

Maintenance or stop and go: What is the standard?

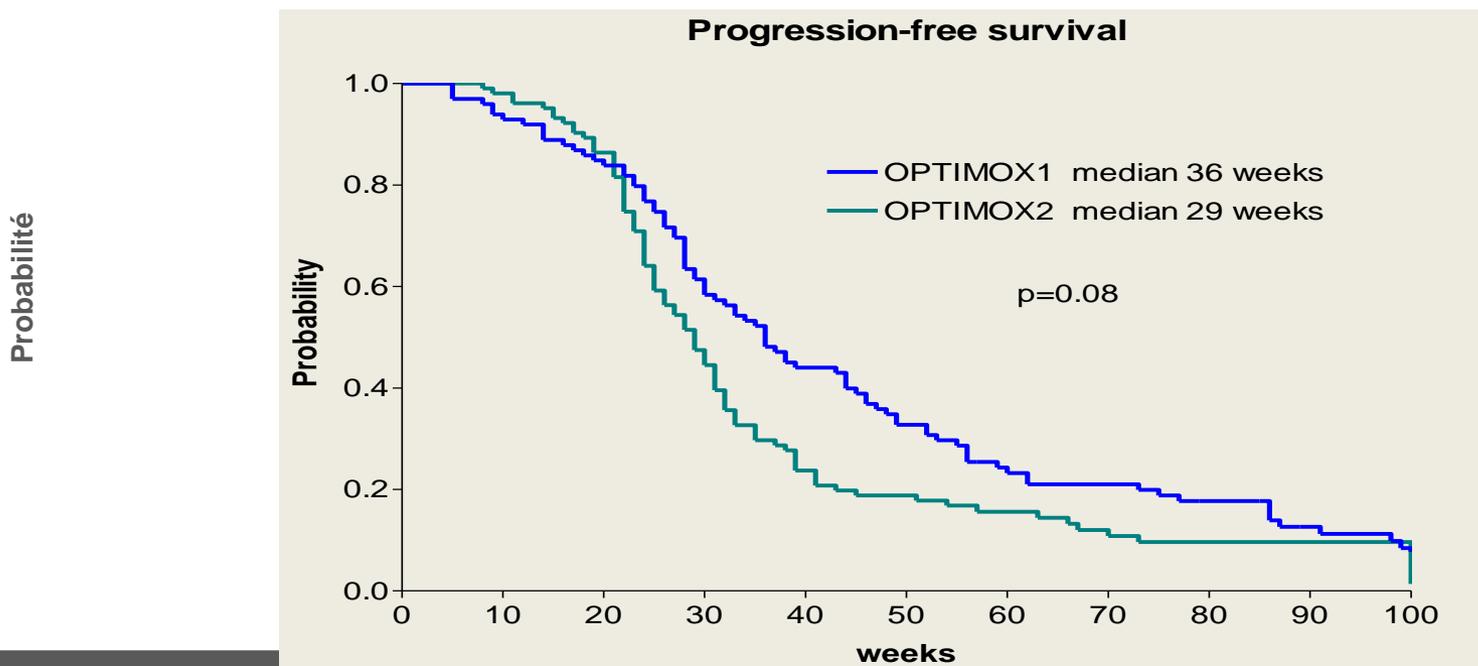
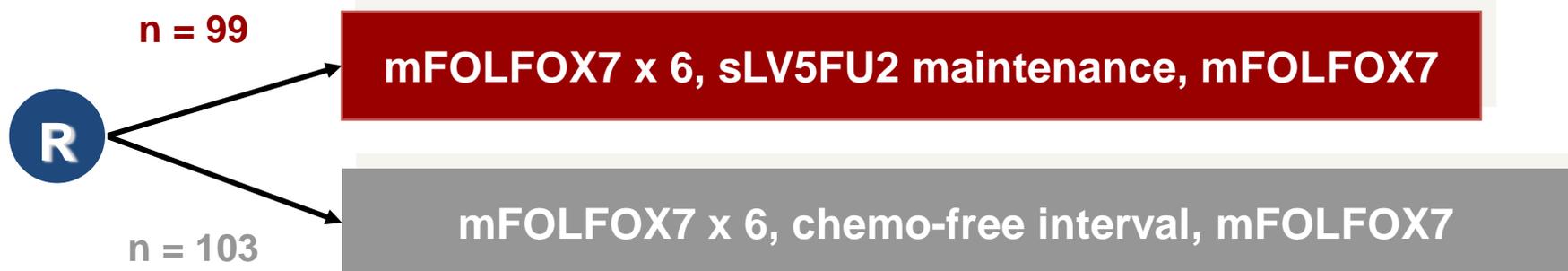
Michel Ducreux

Head of the Gastrointestinal Unit

Pause or maintenance?

Maintenance with chemotherapy versus pause

→ Optimox 2 more difficult to interpretate

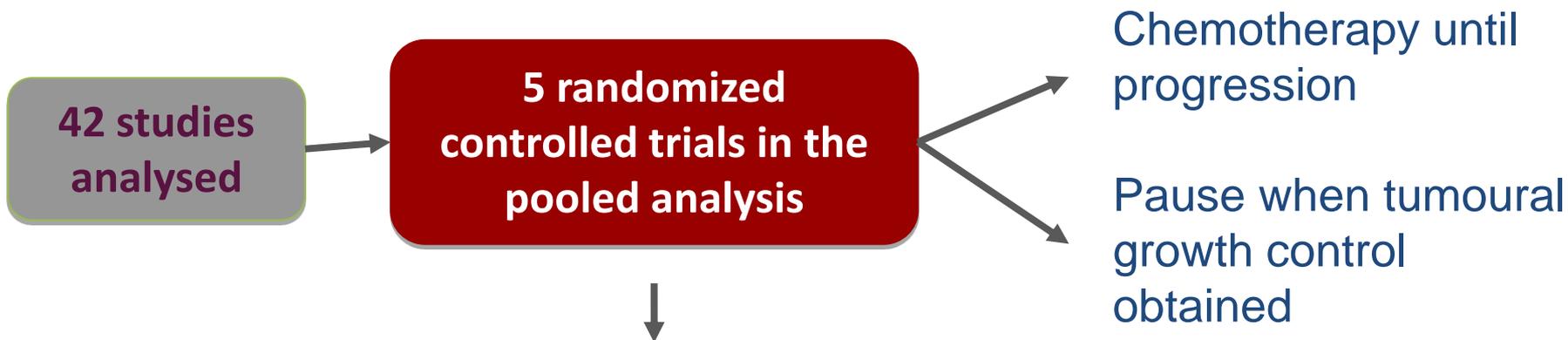


→ Conclusion concerning Chemo-free intervals

- A significant number of patients can benefit from chemotherapy holidays. Baseline characteristics do not allow to select these patients
- Optimal duration of chemotherapy before CFI is 6 months.
- A prolonged CFI (> 6 months) predicts a prolonged survival
- Normal CEA level after chemo was the single identified predictive factor of prolonged survival in patients who had a >3 months CFI

→ Pause and overall survival

Pause, not for everyone



1776 patients evaluables for overall survival
OS infavour of continuation of CT: HR 0.9; IC 95% 0.82 – 0.99; $p=0.03$

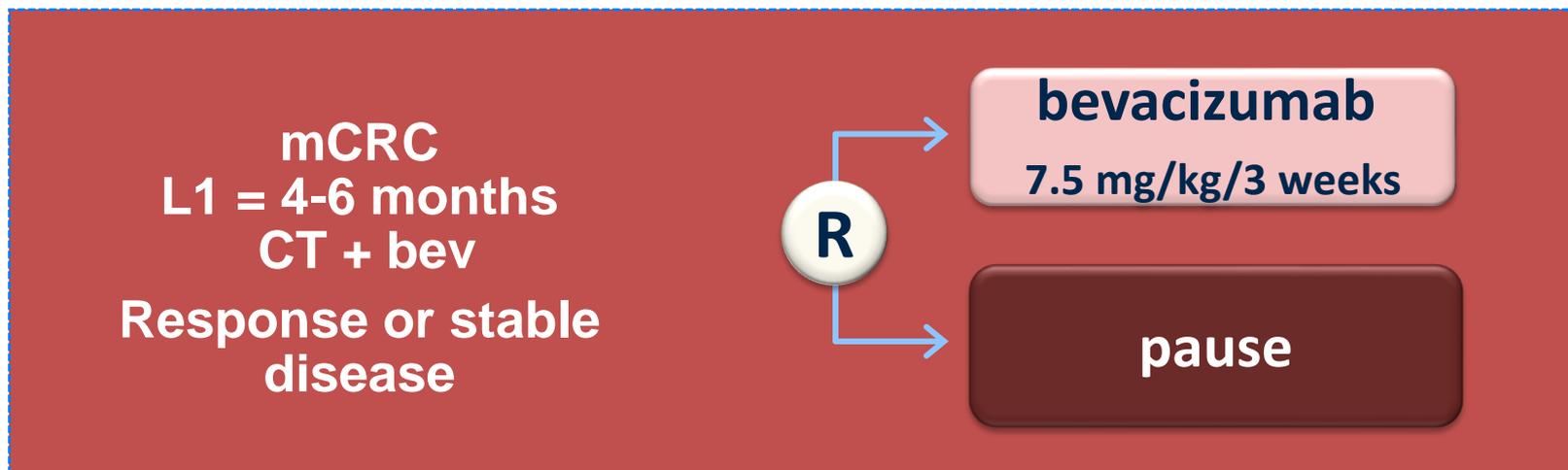
- **Pause should be proposed only to patients with slow growing tumour...**

Pause or maintenance?

