Case #2

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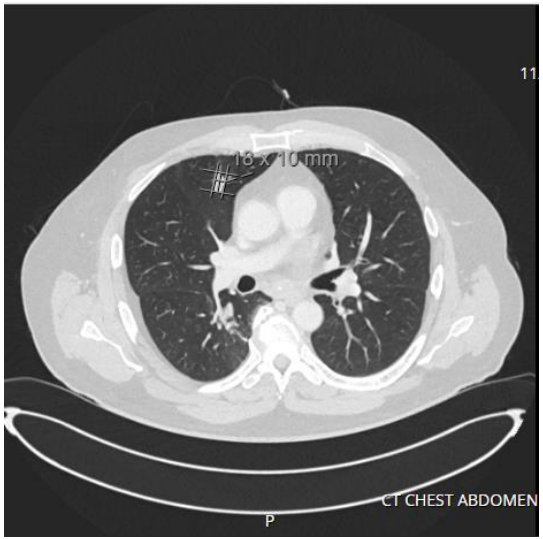
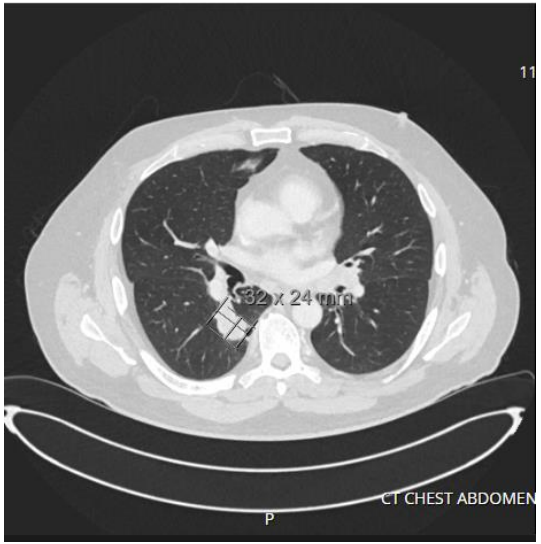
Case #2

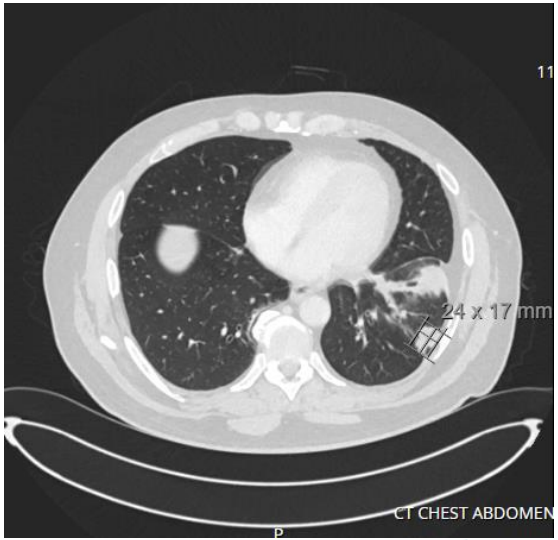
- JA is a 62 y/o gentleman with a history of metastatic recurrent rectal cancer from NE
- ECOG PS = 0
- PMhx: HTN attributed to prior bevacizumab-based therapy
- Fhx: Non-contributory
- SHx: He is a farmer and is very active
- Prior treatment:
    - Neoadjuvant chemoXRT/TME/adjuvant FOLFOX chemotherapy (2 of 14 LN's +) in 2014
    - Recurrent bilateral disease to the lungs noted: 2017. Resumed FOLFOX+ bevacizumab with intermittent maintenance chemotherapy until 2020 with PD and associated development of RPLN
    - 2022: Started FOLFIRI + bevacizumab with PD
    - 2023: TAS-102 + bevacizumab with PD

Case #2: Continued

- He presents to you for treatment recommendations. Unfortunately, there are no openings at this time for a clinical trial. He has progressive bilateral lung mets, mediastinal and hilar LN.
- Incidentally it is noted he has been noncompliant with his meds and his bp is 160/82.

