STREAM - A randomized, blinded, placebo-controlled phase II study of sorafenib treatment of chemo naive patients with metastatic uveal melanoma (MUM)

BACKGROUND
There is no approved systemic treatment for pts with MUM. The STREAM study evaluated the efficacy of the oral multikinase inhibitor sorafenib in chemonaive pts with MUM with the primary endpoint progression-free survival (PFS) in the blinded phase.

METHODS
During the initial 56d run-in period all pts received sorafenib 400 mg bid with concomitant monitoring by magnetic resonance imaging including diffusion weighted imaging (DWI-MRI) (Fig. 1). Pts with partial response (PR) on d56 according to RECIST 1.1 were further treated with open-label sorafenib and monitored. pts with progressive disease (PD) were taken off study, and pts with stable disease (SD) were randomly assigned to blinded sorafenib or placebo and were further monitored every 8 wks and unblinded in case of PD. Pts on sorafenib were taken off study and pts on placebo were offered sorafenib with further monitoring.

RESULTS
Altogether, 117 (79.6%) of 147 pts entering the run-in period were evaluable for response on d56. Two pts had PR (1.7%), 78 pts had SD (66.7%) and 38 pts had PD (26.6%), respectively (Fig. 2). Median PFS from randomization was significantly longer with sorafenib (5.5 mths) than placebo (1.9 mths; p = 0.0079) (Fig. 4). Sorafenib was readministered to 23 pts with PD under placebo (59.0%) with a median PFS of 1.9 mths (range 1.2-15.7 mths). Overall survival (OS) was not different between the sorafenib group (median 13.0 mths, range 0.9-36.2 mths) and the placebo group (median 12.2 mths, range 1.4-53.3 mths).

In the safety set of 147 pts there were 104 Treatment-Emergent Adverse Events (TEAEs) and 22 Treatment-Emergent Serious Adverse Events (TESAEs) with NCI-CTC grade 3/4 (Table 2) with highest incidences for rash (n=20), hypertension (n=14), hand-foot-syndrome (n=10), diarrhea (n=8) and nausea/vomiting (n=8), respectively. Intermittent dose reduction of sorafenib to 200 mg bid or discontinuation were performed, respectively. No pt died from toxicity.

The evaluation of the apparent diffusion coefficient (ADC) ratio derived from DWI-MRI in 47 pts of the run-in period showed a significant difference between pts with SD and pts with PD (p = 0.05) (Fig. 6).

CONCLUSIONS
• The primary endpoint of STREAM was reached.
• Sorafenib is clinically active and tolerable in first-line treatment of pts with MUM with an increase of median PFS from 1.9 mths for placebo to 5.5 mths for sorafenib (p = 0.0079).
• The median OS of 14.8 mths compares favorably with previous findings in pts with MUM.
• Besides morphological MRI features, ADC ratio may be used as an additional functional response criterion.

REFERENCES

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