Maintenance with targeted therapy versus pause

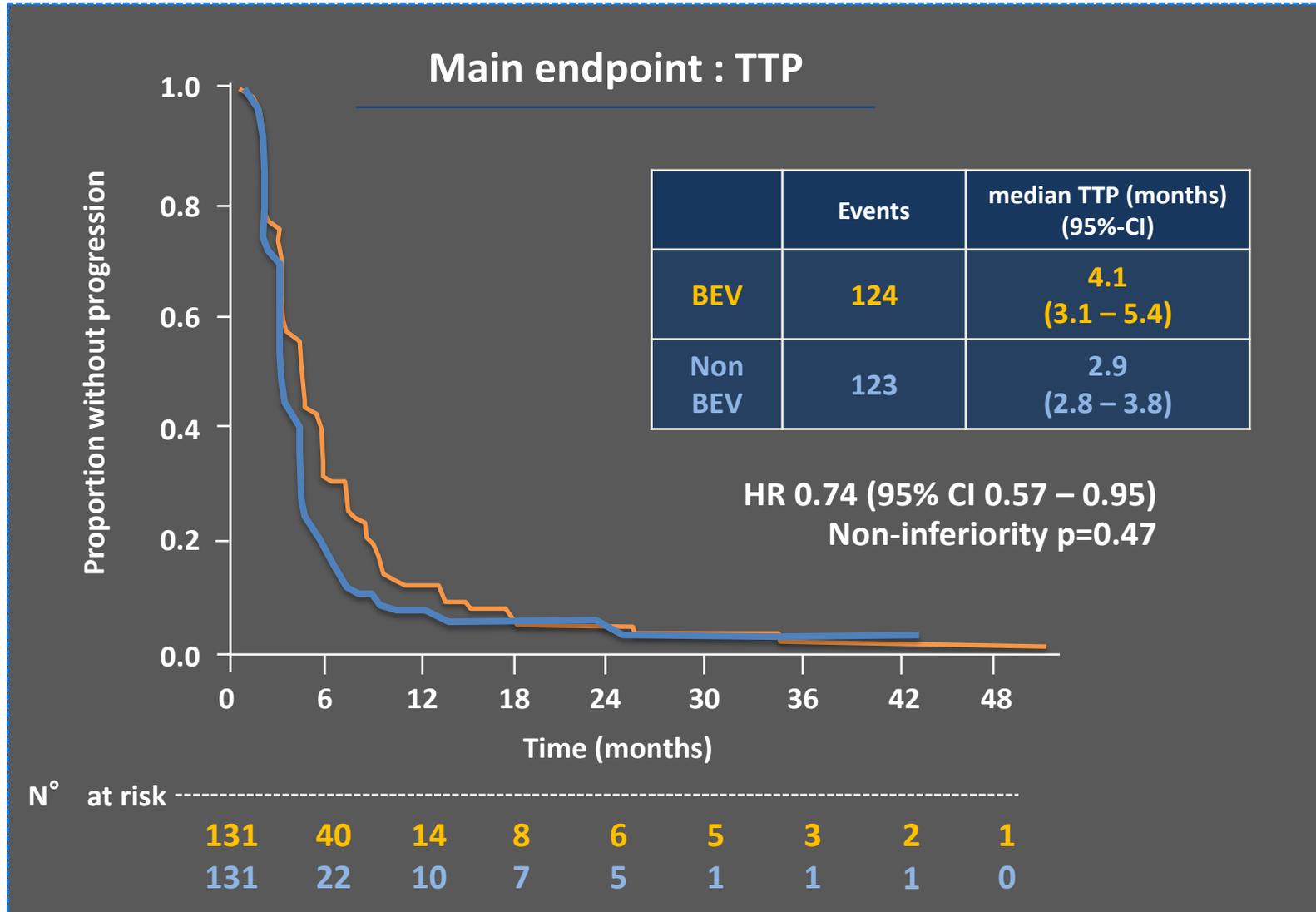
→ Maintenance with bevacizumab alone???

