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A decade of treatment of the primary metastatic colorectal cancer

DISCLOSURE OF INTEREST

- ⦿ No potential conflicts of interest

Patient's profile

73-year-old gentleman. A doctor and pharmacologist, married with kids and grandchildren, smokes for 50 years. Presented with symptoms of intestinal obstruction. ECOG 3-4. Underwent an emergency left hemicolectomy with hepatic S5 resection in 11/21/07:

- ⦿ **Histology and IHC:** adenocarcinoma K/NRAS-, BRAF-wt 09/12
- ⦿ **Initial stadium:** pT3 pN0 pM1a, Stage IV, G2, R0 12/19/07
- ⦿ **Initial tumor markers:** CEA1.7 U/ml, CA-19.9 0.6 U/ml
- ⦿ **Family history of CRC:** none
- ⦿ **Comorbidities:** Z95.0 Presence of cardiac pacemaker E11.42 Type 2 diabetes mellitus with diabetic polyneuropathy; B18.2 Chronic viral hepatitis C; D29.1: Benign neoplasm of prostate; I10 Essential (primary) hypertension; J44.9 Chronic obstructive pulmonary disease

Medical history through the years

1st disease progression in 04/10:
new mts in liver, CEA 7.4 Um/l; liver resection (r0) and 3XELOX/5XELIRI

Allergic reaction to Oxaliplatin

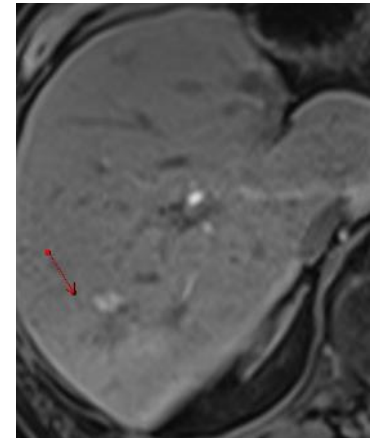
3rd disease progression in 04/14: liver mts growth; Stereotactic radiotherapy (S1-2 lungs, S6(8) liver), 6XELIRI, Capecitabine maintenance therapy

AV-blockade; pacemaker insertion



8 courses of XELOX + 9 Cetuximab injections since 11/07

2nd disease progression in 08/12: new mts in liver, CEA 4.7 Um/l; Radiofrequency thermoablation of hepatic S8+ Capecitabine, Cetuximab



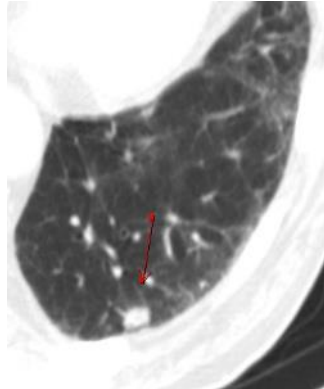
Clinical trials of cetuximab in combination with oxaliplatin-based chemotherapy

Clinical trial	Type of study	KRAS analysis	Treatment	Response rate (%)	R0 resection rate (%)	PFS (mo)	OS (mo)
Arnold et al (1) 2008	Phase Ib/II	No	Cetuximab-FUFOX	57%	4%	8.1	28.2
Tabernero et al (2) 2007	Phase II	No	Cetuximab-FOLFOX4	72%	21%	12.3	30
OPUS, Bokemeyer et al (3) 2009	Phase II	Yes	Cetuximab-FOLFOX4 vs FOLFOX4	57% vs 34% (OR = 2.551, P = 0.0027)	12% vs 3% (P = 0.0242)	8.3 vs 7.2 (HR = 0.567, P = 0.0064)	22.8 vs 18.5 (HR = 0.855, P = 0.39)
COIN, Maughan et al (4) 2011	Phase III	Yes	Cetuximab-mFOLFOX6/XELOX vs mFOLFOX6/XELOX	64% vs 57% (OR = 1.35, P = 0.049)	15% vs 13% (P = 0.74)	8.6 vs 8.6 (HR = 0.96, P = 0.60)	17 vs 17.9 (HR = 1.04, P = 0.67)
NORDIC-VII, Tveit et al (5) 2017	Phase III	Yes	FLOX vs FLOX + Cetuximab vs cont Cetuximab + inter FLOX	61% vs 60% vs 50% (OR = 0.96, P = 0.89) for RAS/BRAF-wt (1)		8.3 vs 8.2 vs 7.4 (HR = 0.95; 1.27, P = 0.67; 0.05)	20.4 vs 19.7 vs 20.3 (HR = 0.92; 1.09, P = 0.43; 0.48)

