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EXPERTS KNOWLEDGE SHARE
with
Prof. Köhne,
Dr. Modest and Dr. Vecchione

Madrid (Spain)
Sunday September 10th 2017

Supported by an independent Educational Grant from Bayer

THE DEBATE

How long should treatment be within an adjuvant setting - 3 or 6 months?

Differing Perspectives	The Experts
The case for 3 month treatment	Dr. Loredana Vecchione
The case for 6 month treatment	Dr. Domink Modest
Concluding Remarks	Prof. Claus-Henning Köhne

3 MONTHS ADJUVANT TREATMENT FOR STAGE III COLON CANCER:

WHAT A TERRIFIC IDEA, ISN´T IT?

Loredana Vecchione

Medical Oncologist
Charité Comprehensive Cancer Center
Berlin

2017 ASCO ANNUAL MEETING
Making a Difference in Cancer Care WITH YOU

ASCO DAILY NEWS

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Risk-Based Approach to Chemotherapy Duration Recommended for Stage III Colon Cancer

JUNE 4, 2017

Shi Q, ASCO 2017

In view of these findings, investigators in the IDEA collaboration reached a clinical consensus to recommend a risk-based approach to selecting adjuvant chemotherapy for stage III colon cancer. The consensus recommends 3 months of adjuvant chemotherapy for patients with low-risk disease, defined as T1-3N1 tumors, which includes approximately 60% of stage III patients. For high-risk patients, defined as patients with T4 or N2 tumors, decisions on use of the shorter course should be based on an individual assessment of tolerability, risk, and choice of regimen.

SCOT: CAPOX for 3 Months Is Not Inferior to 6 Months in Colorectal Cancer

JUNE 13, 2017

Iveson T, ASCO 2017

...SCOT met its non inferiority target....therefore 3 months treatment should now be considered for many patients...

TOSCA Supports Shorter Adjuvant CT Duration for Resected Colon Cancer

JUNE 13, 2017

Sobrero A, ASCO 2017

"Because the difference in RFS is so limited … but the toxicity so much better, 3 months of oxaliplatin-based chemotherapy can be considered another standard option for the adjuvant treatment of resected colon cancer," presenter Alberto F. Sobrero, MD, of the Ospedale San Martino, in Italy, said.

"The last 24 hours, with the Plenary Session and today's talks, will change the lives of hundreds of thousands of [patients with] colorectal cancer each year worldwide," Dr. Meyerhardt said.

On the basis of the results of TOSCA, SCOT, IDEA France, and other IDEA trials, Dr. Meyerhardt plans to offer 6 months of FOLFOX to his patients with T4 or N2 disease. For those with T1-3N1 disease, he will offer 3 months of CAPOX or FOLFOX to reduce toxicity and alleviate the logistical burden of treatment; he cited his preference for CAPOX because of its slightly more preferable efficacy data.

Meyerhardt J, ASCO 2017

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2017 ASCO ANNUAL MEETING
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ASCO DAILY NEWS

Medscape Coverage from the
American Society of Clinical Oncology (ASCO) 2017 Annual Meeting

Less Is More: Patients With Colon Cancer Get a Chemo Break

Kate Johnson
June 04, 2017

CHICAGO — Most patients with low-risk stage III colon cancer will likely have their oxaliplatin-based adjuvant chemotherapy regimen cut in half, based on findings of the largest prospective trial on the issue to date, reported here at the American Society of Clinical Oncology (ASCO) 2017 Annual Meeting.


Dr Axel Grothey

For the 60% of patients who have low-risk tumors "we do not recommend more than 3 months of chemotherapy w[ith] an oxaliplatin-based regimen," he said. "That applies to 20,000 patients per year in the US, and you can easily se[e] that translates to hundreds of thousands of patients worldwide."

"This is a great day for patient[s] throughout the world," comme[nted] ASCO expert Nancy Baxter, MD, who is from St Michael's Hospital in Toronto, Ontario, Canada. "Now, today, up to 60% of my patients with stage III colon cancer will be able to stop after 3 months of therapy and be able to get on with their lives and have a lower risk of permanent problems, such as numbness of their hands and feet. Less is more," she said.


Dr Nancy Baxter

Medscape Coverage from the
American Society of Clinical Oncology (ASCO) 2017 Annual Meeting

COMMENTARY

Good IDEA: Drop Adjuvant Chemo From 6 to 3 Months in CRC

John L. Marshall, MD
DISCLOSURES | June 12, 2017

New standard of care: 3 months of CAPOX chemotherapy for most of your stage III patients. Only in those at higher risk should you consider going to 6 months. In those, I would say use only fluoropyrimidine

UpToDate

UpToDate durchsuchen
Adjuvant therapy for resected stage III (node-positive) colon cancer

Topic Outline
SUMMARY & RECOMMENDATIONS
INTRODUCTION

Adjuvant therapy for resected stage III (node-positive) colon cancer

Authors: Jeffrey W Clark, MD, Hanna K Sanoff, MD, MPH
Section Editor: Richard M Goldberg, MD
Deputy Editor: Diane MF Savarese, MD

DURATION OF THERAPY — The optimal duration of adjuvant chemotherapy for patients with stage III colon cancer is evolving…. we continue to suggest six months of oxaliplatin-based therapy for individuals with high-risk cancers (T4, N2) …On the other hand, given the small predicted loss of disease-free survival (DFS) benefit (absolute difference 0.9 percent at three years) and the significantly lower rates of oxaliplatin neuropathy, it seems reasonable to limit adjuvant therapy to three months in patients with low-risk disease (T1-3,N1), which makes up approximately 60 percent of all stage III colon cancers. However, the data from the IDEA collaboration are preliminary, and overall survival results are not yet mature….

BACKGROUND AND RATIONALE

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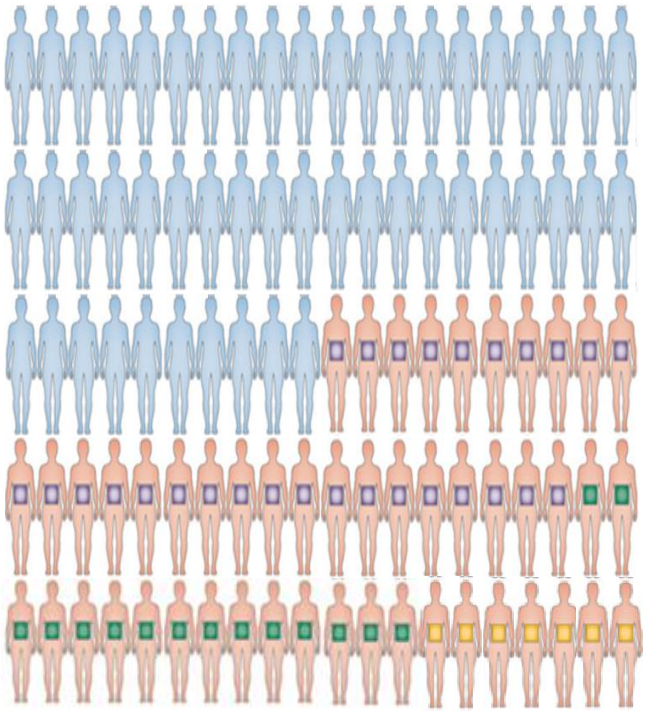
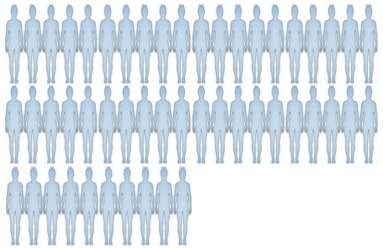
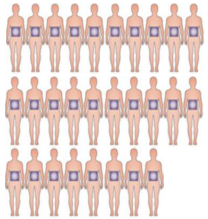
Stage III colon cancer

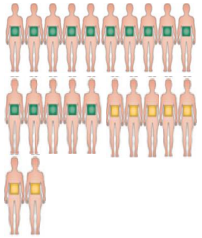




50%
Cured with surgery alone
No added value from chemo



28%
Recur after adj chemo
Chemo did not help



22%
Cured because they received chemo

Moertel CG, N Engl J Med 1990; IMPACT investigators, Lancet 1995; Andre´ T, J Clin Oncol. 2009; Yothers G, J Clin Oncol 2011; Haller D, J Clin Oncol 2011

BACKGROUND AND RATIONALE

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- Can we reduce the duration of oxaliplatin-based adjuvant chemotherapy in stage III CRC:
  - In order to reduce both short and long term toxicities?
  - Without impairing the DFS benefit that 22% of stage III CRC receives from this treatment?

Is 3 months oxaliplatin-based adjuvant chemotherapy not worse than 6 months therapy?

INTERNATIONAL DURATION EVALUATION OF ADJUVANT CHEMOTHERAPY (IDEA) COLLABORATION

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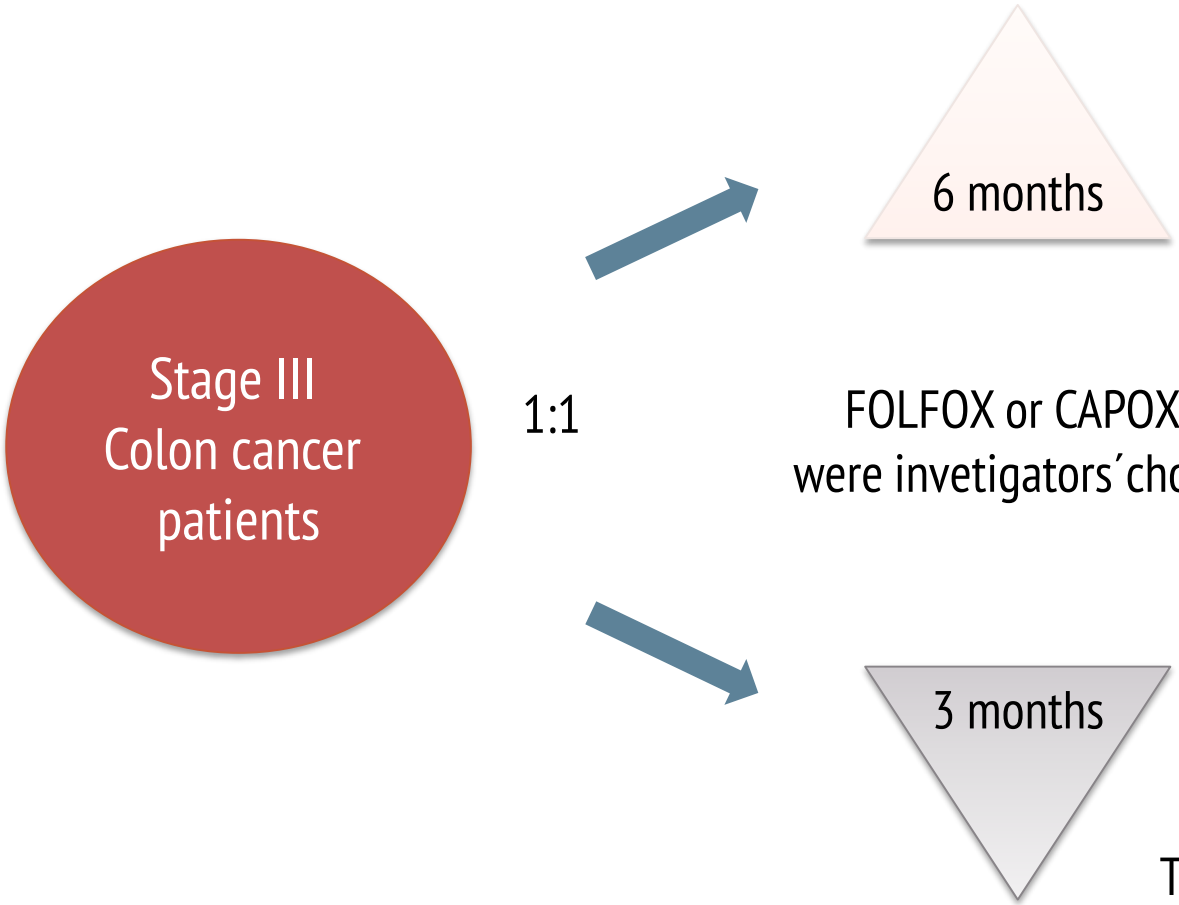
- Prospective pooled analysis of six independent randomized phase III trials (12 countries) investigating the duration of adjuvant chemotherapy, 6 versus 3 months, in early stage CRC patients