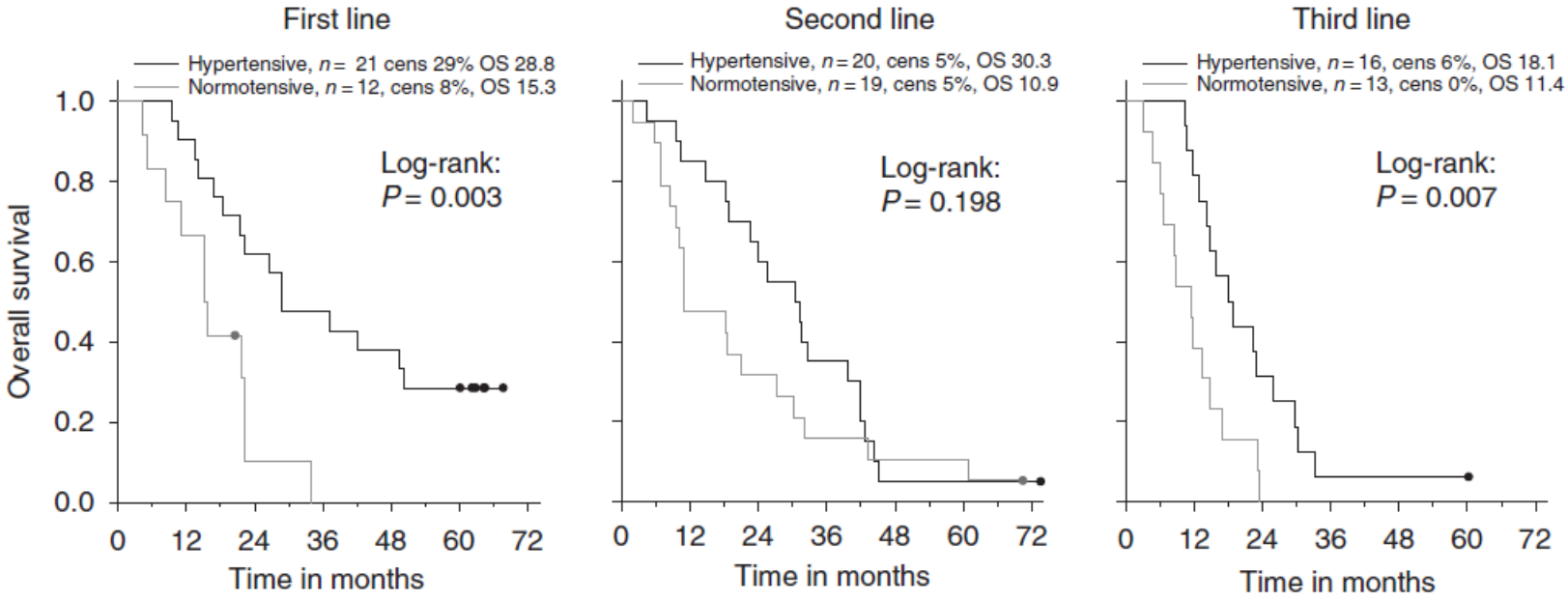






Case #2: Prognosis of HTN/anti-VEGF Therapy

- Class effect of anti-VEGF therapy includes HTN
- Prior data suggested possible benefit of HTN and prognosis



Österlund P et al. *Br J Cancer.* 2011;104(4):599-604.

Case #2: Risk Factors for HTN/anti-VEGF Therapy

Univariate and multivariate analyses of risk factors for grade ≥ 3 HTN

Duration of total anti-VEGF treatment				
≥ 700 days/ < 700 days	3.09 (1.26–7.56)	0.01*	3.61 (1.21–10.79)	0.02*
Baseline pre-existing hypertension				
Present/absent	5.03 (1.83–13.83)	0.002**	4.21 (1.41–12.58)	0.01*
(B)				
Age (years)				
≥ 65/ < 65	2.00 (0.84–4.78)	0.12	0.76 (0.25–2.38)	0.65
Hypoalbuminemia				
Present/absent	2.35 (0.79–6.99)	0.12	3.36 (0.95–11.89)	0.06
Duration of total anti-VEGF treatment				
≥ 700 days/ < 700 days	3.09 (1.26–7.56)	0.01*	4.59 (1.41–14.92)	0.01*
Pre-existing hypertension before anti-VEGF treatment				
Present/absent	8.77 (3.33–23.11)	< 0.0001**	8.74 (2.86–26.72)	0.0001**

Saito Y et al. *Support Care Cancer.* 2022;30(12):10203-10211.

