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CONTENTS

2015 ASCO ANNUAL MEETING PROCEEDINGS

Special Award Lecture Abstracts 1s

Plenary Session
(Abstracts LBA1 - LBA4) 3s

Pathways Clinical Science Symposia
(Abstracts LBA100 - LBA109) 5s

Global Oncology Symposium
(Abstract 200) 8s

Breast Cancer—HER2/ER
Scheduled presentations (Abstracts 500 - TPS642) 9s

Breast Cancer—Triple-Negative/Cytotoxics/Local Therapy
Scheduled presentations (Abstracts 1000 - TPS1113) 45s

Cancer Prevention, Genetics, and Epidemiology
Scheduled presentations (Abstracts 1500 - 1592) 73s

Central Nervous System Tumors
Scheduled presentations (Abstracts 2000 - TPS2081) 96s

Developmental Therapeutics—Clinical Pharmacology and Experimental Therapeutics
Scheduled presentations (Abstracts 2500 - TPS2624) 117s

Developmental Therapeutics—Immunotherapy
Scheduled presentations (Abstracts 3000 - TPS3106) 148s

continued on following page

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7500 Oral Abstract Session, Sat, 3:00 PM-6:00 PM

Bevacizumab 15mg/kg plus cisplatin-pemetrexed (CP) triplet versus CP doublet in Malignant Pleural Mesothelioma (MPM): Results of the IFCT-GFPC-0701 MAPS randomized phase 3 trial. *First Author: Gerard Zalcman, Caen Univ Hosp, Caen, France*

Background: MPM median overall survival (OS) did not exceed 13 months with pemetrexed-platinum doublet, with virtually no surviving patients at 5 years. Vascular endothelial growth factor is a potent mitogen for MPM cells. **Methods:** In this French multicenter randomized phase 3 trial, eligible patients had unresectable, histologically proved MPM, age < 76, no prior chemo, PS 0-2, no thrombosis, nor bleeding. Randomized patients (1:1) received pem 500 mg/m^2, CDDP 75 mg/m^2 at D1, with (arm B) or without bevacizumab (arm A), 15 mg/kg Q21D, for 6 cycles. Arm B non-progressive patients received bevacizumab maintenance therapy until progression or toxicity. Primary endpoint was OS. 445 patients were to be randomized, and 385 events observed, to show a significant OS improvement, with 80% statistical power, 5% a-risk. **Results:** From Feb. 2008 to Jan. 2014, 448 patients were included in 73 centers. Males: 75.4%, median age: 65.7 years (range 34.7-75.9), PS 0-1: 96.7%. The IDMC recommended a second interim analysis after 85% of events. On 01-Jan-2015, the duration since last news was < 30 days in 105 out of 106 still living patients. Overall survival was significantly longer in the experimental arm (median: 18.8 months, 95%CI[15.9-22.6] *vs.* 16.1 months, 95%CI[14.0-17.9] for the reference arm, (adj.HR = 0.76, 95%CI[0.61; 0.94], p = 0.012). With only 46/448 non-progressive patients at the date of analysis, median PFS was 9.6 months, 95%CI[8.5-10.6] in bevacizumab arm *vs.* 7.5 months, 95%CI[6.8-8.1] (adj.HR = 0.62, 95%CI[0.50-0.75], p < 0.0001). G3-4 hematological toxicities did not significantly differ in the two arms (49.5% *vs.* 47.3%). Significantly more G3 proteinuria (0.0 *vs.* 3.1%), G3 hypertension (0.0 *vs.* 23%), G3-4 arterial thrombotic events (0.0 *vs.* 2.7%) were observed in bevacizumab arm. QOL and exploratory biomarkers studies will be also presented at time of the meeting. **Conclusions:** Bevacizumab addition to pemetrexed/cis-platin provides a significantly longer survival in pts with MPM, with acceptable toxicity, making this triplet a new treatment paradigm. Clinical trial information: NCT00651456.

