Case #3: A Patient With pMMR mCRC Progressing After Frontline Triplet Therapy

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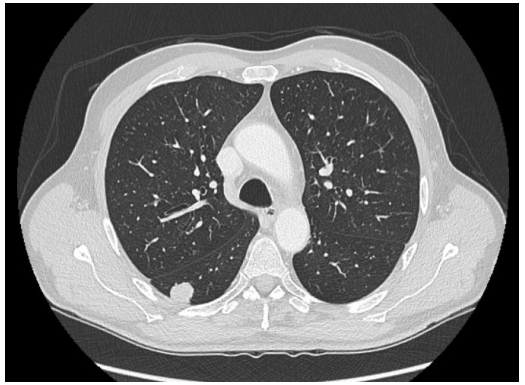
Personal and Disease History

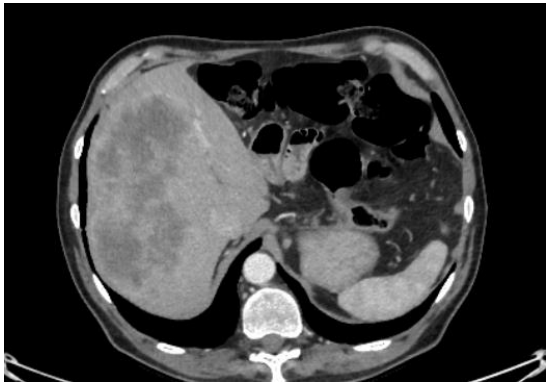
- Male, 71 yo at diagnosis
- No relevant family history
- No concomitant comorbidities

- June 2019: weight loss, SOF+

→ Sigma adenocarcinoma
→ Lung and liver synchronous mets

- pMMR
- KRAS mutated G12V
- NRAS mutated Q61K
- BRAF wild-type





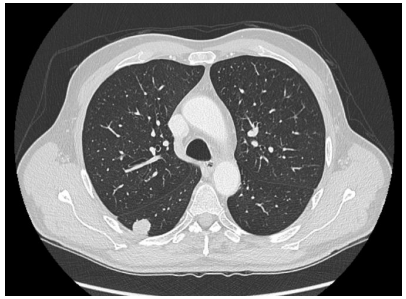
Which First Line Would You Have Proposed?

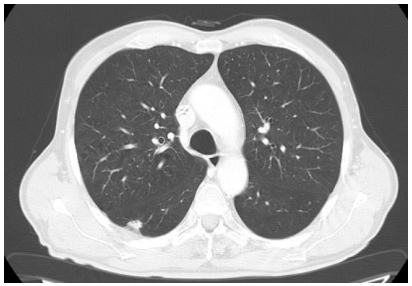
First-Line Treatment

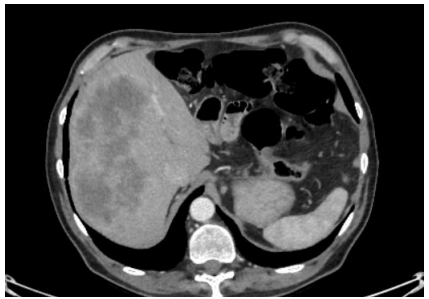
- Left located primary
- Lung and liver mets
- pMMR, RAS mutated

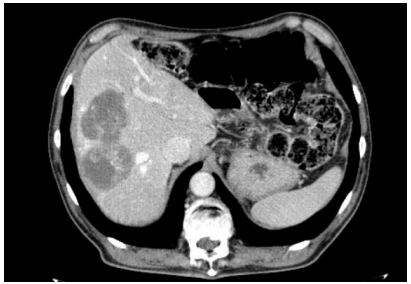
FOLFOXIRI + bev

Jun 2019 NOV 2019





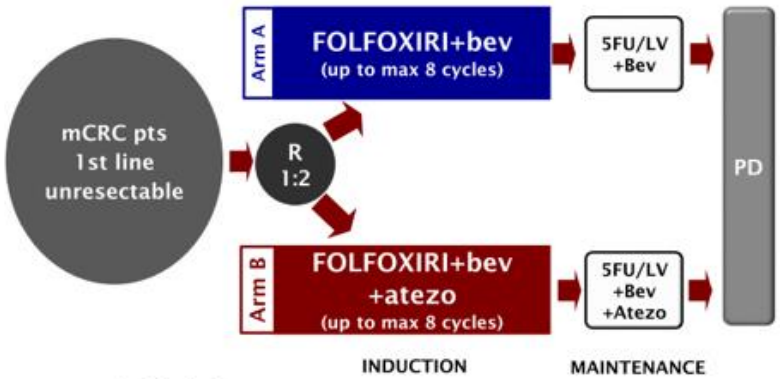




Jul 2019 enrollment in AtezoTRIBE trial randomized to experimental arm: Atezolizumab + bevacizumab + FOLFOXIRI