- Swiss multicentric study

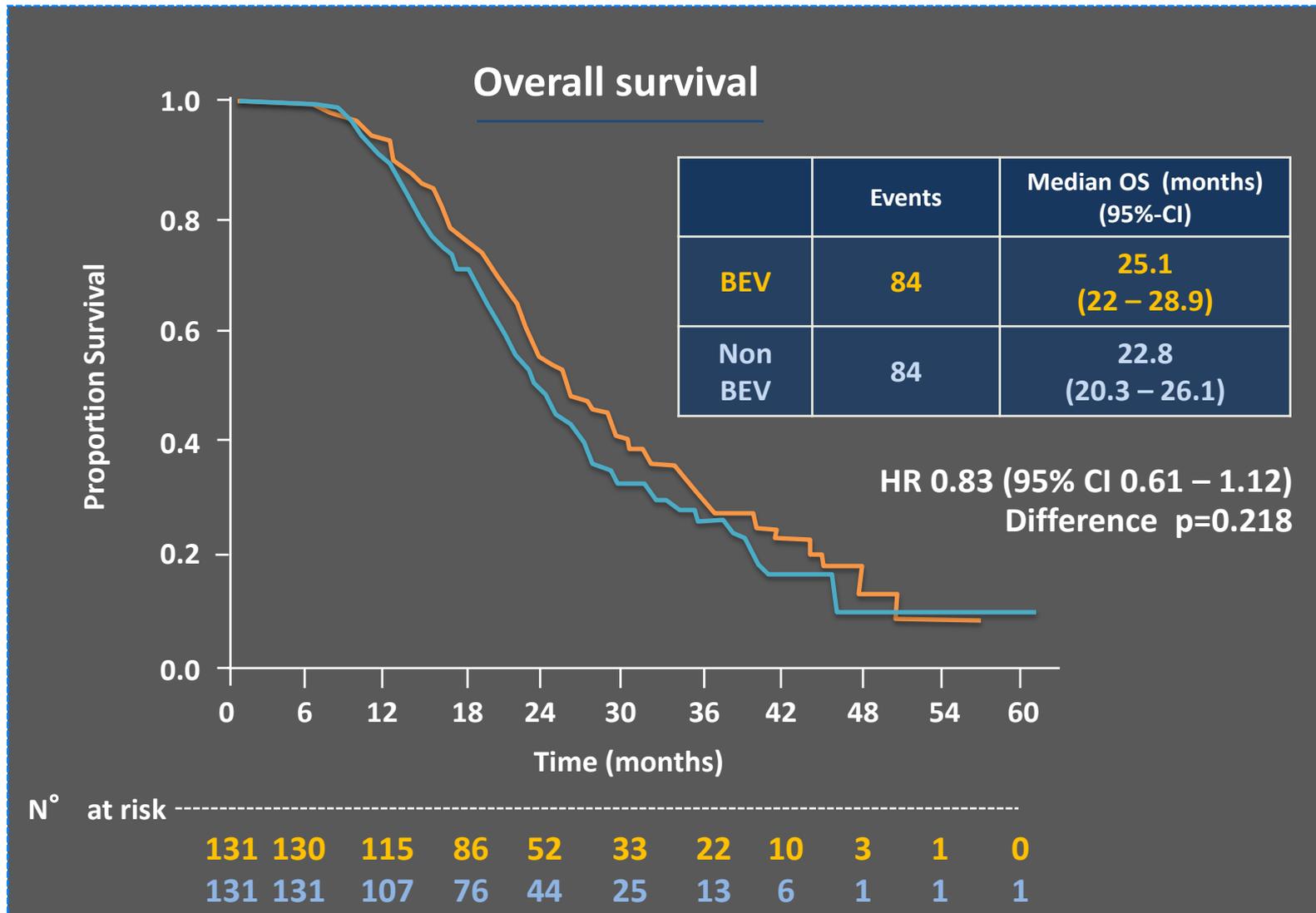


- → Main endpoint: TTF
- Non-inferiority study

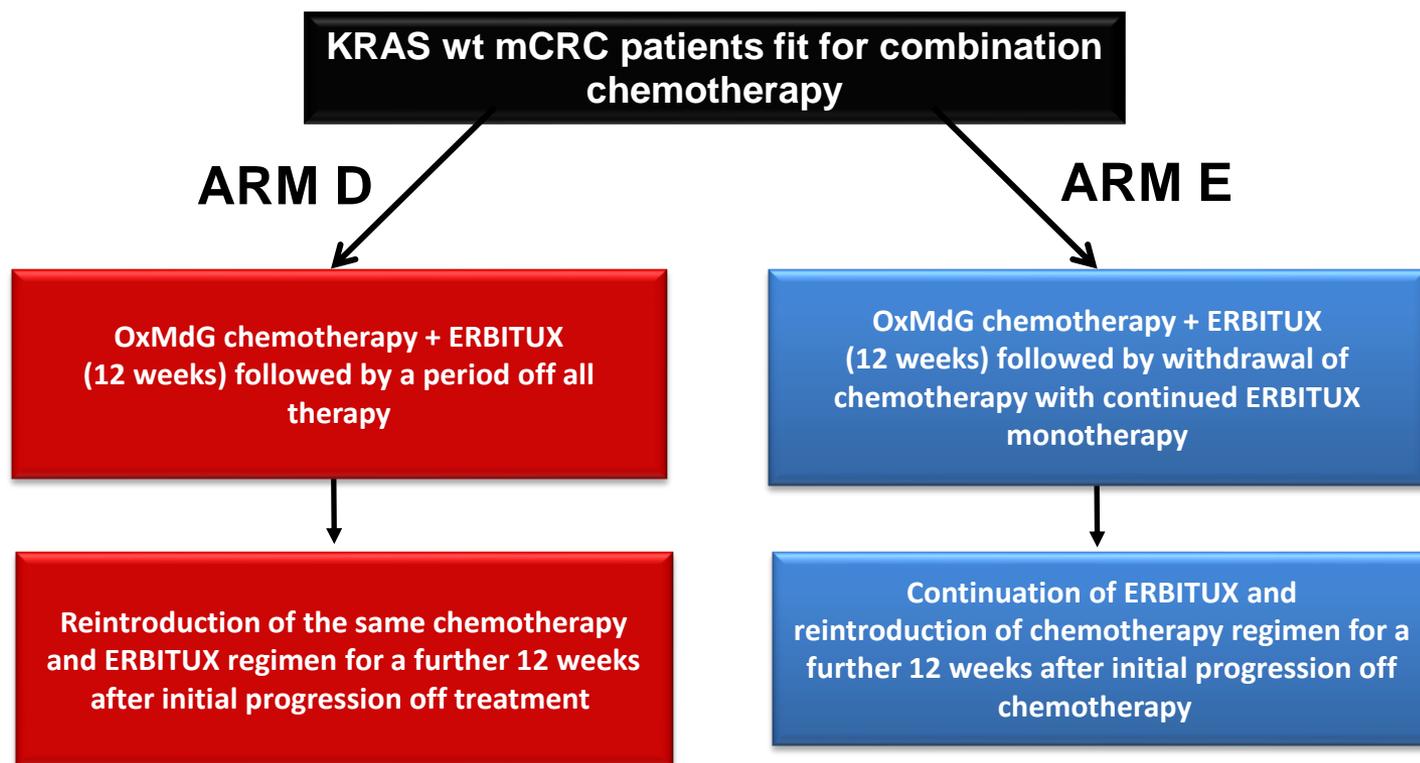
→ Maintenance with bevacizumab alone???



→ Bevacizumab versus control



→ Phase II COIN-B: maintenance with cetuximab in KRAS wt mCRC 1L

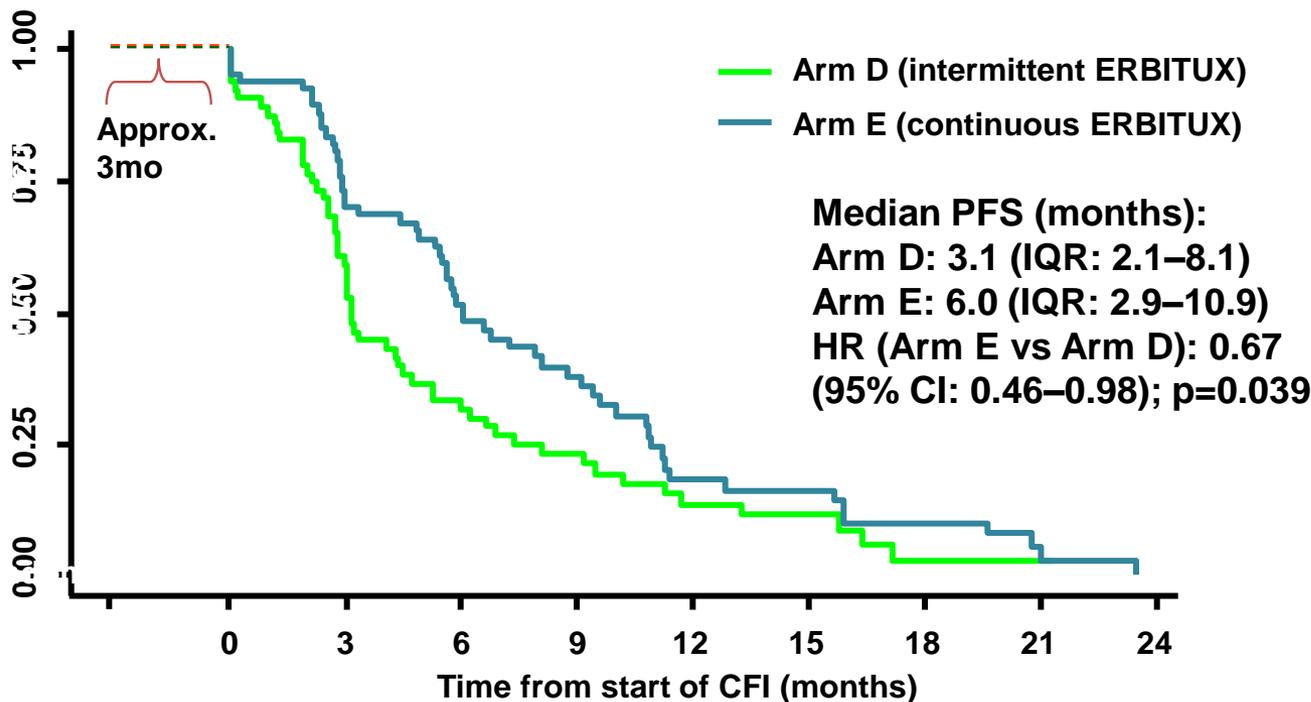


Stop treatment strategy at failure (defined as RECIST PD), *while on combined treatment (i.e. both ERBITUX and chemotherapy)*, cumulative toxicity or patient choice

Primary Endpoint: Failure-free survival (FFS) at 10 months

Secondary Endpoints: OS, PFS, ORR, safety

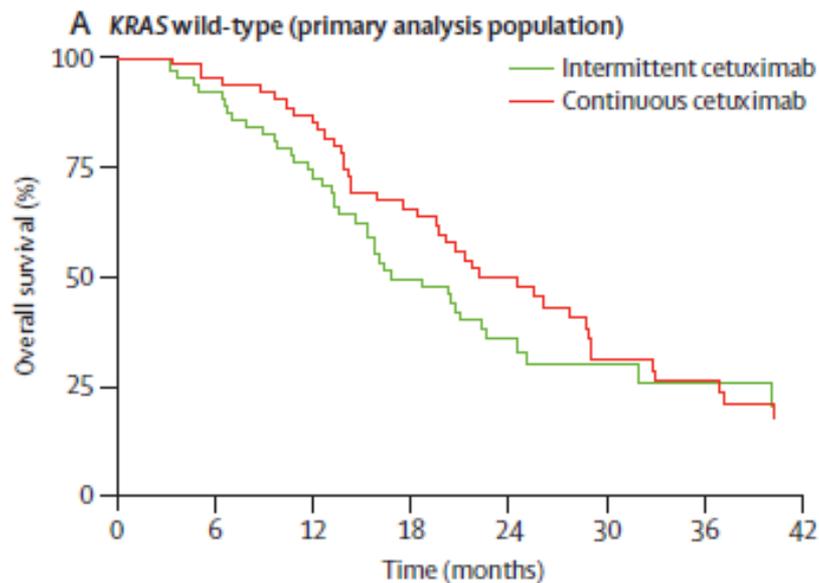
→ COIN-B: PFS from start of 1st CFI in primary analysis cohort