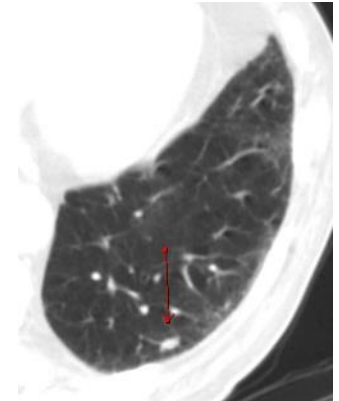
- 1) Arnold D, Höhler T, Dittrich C, Lordick F, Seufferlein T, Riemann J, Wöll E, Herrmann T, Zobel A, Schmoll HJ. Cetuximab in combination with weekly 5-fluorouracil/folinic acid and oxaliplatin (FUFOX) in untreated patients with advanced colorectal cancer: a phase Ib/II study of the AIO GI Group. *Ann Oncol.* 2008;19:1442–1449
- 2) Tabernero J, Van Cutsem E, Díaz-Rubio E, Cervantes A, Humblet Y, André T, Van Laethem JL, Soulié P, Casado E, Verslype C, et al. Phase II trial of cetuximab in combination with fluorouracil, leucovorin, and oxaliplatin in the first-line treatment of metastatic colorectal cancer. *J Clin Oncol.* 2007;25:5225–5232
- 3) Bokemeyer C, Bondarenko I, Makhson A, Hartmann JT, Aparicio J, de Braud F, Donea S, Ludwig H, Schuch G, Stroh C, et al. Fluorouracil, leucovorin, and oxaliplatin with and without cetuximab in the first-line treatment of metastatic colorectal cancer. *J Clin Oncol.* 2009;27:663–671.
- 4) Maughan TS, Adams RA, Smith CG, Meade AM, Seymour MT, Wilson RH, Idziaszczyk S, Harris R, Fisher D, Kenny SL, et al. Addition of cetuximab to oxaliplatin-based first-line combination chemotherapy for treatment of advanced colorectal cancer: results of the randomised phase 3 MRC COIN trial. *Lancet.* 2011;377:2103–2114.
- 5) Cetuximab in treatment of metastatic colorectal cancer: final survival analyses and extended RAS data from the NORDIC-VII study *British Journal of Cancer* (2017) 116, 1271–1278

Medical history through the years

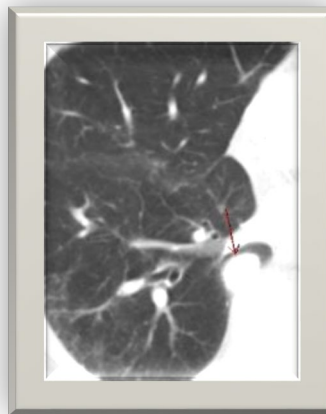
5th disease progression in 04/16: new lungs mts; FOLFIRI (3 SD) + Cetuximab (3PR); Due to toxicity: Irinotecan + Panitumumab 4



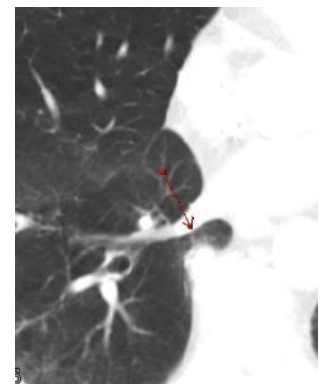
7th disease progression in 11/18: lungs mts; FOLFIRI reinduction + Panitumumab maintenance