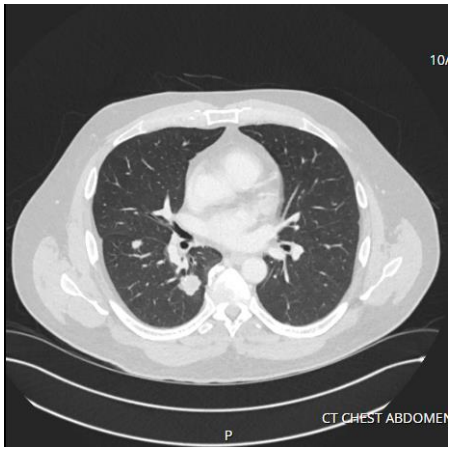
Case #2: SAEs of Existing Trials

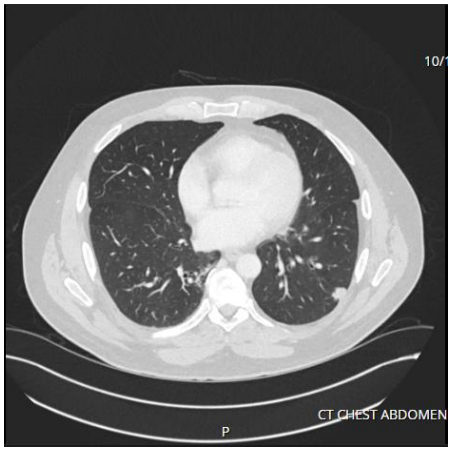
Trial	FRESCO-2		FRESCO		SUNLIGHT		CORRECT	
	Fruquintinib (N=456)	Placebo (N=230)	Fruquintinib (N=278)	Placebo (N=138)	TAS-102 +Bev (N=246)	TAS-102 (N=246)	Regorafenib (N=505)	Placebo (N=255)
Any AE ≥G3 (Safety pop.)	62.7%	50.4%	61.1%	19.7%	72.4%	69.5%	54%	14%
AE Led to dose interruption	46.7%	26.5%	35.3%	10.2%	69.5%	53.3%	61%	22%
AE Led to dose reduction	24.1%	3.9%	24.1%	4.4%	16.3%	12.2%	38%	3%
AE Led to treatment discon.	20.4%	21.3%	15.1%	5.8%	12.6%	12.6%	17%	12%
Hypertension ≥G3	13.6%	0.9%	21.2%	2.2%	5.7%	1.2%	7%	1%
Hand-Foot Syndrome, ≥G3	6.4%	0.0%	10.8%	0.0%	-	-	17%	<1%
ALT increased, ≥G3	3.1%	0.4%	0.7%	1.5%	-	-	-	-
AST increased, ≥G3	2.2%	1.3%	0.4%	0.7%	-	-	-	-
SAE	37.5%	38.3%	15.5%	5.8%	98%	98%	44%	40%

Dasari A et al. *Lancet.* 2023;402(101395):41-53. Li J et al. *JAMA.* 2018;319(24):2486-2496. Prager GW et al. *N Engl J Med.* 2023;388(18):1657-1667. Grothey A et al. *Lancet.* 2013;381(9863):303-312.

Case #2: Continued

- Retrospective analysis (N = 187) of pts on bevacizumab
- Bp was measured at home twice daily and were started on amlodipine if needed
- Two groups: Group A (anti-VEGF induced) and Group B (pre-existing)
- Findings: HTN was controlled ≤7 days under amlodipine in 23/26 (88.5%, 95%CI: 76.2–100) patients in group A, and 8/10 (80%, 95%CI: 55.2–100) patients in group B.
- We re-initiated amlodipine 10 mg daily and his bp returned back to normal 124/78
- Fruquintinib was initiated:





Mir O et al. *Invest New Drugs.* 2012;30(2):702-707.