Presidential Session IV
Tuesday 27 September 2011, 09:00−11:00
12LBA LATE BREAKING ABSTRACT

Cognitive and Cardiac Outcome After Prenatal Exposure to Chemotherapy in Children 18 Months or Older

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Background: The effect of prenatal exposure to chemotherapy on cardiac and neurodevelopmental outcomes is still uncertain.
Methods: This is a prospective multicenter study examining children who were prenatally exposed to maternal cancer staging and treatment, including chemotherapy. Children were examined at the age of 18 months, 5−6, 8−9, 11−12, 15−16 and 18 years. The tests comprised a clinical neurologic examination, testing of the general level of cognitive functioning(Bayley/IQ-test), an electro/echocardiography and questionnaire on general health and development. From the age of 5 years, also an audiometry, Auditory Verbal Learning Test and subtasks of the Children's Memory Scale and Test of Everyday Attention for Children were performed and the Child Behavior Checklist was completed.
Results: In total, 236 cycles of chemotherapy were administered in 68 pregnancies. Seventy children, born at a median gestational age of 35.7 weeks (range, 28.3–41.0; 47/70 <37 weeks), were included with a median follow up period of 22.3months (range, 16.8–211.6). Although neurocognitive outcome results were within normal ranges, the high frequency of preterm birth had a negative influence on cognitive development. A severe neurodevelopmental delay was seen in both members of a twin (3%). Child's behavior, general health, hearing and growth was reported as in a general population. Cardiac dimensions and functions were within normal ranges.
Conclusion: Fetal exposure to chemotherapy was not associated with increased morbidity at the level of the central nervous system, cardiac, and auditory functions, as well as general health and growth. However, prematurity was frequently encountered, and associated with impaired cognitive development.

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13LBA LATE BREAKING ABSTRACT

Efficacy of Veliparib (ABT-888) Plus Temozolomide Versus Temozolomide Alone: a Randomized, Double-blind, Placebo-controlled Trial in Patients with Metastatic Melanoma

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Background: Veliparib (ABT-888) is a novel, orally bioavailable, small molecule, potent inhibitor of the enzymes PARP-1 (Ki 5nM) and PARP-2 (Ki 3nM), involved in DNA repair. Veliparib enhances antitumor activities of multiple cytotoxic agents preclinically, including temozolomide (TMZ).
Materials and Methods: This multicenter, double-blind, placebo (pbo)-controlled trial (ABT-888 in combination with TMZ in metastatic melanoma [MM]; trial ID NCT00804908; sponsor Abbott Laboratories) evaluated the efficacy of veliparib+TMZ vs pbo+TMZ in prolonging progression free survival (PFS). Adult patients (pts) with unresectable Stage III or IV MM, $\geqslant$1 measurable lesion on CT scan (RECIST), and ECOG 0−1, were randomized in a 1:1:1 ratio to pbo BID+TMZ, veliparib 20 mg BID+TMZ or veliparib 40 mg BID+TMZ. Toxicity was assessed by NCI-CTCAE v3.0. Efficacy endpoints included PFS, overall survival (OS), and objective response rate (ORR). Tumor response and disease progression were evaluated every 8 weeks (per RECIST), with CT scans reviewed centrally.
Results: Between February 2009 and January 2010, 346 pts were randomized. Although median PFS nearly doubled numerically in the veliparib groups vs pbo (table), these differences were not statistically significant.

Efficacy endpoints	Pbo +TMZ (N = 115)	Veliparib 20 mg +TMZ (N = 116)	Veliparib 40 mg +TMZ (N = 115)	Hazard Ratio (HR); P-value Veliparib 20 mg vs Pbo	Veliparib 40 mg vs Pbo
Median PFS, days [95% CI]	60 [57,111]	113 [92,168]	110 [57,125]	HR = 0.737 p = 0.071[a]	HR = 0.822 p = 0.233[a]
Median OS, days [95% CI]	390 [299,436]	327 [274,399]	412 [346,483]	HR = 1.009 p = 0.955[a]	HR = 0.790 p = 0.162[a]
ORR, n (%)	8 (7.0)	12 (10.3)	10 (8.7)	p = 0.372[b]	p = 0.598[b]

[a]Stratified log-rank test. [b]Stratified CMH test.

Toxicities were as expected for TMZ. The frequency of thrombocytopenia, neutropenia and leukopenia increased significantly in the veliparib groups. Grade 3/4 adverse events (AEs), mainly of hematological toxicities, were seen in 38% (pbo), 54% (veliparib 20 mg), 57% (veliparib 40 mg) of pts. Veliparib-//pbo-related AEs were reported by 79% (pbo), 89% (veliparib 20 mg), 93% (veliparib 40 mg) of pts, and TMZ-related AEs were reported by 89% (pbo), 93% (veliparib 20 mg), 96% (veliparib 40 mg).
Conclusion: Veliparib-treated pts had numerically increased median PFS (20 and 40 mg) and median OS (40 mg), but these trends were not significant. No new toxicity signals were identified.

Presidential Session IV
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14LBA LATE BREAKING ABSTRACT

A Phase I/II, Open-label, Randomised Study of BIBF 1120 Plus mFOLFOX6 Compared to Bevacizumab Plus mFOLFOX6 in Patients with Metastatic Colorectal Cancer

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Background: This Phase I/II study evaluated BIBF 1120, an oral triple angiokinase inhibitor of VEGFR 1−3, PDGFR-α and -β, and FGFR 1−3, plus modified FOLFOX6 (mFOLFOX6) compared to bevacizumab (BEV) plus mFOLFOX6 in chemo-naïve metastatic colorectal cancer (mCRC) patients (pts).
Material and Methods: Eligible pts had unresectable, measurable histologically confirmed mCRC (adenocarcinoma) and ECOG PS $\leqslant$2 with adequate organ function. Pts stratified by ECOG PS, LDH levels, and receipt of adjuvant treatment were randomised 2:1 to receive first-line treatment with continuous BIBF 1120 plus mFOLFOX6 q2w (BIBF 1120 arm) or 5 mg/kg IV BEV plus mFOLFOX6 q2w (BEV arm) until disease progression or non-tolerable toxicity. Primary endpoint was progression-free survival (PFS) rate at 9 months; secondary endpoints included additional efficacy measures (PFS, objective response rate [ORR], resection rate) and adverse event (AE) profile.
Results: 128 pts were randomised (BIBF 1120 arm: 85 pts; BEV arm: 41 pts; not treated: 2 pts), with balanced baseline characteristics (mean age 63 years, 48% women). Three and 11 pts received 150 and 200 mg bid BIBF 1120, respectively, in the Phase I part. Interim database lock was performed 9 months after the last patient was first treated. At database lock, 47 pts (37%) continued on the study (BIBF 1120 arm, 35% vs BEV arm, 41%). The Kaplan–Meier 9-month PFS rate was 63% (95% CI: 50−75%) in the BIBF 1120 arm and 69% (95% CI: 53−86%) in the BEV arm. Median PFS was 10.6 months in both arms; confirmed ORR was 61% vs 54% and resection rate was 14% vs 20%, BIBF 1120 vs BEV arms, respectively. Treatment with BIBF 1120 did not impact exposure and intensity of mFOLFOX6 treatment compared with BEV.