A Phase Ib/II, open-label, multicenter study of INC280 (capmatinib) alone and in combination with buparlisib (BKM120) in adult patients with recurrent glioblastoma

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PURPOSE
To estimate the maximum tolerated dose (MTD) and/or identify the recommended Phase II dose (RP2D) for combined INC280 and buparlisib in patients with recurrent glioblastoma with homozygous phosphatase and tensin homolog (PTEN) deletion, mutation or protein loss.

METHODS
This multicenter, open-label, Phase Ib/II study included adult patients with glioblastoma with mesenchymal-epithelial transcription factor (c-Met) amplification. In Phase Ib, patients received INC280 as capsules or tablets in combination with buparlisib. In Phase II, patients received INC280 only. Response was assessed centrally using Response Assessment in Neuro-Oncology response criteria for high-grade gliomas. All adverse events (AEs) were recorded and graded.

RESULTS
33 patients entered Phase Ib, 32 with altered PTEN. RP2D was not declared due to potential drug-drug interactions, which may have resulted in lack of efficacy; thus, Phase II, including 10 patients, was continued with INC280 monotherapy only. Best response was stable disease in 30% of patients. In the selected patient population, enrollment was halted due to limited activity with INC280 monotherapy. In Phase Ib, the most common treatment-related AEs were fatigue (36.4%), nausea (30.3%) and increased alanine aminotransferase (30.3%). MTD was identified at INC280 Tab 300 mg twice daily + buparlisib 80 mg once daily. In Phase II, the most common AEs were headache (40.0%), constipation (30.0%), fatigue (30.0%) and increased lipase (30.0%).

CONCLUSION
The combination of INC280/buparlisib resulted in no clear activity in patients with recurrent PTEN-deficient glioblastoma. More stringent molecular selection

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strategies might produce better outcomes.

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