Trial	SCOT	Alliance/ SWOG 80702	TOSCA	IDEA France	ACHIEVE	HORG
Regimen	CAPOX or mFOLFOX6	mFOLFOX6	CAPOX or FOLFOX4	CAPOX or mFOLFOX6	CAPOX or mFOLFOX6	CAPOX or FOLFOX4
N of pts enrolled	3983	2440	2402	2010	1291	708
Countries	UK Denmark Spain Australia Sweden New Zeland	US, Canada	Italy	France	Japan	Greece

STUDY DESIGN



Total planned accrual ⩾ 10,500

STUDY OBJECTIVES

- Primary endpoint
  - Disease Free survival (DFS)

- Primary analyisis Population:
  - Modified Intent-to-Treat

- DFS Hazard ratio (HR 3m vs 6 m) and two-sided 95% Confidence Interval (CI) were estimated by Cox model stratified by study

- Pre-planned subgroup analyses:
  - By **regimen** and **T/N stage**

RATIONALE FOR NON-INFERIORITY MARGIN

Historical data from MOSAIC

5FU/LV + Oxaliplatin
vs 5-FU/LV

24% relative risk reduction

IDEA consensus

Oxaliplatin-based treatment:
3m vs 6 m

<12% relative risk increase *(upper 95%CI)* of relapse to be sufficient to show the NI of 3m vs 6 m

↓

Non-inferiority Margin:
DFS HR = 1.12

NON-INFERIORITY HYPOTHESIS TESTING

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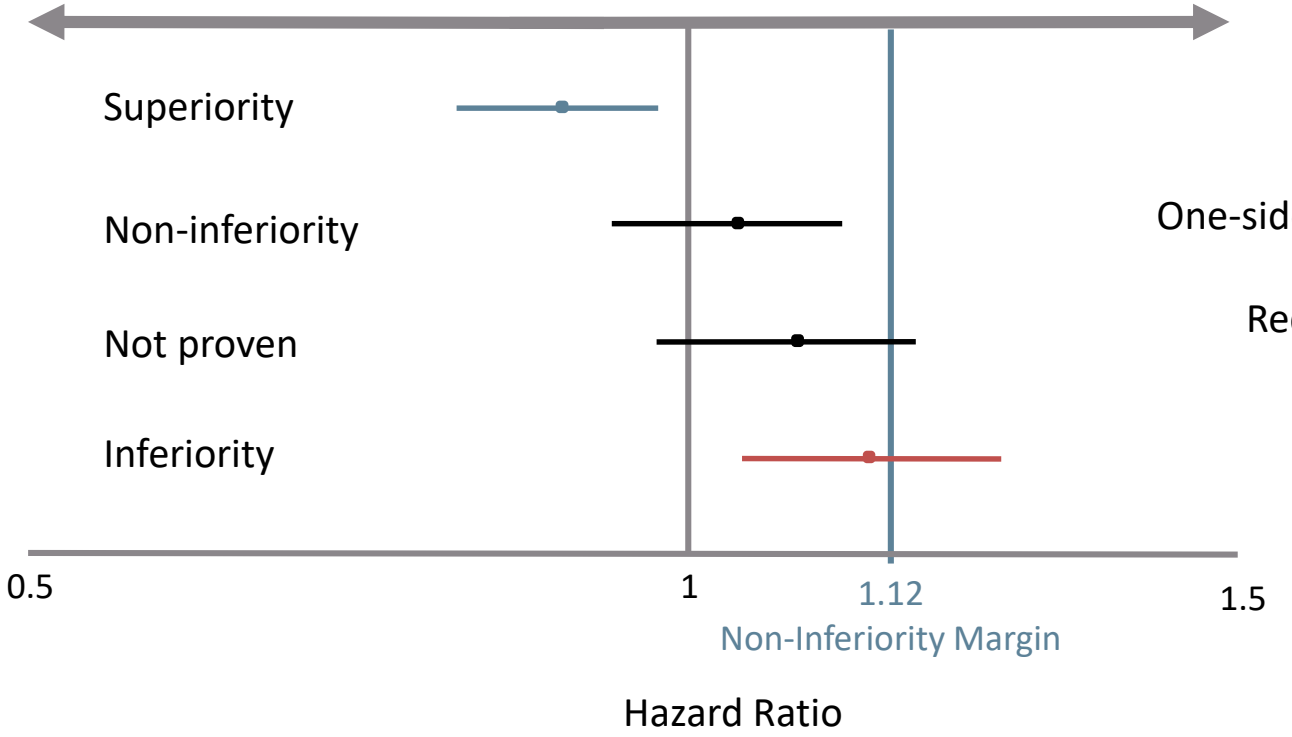
STATISTICAL CONCLUSIONS UNDER DIFFERENT SCENARIOS IN NON-INFERIORITY TRIALS



One-sides Type I Error Rate = 0.025
Power = 90%
Require 3390 DFS Events

Piaggio et al. Jama 2006 and 2012

POSSIBLE SCENARIOS OF OBSERVED TREATMENT DIFFERENCES FOR ADVERSE OUTCOMES(HARMS) IN NONINFERIORITY TRIALS

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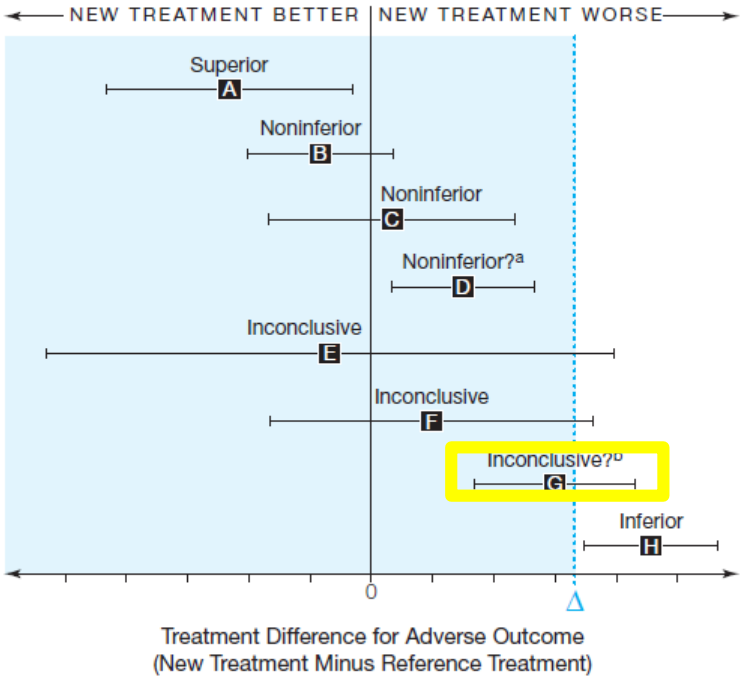

Error bars indicate 2-sided 95% CIs. The blue dashed line at x=Δ indicates the noninferiority margin; the blue tinted region to the left of x=Δ indicates the zone of inferiority. A, If the CI lies wholly to the left of zero, the new treatment is superior. B and C, If the CI lies to the left of Δ and includes zero, the new treatment is noninferior but not shown to be superior. D, If the CI lies wholly to the left of Δ and wholly to the right of zero, the new treatment is noninferior in the sense already defined but also inferior in the sense that a null treatment difference is excluded. This puzzling circumstance is rare, because it requires a very large sample size. It also can result from a noninferiority margin that is too wide. E and F, If the CI includes Δ and zero, the difference is nonsignificant but the result regarding noninferiority is inconclusive. G, If the CI includes Δ and is wholly to the right of zero, the difference is statistically significant but the result is inconclusive regarding possible inferiority of magnitude Δ or worse. H, If the CI is wholly above Δ, the new treatment is inferior.
[a]This CI indicates noninferiority in the sense that it does not include Δ, but the new treatment is significantly

[b]This CI is inconclusive in that it is still plausible that the true treatment difference is less than Δ, but the new treatment is significantly worse than the standard. Adapted from Piaggio et al.[6]

Piaggio et al, Jama 2006 and 2012

IDEA TRIALS: MAIN CHARACTERISTICS

Trial	Regimen(s)	Stage	T4 (within stage III)	Tumor Location	% CAPOX
TOSCA	CAPOX or FOLFOX4	II, III	12%	Colon	35
SCOT	CAPOX or mFOLFOX6	II, III	29%	Colon, Rectum	67
IDEA France	CAPOX or mFOLFOX6	III	18%	Colon	10
C80702	mFOLFOX6	III	15%	Colon	0
HORG	CAPOX or FOLFOX4	II, III	14%	Colon	58
ACHIEVE	CAPOX or mFOLFOX6	III	28%	Colon	75

Modified from Shi Q, ASCO 2017

PATIENTS CHARACTERISTICS

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	FOLFOX		CAPOX	
Patient characteristics	**3m (n=3870)**	**6m (n=3893)**	**3m (n=2554)**	**6m (n=2517)**
Median Agne, years	64	64	65	65
ECOG PS*				
0	77%	77%	82%	81%
1	22%	22%	18%	19%
T stage				
T1-2	13%	14%	13%	12%
T3	68%	67%	63%	63%
T4	19%	19%	24%	25%
N Stage				
N1	72%	73%	71%	71%
N2	28%	27%	29%	29%

* 1% of PS 2 in the FOLFOX group

Presented at ASCO 2017 by: Qian Shi, PhD on behalf of IDEA collaborators

TOXICITY

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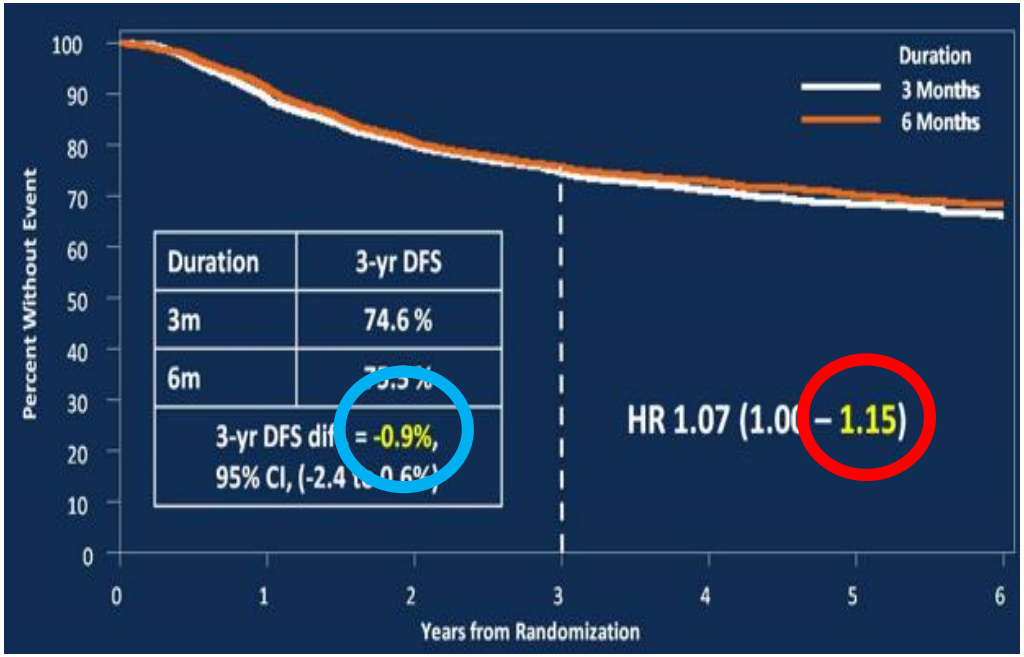
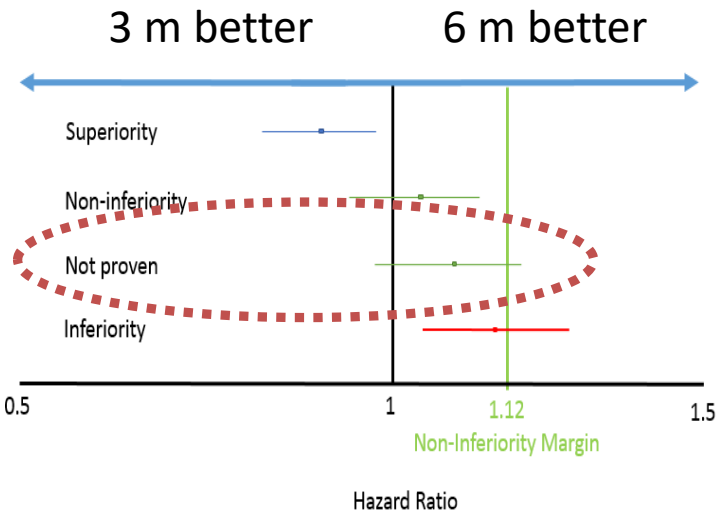
	FOLFOX			CAPOX		
Adverse events	**3m**	**6m**	**p-value [1]**	**3m**	**6m**	**p-value [1]**
Overall						
G2	32%	32%	<0.0001	41%	48%	<0.0001
G3-4	38%	57%		24%	37%	
Neurotoxocity						
G2	14%	**32%**	<0.0001	12%	**36%**	<0.0001
G3-4	3%	**16%**		3%	**9%**	
Diarrhea						
G2	11%	13%	<0.0001	10%	13%	0.0117
G3-4	5%	7%		7%	9%	