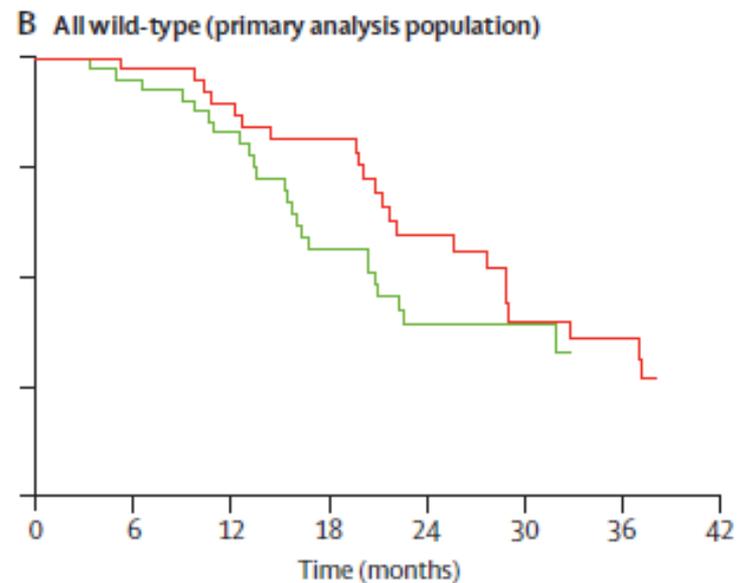
Arm D	65	37	19	13	7	4	1	1	0
Arm E	67	47	33	21	9	8	5	2	0

- PFS from start of study treatment is approximately 3 months greater than values given above

→ Coin overall survival



Number at risk		0	6	12	18	24	30	36	42
Intermittent cetuximab	64	58	45	27	13	9	5	4	
Continuous cetuximab	66	61	49	34	24	13	11	6	



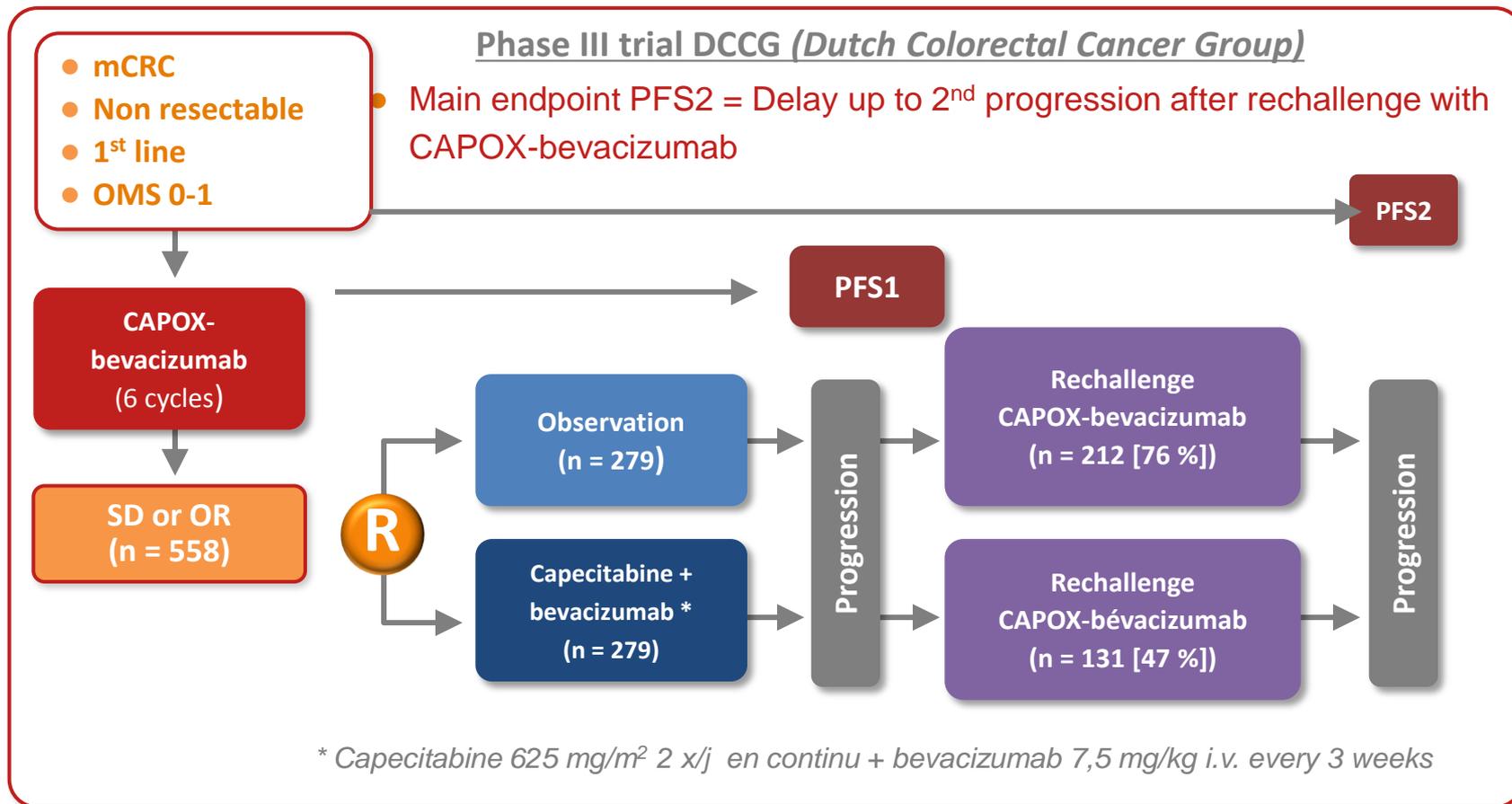
Number at risk		0	6	12	18	24	30	36	42
Intermittent cetuximab	42	40	33	21	10	8	4	4	
Continuous cetuximab	43	40	33	27	18	10	9	5	

Figure 4: Kaplan-Meier analyses of overall survival

Pause or maintenance?

Maintenance with chemotherapy + bevacizumab
versus pause

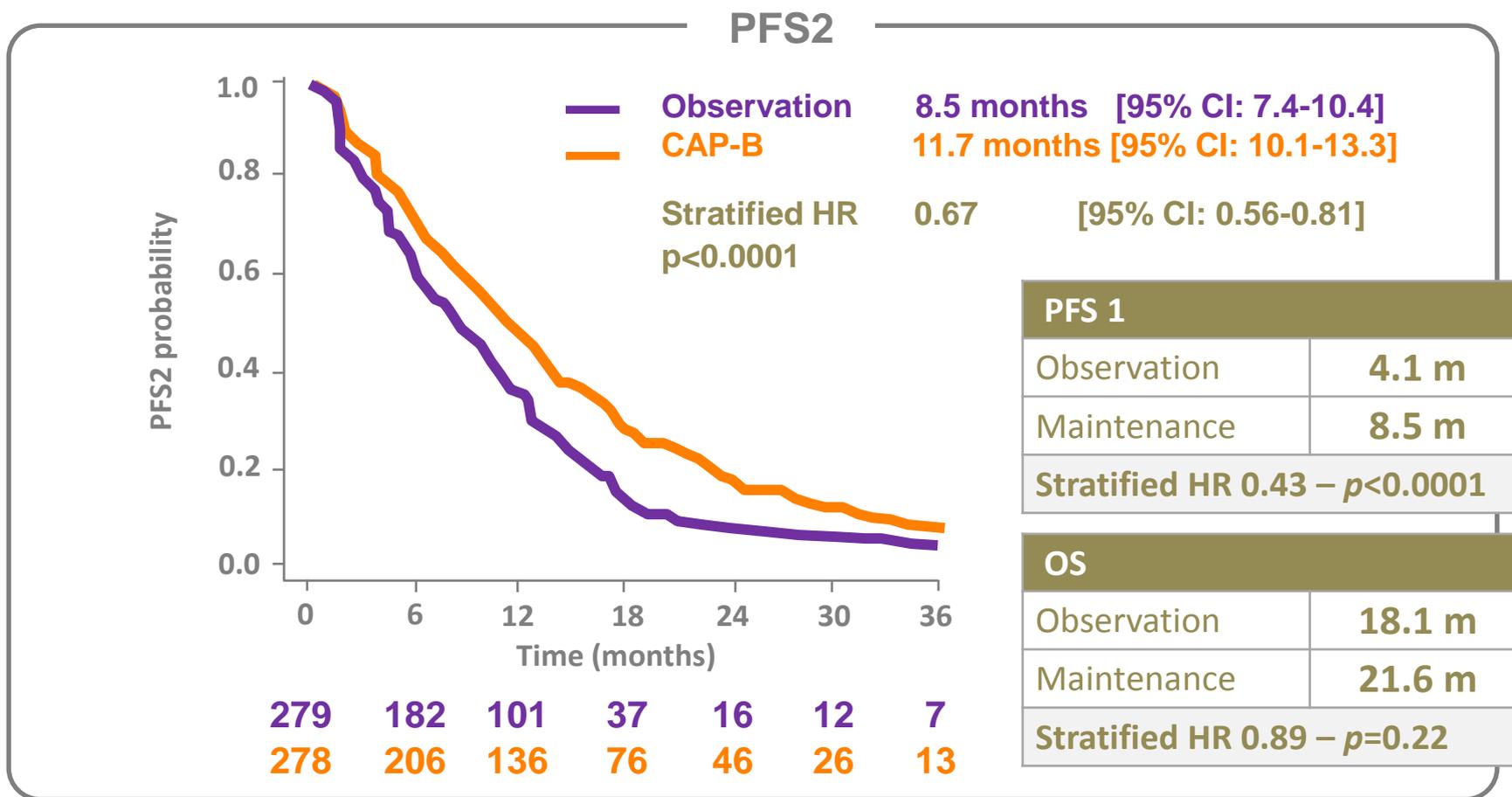
➔ Maintenance with bevacizumab and capecitabine: CAIRO3



