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* The researcher claims no conflicts of interest.

Background

- Bevacizumab (BVZ) is known to be effective to control radiation necrosis (RN) following stereotactic radiosurgery (SRS) for brain metastases (BMs), although treatment failure may occur.
- Here, we investigated the incidence and pattern of local failure after BVZ therapy for RN and its underlying biological mechanism.

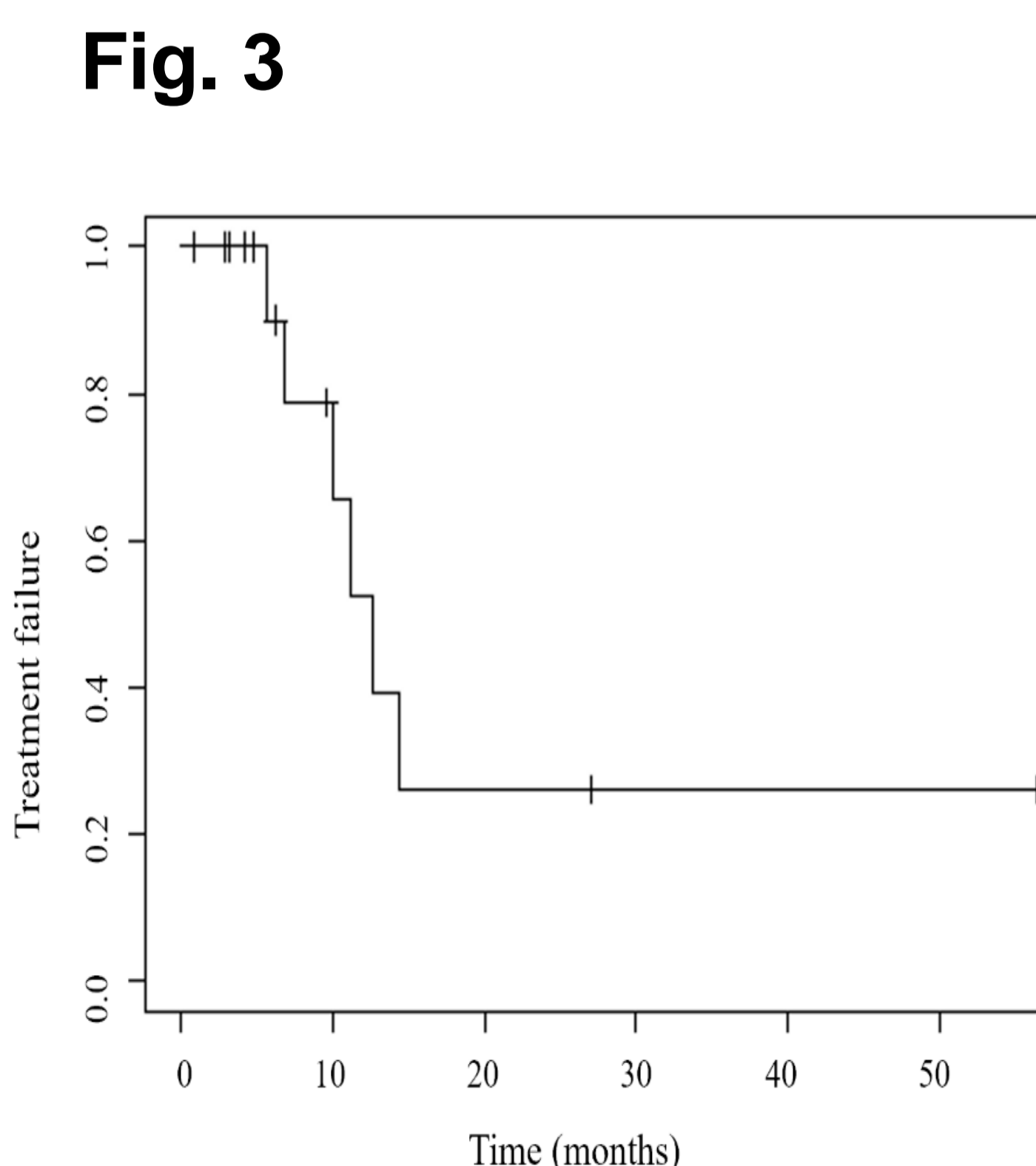