[1] Chi-squared test for trend; Total of 19 grade 5 events; Adverse events only collected on first 617 pts from SCOT trial

PRIMARY DFS ANALYSIS (mITT)

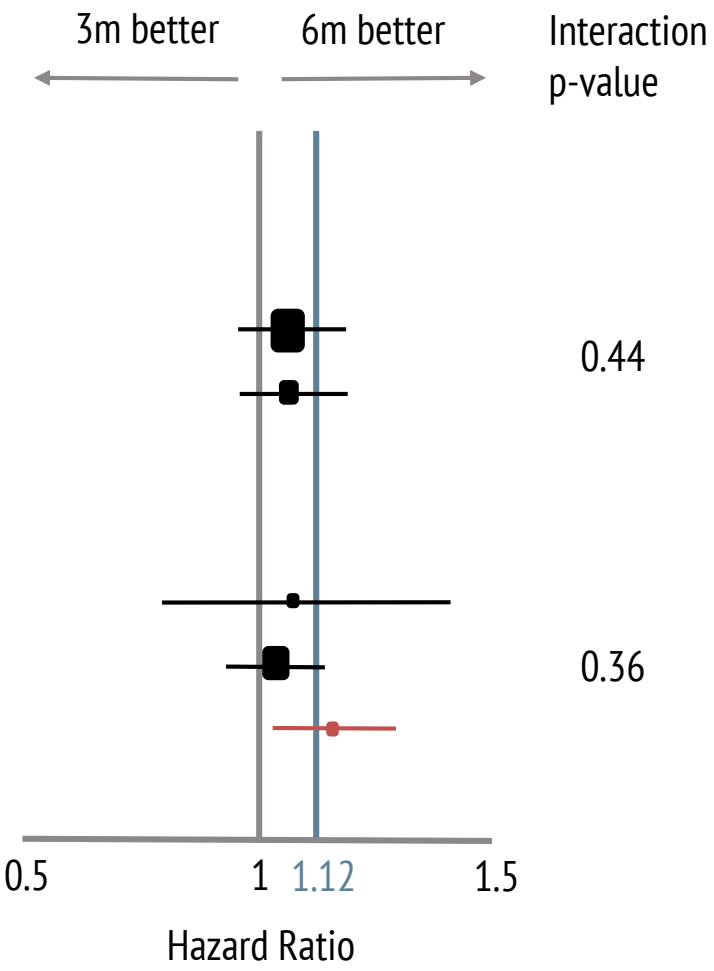


N Pts	6424	5446	4464	3000	1609	826	321
At risk	6410	5530	4477	3065	1679	873	334



PRE-PLANNED ANALYSIS: DSF COMPARISON BY STAGE

	Pts 3m	Pts 6m	HR (3m/6m)	Interaction p-value
N stage				
N1	4583	4585	1.07	0.44
N2	1798	1769	1.07	
T stage				
T1/2	849	841	1.07	0.36
T3	4219	4181	1.04	
T4	**1320**	**1335**	**1.16**	



DFS BY STAGE

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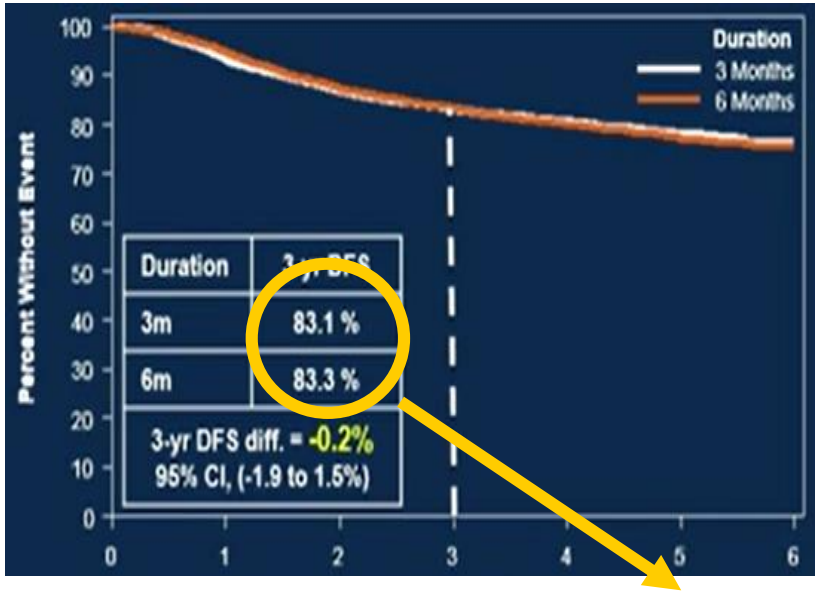
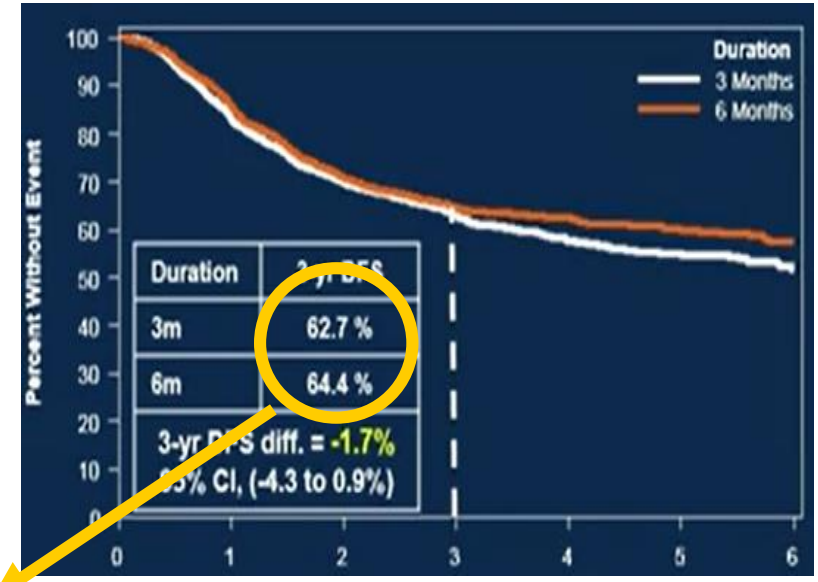
T1-3 N1 (25.7%)



N Pts	3744	3313	2796	1934	1064	
At risk	3727	3336	2788	1949	1081	

T4 or N2 (41.3%)

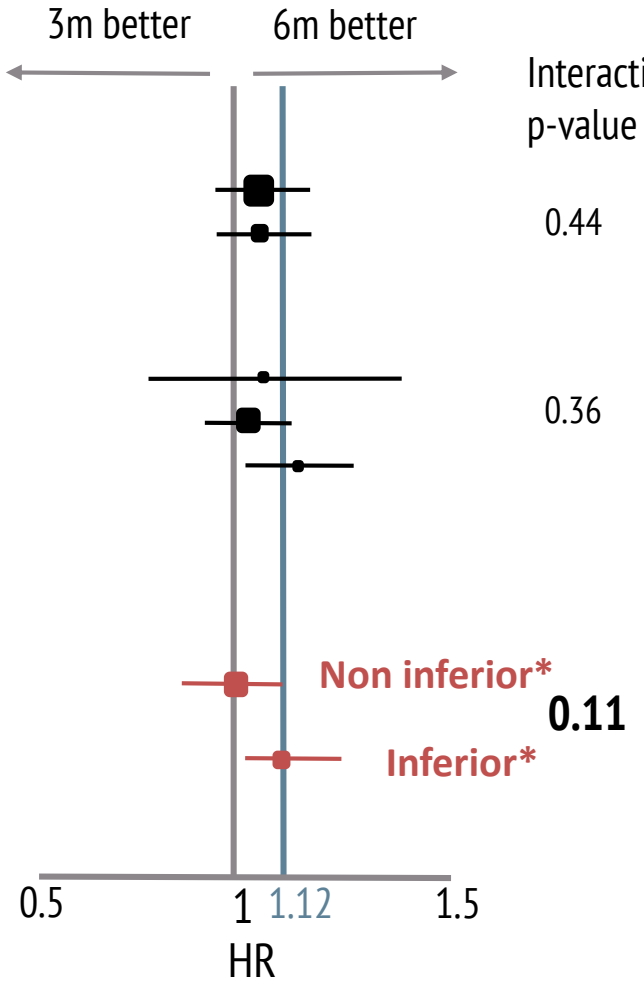


N Pts	2634	2099	1640	1044	531	292	107
At risk	2622	2151	1655	1094	586	301	110

Δ 20%

DSF COMPARISON BY RISK GROUPS

	Pts 3m	Pts 6m	HR (3m/6m)	Interaction p-value
N stage				
N1	4583	4585	1.07	
N2	1798	1769	1.07	0.44
T stage				
T1/2	849	841	1.07	
T3	4219	4181	1.04	
T4	**1320**	**1335**	**1.16**	0.36
Risk Group				
T1-3 N1	3744	3727	1.01	
T4 or N2	2634	2622	1.12	**0.11**



PRE-PLANNED ANALYSIS: DSF COMPARISON BY REGIMEN

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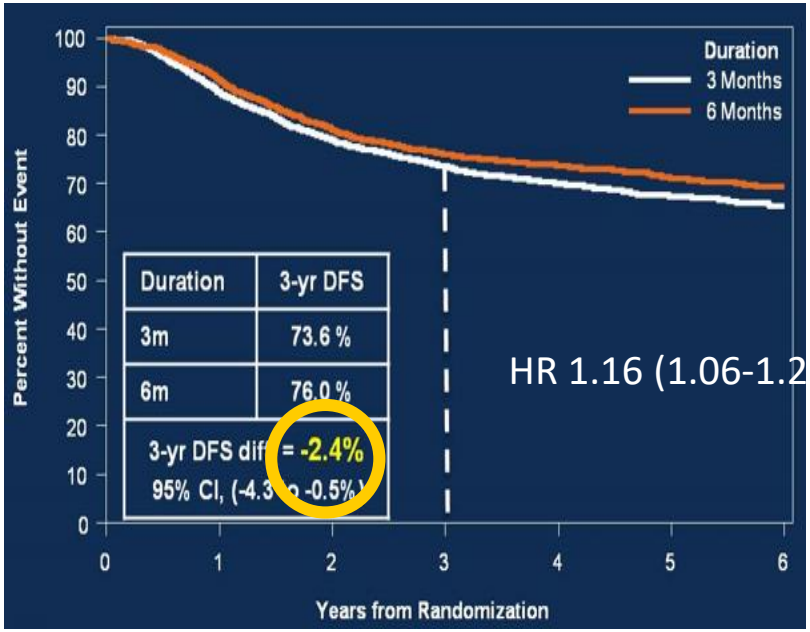
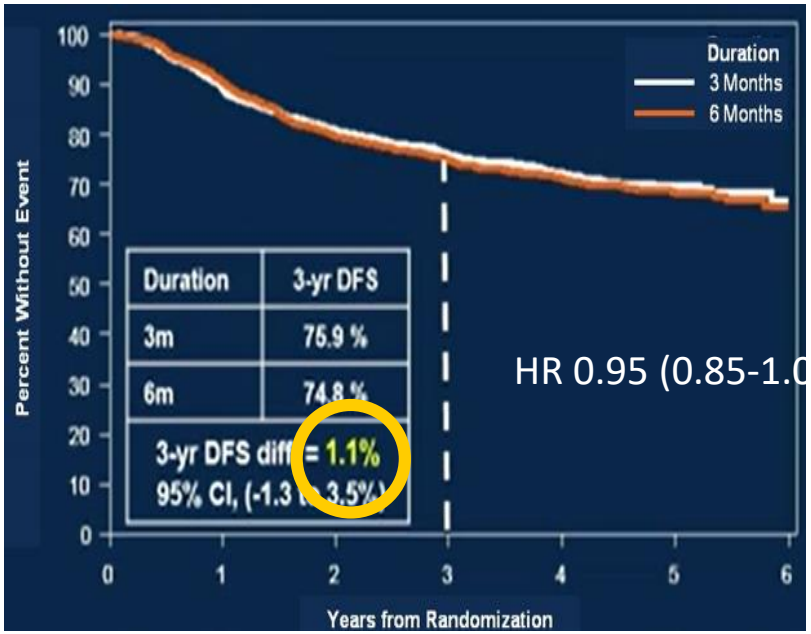
FOLFOX



