Background:
Furmonertinib (AST2818) is a selective third-generation epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI), which can irreversibly inhibit both EGFR sensitizing and T790M resistant mutations. However, like other EGFR-TKIs, progression is still unavoidable when treated with furmonertinib.

Methods: In a multi-center, single-arm phase IIb study (NCT03452592), non-small cell lung cancer (NSCLC) patients with EGFR T790M mutation received furmonertinib 80mg/d treatment until disease progression, death or treatment cessations for other reasons. This is a post-hoc analysis of the progression pattern and post-progression treatment.**Results:**A total of 220 patients were enrolled in this study. At baseline, 105 (48%) patients had central nervous system (CNS) metastases, 84 (38%) were EGFR L858R mutated and 9 (4%) were ECOG performance status 2. At data cut-off (December 31, 2020), 179 out of 220 (81%) patients had progressed assessed by investigators (patients who died before assessed as progression were excluded). The most frequent progression site was lung (n = 106，48%), followed by CNS (n = 33, 15%), lymph node (n = 22, 10%), liver (n = 20, 9%) and bone (n = 16, 7%). CNS progression rate were 3%, 8%, 13% and 15% at 3, 6, 12 and 18 months, respectively. After progression, 52% (93/179) patients continued furmonertinib monotherapy based on the judgement of continuous benefit by investigators which was permitted in the protocol. The median post-progression treatment time of furmonertinib was 3.02 months (range 0.03-18.27). Overall, 48% (86/179) patients discontinued furmonertinib and later-line treatments were decided by investigators. The post-progression survival (PPS) was 17.3 months in the furmonertinib-continued group and 12.4 months in the furmonertinib-not-continued group (HR 0.57 [95%CI 0.40-0.80], p = 0.0048).**Conclusions:**Although about half patients had CNS metastases at baseline, CNS progression rate was relatively low in this study. Post-progression continuous treatment of furmonertinib monotherapy might still bring survival benefit to certain NSCLC patients with EGFR T790M mutation which need further exploration. Clinical trial information: NCT03452592