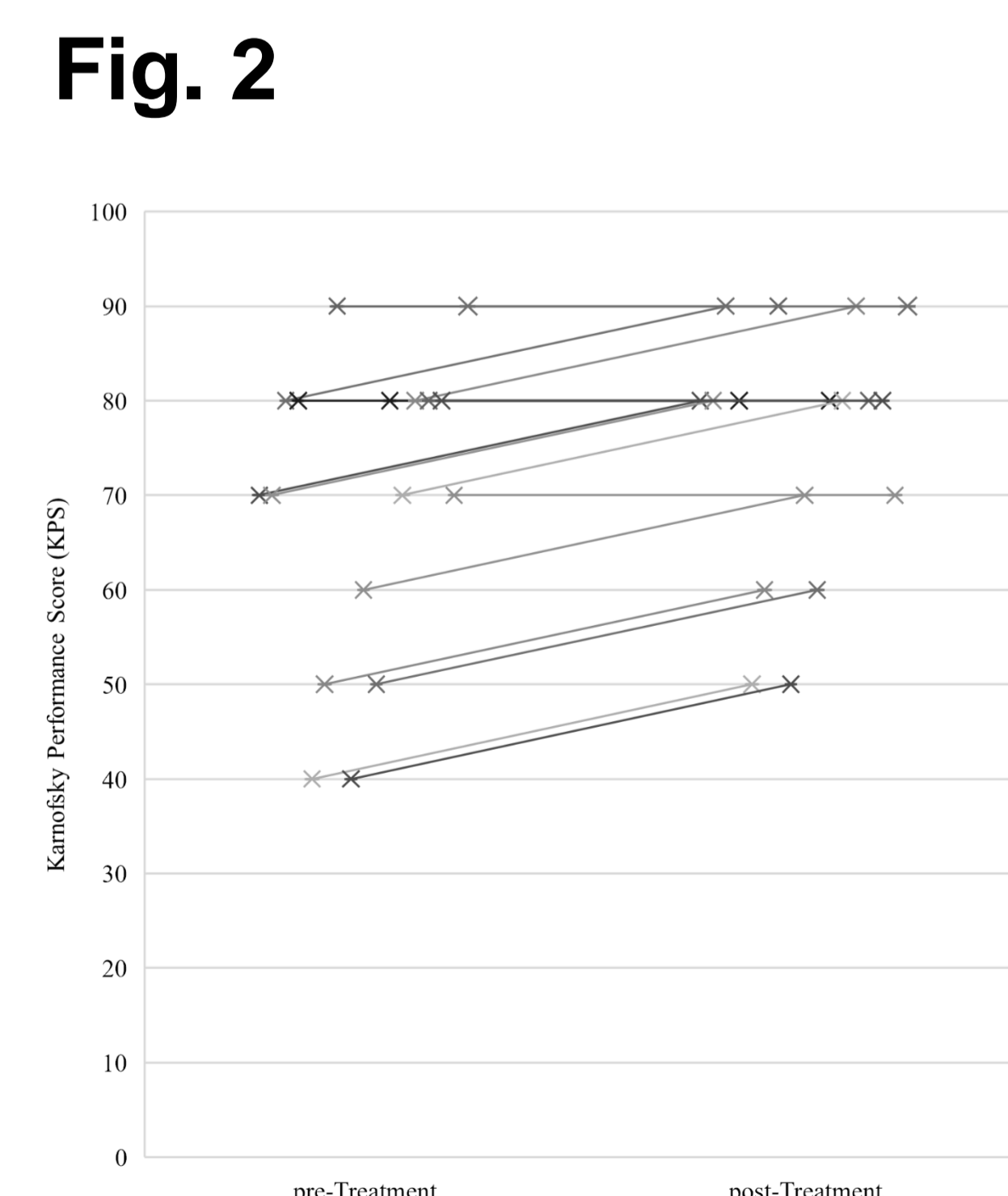
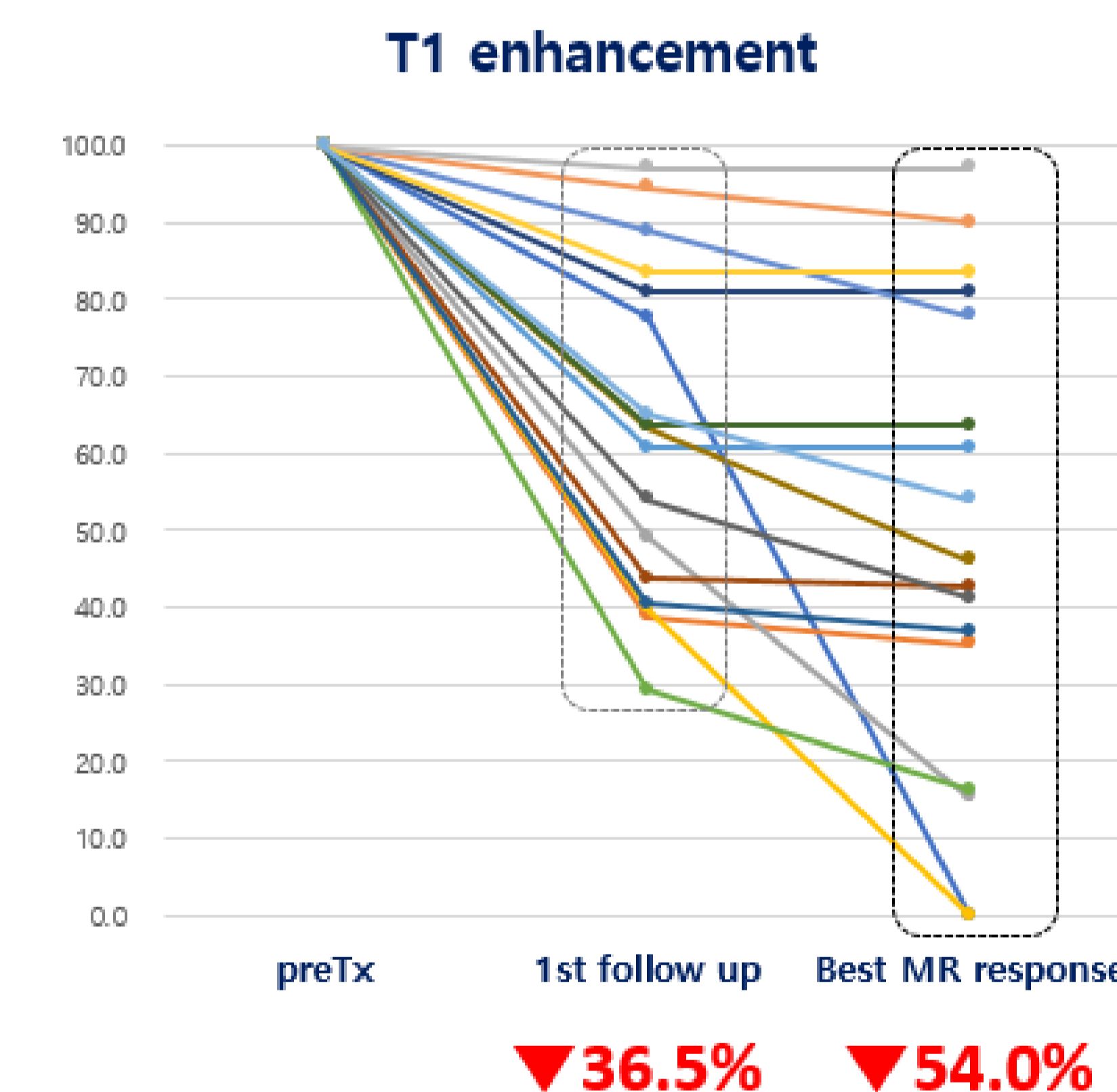
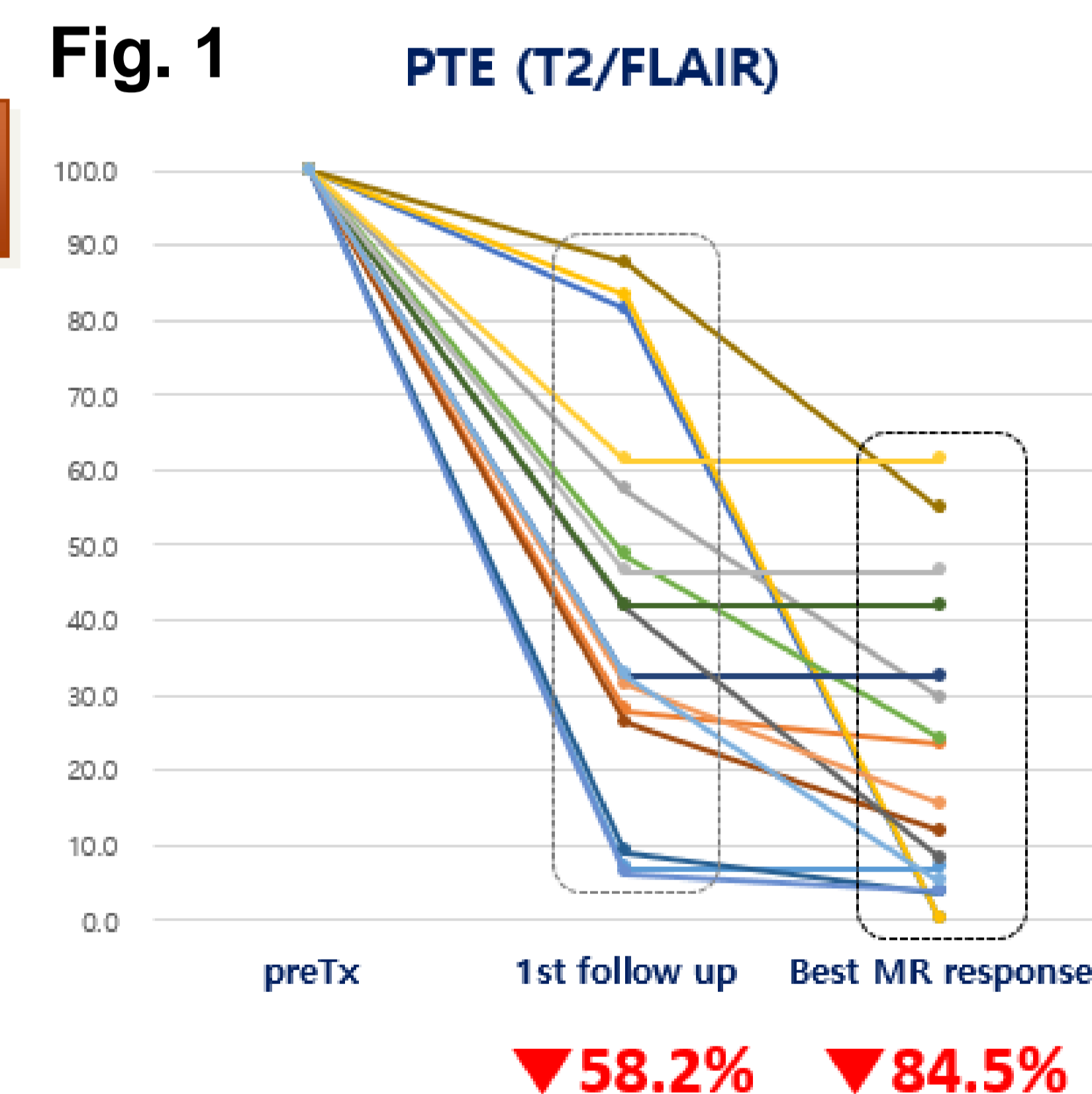
Materials and Methods