- **Secondary endpoints : PFS1, TTP2, OS**

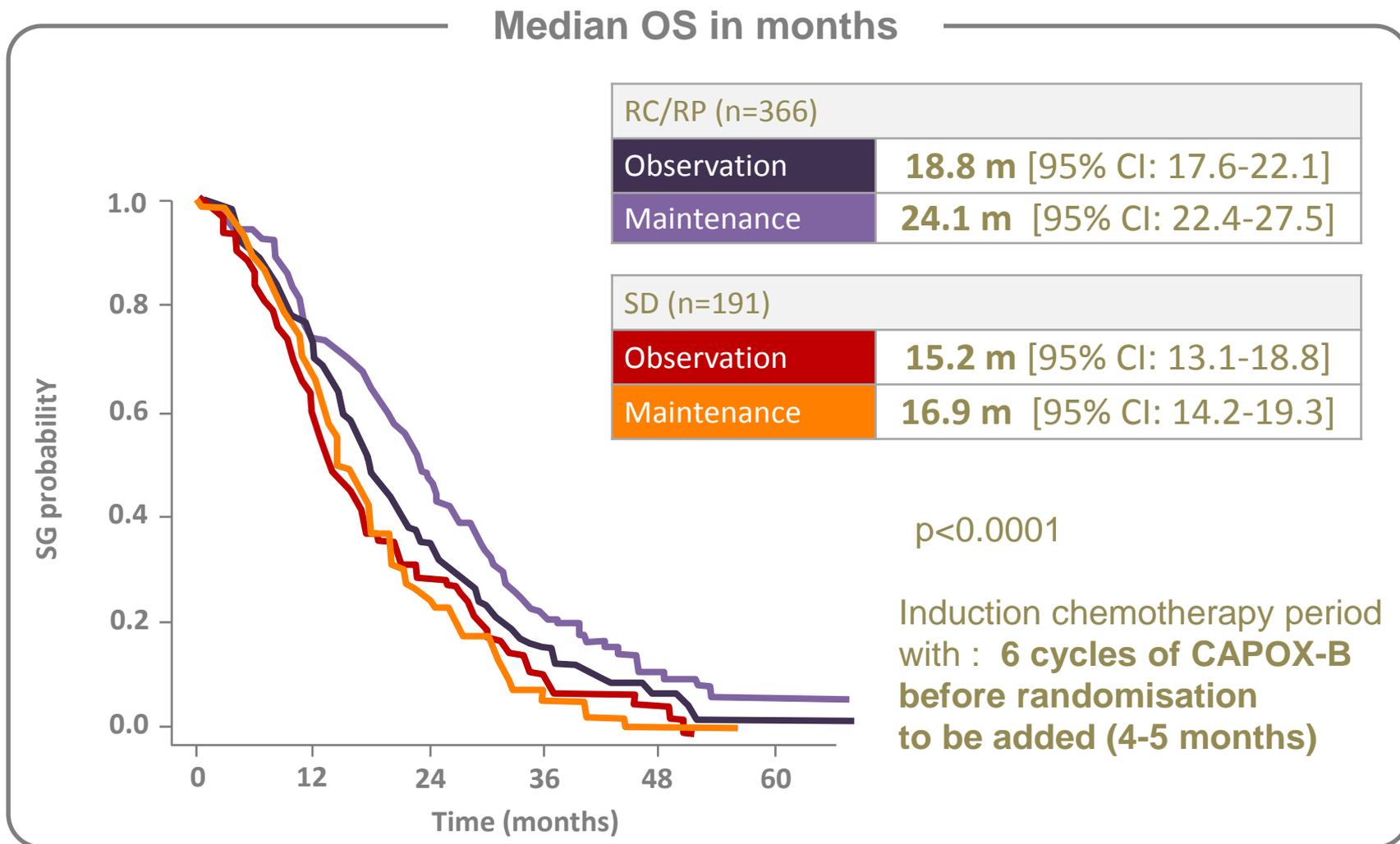
➔ TTP2 : time to progression or death after first progression, whatever the treatment used

→ CAIRO 3 : Actualized results



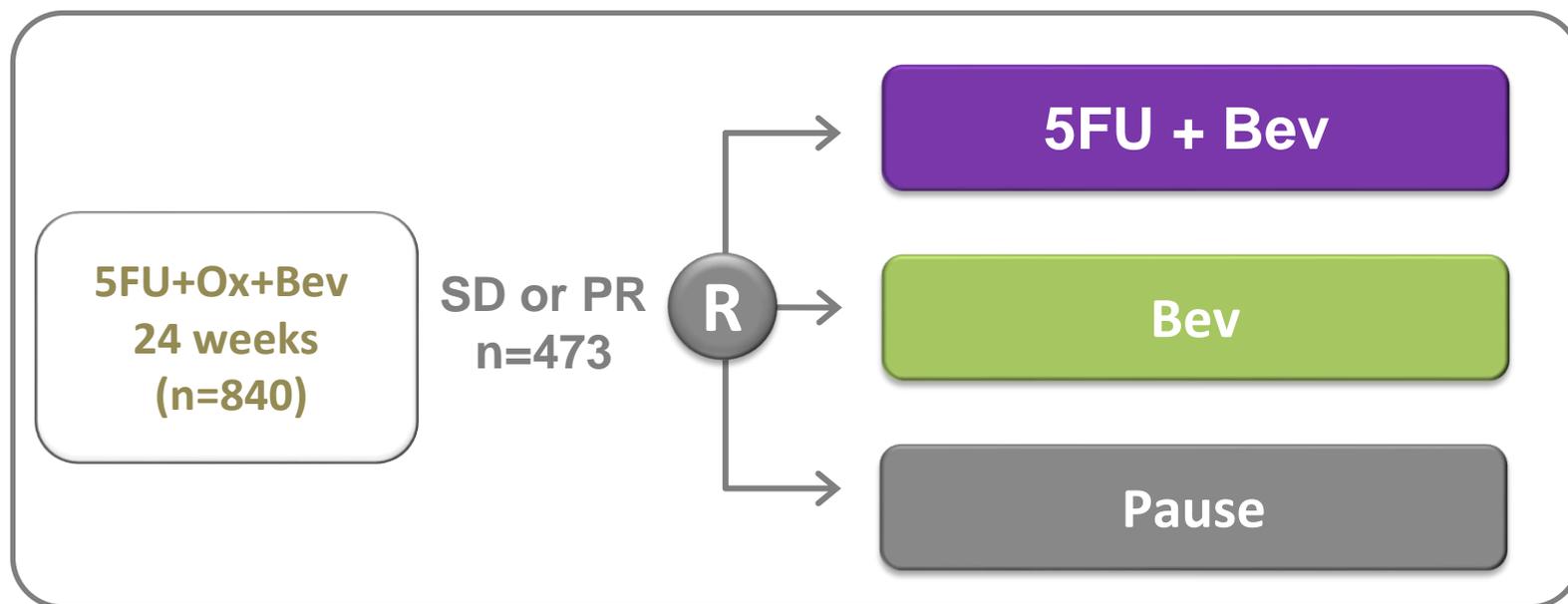
▶ **Study in favour of maintenance**
PFS2 benefit seen across all subgroups

