

RANDOMIZED PHASE III STUDY OF 5-FLUOROURACIL/
FOLINATE/OXALIPLATIN GIVEN CONTINUOUSLY OR INTERMITTENTLY
WITH OR WITHOUT CETUXIMAB, AS FIRST-LINE TREATMENT OF
METASTATIC COLORECTAL CANCER: THE NORDIC VII STUDY
(NCT00145314), BY THE NORDIC COLORECTAL CANCER
BIOMODULATION GROUP

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Date posted: Nov 8 2010



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Study Design

N= 566 (ITT)

Primary
Outcome: PFS

R

Nordic FLOX (q2w)

**Nordic FLOX (q2w) +
Cetuximab (Continuous)**

**First Line
mCRC**

**Nordic FLOX (q2w) +
Cetuximab (Intermittent)**

Response Rate

Population	FLOX	Cont FLOX +C	Int FLOX +C	HR (B vs A)
ITT (N=566)	41	49	47	1.35
All KRAS (N=498)	45	47	48	1.12
KRAS WT (N=303)	47	46	51	0.96
KRAS Mut (N=195)	40	49	42	1.44

PFS

Population	FLOX	Cont FLOX +C	HR (B vs A)
ITT (N=566)	7.9	8.3	0.89
All KRAS (N=498)	8.3	8.3	0.92
KRAS WT (N=303)	8.7	7.9	1.07
KRAS Mut (N=195)	7.8	9.2	0.71

Overall Survival

Population	FLOX	Cont FLOX +C	Int FLOX +C	HR (B vs A)
ITT (N=566)	20.4	19.7	20.3	1.06
All KRAS (N=498)	22.0	20.1	20.6	1.10
KRAS WT (N=303)	22.0	20.1	21.4	1.14
KRAS Mut (N=195)	20.4	21.1	20.5	1.03

Gr 3/4 TOXICITY

	FLOX	Cont FLOX +C	Int FLOX +C
Thrombocytopenia	3	4	2
Neutropenia	47	46	49
Febrile neutropenia	11	13	10
Infection without neutropenia	5	7	10
Diarrhoea	10	17	16
Sensory neuropathy	22	16	14
Motor neuropathy	10	7	5
Nail disorder	1	3	6
Skin/rash	1	22	29
Allergic reaction	3	7	6
Fatigue	10	16	11
Nausea	3	4	5



STUDY SUMMARY

- **The major findings of this study:**
 - Cetuximab does not improve the RR, PFS or OS of NORDIC FLOX
 - Intermittent NORDIC FLOX provides the same benefit as continuous NORDIC FLOX
- **This trial showed a trend for a benefit of adding cetuximab in the KRAS mutant subset of patients**
- **This is unlike all other trials of Oxaliplatin based chemotherapy, where a detriment has been seen with the addition of EGFR inhibitors in the KRAS mutant subset**



STUDY COMMENTARY

- **? Why no added benefit to adding cetuximab to NORDIC FLOX**
 - ? Bolus 5FU in NORDIC FLOX
 - Higher rates of diarrhea in cetuximab arms but in response to a question, Dr Tveit stated that exposure to chemo did not appear to be a factor in trial results
 - ? Oxaliplatin in NORDIC FLOX
 - But PRIME, OPUS and FOLFOX subset of COIN have all shown benefits when EGFR inhibitor added to FOLFOX



STUDY COMMENTARY

- **? Why did Patients with KRAS mutant tumours appear to do better than patients with KRAS WT tumours - a finding inconsistent with all other trials of EGFR inhibitors added to oxaliplatin based therapies**
 - **? Chance**



BOTTOM LINE FOR CANADIAN MEDICAL ONCOLOGISTS

- Cetuximab should not be added to NORDIC FLOX - but since this regimen is not used outside of Scandanavia there is little direct impact of this trial for Canadians
- Like the COIN trial, this affirms that choice chemo backbone appears to be an important consideration in the use of chemo and EGFR inhibitors. The benefits of adding EGFR inhibitors have only been seen when added to FOLFIRI or FOLFOX