N Pts	3870	3227	2561	1825	1121	633	291
At risk	3893	3308	2633	1880	1150	666	309

CAPOX



N Pts	2554	2219	1903	1175	488	193	30
At risk	2517	2222	1844	1185	529	207	25

Interaction p-value = 0.0051

DIFFERENT RESULTS IN RFS/DFS IN THE OVERALL POPULATION FOR THE TRIALS PRESENTED AT ASCO

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Trials	3m	6m	HR	3 yrs DFS Δ	Non Inferiority
SCOT	76.7%	77.1%	1.006 (0.909-1.114)	-0.4%	Proven (upper margin 1.13)
TOSCA	81.1%	83%	1.14 (0.99-1.32)	-1.9%	Not proven (upper margin > 1.2)
IDEA France	72%	76%	1.24 (1.05-1.46)	4%	Inferiority

Nevertheless.....

DFS COMPARISON BY REGIMEN ACROSS THE DIFFERENT TRIALS

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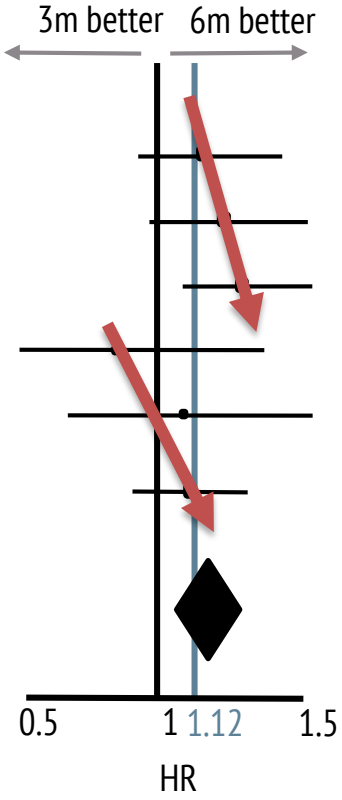
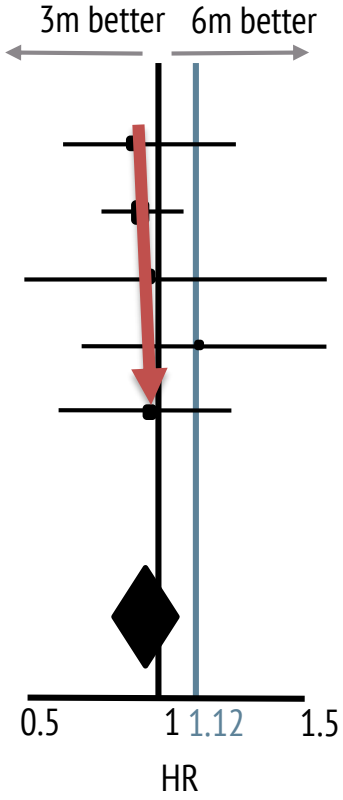
FOLFOX

	Pts 3m	Pts 6m	HR 3m/6m
TOSCA	770	792	1.14
SCOT	662	672	1.21
IDEA France	895	914	1.27
HORG	148	148	0.87
ACHIEVE	163	159	1.08
C8072	1232	1208	1.10
Overall	3870	3893	1.16



CAPOX

	Pts 3m	Pts 6m	HR 3m/6m
TOSCA	424	416	0.92
SCOT	1130	1319	0.94
IDEA France	107	94	0.97
HORG	206	206	1.12
ACHIEVE	487	482	0.92
Overall	2554	2517	0.95



IS THE REGIMEN´S CHOICE IMPORTANT?

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YES

- More continuous 5FU infusion seems to be better (Twelves et al, 2005; Chau et al, 2005)
- The dose of oxaliplatin in the first 4 weeks of CAPOX is 260 mg/m^2, while for FOLFOX is 170 mg/m^2
- Compliance and overall dose intensity better

TREATMENT COMPLIANCE IN IDEA

	FOLFOX		CAPOX	
Treatment compliance	**3m**	**6m**	**3m**	**6m**
Total no. weeks received treatment Median (Q1-Q3)	12 (12-12)	24 (20-24)	12 (12-12)	24(18-24)
Reached the planned last cycle[1]	90%	71%	86%	65%

% of dose actually delivered, Mean (SD)				
5FU[2]	92.4 (22.7)	81.6 (26.6)	----------	
Capecitabine	----------		91.2 (23.5)	78 (29.4)
Oxaliplatin	91.4 (19.9)	72.8 (25.6)	89.8 (21.7)	69.3 (28.3)

FOLFOX 3m-6m vs CAPOX 3m-6m

5FU Δ 12%

Oxaliplatin Δ 20%

[1] 1% of pts of the 3m arm (both FOLFOX and CAPOX) received >3m of treatment; [2] both infusion and bolus

TREATMENT COOMPLIANCE IN IDEA

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	FOLFOX		CAPOX	
Treatment compliance	3m	6m	3m	6m
Oxaliplatin dose	510mg/m²	1020 mg/m²	520mg/m² 1040mg/m²	
n. of planned cycles	6	12	4	8
% of dose actually delivered, Mean (SD)				
5FU[2]	92.4 (22.7)	81.6 (26.6)	-	
Capecitabine	----------		91.2 (23.5)	78 (29.4)
Oxaliplatin	91.4 (19.9) 466 mg/m² 5.5 cycles	72.8 (25.6) 742 mg/m² 8.7 cycles	89.8 (21.7) 466 mg/m² 3.5 cycles	69.3 (28.3) 720mg/m² 5.5 cycles
DFS low risk	81.9%	83.5%	85%	83.1%
DFS high risk	61.5%	64.7%	64.1%	64%

Modified from Shi Q, ASCO 2017

IS THE REGIMEN´S CHOICE IMPORTANT?

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YES

- More continuous 5FU infusion seems to be better (Twelves et al, 2005; Chau et al, 2005)
- The dose of oxaliplatin in the first 4 weeks of CAPOX is 260 mg/m^2, while for FOLFOX is 170 mg/m^2
- Compliance and overall dose intensity better

NO

- No differences in metastatic setting (Cassidy et al, 2011)

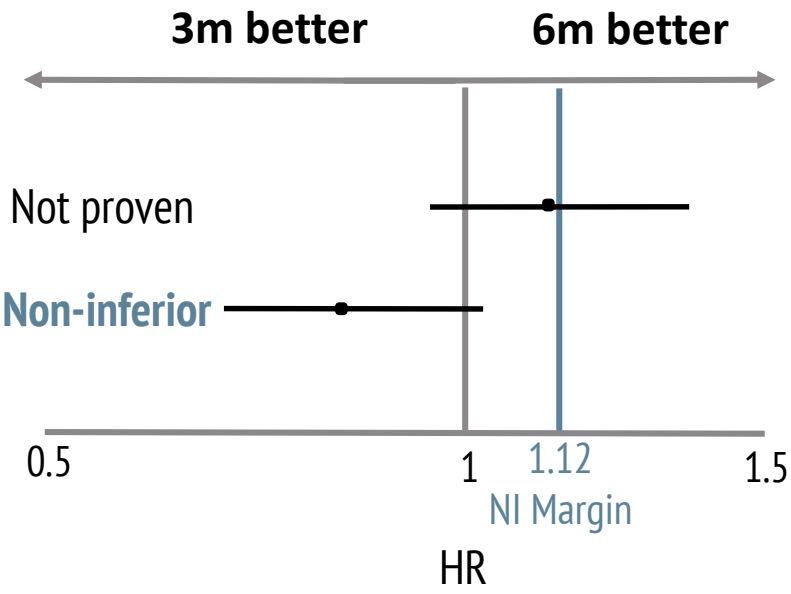
↓

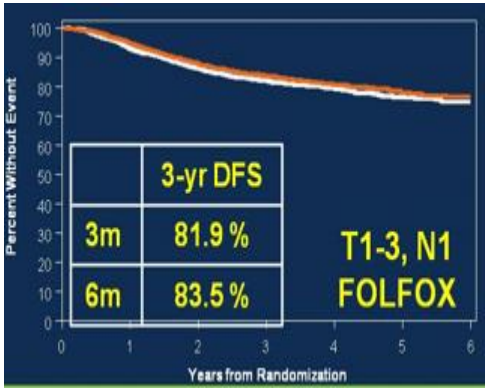
Please consider also the example of FOLFIRI efficacy in metastatic vs adjuvant setting!

- Bias by indication: factors for favourable outcome for patient who got CAPOX

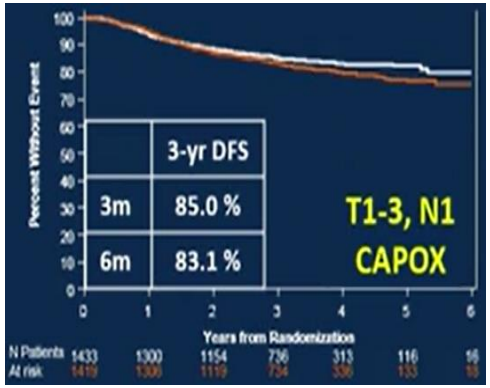
DFS COMPARISON BY RISK GROUP AND REGIMEN

Risk Group	Regimen	DFS HR; 95% CI
T1-3 N1	FOLFOX	1.10 (0.96-1.26)
	CAPOX	**0.85 (0.71-1.01)**