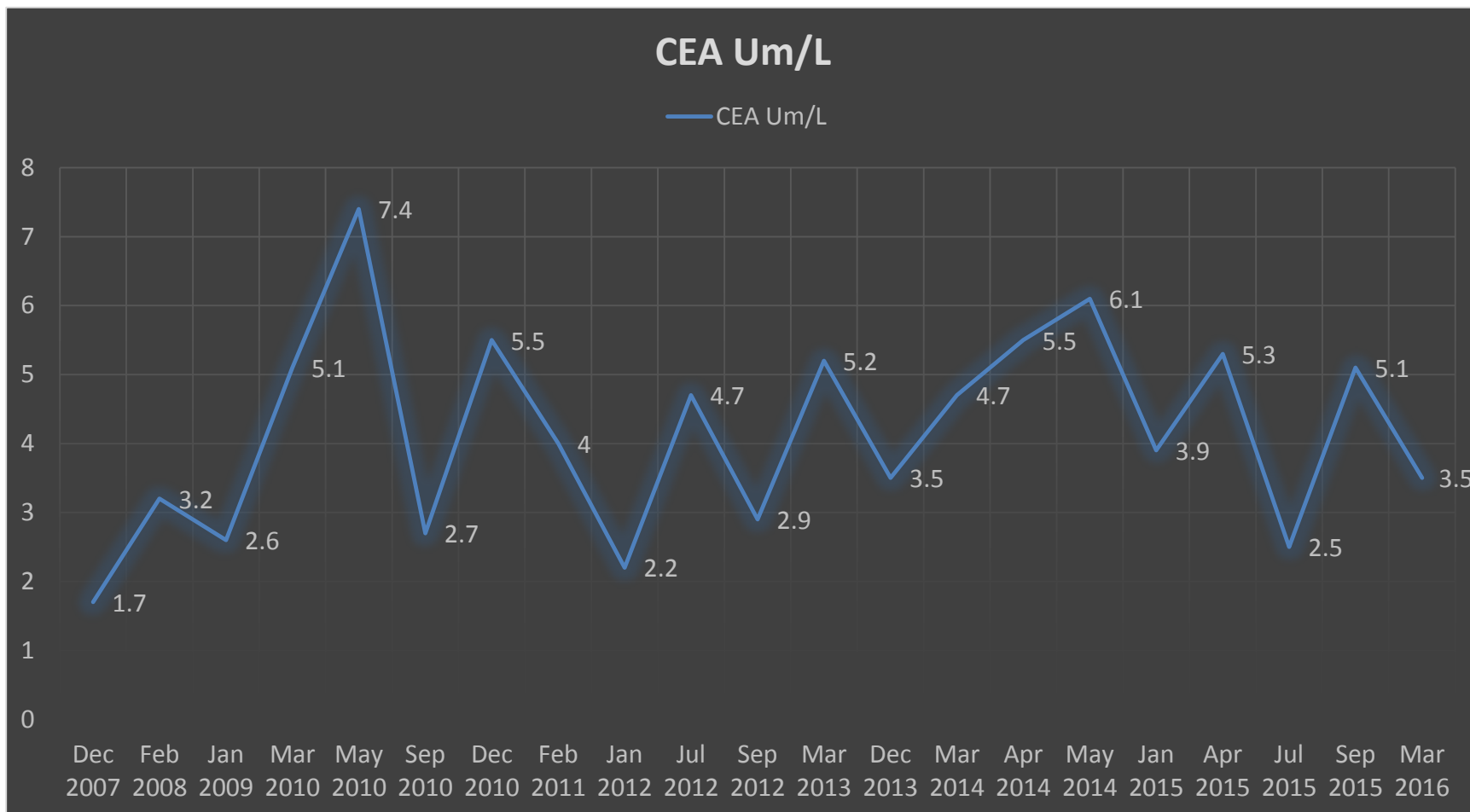
4th disease progression in 05/15: lungs mts; atypical resection, 4 5-FU/leucovorin Roswell Park regimen



Maintenance therapy with Panitumumab since 11/17; 6th disease progression in 07/17; lungs mts;



Tumor's marker level and disease progression



Summary

- ⦿ According to literature, 5-year OS in patients with primary metastatic CRC is 14%
- ⦿ Mr. V is still alive for more than 11,5+ years since the initial diagnosis
- ⦿ Due to active tactics of treatment + usage of all the available options including supportive care
- ⦿ Good quality of life: still working, active lifestyle, still heavily smokes 😊
- ⦿ Also more than 5 years after radiological treatment with no additional surgical treatment

Thank you for your attention!