→ Overall survival according to response to initial treatment



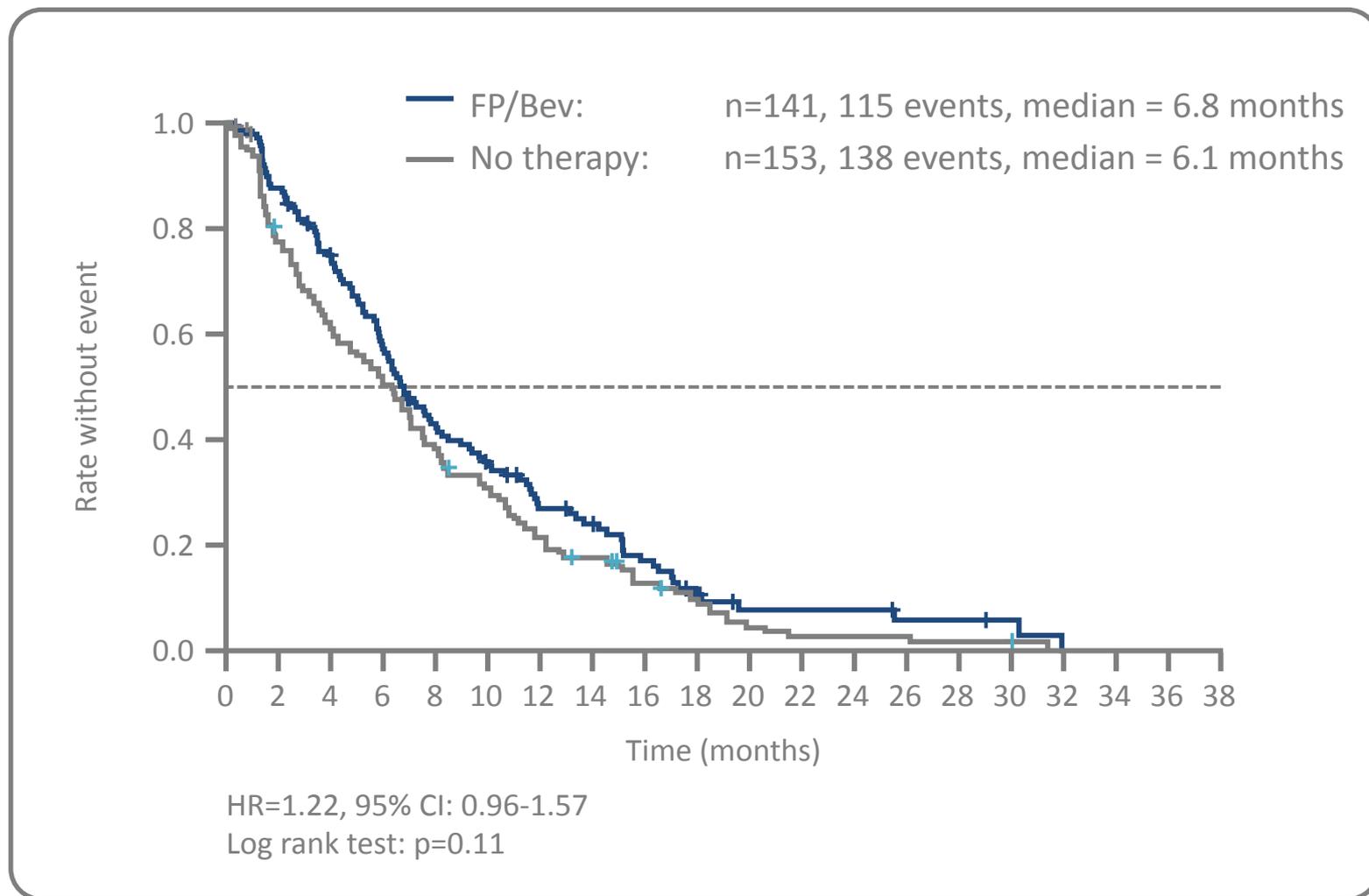
→ AIO trial ASCO 2014.....

- **mCRC L1, non inferiority study**

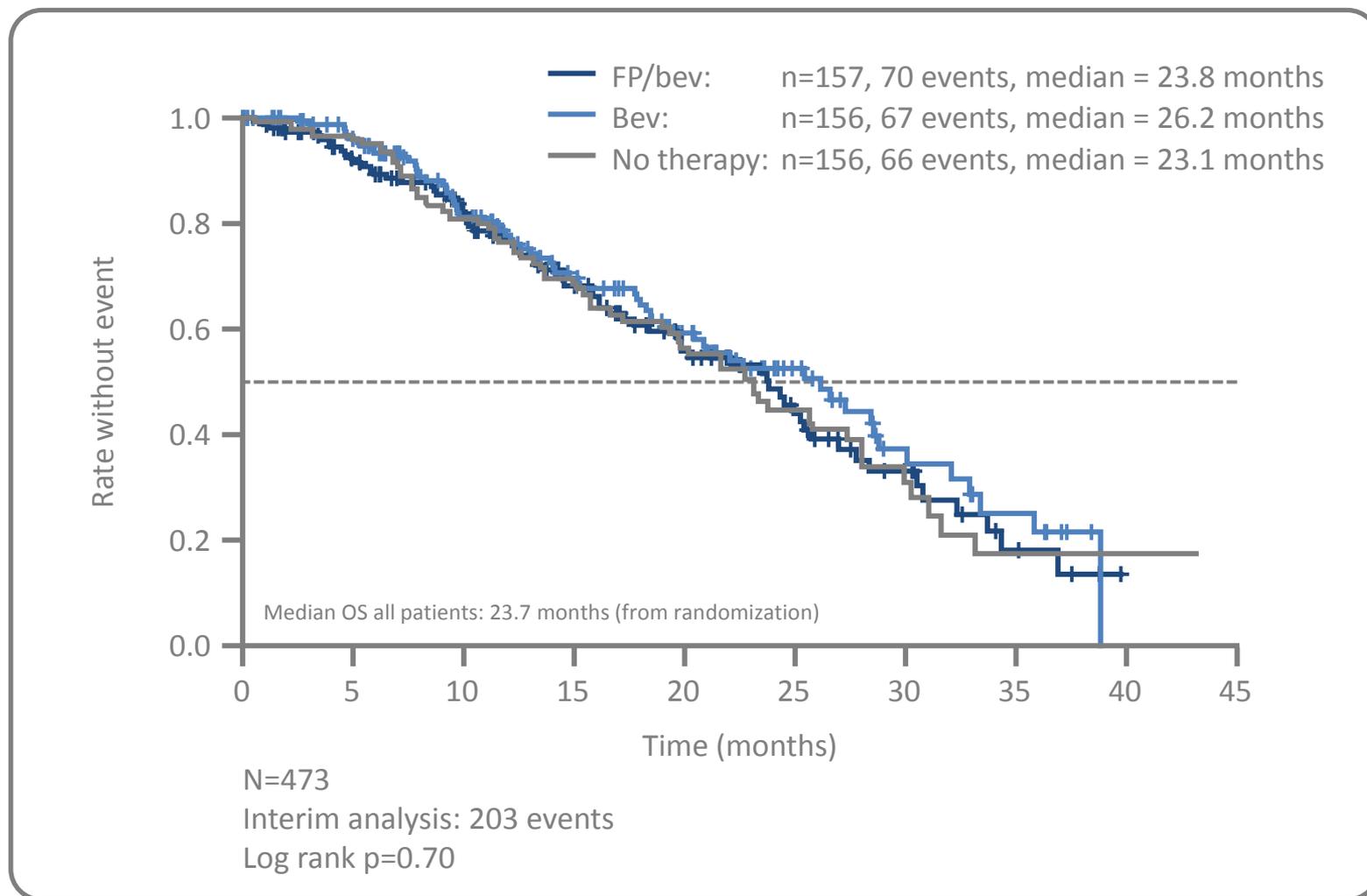


- Main endpoint TTFS (equal to PFS 1 if no reintroduction)
- Secondary endpoints: PFS, OS
- Median follow-up = 27 monts

→ Primary endpoint TFS: No therapy vs. FP/Bev



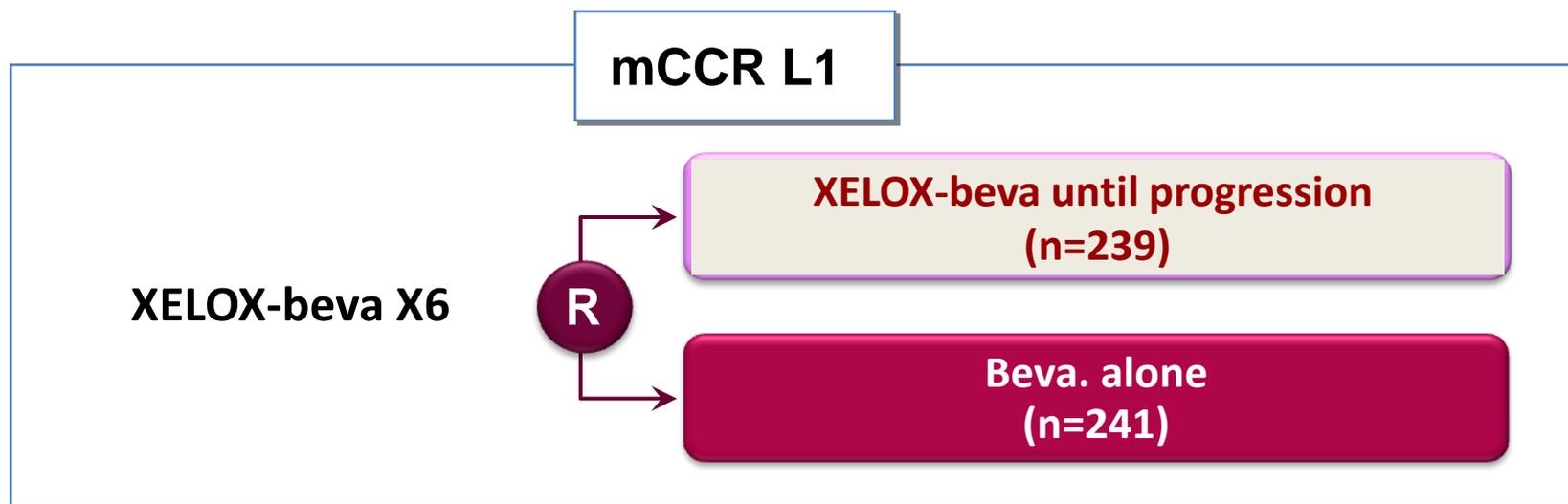
→ OS from start of maintenance



Pause or maintenance?