7501 Oral Abstract Session, Sat, 3:00 PM-6:00 PM

Phase III trial (NGR015) with NGR-hTNF plus best investigator choice (BIC) versus placebo plus BIC in previously treated patients with advanced malignant pleural mesothelioma (MPM). *First Author: Rabab M. Gaafar, National Cancer Institute, Cairo University, Cairo, Egypt*

Background: Currently, there are no standard options for MPM patients who failed a pemetrexed-based chemotherapy (CT). NGR-hTNF, a tumor-targeted antivascular agent, displays antitumor activity through a vessel normalization that improves intratumor CT uptake and T-cell infiltration. **Methods:** MPM patients who progressed on or after a front-line pemetrexed-based regimen, stratified for performance status (PS) and CT agent, were randomly assigned to receive weekly NGR-hTNF 0.8 μg/m^2 (arm A; n = 200) or placebo (arm B; n = 200), both given with BIC (gemcitabine [G], vinorelbine [V], doxorubicin [D] or supportive care). Primary endpoint was overall survival (OS). Hypothesis testing: hazard ratio (HR) = 0.72, 1-β = 0.80, α = 0.05. **Results:** Baseline characteristics were balanced between arms (A vs B): median age (65 vs 67 years); men (76% vs 74%); PS ≥ 1 (72% vs 69%); nonepithelial histology (15% vs 19%); poor EORTC score (30% vs 23%); prior treatment-free interval (TFI) < median of 4.8 months (47% vs 53%). Investigator-selected CT (n = 381, 95%): G 55%, V 42%, D 3%. Patients completing six CT cycles: 41% vs 32% (p = 0.08). Most common grade 3/4 toxicity: neutropenia (17% vs 19%) and fatigue (5% vs 8%). After a median follow-up of 18.9 months, OS did not differ significantly between arms in ITT analysis (median 8.4 vs 7.9 months; HR = 0.94 p = 0.61). By predefined OS analyses, there was a significant interaction only between treatment group and TFI (p = 0.008). In 198 patients with TFI shorter than 4.8 months after first-line therapy, median OS for NGR-hTNF vs placebo was 9.0 vs 6.3 months and 1-year OS was 39% vs 23%, respectively (HR = 0.69 p = 0.02; stratified HR = 0.65 p = 0.01). By CT agent, median OS for NGR-hTNF plus G vs placebo plus G was 9.0 vs 6.2 months and for NGR-hTNF plus V vs placebo plus V was 9.7 vs 6.9 months. A significant treatment-by-TFI interaction was also observed for PFS (p = 0.009), with 6-month rates in the short TFI subset of 25% for NGR-hTNF and 12% for placebo (HR = 0.71 p = 0.03). **Conclusions:** Though the primary endpoint was not met, OS and PFS benefit reported with NGR-hTNF plus CT in patients with short TFI deserves a confirmatory first-line phase III trial. Clinical trial information: NCT01098266.

7502 Oral Abstract Session, Sat, 3:00 PM-6:00 PM

Pembrolizumab (MK-3475) in patients (pts) with extensive-stage small cell lung cancer (SCLC): Preliminary safety and efficacy results from KEYNOTE-028. *First Author: Patrick Alexander Ott, Dana-Farber Cancer Institute, Boston, MA*

Background: Treatment options for pts with SCLC that progresses on platinum-based chemotherapy are limited. Pembrolizumab, an anti–PD-1 monoclonal antibody designed to block the interaction between PD-1 and its ligands PD-L1 and PD-L2, has shown antitumor activity in multiple advanced malignancies, including non-small cell lung cancer. We assessed the safety and efficacy of pembrolizumab in pts with PD-L1$^+$ SCLC. **Methods:** KEYNOTE-028 (ClinicalTrials.gov, NCT02054806) is an ongoing multicohort, phase Ib study of pembrolizumab in pts with PD-L1$^+$ advanced solid tumors. Key eligibility criteria for the SCLC cohort include: confirmed, measurable disease; PD-L1 expression in ≥ 1% of cells in tumor nests or PD-L1$^+$ bands in stroma as assessed by IHC at a central laboratory; failure of standard therapy; and absence of autoimmune disease or interstitial lung disease. Pembrolizumab 10 mg/kg is given every 2 wk for up to 2 y or until confirmed progression or unacceptable toxicity. Primary end points are safety, tolerability, and response assessed per RECIST v1.1 by investigator review every 8 wk for the first 6 mo and every 12 wk thereafter. **Results:** Of the 135 pts with SCLC screened, 37 (27%) had PD-L1$^+$ tumors. Seventeen pts were enrolled from March 2014 through January 2015 (59% men; median age, 62 y; 59% ECOG PS 1). One pt was misenrolled and did not receive pembrolizumab. All 16 treated pts received prior platinum and etoposide. 9 pts (53%) experienced a drug-related AE (DRAE); only 1 pt had a grade ≥ 3 DRAE. There were no treatment-related deaths or discontinuations due to DRAEs. Four of 16 (25%) evaluable pts had a partial response. One (7%) pt had stable disease, resulting in a disease control rate of 31%. Six (37%) pts had progressive disease as their best response, and 5 pts had no assessment at the time of analysis. Responses are durable, with all responders on treatment for 16+ wks with ongoing response. **Conclusions:** Pembrolizumab is generally well tolerated and has promising antitumor activity in pts with PD-L1$^+$ SCLC who have progressed on prior platinum-based therapy. Enrollment in the SCLC cohort of KEYNOTE-028 is ongoing. Clinical trial information: NCT02054806.

