



Cabozantinib therapy in patients with previously treated well differentiated grade 3 neuroendocrine tumors (G3 NETs)

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BACKGROUND

- Well differentiated G3 NETs (G3 NETs) behave very differently than poorly differentiated neuroendocrine carcinomas (NECs)
- The optimal therapy is uncertain
- Chemotherapy such as CAPTEM and FOLFOX has activity
- ¹⁷⁷Lu DOTATATE PRRT is active in untreated G3 NETs (NETTER-2)
- Cabozantinib has activity in previously treated G3 NETs (CABINET) but the number of G3 NET patients was small
- This study aimed to provide further data on cabozantinib in G3 NETs

STUDY AIM

- To evaluate the efficacy and safety of single-agent cabozantinib in a cohort of heavily pretreated patients with progressive G3 NETs

METHODS

- Patients were identified using the Mayo Clinic Electronic Medical Record
- Inclusion criteria:
 - Well differentiated G3 NETs
 - Progression on previous chemotherapy regimens
 - Prior SSA and PRRT allowed
 - Patients actively followed at Mayo Clinic Rochester with all imaging studies available
- RECIST 1.1 criteria were applied retrospectively

RESULTS

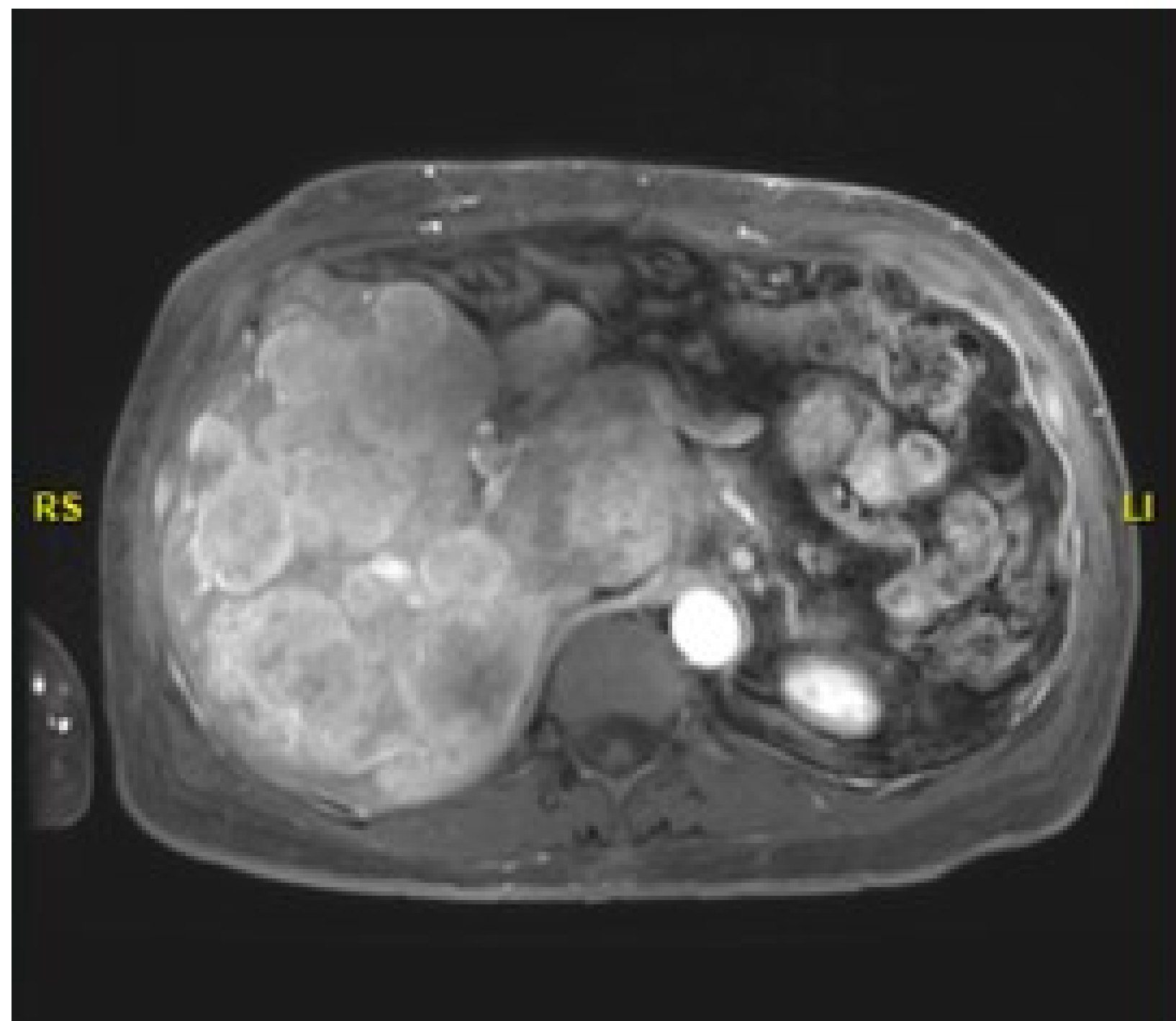
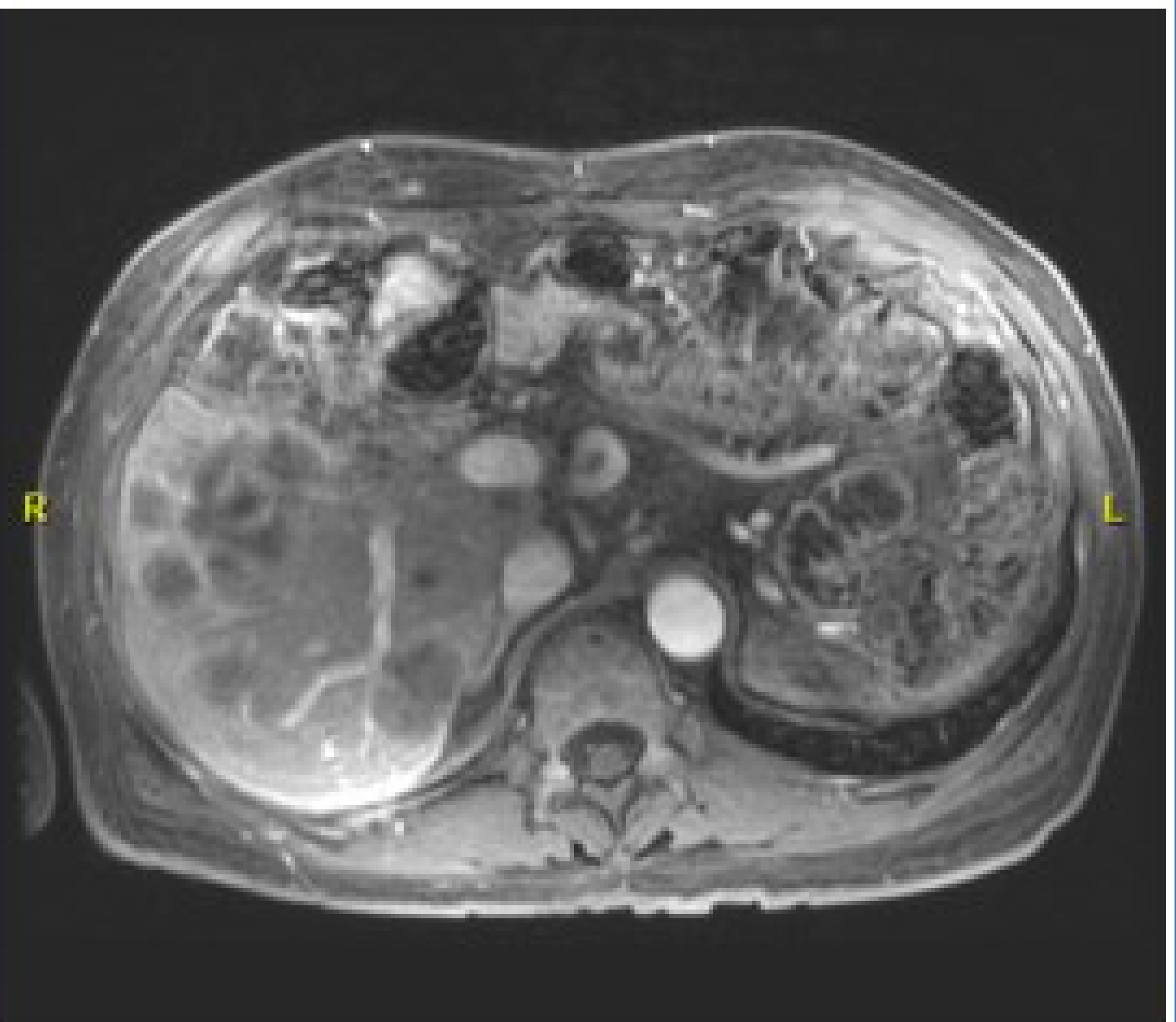
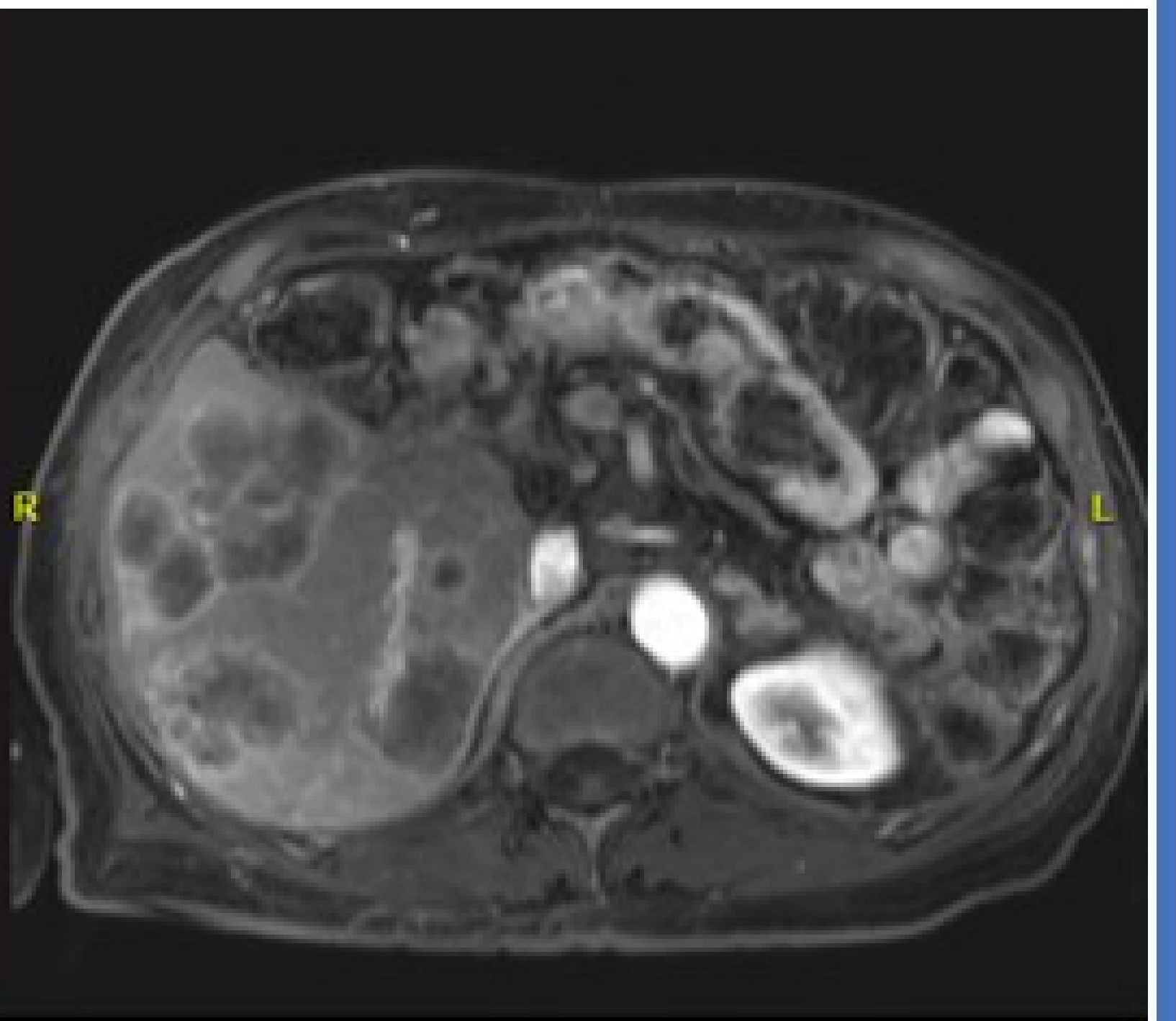
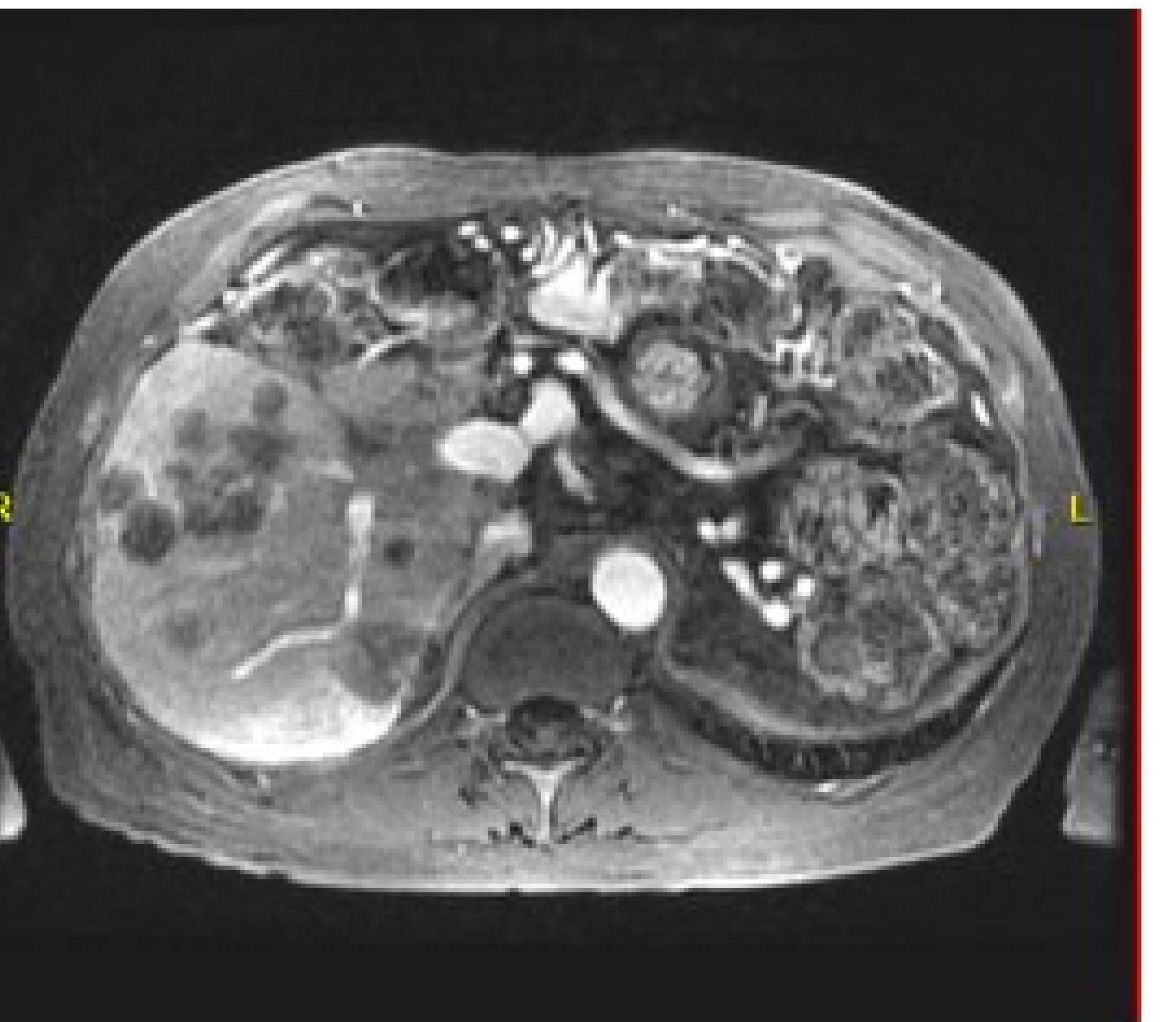
Patient/Tumor Factors	Value