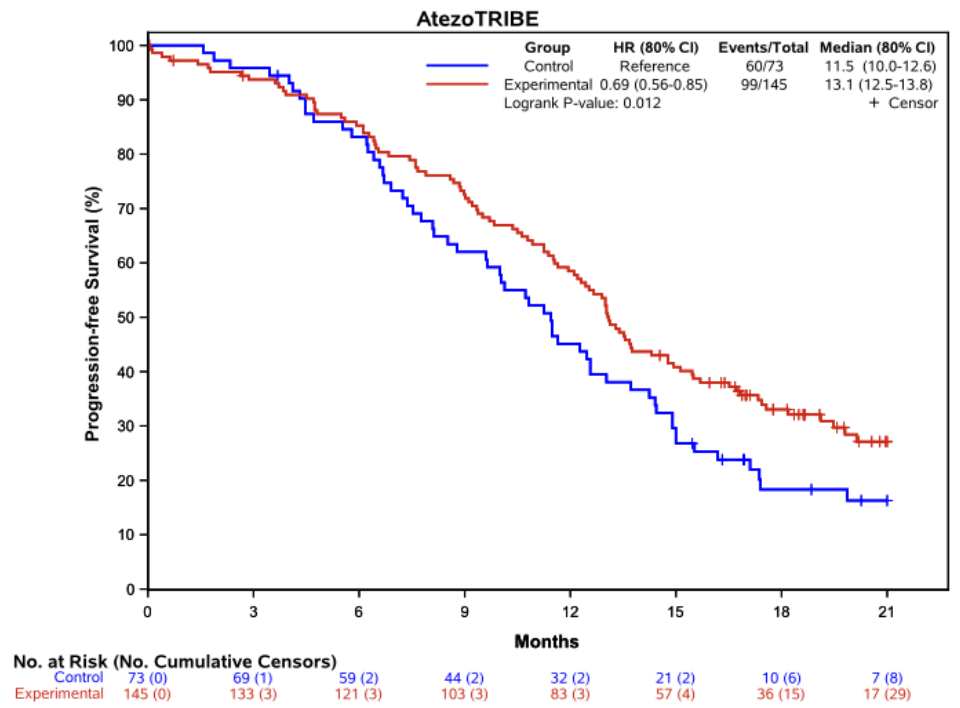
- 17/07/2019-31/10/2019: ATEZO-BEVA-FOLFOXIRI 8 cycles **partial response**
- 19/11/2019 - 22/06/20: 5FU-ATEZO-BEVA maintenance

AtezoTRIBE Results



Stratification factors:

- Center
- PS 0 vs 1-2;
- primary tumor location (right vs left or rectum);
- Previous adjuvant CT



Antoniotti C et al. *Lancet Oncol*. 2022;23(7):876-887.

Subsequent Therapies

- July 2020: slight liver progression with CEA and CA19.9 increase

→ 11 months PFS (7 after maintenance initiation)

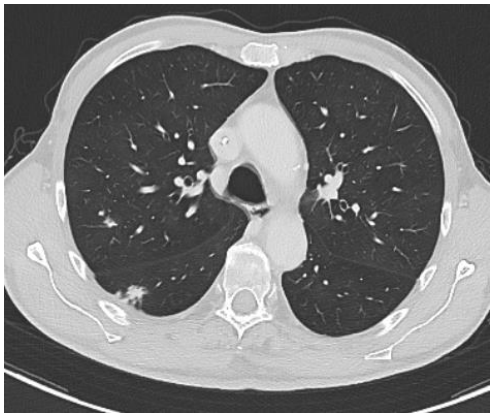
What to do now?

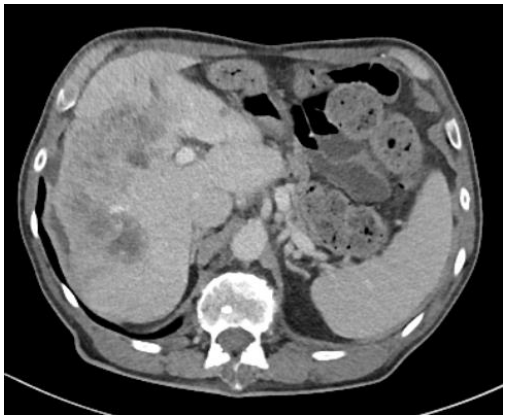
We decided to reintroduce induction regime (good and long-lasting response, no residual neurotoxicity)

- 06/07/2020- 08/09/2020: reinduction with ATEZO-BEVA-FOLFOXIRI 5 cycles - - 31/10/2020: progressive disease

Subsequent Therapies

Third Line:
- 09/11/2020 - 12/02/2021: Regorafenib ReDOS (2 cycles 3 capules/day, 1 cycle 2 capsules/day)
- stable disease at first CT scan
- 13/03/2021: liver progression
PFS: 4 months





Is this patient lost?