3-yrs DFS 3m-6m
Δ -1.6%

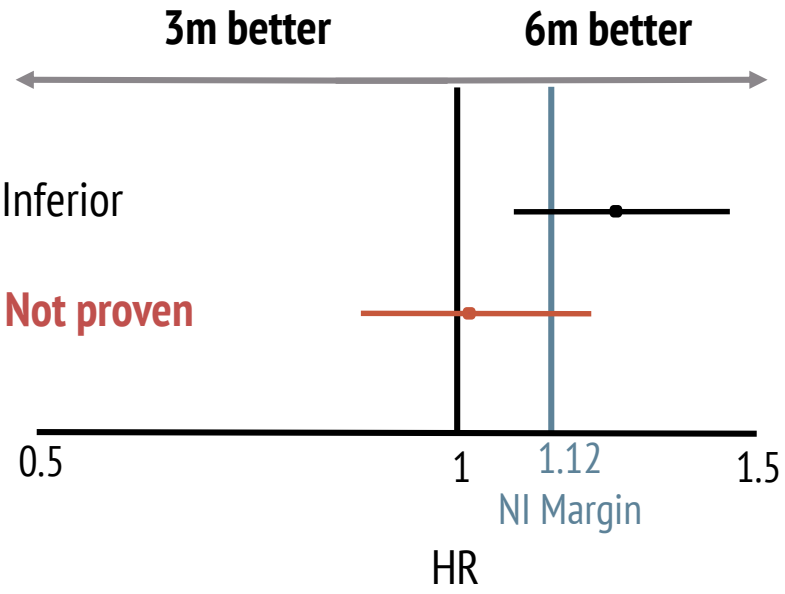


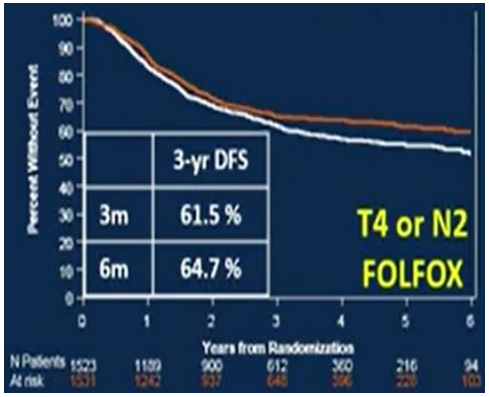
3-yrs DFS 3m-6m
Δ 1.9%

Modified from Shi Q, ASCO 2017

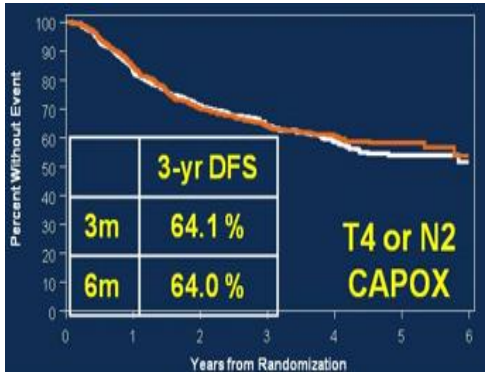
DFS COMPARISON BY RISK GROUP AND REGIMEN

Risk Group	Regimen		DFS HR; 95% CI
T4 or N2	FOLFOX	Inferior	1.20 (1.07-1.35)
	CAPOX	**Not proven**	**1.02 (0.89-1.17)**





3-yrs DFS 3m-6m
Δ -3.2%

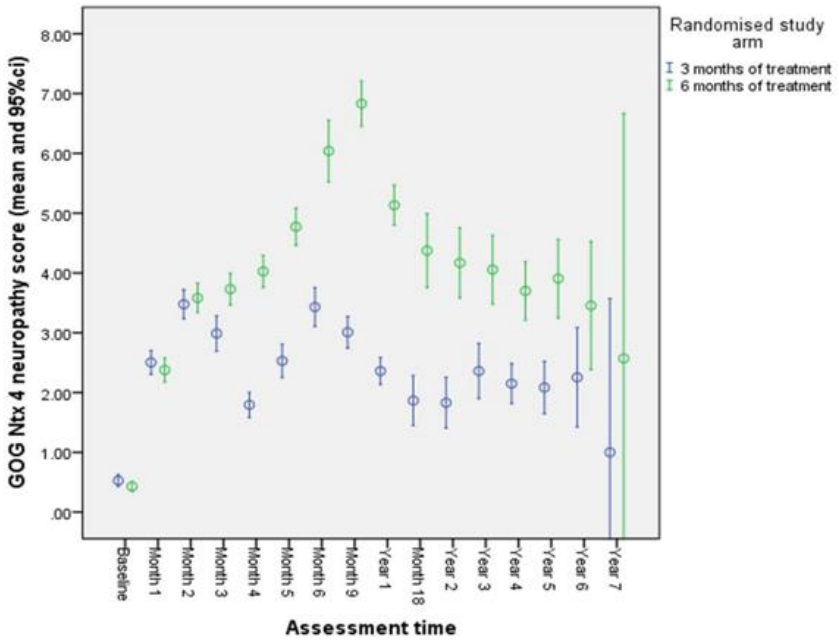


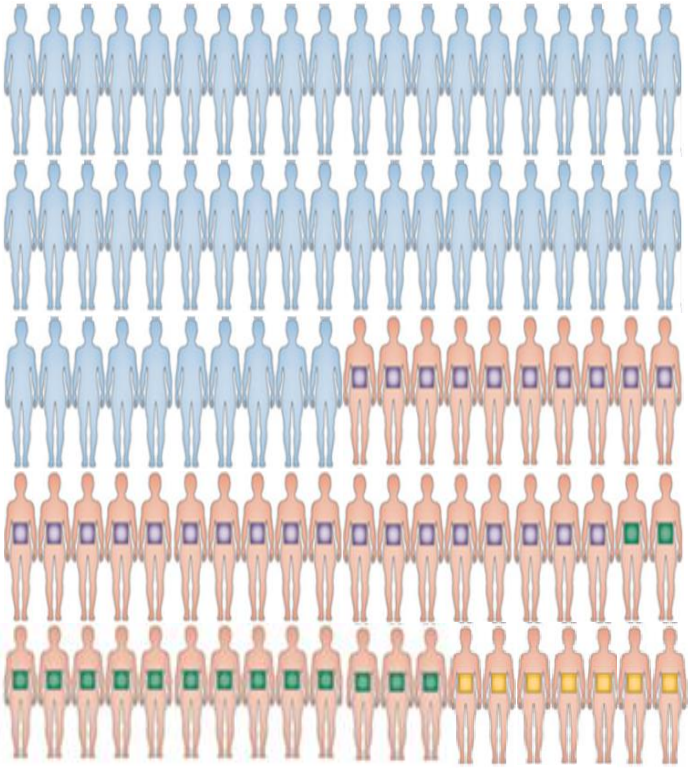
3-yrs DFS 3m-6m
Δ 0-1%

Modified from Shi Q, ASCO 2017

PRE-CONCLUSION

NEUROPATHY MEASURED BY PATIENT QUESTIONNAIRE OVER TIME BY TREATMENT DURATION





PRE-CONCLUSION

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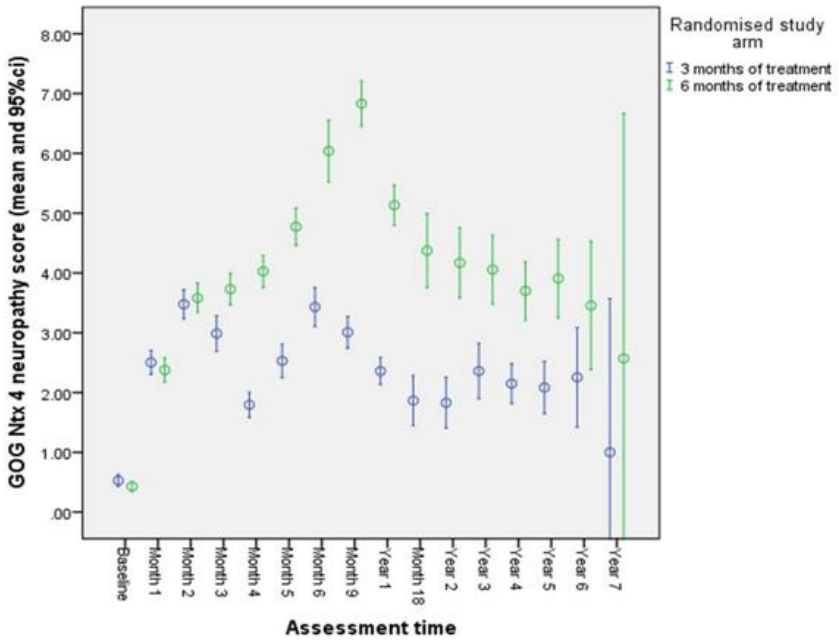
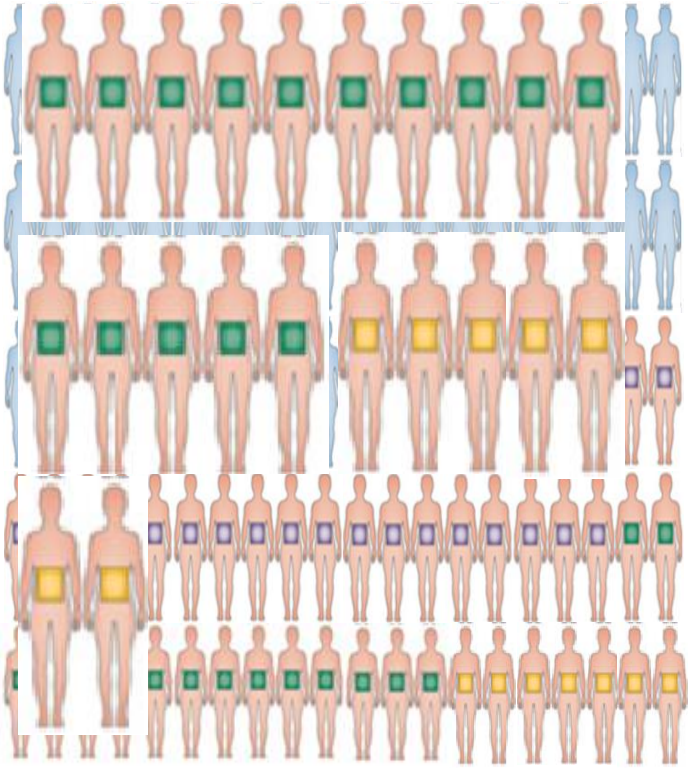
NEUROPATHY MEASURED BY PATIENT QUESTIONNAIRE OVER TIME BY TREATMENT DURATION





Conclusions

- 3m treatment showed higher treatment compliance and lower G2+ neurotoxicity compared to 6m treatment
- Non- inferiority for DFS was not proven in overall stage III colon cancer
- Large difference in overall prognosis between low risk (T1-3 N1) and high risk (T4 or N2): 3 yrs DFS Δ20%
- Results comparing DFS between 3m and 6m treatment depend on risk groups and regimen
- In particular, for low risk group 3m CAPOX is non inferior (NOT WORSE) to 6m and in high risk group 3m are not proven to be inferior as compared to 6m
- OS data are needed to show the robusteness of the results, nevertheless DFS has been proven to be a good predictor of 5yrs OS

HOW WILL I TREAT MY NEXT STAGE III COLON CANCER PATIENT?

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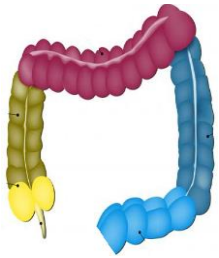
T1-3 N1

Low risk

3 months therapy

High risk



T4 and/orN2

6 months FOLFOX

3 MONTHS OF ADJUVANT TREATMENT

ARE WE READY FOR IT?

Dominik Modest
Medical Oncologist
Medical Dept III, University of Munich (LMU)
Comprehensive Cancer Center Munich, Munich

2017 ASCO ANNUAL MEETING
Making a Difference in Cancer Care WITH YOU

ASCO DAILY NEWS

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Risk-Based Approach to Chemotherapy Duration Recommended for Stage III Colon Cancer

JUNE 4, 2017

Shi Q, ASCO 2017

In view of these findings, investigators in the IDEA collaboration reached a clinical consensus to recommend a risk-based approach to selecting adjuvant chemotherapy for stage III colon cancer. The consensus recommends 3 months of adjuvant chemotherapy for patients with low-risk disease, defined as T1-3N1 tumors, which includes approximately 60% of stage III patients. For high-risk patients, defined as patients with T4 or N2 tumors, decisions on use of the shorter course should be based on an individual assessment of tolerability, risk, and choice of regimen.

SCOT: CAPOX for 3 Months Is Not Inferior to 6 Months in Colorectal Cancer

JUNE 13, 2017

Iveson T, ASCO 2017

...SCOT met its non inferiority ta... therefore 3 months treatment should now be considered for many patients...

Dr Axel Grothey

For the 60% of patients who have low-risk tumors "we do not recommend more than 3 months of chemotherapy wi an oxaliplatin-based regimen," he said. "That applies to 20,000 patients per year in the US, and you can easily se that translates to hundreds of thousands of patients ...dwide."

...is a great day for patients thro...out the world," commented ASCO expert Nancy Baxter, MD, who is from St Michael's Hospital in Toronto, Ontario, Canada. "Now, today, up to 60% of my patients with stage III colon cancer will be able to stop after 3 months of therapy and be able to get on with their lives and have a lower risk of permanent problems, such as numbness of their hands and feet. Less is more," she said.