Maintenance with bevacizumab + chemotherapy
versus bevacizumab alone

→ Maintenance study: MACRO



- Main endpoint : non-infériority accepted HR .,32
- Bevacizumab : 7.5 mg/kg /3 weeks.
- Xelox : oxaliplatin 130 mg/m² IV D1
capecitabine 1000 mg/m² p.o. D1-14
D1'=D21

→ Maintenance study: MACRO

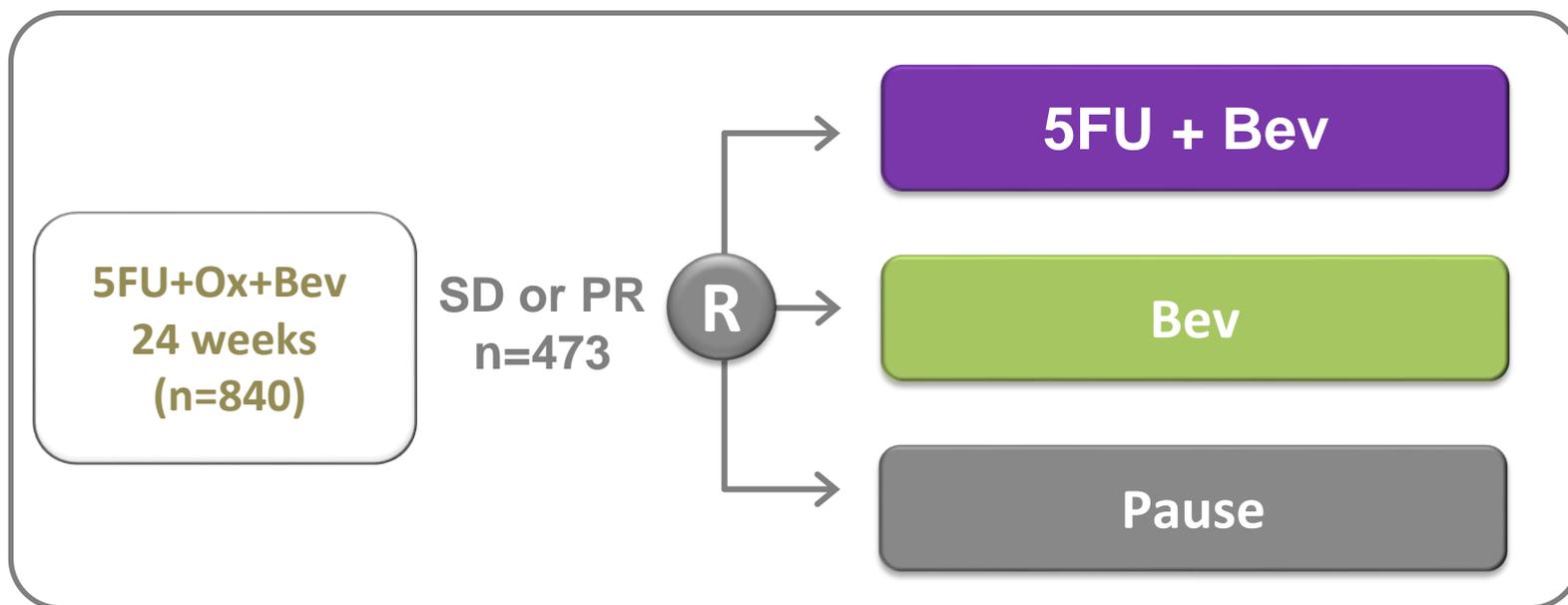
	Xelox-Beva	Beva	
Median PFS (months)	10.4	9.7	NS
Median OS (months)	23.4	21.7	NS
ORR (%)	46	49	NS
RO resections	8.8	5.8	NS

→ Non inferiority non formally demonstrated
HR 1,11 [0.89-1.37]

→ No control arm....

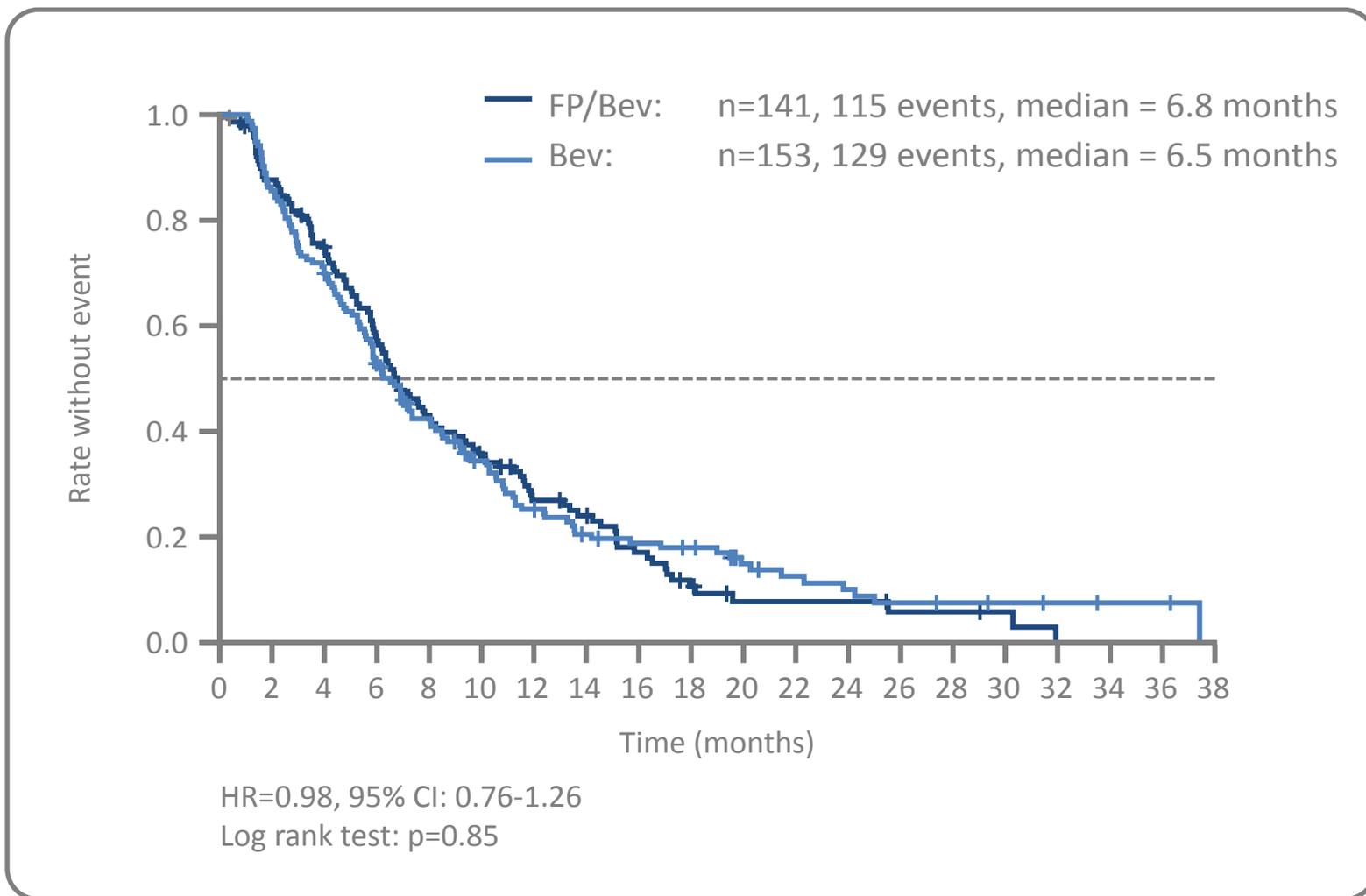
→ AIO trial ASCO 2014.....