→ Enrollment in the FRESCO-2 Trial

FRESCO-2 Trial Enrollment

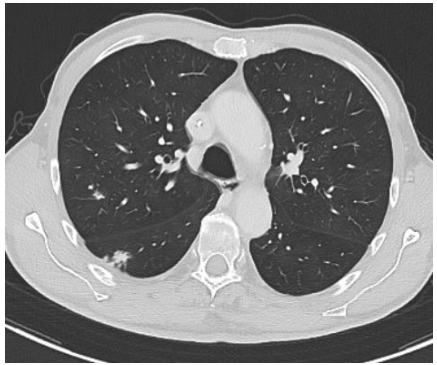
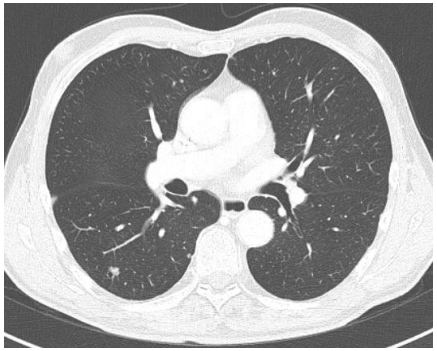
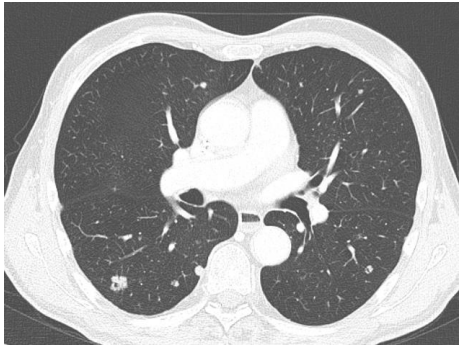
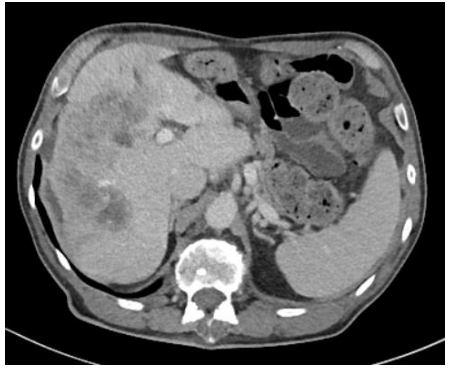
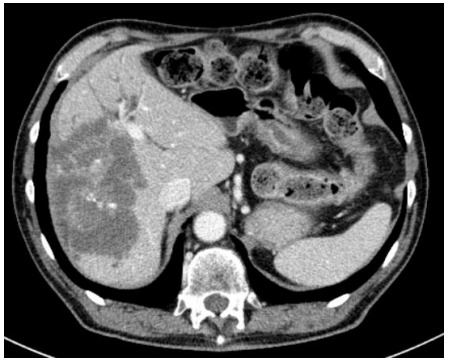
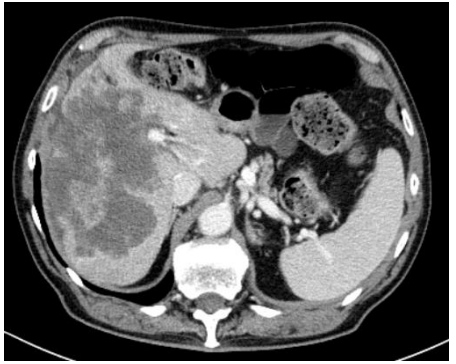
- Fourth Line:
- - 06/04/2021- 17/03/2022: Fruquintinib/Placebo

- Response:
- Stable disease per RECIST criteria
- BUT clinical benefit:
- Weight increase
- CEA and CA 19.9 decrease

- Toxicity: H-F sdr g2, asthenia g1, hypertension g3 (resolved with therapy introduction)

- PFS: 11 months

Radiological Evaluation During Fruquintinib Treatment

March 2021	November 2021	March 2022
		
		

Conclusion

- 3 years OS in RAS mut, high burden mCRC
- **Take-home messages:**
  - Choice of first line is crucial, especially in high metastatic disease burden
  - Lack of benefit from regorafenib does not preclude benefit from fruquintinib
  - Sequencing of treatment is of paramount importance to prolong survival and improve QoL