Dr Nancy Baxter

TOSCA Supports Shorter Adjuvant CT Duration for Resected Colon Cancer

JUNE 13, 2017

Sobrero A, ASCO 2017

"Because the difference in RFS is so limited ... but the toxicity so much better, 3 months of ...aliplatin-based chemotherapy can be considered another standard option for the adjuvant ...eatment of resected colon cancer," presenter Alberto F. Sobrero, MD, of the Ospedale San M...o, in Italy, said.

PIs of studies or IDEA consortium.

"The last 24 hours, with the Ple... ...ession and today's talks, will change the lives of hundreds of thousands of [patients with] colorectal cancer each year worldwide," Dr. Meyerhardt ...d.

On the basis ... results of TOSCA, SCOT, IDEA France, and other IDEA trials, Dr. Meyerhardt plans to offer 6 months of FOLFOX to his patients with T4 or N2 disease. For those with T1-3N1 disease, he will offer 3 months of CAPOX or FOLFOX to reduce toxicity and alleviate the logistical burden of treatment; he cited his preference for CAPOX because of its slightly more preferable efficacy data.

Meyerhardt J, ASCO 2017

HOW DO WE DEAL WITH FRESH STUDY DATA?

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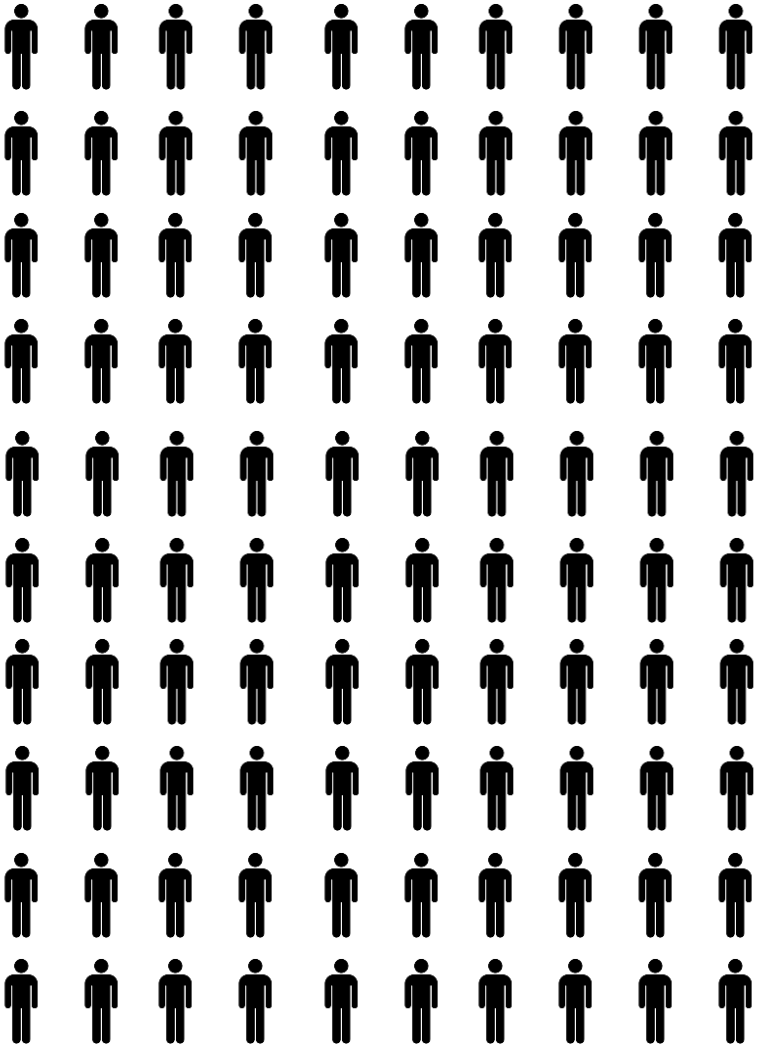
Three questions should be asked in general:

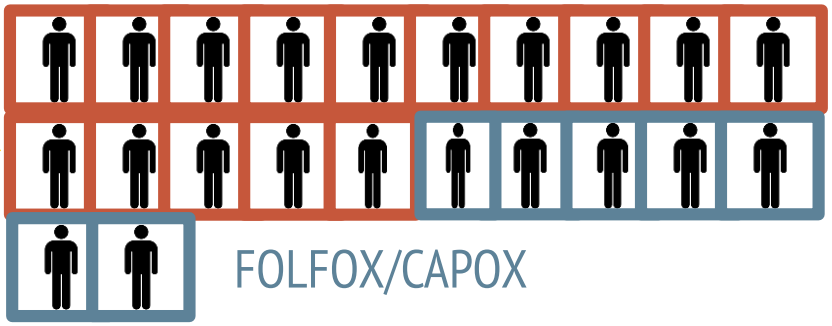
Is the data:

- True?
- New?
- Does it matter?

STAGE III COLON CANCER



Cured because they got adjuvant therapy after surgery



Only ones that benefit from chemo (as measured by cure)

PRE-CONCLUSION

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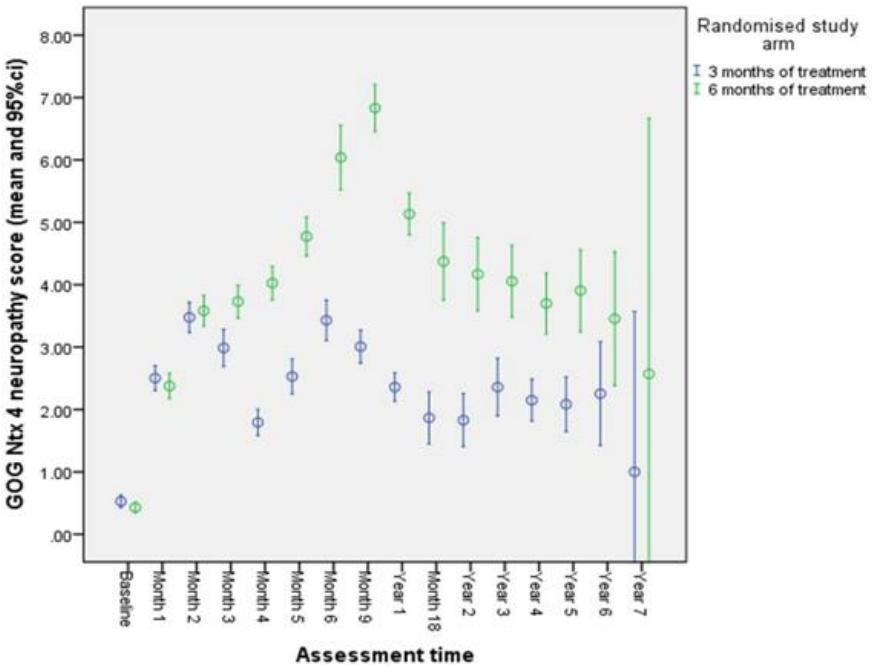

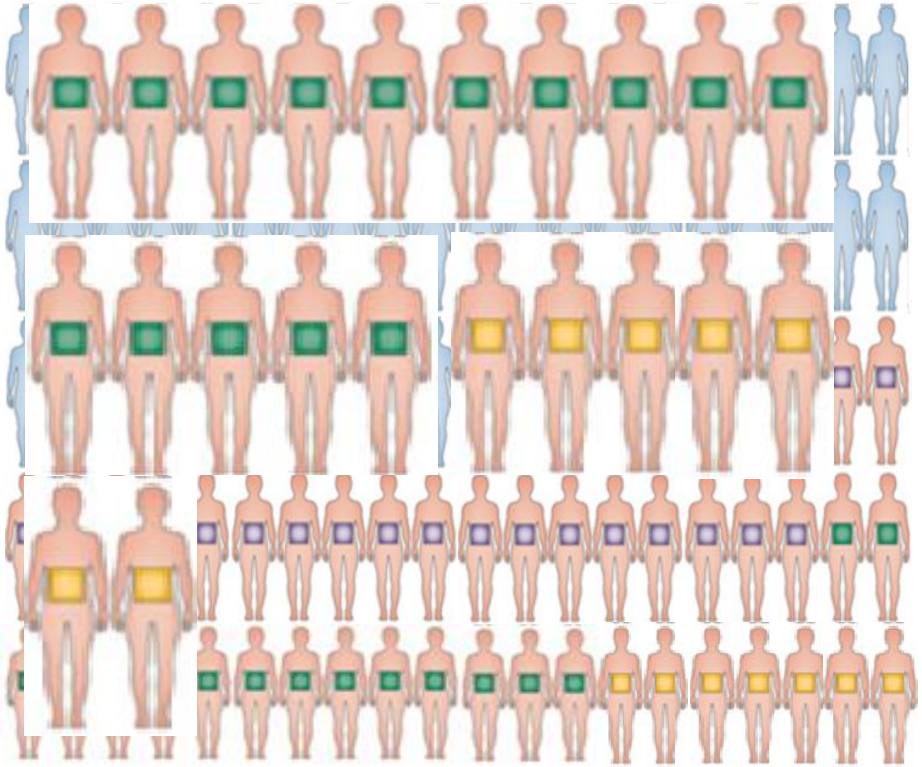

BACKGROUND OF IDEA

With 6 mo Ox-based chemo, we cure a minority and harm a majority

Aiming to reduce toxicity and maintain the benefit is important

It applies to large no. of patients worldwide

This is highly relevant

The question is unanswered and therefore, new

WHAT ARE THE MAIN CONCLUSIONS?

ARE THEY TRUE?

PRIMARY DFS ANALYSIS (mITT), CONT.

