enrolled in a Belgian academic multi-centre phase II trial, following a Simon's two-stage design. Patients received treatment with sunitinib in 6 weekly cycles comprising of a 50 mg once daily dosing for 4 consecutive weeks, followed by a 2-week off-treatment period. The primary end point of the study was RECIST-defined objective response. Angiogenic biomarkers were collected to study their potential predictive value for response. Peripheral blood was drawn every 2 weeks during the first treatment cycle and serum VEGF, VEGFR-1, VEGFR-2 and PlGF levels were determined by ELISA. The number of circulating endothelial cells was enumerated weekly by FACS during the 1st cycle and at day 1 of following cycles.
Results: At present, 21 patients (18 evaluable) with metastatic melanoma have been enrolled in the first stage of the study. Three patients were not evaluable for response because of early discontinuation of sunitinib, due to adverse events (1 cardiac insufficiency, 1 cerebral haemorraghia) and inability to swallow medication (1). Two patients (11.1% of evaluable) demonstrated partial response as best response with a mean duration of 5.4 months, 5 had stable disease (27.8%) with a mean duration of 4.4 months and 11 had progressive disease (61.1%). The most frequent toxicities were asthenia (61.9%), anorexia (33.3%) and nausea (42.9%). No grade 4 toxicity was observed. The correlative data with response analysis of the angiogenic biomarkers is ongoing and will be reported.
Conclusion: In the present phase II trial, early antitumor activity of sunitinib was detected in advanced melanoma patients, with an overall clinical benefit rate of 33%. The recruitment into the second stage of the study is ongoing. Angiogenic biomarkers are being correlated with clinical activity.

9306 ORAL

Phase II multi-institution trial of ipilimumab for patients with melanoma and brain metastasis

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Background: Ipilimumab (ipi) is a fully-human antibody (Ab) that blocks the engagement of CTLA4 on activated T lymphocytes with ligands on antigen-presenting cells. As a single agent, ipi has activity in advanced melanoma (mel), induces antigen-specific immune responses, and has been reported effective in patients with brain metastasis (met). We performed this phase II trial (CA-184−042) to better assess the activity of ipi against mel with brain met.
Patients and Methods: Patients (pts) had measurable brain met(s) with at least one lesion >0.5 cm or 2 lesions >0.3 cm and none >3 cm in diameter. Any size and site of extracranial met was also permitted. Prior-therapy (Rx) exclusions included investigational Ab and focused radiotherapy (RT) to the index lesion(s). Prior whole brain (WB) RT was allowed. Steroid Rx was prohibited except for Rx of immune-related adverse events (irAE), which, if severe, could be treated with glucocorticosteroid and additional immunosuppressants according to established algorithms. Ipi, 10 mg/kg, was administered intravenously over 90 minutes every 3 weeks for 4 doses, and stable or responding pts could continue to receive ipi on a q 12 week maintenance schedule. A 2-stage accrual design required >2 objective responses among the first 21 pts in order to proceed to stage 2 (21 additional pts)[Arm A]. A separate cohort of 21 pts on glucocorticoid Rx (Arm B) was then treated at the same time that Arm A was re-opened for second-stage accrual to the total of 41 patients.
Results: All patients have been accrued to both Arm A (41 pts) and Arm B (21 pts), and data will be complete for both cohorts by August, 2009. Complete data are provided for the 21 pts in first-stage accrual of arm A: Eight had prior WBRT with or without additional SRT to lesions not used for response assessment in this study. All pts had one or more prior systemic Rx. The World Health Organization response criteria were modified to take immune-related changes into account. Three pts had confirmed partial responses by World Health Organization criteria, all of which were continuing at the time of reporting, with durations of 7+, 6+ and 2+ months. One pt had an extracranial partial response but progressed in the brain. The frequency, grade and nature of irAE was similar to those reported in large trials of ipi for mel with colitis as the major toxicity requiring Rx discontinuation.
Conclusions: Ipi appears to have activity in mel met to the brain at a level consistent with reports of its activity in pts without brain met. For pts with recurrent brain met following surgery, focused RT and/or WBRT, ipi is an appropriate Rx alternative.
Support: Bristol-Myers Squibb

Poster presentations (Tue, 22 Sep, 14:00−17:00)
Melanoma and skin cancer

9307 POSTER

Long-term survival in advanced melanoma patients treated with ipilimumab at 10 mg/kg: ongoing analyses from completed Phase II trials

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Background: The monoclonal antibody ipilimumab blocks cytotoxic T lymphocyte antigen-4, thereby activating an antitumor immune response. Updated survival data from ipilimumab studies in previously treated (⩾1 prior anti-cancer therapy) and treatment-naïve patients (pts) with advanced melanoma are reported.
Methods: Follow-up of pts treated with ipilimumab at 10 mg/kg in three completed Phase II trials is ongoing (CA184008 was an open-label, single-arm study of ipilimumab at 10 mg/kg; CA184022 was a dose-ranging study of pts randomized to ipilimumab at 0.3, 3, or 10 mg/kg; CA184007 was a randomized study in which pts were treated with ipilimumab at 10 mg/kg with or without prophylactic budesonide). Ipilimumab was given every 3 weeks (Q3W) ×4 (induction); eligible pts could receive maintenance ipilimumab Q12W from Week 24.
Results: Median overall survival and 18-month survival rates after a median follow-up ranging from 10.1 to 16.3 months for pts receiving ipilimumab at 10 mg/kg are presented (Table). Across the three studies, the number of prior therapies was not associated with response to ipilimumab. Long-term survivors included pts with progressive disease (PD) [per modified World Health Organization (mWHO) criteria] at the first tumor assessment (Week 12).

Study	Median overall survival, months [95% CI]	12-month survival rate, % [95% CI]	18-month survival rate, % [95% CI]	Longest survival time, months*
CA184008 (N = 155)				
(previously treated)	10.2 [7.6, 16.3]	47.2 [39.5, 55.1]	39.4 [31.7, 47.2]	28.6
CA184022 (N = 214)				
10 mg/kg (n = 71) (previously treated)	11.4 [6.9, 16.1]	48.6 [36.8, 60.4]	34.5 [23.6, 46.2]	26.9
CA184007 (N = 115)				
Ipilimumab+placebo (n = 57)	19.3 [12.0, NR]	62.4 [49.4, 75.1]	50.9 [37.5, 64.1]	29.2
Treatment-naive (N = 32)	NR [13.9, NR]	71.4 [55.2, 87.2]	61.0 [43.4, 77.7]	28.7
Previously treated (N = 25)	14.7 [6.6, 20.5]	50.8 [31.5, 71.1]	38.1 [20.0, 57.6]	29.2
Ipilimumab+budesonide (n = 58)	17.7 [6.8, NR]	55.9 [42.7, 68.8]	47.9 [34.7, 61.2]	32.5
Treatment-naive (N = 21)	22.5 [11.7, NR]	65.9 [45.0, 85.7]	65.9 [45.0, 85.7]	29.9
Previously treated (N = 37)	8.4 [6.0, 22.6]	49.9 [33.3, 66.6]	37.9 [22.2, 54.3]	32.5

NR, not reached; *follow-up ongoing

Conclusions: Ipilimumab therapy resulted in long-term survival in a sizeable proportion of previously treated and treatment-naïve pts, including some pts characterized as PD by mWHO criteria at Week 12. Follow-up of pts from the three studies is ongoing and 24-month survival data will be presented at the meeting.