7503 Oral Abstract Session, Sat, 3:00 PM-6:00 PM

Phase I/II study of nivolumab with or without ipilimumab for treatment of recurrent small cell lung cancer (SCLC): CA209-032. *First Author: Scott Joseph Antonia, Moffitt Cancer Center, Tampa, FL*

Background: Patients (pts) with SCLC respond to initial platinum (PLT) based chemotherapy (CT), but rapidly progress. Combined blockade of PD-1 and CTLA-4 immune checkpoint pathways has anti-tumor activity with a manageable safety profile. Nivolumab (NIVO) is a fully human IgG4 PD-1 immune checkpoint inhibitor approved in the US & Japan. Interim safety and efficacy of NIVO +\- ipilimumab (IPI), a CTLA-4 checkpoint inhibitor, in pretreated SCLC pts are reported. **Methods:** Pts who were PLT sensitive or refractory and had progressive disease were enrolled regardless of tumor PD-L1 status or number of prior CT regimens. This open-label study randomized pts to NIVO 3 mg/kg IV Q2W or NIVO+IPI (1 + 1 mg/kg, 1 + 3 mg/kg or 3 + 1 mg/kg) IV Q3W for 4 cycles followed by NIVO 3 mg/kg Q2W. Primary objective was overall response rate (ORR). Other objectives were safety, PFS, OS and biomarker analysis. **Results:** Seventy-five pts were enrolled (NIVO, n = 40; NIVO+IPI, n = 35); 59% had ≥ 2 prior regimens. Drug-related adverse events (DrAEs) in ≥ 10% were fatigue (18%), diarrhea (13%), nausea (10%), and decreased appetite (10%) with NIVO; and fatigue (29%), diarrhea (17%), pruritus (14%), nausea, endocrine disorders and rash (11% each) with NIVO+IPI. Gr 3/4 DrAE in ≥ 5% included diarrhea and rash (6% each; NIVO+IPI). Drug-related pneumonitis occurred in 2 pts (1 per arm). One pt experienced a drug-related SAE of myasthenia gravis on study which was fatal. Of 40 evaluable NIVO pts, partial response (PR) was seen in 6, 15% (duration of ongoing responses [DOR] 80-251+ days); stable disease (SD) in 9, 22.5%; and progressive disease (PD) in 25, 62.5%. In 20 evaluable NIVO+IPI pts, 1 had complete response (CR), 5% (DOR 322+ days); 4 had a PR, 20% (DOR 41-83+ days); 6 had SD, 30%, and 9 had PD, 45%. In the NIVO+IPI arm, 12 pts had not reached first tumor assessment and 3 were not evaluable. Nine pts (23%) continue treatment with NIVO and 19 (54%) with NIVO+IPI. **Conclusions:** In this PD-L1 unselected SCLC population with progression post-PLT, NIVO alone or combined with IPI was tolerable. ORR was 15% (NIVO) and 25% (NIVO+IPI) for evaluable pts; durable responses were noted. Updated safety, clinical activity and biomarker analysis will be presented. Clinical trial information: NCT1928394.