- We conducted a retrospective analysis on 17 patients who had been treated with BVZ for RN following SRS for BMs between 2016 and 2021.
- In each patient, the diagnosis of RN was made based on the conventional and advanced MR with or without positron emission tomography.
- Median 5 cycles (range, 2-10 cycles) of BVZ (5 mg/kg) were administered at 2-week intervals.
- Treatment response was assessed by volumetric changes of the lesions on MR and patients' neurological status.

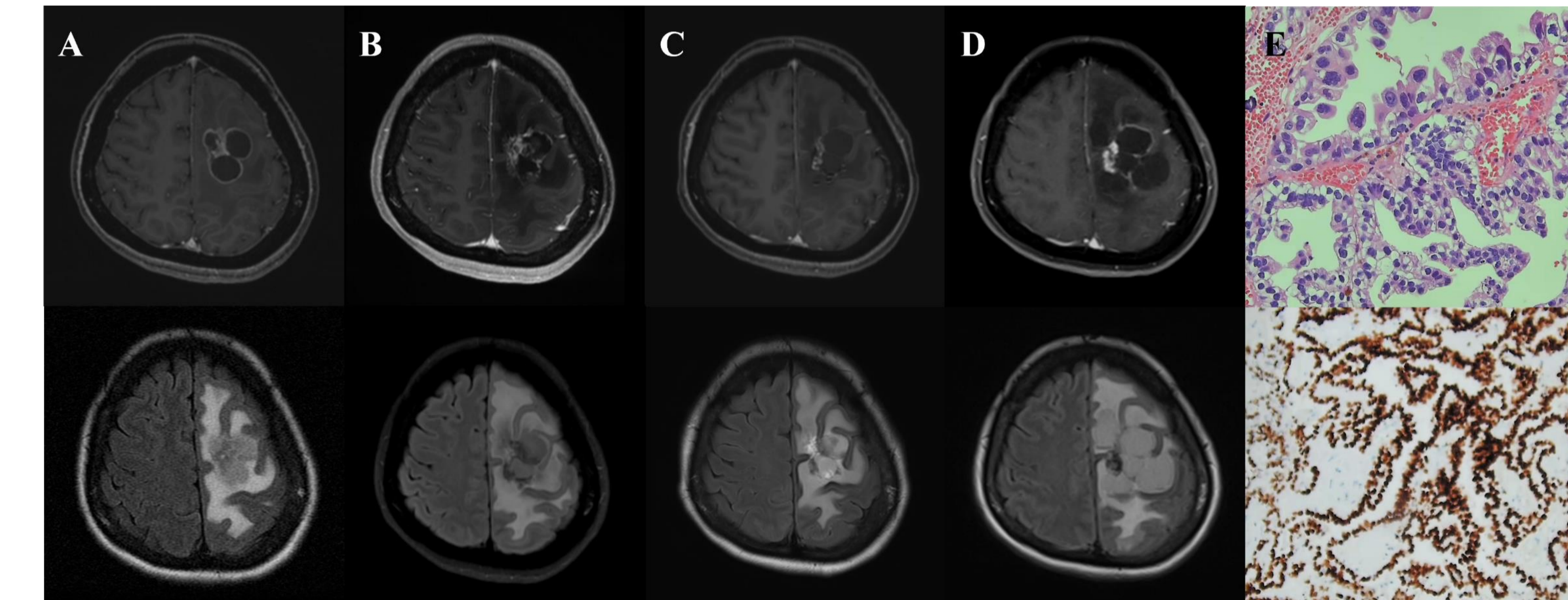
Results

- Treatment response was typically brisk and substantial.
- Best MR response was seen at median 13 weeks (range, 3-56 weeks) after the start of BVZ with a median volume decrease of 84.5% (range, 38.7-100%) of perilesional brain edema on T2WI and of 54% (range, 2.9-100%) of contrast enhancing lesions on T1WI (Fig. 1).
- Patients' neurological status improved in 16 patients (94.1%) and was stationary in 1 (5.9%) (Fig. 2).

- During the median follow-up of 12 months (range, 2-60 months), delayed local failure was observed in 6 patients (35.3%) at median 10 months (range, 6-14 months) after starting BVZ treatment, where viable tumor recurrence was demonstrated in all of them (Fig. 3).
- No reconstitution of RN without viable tumor was observed during the follow-up.



Illustrative case for tumor recurrence after bevacizumab treatment



- A) The metastatic lesion located adjacent to the motor cortex before SRS treatment.
- B) Two years after SRS treatment, radiation necrosis was observed.
- C) Five months after bevacizumab treatment, peritumoral edema was decreased.
- D) 14 months after bevacizumab treatment, non-enhancing tumor lesion increased.
- E) Histopathological examination revealed a metastatic adenocarcinoma, with hematoxylin-eosin stain and thyroid transcription factor-1 (TTF-1) stain.

Conclusion

- Although BVZ was highly effective to control RN following SRS for BMs, delayed local failure frequently occurs owing to viable tumor recurrence.
- This may imply that much predominant vascular stabilizing effect of BVZ over anti-tumor effect transiently obscures the presence of potential viable tumor cells but does not prevent them from eventual recurrence.