- mCRC L1, non inferiority study



- Main endpoint TTFS (equal to PFS 1 if no reintroduction)
- Secondary endpoints: PFS, OS
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→ Primary endpoint TFS : Bev vs. FP/Bev



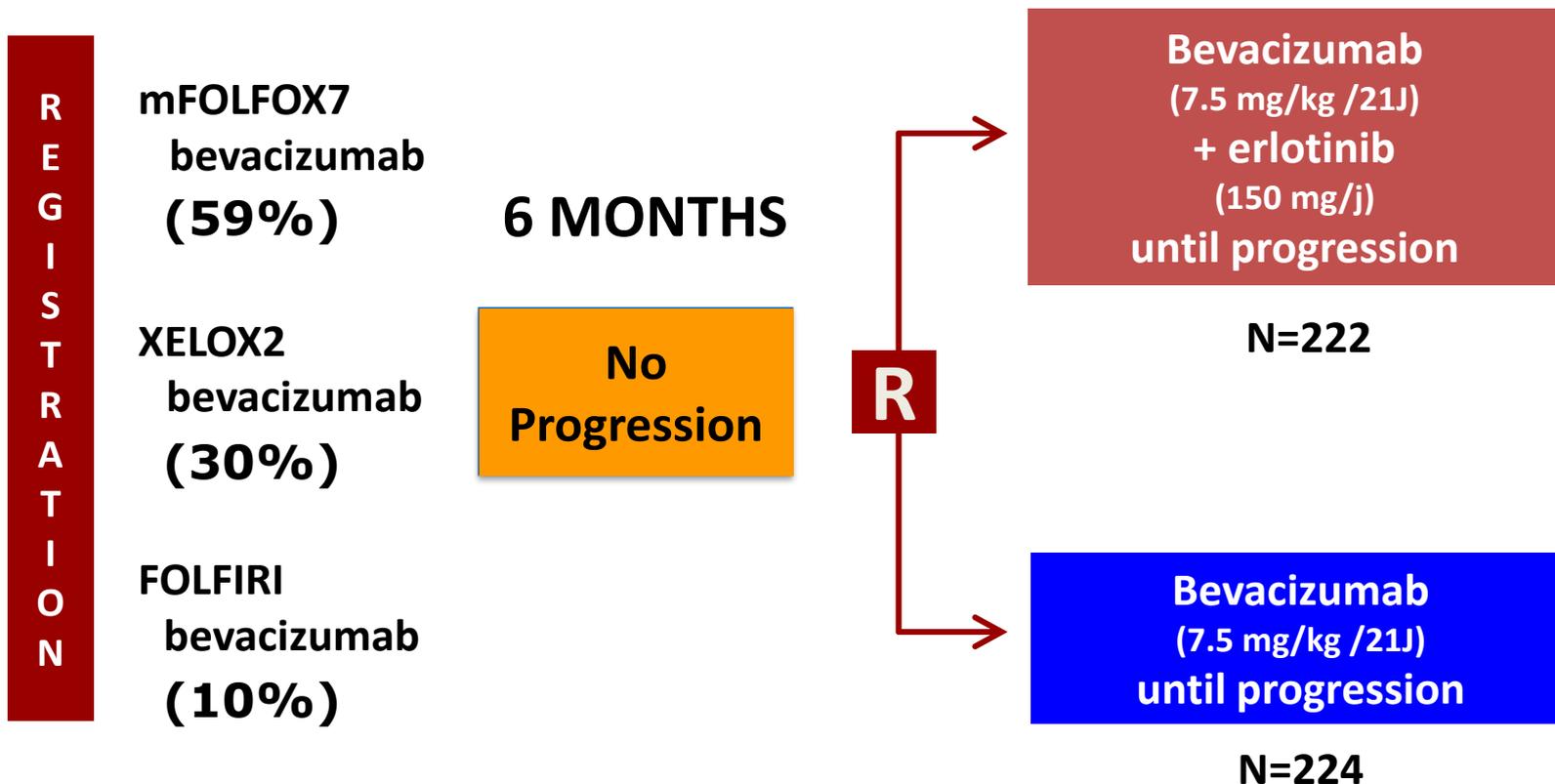
Pause or maintenance?

Maintenance with bevacizumab + erlotinib
versus bevacizumab alone

→ Maintenance: Bev + erlotinib DREAM

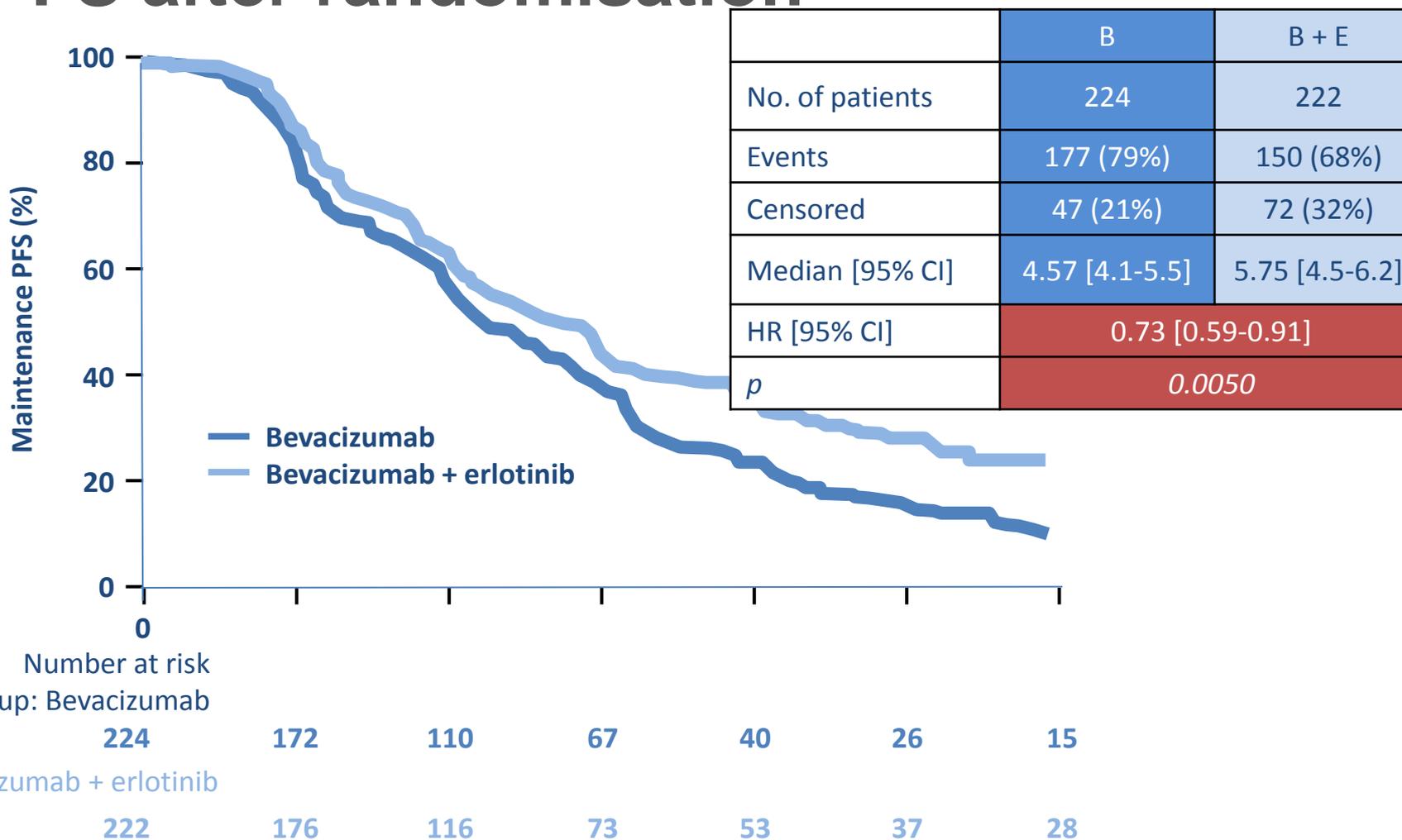
Induction, N=700

Maintenance, N=446



4.1.07 – 13.10.11

→ DREAM-OPTIMOX 3 : PFS after randomisation



→ Conclusion

- More data with bevacizumab than with cetuximab
- Maintenance seems to be better than no treatment in metastatic colorectal cancer in terms of progression-free survival
- No clear advantage in terms of overall survival
- Combination of capecitabine + bevacizumab seems to be a little bit more active than bevacizumab alone
- Pause remain useful in patients with:
 - Normalisation of CEA
 - Slow-growing tumours??
 - Response to initial therapy ???...