Number of patients	11
Male/Female	7/4
Pancreatic primary	7
Median initial Ki67	15.5%
Range	23% - 55%
Median Highest Ki67	51.4%
Range	23-77%

Prior Therapy	Number
SSA	9
PRRT	6
Re-PRRT	4
CAPTEM	11
Other chemo	9
Immunotherapy	4
Everolimus	4

OUTCOMES

- Objective response rate: 45% (5 of 11 patients)
- Nine patients (82%) had progression on therapy
- Two patients had to discontinue cabozantinib for toxicity
- Dose reduction for toxicity was needed in 3 patients
- The median progression-free survival on cabozantinib was 2.8 months (range: 2.2 to 14 months)
- The longest response duration was 14 months
- The overall survival from initiation of cabozantinib was 24.5 months

REPRESENTATIVE IMAGING STUDIES

Pre cabozantinib	First restaging on cabozantinib	After a brief hold of cabozantinib for toxicity	Back on cabozantinib
			
Day 0	After 2 months	3-week cabo hold	6 weeks after restarting 6 months after starting cabo

CONCLUSION

- In this heavily pretreated cohort of G3 NET patients, cabozantinib has clinical activity
- Although the overall PFS was short, some patients had a durable response
- Some patients had profound radiographical response but usually not durable
- The CABINET trial will provide additional information on efficacy in G3 NETs once results of subgroup analyses are presented

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