results of the initial phase results ($n = 150$), the cisplatin arm was dropped due to less activity than the IP carboplatin arm as pre-designed in the study. The second stage results evaluated 101 patients in the IV carboplatin/paclitaxel arm versus 102 patients in the IP carboplatin/IV-IP paclitaxel arm. There was an improvement in progressive disease at 9 months in the IP carboplatin/paclitaxel arm versus the IV arm (23.3% vs. 42.2% $p = 0.03$). This is not a common endpoint and was adjusted due to low accrual in the second phase of the study. The traditional progression free survival (PFS) was not significantly different (12.5 months vs. 11.3 months favoring the IP arm) but the study was not powered to detect a difference. Interestingly, the overall survival (OS) favored the IP arm at 59.3 months versus 38.1 months but this difference did not reach statistical significance ($p = 0.4$).

A second IP study was presented by a group from Japan, combining the concepts of dose dense paclitaxel and IP platinum in patients with suboptimally debulked primary epithelial ovarian cancer. These authors considered the combination of these strategies, which had both showed prior improvements in OS in ovarian cancer patients, to be a novel tactic in the upfront treatment of this high risk disease. This was a multicenter single arm Phase II study that enrolled 76 patients with RECIST measurable disease (Abstract #5504). Carboplatin AUC 6 was given IP on day 1 and paclitaxel at 80 mg/m^2 was given on days 1, 8, and 15 of a 21-day cycle. Only 60.5% of patients completed the planned 6 cycles of therapy and a remarkable 50.9% had a delay due to toxicity prior to their 5th cycle of treatment. Grade 3 or 4 neutropenia was seen in 84% of patients. The neuropathy of this regimen was significant with 10.5% of patients experiencing grade 3 or 4 symptoms. The PFS was 18.5 months and the OS was 55.5 months in this study. The overall response rate (ORR) was reported as 83.1%. Of note, only 9 patients had a reported complete response by RECIST criteria. This study represents a novel mechanism for the treatment of suboptimally debulked patients and further studies will be needed to determine if this regimen is more effective than IV treatment in a randomized study.

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Table 1
Phase II trials of novel drug and cytotoxic treatment strategies in ovarian, fallopian tube, and primary peritoneal carcinomas.

Type	Abs no.	Agents/dose	Mechanism	Type of patients	Results	HR	p-Value	Major toxicities
Phase II single agent	5532	Oral veliparib (300 mg) BID monotherapy, 28-day cycle	PARP inhibitor	Primary EOC/FTC/PPC, BRCA1/2 mutations, Pt-R or intermediate sensitive relapse of OC, measurable disease by either RECIST or GCIG CA125 (n = 32)	ORR = 65.7% CR = 6.3% PR = 59.4% PFS = 5.5 months OS = 15.2 months	–	–	Grade 2: f (22%), n (22%), v (9%)
	5533	IV avelumab (10 mg/kg), q2w	Fully human anti-PD-L1 IgG1 antibody	Recurrent/refractory OC (n = 124)	Median PFS = 11.3 weeks Median OS = 10.8 months ORR = 9.7% ORR in PD-L1 + vs. PD-L1 − pts = 12.3% vs. 5.9% PR = 12 (9.7%) SD = 55 (44.4%) DCR = 54.0%	–	–	Treatment-related AEs in 82 (66.1%): f (13.7%), infusion-related reaction (12.1%), d (11.3%)
	5540	Oral rucaparib (600 mg) BID	PARP inhibitor	Measurable, relapsed, Pt-S, high-grade EOC/FTC/PPC (n = 204) classified as either *BRCAm* (n = 40, Group 1), *BRCA*^{wt}/LOH^{high} (*BRCA*-like) (n = 82, Group 2), or *BRCA*^{wt}/LOH^{low} (n = 70, Group 3)	Confirmed rORR for BRCAm pts (n = 20 each) = germline (85%) vs. somatic (75%) 3 pts died from PD Prespecified LOH cutoff: rORR = 80 vs. 35.4 vs. 12.9% DoR = 11.2 vs. 10.8 vs. 5.9 months PFS = 12.8 vs. 5.7 vs. 5.2 months Refined LOH cutoff: rORR = 80 vs. 39.1 vs. 13.3% DoR = 11.2 vs. 10.8 vs. 5.7 months PFS = 12.8 vs. 7.2 vs. 5.0 months	0.27, 0.62 0.25, 0.51	<0.001 0.011 <0.001 <0.001	n (71%), f (59%), ALT/AST increase (41%), An (30%); Grade ≥ 3: n (3%), f (6%), ALT/AST increase (11%), An (19%)
	5557	Oral palbociclib (125 mg) daily for 3 weeks w/ 1 week off, q28d	CDK4/6 inhibitor	Asymptomatic pts with RECIST and/or CA125 measurable disease failing ct or anti-hormonal therapy (n = 37)	PFS-6 months = 9/30 (30%) RECIST: Median PFS = 3.7 months PR = 1/26 (4%) SD = 17/26 (65%) PD = 8/26 (31%) GCIG CA125: Median PFS = 4.0 months CR = 1/30 (3%) PR = 3/30 (10%) SD = 18/30 (60%) PD = 8/30 (27%)	–	–	Grade 3/4: ANC (5), PLTS (4), hypokalemia (1), emesis (1) Grade 2: An (2), n (1), abdominal pain (1); 1 bowel obstruction; 1 death due to PD w/n 30 days of discontinuation
	5564	Oral ENMD-2076 (275 mg) daily, 28-day cycle	Anti-angiogenic/anti-proliferative kinase inhibitor with activity against the Aurora A mitotic kinase	Recurrent CCOC, ECOG ≤ 2, measurable disease, prior platinum therapy (n = 32)	Evaluable pts (n = 26): SD = 19 (73%) Median tumor reduction of −13% in 17 (65%) pts No objective responses by RECIST Median PFS = 3.9 months PFS-6 month = 23% Pts w/ ARID1A loss had longer PFS and therapy duration 7.27 vs. 2.55 months	–	<0.028	AEs in 24/28 (86%), most common were Grade 1/2 f. n, v, htn, d; Grade ≥ 3 AEs in 46% of pts; AEs caused dose-reduction in 11 (39%) and discontinuation in 3 (11%)
Phase II combination	2551	Oral afuresertib (125 mg) + IV paclitaxel (175 mg/m^2) + carboplatin (AUC 5), q3w, ≤6 cycles followed by afuresertib maintenance	Pan-AKT inhibitor; cytotoxic agents	Recurrent Pt-R/Pt-Ref OC (n = 30)	Among Pt-R pts (n = 26) ORR (RECIST) = 32.1% ORR (CA-125, n = 25) = 52% Median PFS = 7.1 months ORR correlates with duration of sensitivity to prior platinum regimen and PFIs	–	–	Grade 3/4 AEs: d (20%), f (10%), rash (10%), v (7%), n (3%)
	2584	Oral veliparib (250 mg) BID days 1–21 on 3, 28-day cycles + low-dose fractionated whole	PARP inhibitor; radiation therapy	Advanced solid malignancies/peritoneal carcinomatosis (n = 32)	Median PFS = 3.6 months Median OS = 9.1 months OC/FTC survival was not significantly	–	0.885	Grade 3/4 AEs: lymphopenia (59%), An (9%), PTLS (12%), ANC (6%), leukopenia (6%), n