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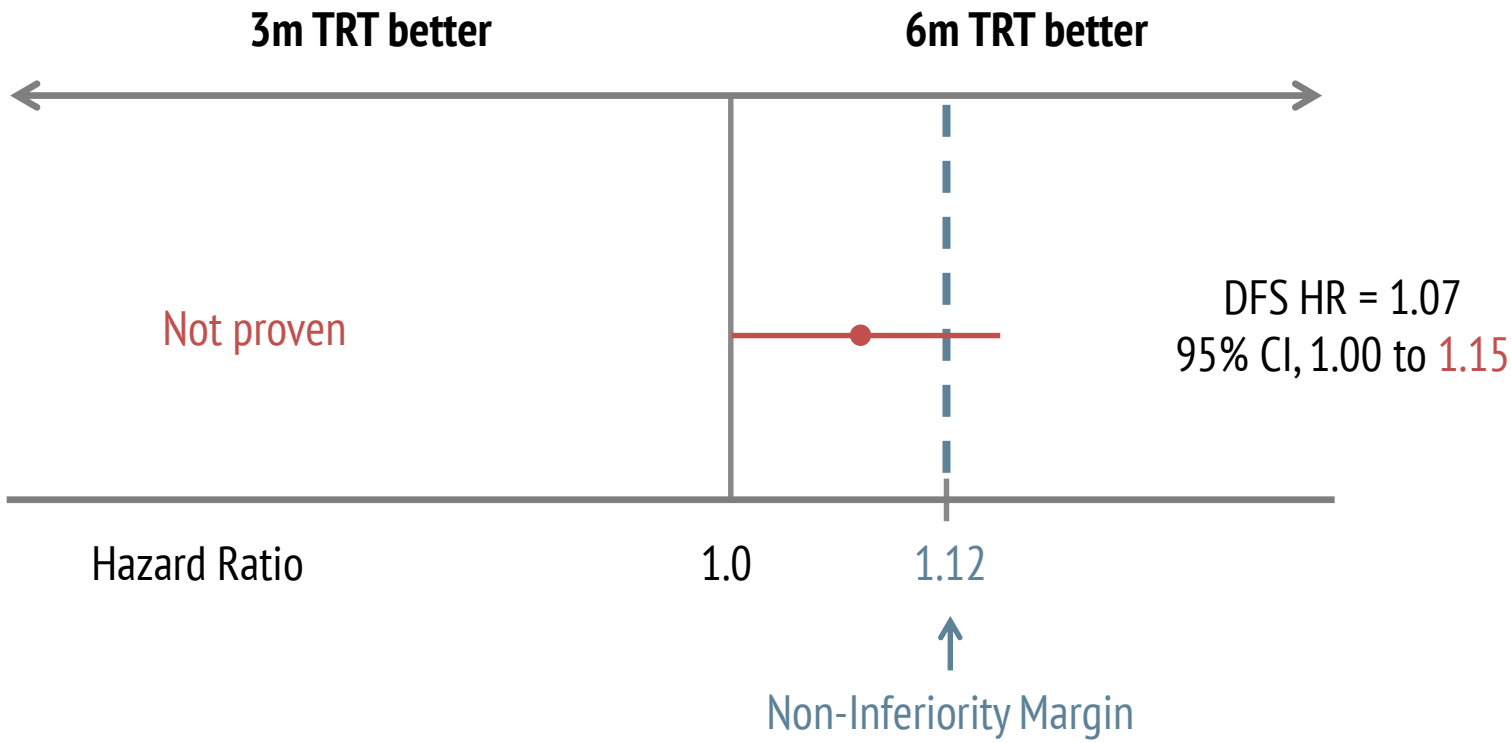
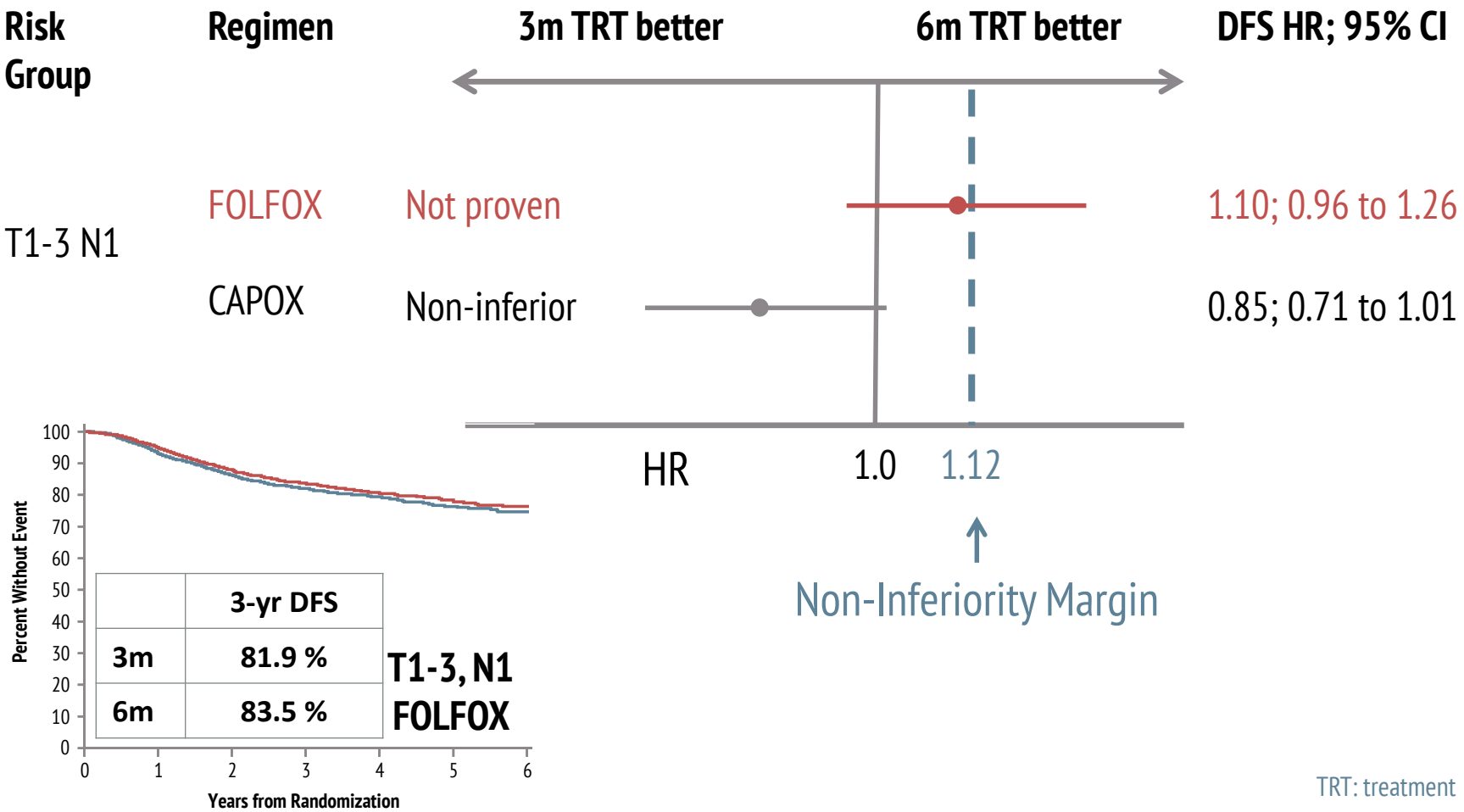
STATISTICAL CONCLUSIONS



TRT: treatment

DFS COMPARISON BY RISK GROUP AND REGIMEN



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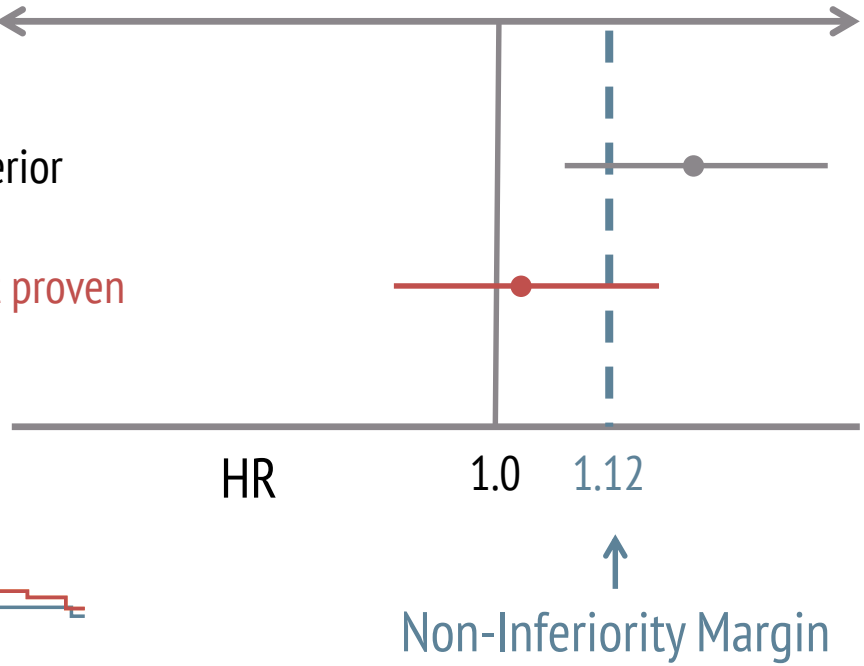

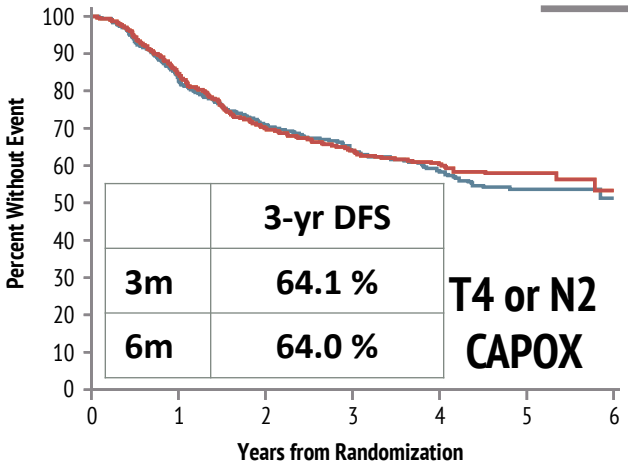

	3-yr DFS
3m	64.1 %
6m	64.0 %

T4 or N2
CAPOX

TRT: treatment

IDEA CLINICAL CONSENSUS: RISK-BASED APPROACH TO ADJUVANT CHEMOTHERAPY IN STAGE III COLON CANCER

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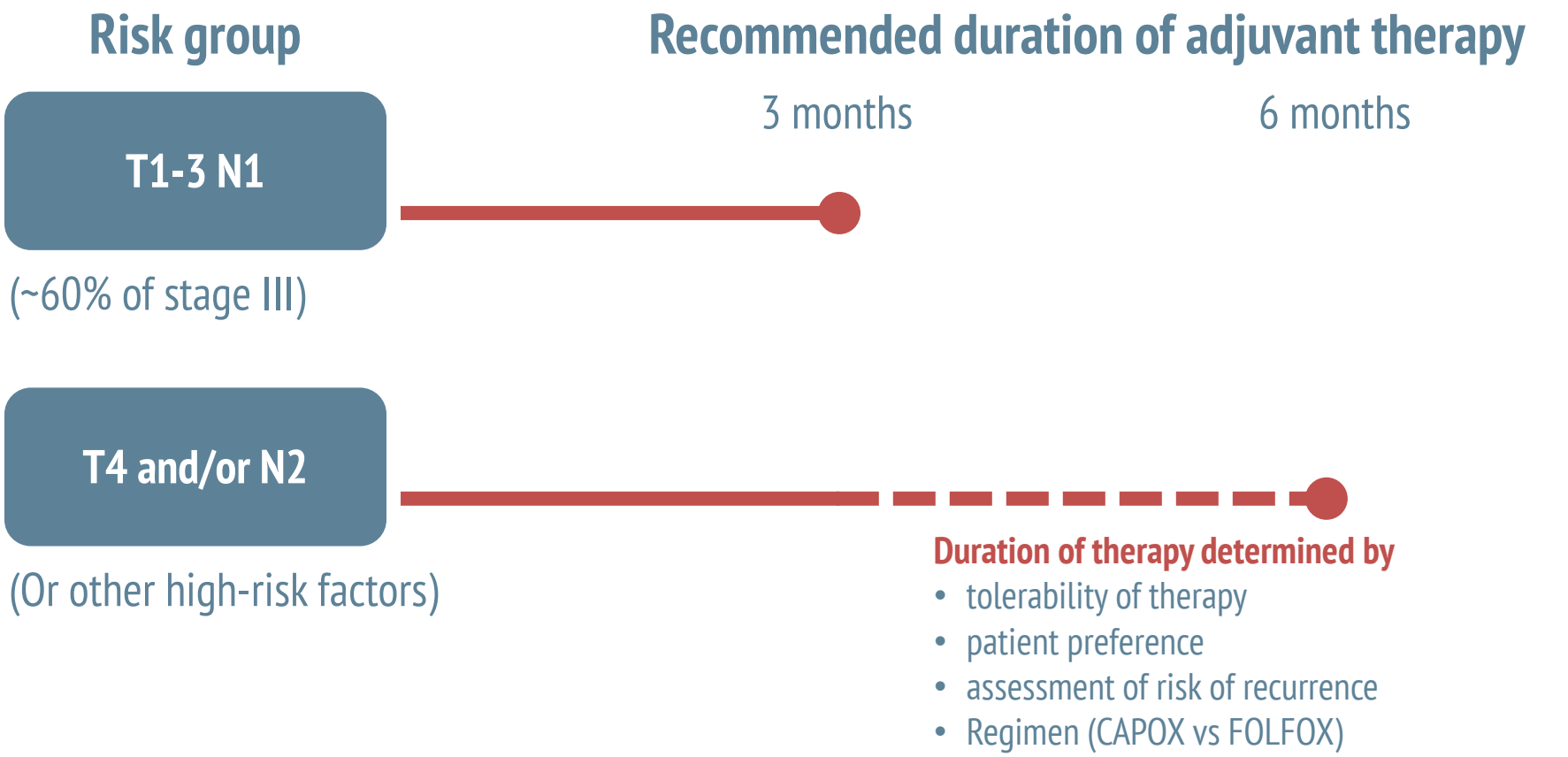

CENTRAL STATEMENT @ASCO

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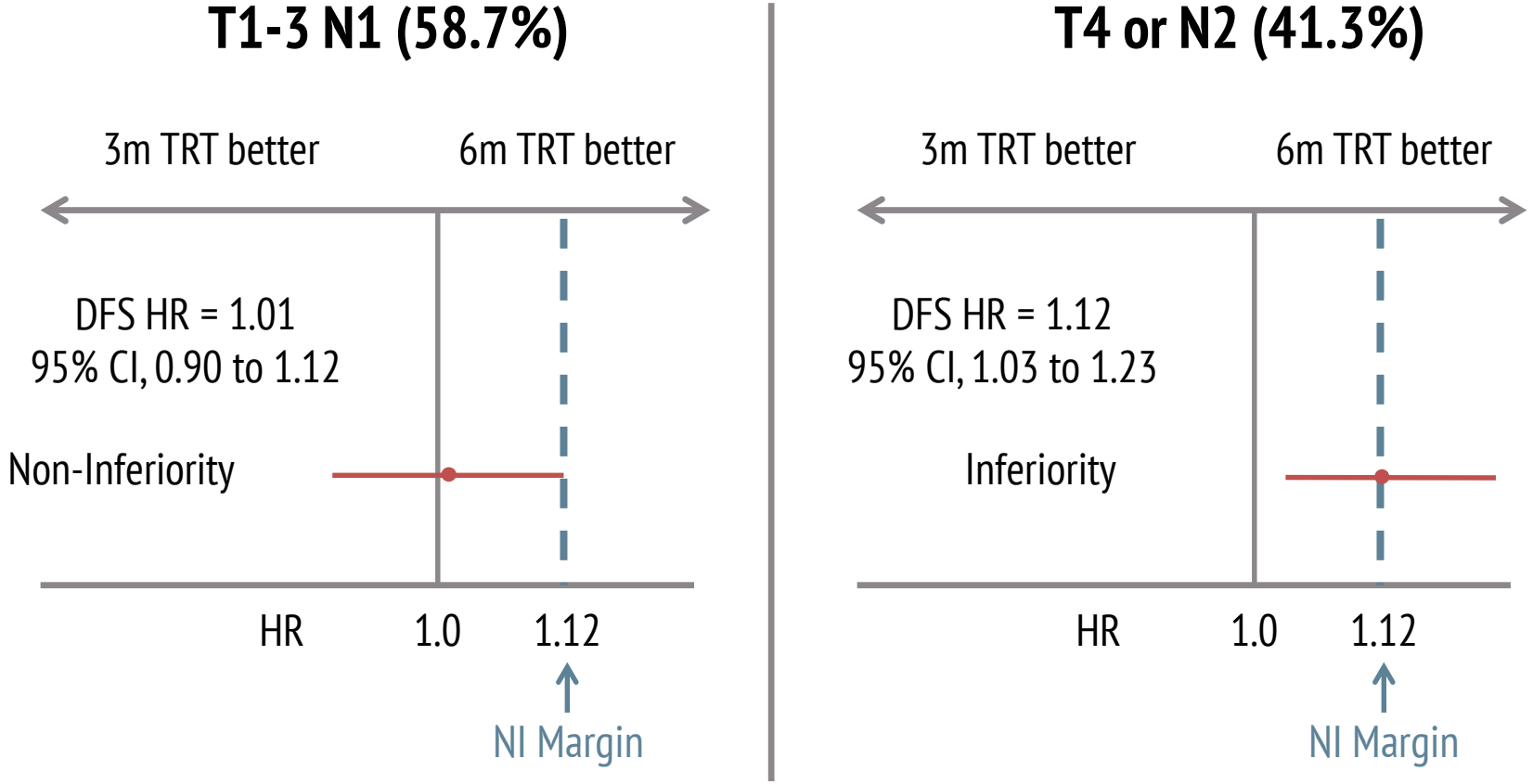
- My next patient who has T4 or N2 disease, I will offer 6 months FOLFOX

- My next patient who has T1-3, N1 disease, I will discuss differences in toxicities and logistics of CAPOX or FOLFOX. I will offer 3 months CAPOX or FOLFOX and explain I am more confident in the data for CAPOX

SUMMARY & BASIC INTERPRETATION OF IDEA

- This is a negative trial
- Overall analysis (DFS): 6mo rather superior (borderline-sign.) than 3mo non-inf.
- Two subgroups are defined: low risk T3/N1 and CAPOX
- T3/N1-story only “true” with CAPOX?
- T4/N2 clearly not non-inf.

DFS COMPARISON BY RISK GROUPS, CONT.



Interaction p-value = 0.11

TRT: treatment

STAGE DEPENDING EFFECT T3/ N1 VS T4/N2 ?

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IS THIS TRUE?

No interaction of stage and treatment can be proven based on the whole IDEA consortium of >12.000 pts.

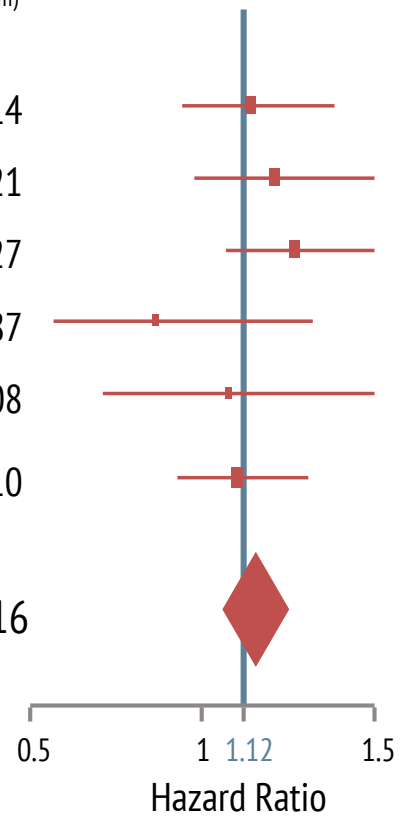
Without clear interaction, we should be very careful

- To declare differences in outcome based on TX and stage
- To define differing treatment choices

DFS COMPARISON BY REGIMEN, CONT.

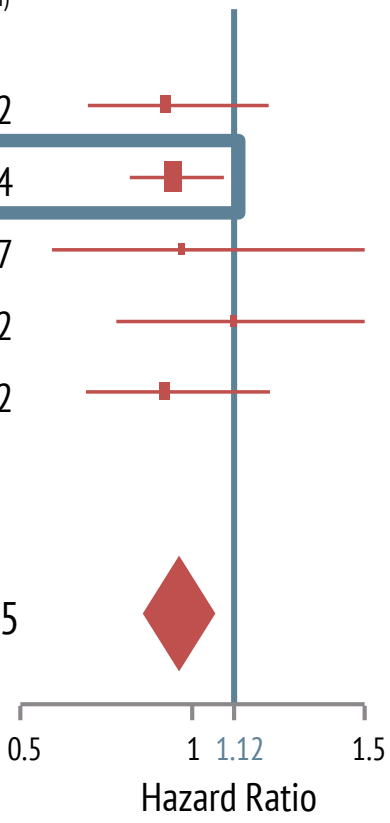
FOLFOX

	Patients 3m arm	Patients 6m arm	HR (3m/6m)
TOSCA	770	792	1.14
SCOT	662	672	1.21
IDEA France	895	914	1.27
HORG	148	148	0.87
ACHIEVE	163	159	1.08
C80702	1232	1208	1.10
Overall	3870	3893	1.16



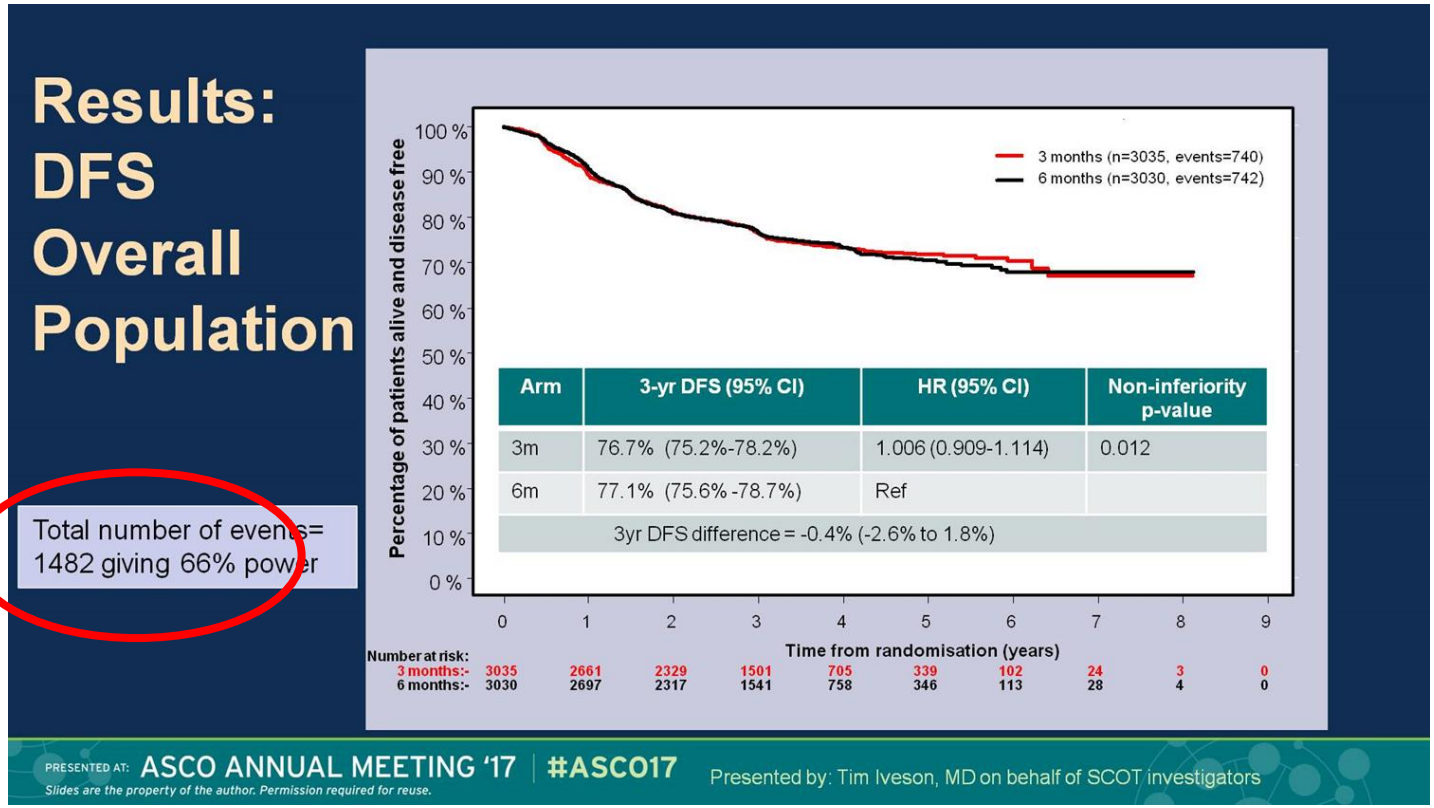
CAPOX

	Patients 3m arm	Patients 6m arm	HR (3m/6m)
TOSCA	424	416	0.92
SCOT	1330	1319	0.94
IDEA France	107	94	0.97
HORG	206	206	1.12
ACHIEVE	487	482	0.92
Overall	2554	2517	0.95



IS THE CAPOX EFFECT RELEVANT/TRUE?

- Majority of CAPOX pts from on one study (SCOT), **> 56%!**



CAPOX...

It could be true, but is maybe biased by:

- No randomisation/ bias of prognosis
- One study with event rate of <25% (SCOT)

My interpretation:

If you go for CAPOX, you may stop at 3 months- but:

Is this equal to: you should go for CAPOX at T3/N1??

SUMMARY 1

- IDEA did not show non-inferiority of 3mo, rather superiority of standard (6mo) based on a sample size of >12.000 pts

- Conflicting results of three single studies with differences in design

- The subset of T3/N1 and T4/N2 did **not show** a significant interaction
  - Is it reasonable to base recommendations based on this finding?

- CAPOX appeared to do better that FOLFOX
  - 56% of CAPOX data originate from SCOT, a study with 66% Power and 24% events

SUMMARY 2

We promote adjuvant treatment to save lives.
Have you seen overall survival data?

➔ There are no overall survival data!

The IDEA data are not robust enough to define a new standard, yet.

CONCLUSION

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The data are new and relevant

True? **Maybe**

Is it already time to define a new standard? **No**

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